Progress in Nuclear Magnetic Resonance Spectroscopy 57 (2010) 111–158

Contents lists available at ScienceDirect

Progress in Nuclear Magnetic Resonance Spectroscopy

journal homepage: www.elsevier.com/locate/pnmrs

Nuclear spin relaxation in isotropic and anisotropic media

Matthew P. Nicholas [a,1], Ertan Eryilmaz [b,c], Fabien Ferrage [a,d], David Cowburn [a], Ranajeet Ghose [b,c,*]

[a] *New York Structural Biology Center, 89 Convent Avenue, Park Building at 133rd St., New York, NY 10027, USA*
[b] *Department of Chemistry, The City College of New York, 160 Convent Avenue, New York, NY 10031, USA*
[c] *Graduate Center of the City University of New York, 365 5th Avenue, New York, NY 10016, USA*
[d] *Département de Chimie, Ecole Normale Supérieure, and CNRS, UMR 7203; 24 rue Lhomond, 75231 Paris cedex 05, France*

ARTICLE INFO

Article history:
Received 28 January 2010
Accepted 13 April 2010
Available online 29 April 2010

Keywords:
Spin relaxation
Rotational diffusion
Stochastic processes
Chemical shift
Dipolar coupling

Contents

---

[*] Corresponding author. Tel.: +1 212 650 6049; fax: +1 212 650 6107.
E-mail address: rghose@sci.ccny.cuny.edu (R. Ghose).

[1] Present address: Albert Einstein College of Medicine, Medical Scientist Training Program, Department of Anatomy and Structural Biology, 1300 Morris Park Avenue; Bronx, NY 10461, USA.

doi:10.1016/j.pnmrs.2010.04.003

1. Introduction

A typical NMR experiment consists of a sample of nuclei of spin $\mathscr{I}$ placed in a strong, uniform magnetic field $\vec{B}_0$ (the magnetic field is taken to be along the laboratory z-axis; $B_z = B_0, B_x = B_y = 0$ and $\mathscr{I}$ is the nuclear spin quantum number) until the sample reaches thermal equilibrium. In an external field, the magnetic moment $\vec{\mu} = \gamma \hat{\mathscr{I}}$ of each spin precesses around $\vec{B}_0$ at the Larmor frequency $\omega_0 = -\gamma B_0$, where γ is the gyromagnetic ratio, which depends on the type of nucleus in question. For each spin, we know the z-component of its angular momentum; at the same time, due to quantum mechanical uncertainty, the x- and y-components are unknown and all possible orientations along the surface of a cone for $\vec{\mu}$ are allowed. We thus employ the idea of the precession of $\vec{\mu}$, but the exact location of the vector at any given time cannot be predicted. Although the model of precession is physically inaccurate, it is a useful analogy to classical mechanics nonetheless. The z-component of $\vec{\mu}$, μ_z, may assume one of $2\mathscr{I}+1$ values, each with corresponding energies separated by $\hbar\omega_0$. Each energy state (orientation) is populated according to the Boltzmann distribution. For spin-1/2 ($\mathscr{I} = 1/2$) particles, two energy states are allowed (two-level system): the spins may have μ_z components either parallel (positive μ_z) or antiparallel (negative μ_z) to the external field.

At equilibrium, because each spin in the sample precesses with arbitrary phase, the components of the magnetic moments in the xy-plane perpendicular to B_0 cancel. Moreover, a slightly higher number of spins populate the lower-energy states, so that the total (or 'bulk') magnetization, $\vec{M}$, lies along the z-axis at equilibrium: $M_0 = M_z$.

Radio frequency (RF) pulses perturb the equilibrium population distribution, to generate phase coherence among the various spins (see Section 2.1.1.2). For a given spin, the z-component of angular momentum is precisely defined, while the x- and y-components stay indeterminate. Thus, the x- and y- components of the bulk-magnetization M_x and M_y oscillate in time.

Relaxation is the irreversible evolution of the spin system towards a steady state [1,2]. For instance, the system returns to equilibrium after a perturbation by an RF pulse or series of RF pulses. Traditionally, the approach to equilibrium has been classified into two broad types – *longitudinal* relaxation and *transverse* relaxation. Longitudinal relaxation, also called *spin–lattice* relaxation, describes the dissipation of energy by the spins into their surroundings (called the *lattice*), which tends to restore the equilibrium population distribution (with slightly more spins in the lower energy states as dictated by the Boltzmann distribution at a given temperature), and consequently reestablishes the z-component of the magnetization (colinear with the external field). Transverse relaxation, sometimes called *spin–spin* relaxation, describes the dephasing (loss of precessional coherence among the spins) that takes place in the xy-plane, leading to a decay in transverse magnetization. Both types of relaxation result from random fluctuations of local magnetic fields, produced by a variety of intramolecular and intermolecular magnetic interactions that are modulated by the stochastic (Brownian) coupling of the spin-system to the lattice.

Longitudinal and transverse relaxation are each characterized by a time constant (T_1 and T_2, respectively) and a corresponding relaxation rate ($R_1 = 1/T_1$ and $R_2 = 1/T_2$). Transverse relaxation takes place more rapidly than does longitudinal relaxation; that is, the decay in transverse magnetization (primarily due to a loss of precessional coherence) takes place faster than the restoration of the equilibrium magnetization (as a result of dissipation of energy by the spins into the lattice, thereby restoring equilibrium populations of the various energy levels). Generally, $2R_2 \geq R_1$, though exceptions to this have been noted [3,4].

In this review, we shall focus primarily on the chemical shift anisotropy (CSA) and dipole–dipole (DD) interactions, which are by far the two most significant interactions contributing to the relaxation of spin-1/2 nuclei in the solution state. Both are essentially intramolecular interactions modulated by random molecular tumbling in solution.

Since molecular rotational diffusion and internal dynamics determine the nature of the stochastic processes that modulate the interactions contributing to relaxation, an understanding of the Brownian motion of spin-containing molecules enables one to determine information regarding their diffusive, shape dependent, and dynamical properties based upon observed relaxation rates. This determination is the ultimate goal of the theory described in this review.

1.1. Outline of the discussion

In the following, we begin by presenting the Wangsness–Bloch–Redfield [5–15,1] density matrix relaxation theory (Section 2), which leads to a discussion of the rotational Brownian motion that modulates the spin interactions (Section 3) leading to relaxation. We consider first the rotational diffusion of single-domain, rigid molecules rotating within various orienting potentials that may result from, for example, a liquid crystalline medium (Section 4 and 5). As a special case, we treat the zero-potential, that is, the diffusion of rigid molecules in an isotropic solvent.

Next, we consider the results of rotational diffusion theory within the framework of relaxation theory, in order to predict relaxation rates measured through NMR spectroscopy. These models may be fitted to experimentally measured NMR relaxation data in order to determine the diffusive hydrodynamic properties (shape, rigidity, etc.) of the macromolecules studied [16–18]. Throughout this review, our goal is to provide thorough, detailed, and (where possible) self-contained explanations, starting from first principles. Emphasis is placed upon completeness and clarity rather than brevity or mathematical elegance. Where extended calculations or background information obfuscate the overarching arguments of the review, we make reference to appendices containing more detailed explanations and derivations.

Several excellent publications have discussed individual topics covered in this review at length. However, we felt that a comprehensive, *ab initio*, self-consistent treatise of all theoretical principles of interest in the calculation of spin-relaxation rates in modern biomolecular NMR, was lacking. We have attempted to provide such a treatment in this review. All relevant aspects of quantum statistics, diffusion theory, NMR interactions and relaxation theory have been introduced assuming no prior background.

We focus here on the theory rather than applications providing detailed analytical expressions wherever possible.

2. Density matrix relaxation theory

Consider an ensemble of identical spins in solution, in which each spin is surrounded by the neighboring spins; the rest of the universe excluding the specific spins under consideration is referred to as the *lattice* or *bath*. Interactions between the spins and the external static field of the NMR spectrometer are treated quantum mechanically. The larger lattice is treated classically with continuous energy levels due its large number of degrees of freedom. The temperature of the lattice is assumed to remain constant, even as energy is exchanged with the spins (the lattice's heat capacity is considered to be infinite).

This treatment describes a weak stochastic coupling between the two systems (spins and lattice) arising from the modulation of the local magnetic environment surrounding each spin, due to the Brownian motion of the particles containing the spins. That is, each spin, in addition to interacting with the static spectrometer field, interacts with local magnetic fields (originating from the lattice) that are time-dependent and random due to the molecular diffusion.

During relaxation, longitudinal (i.e. parallel to the static field) components of the local fields act to either augment or oppose the applied field, and thereby cause the Larmor frequencies of the spins to vary because the spins 'see' an external field that varies with time. This process is adiabatic in the sense that there is no exchange of energy between the spins and lattice, but it contributes to the loss of phase coherence that produces the macroscopic phenomenon of transverse relaxation. Thus, stochastic variations in longitudinal local field components cause transverse relaxation.

Transverse components of the local random fields, if fluctuating at a frequency corresponding to the energy difference between two states of the spin system, may induce a transition in a nearby spin, with an accompanying and opposite transition in the lattice. This process is non-adiabatic: the spin system and lattice directly exchange energy. Since the lattice is assumed to remain in thermal equilibrium, with far greater population of the lower energy states, it is more probable that such interactions involve a transition in the lattice from lower to higher energy, and a spin transition from higher to lower energy, thus reducing the population of higher energy levels in the spin system and ultimately returning it to equilibrium. Thus, fluctuations in the transverse local field components cause longitudinal relaxation.

Because the lattice is treated classically, while the individual spins are treated quantum mechanically, this theory is usually referred to as *semiclassical* relaxation theory. The results of semiclassical relaxation theory can be confirmed by a rigorous quantum mechanical treatment of the problem [1,10], considering the limiting case of an infinite lattice temperature.

2.1. The density operator

2.1.1. Definition and properties

Most relaxation analyses monitor the behavior of bulk magnetization, i.e. that of an ensemble of spins in a finite sample. In order to formulate an analytical theory of this behavior and reconcile it with semiclassical relaxation theory, a quantum mechanical formalism describing the ensemble of spins is necessary. The mathematical tool used to describe a quantum mechanical ensemble such as a system of spins is the density operator [19].

2.1.1.1. Description of a statistical ensemble using a density operator. Consider a statistical ensemble composed of N identical particles, each described by a normalized wave function $|\Phi_k\rangle$ $(k = 1,2,3,\ldots N)$ describing its position in a Hilbert space. Formally, we may consider each normalized ket as corresponding a point Φ_k on the surface $\mathbb{C}$ of a unit 'Hilbert-sphere'.

We would have complete knowledge of the system if we knew the exact wave function of each particle, that is, if we knew $\{|\Phi_1\rangle \ldots |\Phi_N\rangle\}$ at all times. Generally we do *not* know the exact wave function of every particle; that is, we do not know the exact location of each ket on $\mathbb{C}$. Instead, we may know the *probability* of finding the state of a particle within a surface element dS around Φ_k. Let us denote this probability distribution as $P(\Phi_k)$.

If the system is in some arbitrary state $|\Phi_k\rangle$, the expectation value of any state-dependent operator $\widehat{\mathscr{A}}$ is

$$\left\langle \widehat{\mathscr{A}} \right\rangle = \left\langle \Phi_k \middle| \widehat{\mathscr{A}} \middle| \Phi_k \right\rangle. \tag{1}$$

Again, since we do not know the exact state $|\Phi_k\rangle$ with certainty, we may consider only the average value of $\langle \widehat{\mathscr{A}} \rangle$ based on the probability distribution of the states $|\Phi_k\rangle$. We denote this with an overbar:

$$\overline{\left\langle \widehat{\mathscr{A}} \right\rangle} = \int P(\Phi_k) \langle \Phi_k | \widehat{\mathscr{A}} | \Phi_k \rangle \, dS. \tag{2}$$

The average is an ensemble average; that is, the average of the values measured for each member of the ensemble at a given point in time. Due to *ergodicity*, the ensemble average may be replaced by a time average, where all members of the ensemble are identical. Note that Eq. (2) accounts for two independent sources of uncertainty by introducing two corresponding averages. First, there is the *quantum mechanical* uncertainty inherent in the measurement process, leading to an expectation value of a given operator *even when the state of a particle is perfectly well known* (i.e. a pure state). We denote the associated average by the '$\langle\ \rangle$'. Second, there is the *statistical* uncertainty that prevents us from knowing exactly which state each particle is in when the measurement is taken. This is equivalent to an ensemble average (or time average for ergodic systems), which we denote with the overbar.

Now, we expand Eq. (2) in an n-dimensional orthonormal basis set consisting of kets $\{|i\rangle\}$ that span the Hilbert space containing $|\Phi_k\rangle$. According to the closure theorem,

$$\sum_{i=1}^{n} |i\rangle\langle i| = \mathbb{1}_n. \tag{3}$$

where $\mathbb{1}_n$ is the $n \times n$ identity matrix. Applying the closure theorem twice, we have

$$\widehat{\mathscr{A}}|\Phi_k\rangle = \left(\sum_{i=1}^{n} |i\rangle\langle i|\right) \widehat{\mathscr{A}} \left(\sum_{j=1}^{n} |j\rangle\langle j|\right) |\Phi_k\rangle = \sum_{i,j=1}^{n} |i\rangle\langle i|\widehat{\mathscr{A}}|j\rangle\langle j|\Phi_k\rangle. \tag{4}$$

so

$$\langle \Phi_k|\widehat{\mathscr{A}}|\Phi_k\rangle = \sum_{i,j=1}^{n} \langle \Phi_k|i\rangle\langle i|\widehat{\mathscr{A}}|j\rangle\langle j|\Phi_k\rangle. \tag{5}$$

Since $\langle i|\widehat{\mathscr{A}}|j\rangle, \langle \Phi_k \mid i\rangle, \langle j \mid \Phi_k\rangle$ are all scalars, we may rearrange the terms in Eq. (5):

$$\langle \Phi_k|\widehat{\mathscr{A}}|\Phi_k\rangle = \sum_{i,j=1}^{n} \langle i|\widehat{\mathscr{A}}|j\rangle\langle j|\Phi_k\rangle\langle \Phi_k|i\rangle. \tag{6}$$

Eq. (2) may then be rewritten as

$$\overline{\left\langle \widehat{\mathscr{A}} \right\rangle} = \sum_{i,j}^{n} \langle i|\widehat{\mathscr{A}}|j\rangle\langle j| \int P(\Phi_k)|\Phi_k\rangle\langle \Phi_k|i\rangle dS. \tag{7}$$

Eq. (7) defines the density (i.e. probability density) operator $\hat{\rho}$, which has extensive applications in quantum mechanics:

$$\hat{\rho} = \int P(\Phi_k)|\Phi_k\rangle\langle\Phi_k|dS. \tag{8}$$

2.1.1.2. Selected properties and applications. Property 1 – Operation on $|\Phi_m\rangle$. Notice that the operation of the density operator on a state $|\Phi_m\rangle$ is to scale each state $|\Phi_k\rangle$ by the projection of $|\Phi_m\rangle$ onto that state (i.e. by $\langle\Phi_k \mid \Phi_m\rangle$), and to add each of these scaled kets, weighted by the probability of being in each state $|\Phi_k\rangle$ (the integral extends over every possible state, i.e. over the entire $\mathbb{C}$-surface):

$$\hat{\rho}|\Phi_m\rangle = \int P(\Phi_k)\langle\Phi_k \mid \Phi_m\rangle|\Phi_k\rangle dS. \tag{9}$$

Property 2 – Hermiticity:

Since the probability $P(\Phi_k)$ is real, the density operator is Hermitian:

$$\hat{\rho}^\dagger = \left(\int P(\Phi_k)|\Phi_k\rangle\langle\Phi_k|dS\right)^\dagger = \int P^*(\Phi_k)\langle\Phi_k|^\dagger|\Phi_k\rangle^\dagger dS = \hat{\rho}. \tag{10}$$

Application 1 – Expectation values:

Inserting Eq. (8) in Eq. (7), we have

$$\overline{\left\langle\widehat{\mathscr{A}}\right\rangle} = \sum_{i,j}^{n}\langle i|\widehat{\mathscr{A}}|j\rangle\langle j|\hat{\rho}|i\rangle, \tag{11}$$

which, using the closure theorem (Eq. (3)) once more, can be written as

$$\overline{\left\langle\widehat{\mathscr{A}}\right\rangle} = \sum_{i}^{n}\langle i|\widehat{\mathscr{A}}\hat{\rho}|i\rangle, \tag{12}$$

which is the trace of the matrix $\mathscr{A}\rho$:

$$\overline{\left\langle\widehat{\mathscr{A}}\right\rangle} = \mathrm{Tr}(\mathscr{A}\rho). \tag{13}$$

Definition 1 – Populations:

The diagonal elements of the density matrix

$$\rho_{ii} = \langle i|\hat{\rho}|i\rangle = \int P(\Phi_k)|\langle i|\Phi_k\rangle|^2 dS, \tag{14}$$

are real, and may be regarded as the average probability of finding upon measurement that the system is in the state $|i\rangle$. For this reason, the diagonal element ρ_{ii} is referred to as the *population* of state $|i\rangle$. Notice that from the expectation value of the identity operator, i.e. $\mathscr{A} = \mathbb{1}$, we deduce from Eq. (13) that the trace of the density matrix is equal to unity, which befits probabilities.

$$\mathrm{Tr}(\rho) = 1. \tag{15}$$

Definition 2 – Coherences:

The off-diagonal elements

$$\rho_{ij} = \langle i|\hat{\rho}|j\rangle = \int P(\Phi_k)\langle i|\Phi_k\rangle\langle\Phi_k|j\rangle dS, \tag{16}$$

in contrast to the diagonal elements, represent averages of complex numbers. Nonzero elements (ρ_{ij}) indicate that, on average, the correlation is non-vanishing between the two states, $|i\rangle$ and $|j\rangle$. For this reason, off-diagonal elements are referred to as *coherences*.

Application 2: Partial traces

Finally, we make note of the concept of partial traces. For two non-interacting subsystems a and b with corresponding density operators $\hat{\rho}^{(a)}$ (acting in a Hilbert space of dimension m) and $\hat{\rho}^{(b)}$ (acting in a Hilbert space of dimension n), respectively, the global system $a+b$ is described by a density operator $\hat{\rho}^{(ab)}$ given by the direct (tensorial) product of the two constituent subsystems:

$$\hat{\rho}^{(ab)} = \hat{\rho}^{(a)} \otimes \hat{\rho}^{(b)}. \tag{17}$$

The global operator acts in an $m \times n$-dimensional direct product space spanned by the complete set of tensorial products $\{|i^{(a)}\rangle \otimes |i^{(b)}\rangle\}$ of the m basis kets $\{|i^{(a)}\rangle\}$ (of the space in which $\hat{\rho}^{(a)}$ acts) and the n basis kets $\{|i^{(b)}\rangle\}$ (of the space in which $\hat{\rho}^{(b)}$ acts). The (total) trace of this operator is given by [19]:

$$\mathrm{Tr}\left(\hat{\rho}^{(ab)}\right) = \sum_{i^{(a)}}\sum_{i^{(b)}}\left(\left(\left\langle i^{(b)}\right| \otimes \left\langle i^{(a)}\right|\right)\hat{\rho}^{(ab)}\left(\left|i^{(a)}\right\rangle \otimes \left|i^{(b)}\right\rangle\right)\right). \tag{18}$$

The matrix elements of the substituent density operator $\hat{\rho}^{(a)}$ (with an analogous equation for $\hat{\rho}^{(b)}$) are given by

$$\rho_{ij}^{(a)} = \left\langle i^{(a)}\middle|\hat{\rho}^{(a)}\middle|j^{(a)}\right\rangle = \sum_{i^{(b)}}\left(\left(\left\langle i^{(b)}\right| \otimes \left\langle i^{(a)}\right|\right)\hat{\rho}^{(ab)}\left(\left|j^{(a)}\right\rangle \otimes \left|i^{(b)}\right\rangle\right)\right). \tag{19}$$

In analogy to Eq. (18), this operation is referred to as the *partial trace over b*, $\mathrm{Tr}_b(\ldots)$, and enables us to compute from $\hat{\rho}^{(ab)}$ the density matrix $\hat{\rho}^{(a)}$ describing the statistical properties of measurements bearing on system a alone (and analogously for system b). That is,

$$\mathrm{Tr}_b\left(\hat{\rho}^{(ab)}\right) = \hat{\rho}^{(a)}; \quad \mathrm{Tr}_a\left(\hat{\rho}^{(ab)}\right) = \hat{\rho}^{(b)}. \tag{20}$$

In this article, we concern ourselves with only a narrow subset of possible density operator applications. Extensive treatments of the density operator and additional applications may be found elsewhere [19–23]. The key concept to bear in mind is that the density operator contains all quantum mechanical and statistical information necessary to completely describe a general statistical ensemble of particles.

2.1.2. Time evolution

For the problem of nuclear spin relaxation, we are interested in the time evolution of the populations and coherence in an ensemble of spins. We therefore seek to derive and solve an equation of motion for the density operator.

The time evolution of a particle in state $|\Phi_k\rangle$ under the influence of a Hamiltonian $\widehat{\mathscr{H}}$ is given by the Schrödinger equation:

$$\hbar\frac{\partial}{\partial t}|\Phi_k\rangle = -i\widehat{\mathscr{H}}|\Phi_k\rangle, \tag{21}$$

and therefore, for the bra (adjoint) the corresponding equation is:

$$\hbar\frac{\partial}{\partial t}\langle\Phi_k| = i\langle\Phi_k|\widehat{\mathscr{H}}^\dagger = i\langle\Phi_k|\widehat{\mathscr{H}}, \tag{22}$$

since the Hamiltonian is Hermitian, $\widehat{\mathscr{H}}^\dagger = \widehat{\mathscr{H}}$.

For the time evolution of the density operator, we may consider only the time-dependent part, and employing Eqs. (21) and (22)

$$\begin{aligned}\hbar\frac{\partial}{\partial t}\hat{\rho} &= \hbar\frac{\partial}{dt}(|\Phi_k\rangle\langle\Phi_k|) = \hbar\left(\frac{\partial}{dt}|\Phi_k\rangle\langle\Phi_k| + |\Phi_k\rangle\frac{\partial}{dt}\langle\Phi_k|\right)\\ &= -i\widehat{\mathscr{H}}|\Phi_k\rangle\langle\Phi_k| + i|\Phi_k\rangle\langle\Phi_k|\widehat{\mathscr{H}} = -i\left(\widehat{\mathscr{H}}\hat{\rho} - \hat{\rho}\widehat{\mathscr{H}}\right) = -i\left[\widehat{\mathscr{H}}, \hat{\rho}\right].\end{aligned} \tag{23}$$

Writing the Hamiltonian in units of $\hbar$ (so-called Planck or Dirac units), we may write simply

$$\frac{\partial}{\partial t}\hat{\rho} = -i[\widehat{\mathscr{H}}, \hat{\rho}], \tag{24}$$

which is known as the Liouville–von Neumann equation.

Notice that if we expand the density operator in an eigenbasis $\{|j\rangle\}$ consisting of eigenstates of a time independent (i.e. static) Hamiltonian

$$\widehat{\mathscr{H}}|j\rangle = E_j|j\rangle, \tag{25}$$

(given the use of Dirac units, E_j are angular frequencies), we obtain from Eq. (24) by employing closure

$$\begin{aligned}\frac{\partial}{\partial t}\rho_{jk} &= \langle j|\left(i\hat{\rho}\widehat{\mathscr{H}} - i\widehat{\mathscr{H}}\hat{\rho}\right)|k\rangle \\ &= i\sum_{l}\langle j|\hat{\rho}|l\rangle\langle l|\widehat{\mathscr{H}}|k\rangle - i\sum_{m}\langle j|\widehat{\mathscr{H}}|m\rangle\langle m|\hat{\rho}|k\rangle,\end{aligned} \tag{26}$$

since $\langle j|\widehat{\mathscr{H}}|k\rangle = \langle j|k\rangle E_k = \delta_{jk}E_k$, where δ_{jk} is the Kronecker delta ($\delta_{jk} = 1$ for $j = k$, and $\delta_{jk} = 0$ otherwise),

$$\frac{\partial}{\partial t}\ \rho_{jk} = i(E_k - E_j)\rho_{jk}. \tag{27}$$

Thus, under the effect of a time-independent Hamiltonian, the populations ($j = k$) are constant, while the coherences ($j \neq k$) oscillate at the Bohr frequencies (i.e. $E_k - E_j$) of the system.

2.1.3. Product operators: a useful basis set for the density operator

It is often more useful to describe the density operator in a basis of orthonormal spin-operators (that describe experimentally measurable variables) rather than an eigenbasis of the Hamiltonian in Hilbert space as described in the previous section. This basis represents a ket vector in Liouville space. The so-called product operators [2,24,25] comprise a suitable operator basis used in the NMR literature.

The product operator formalism is a very compact and intuitive way to describe the evolution of the density operator. Only the deviations of the density operator from identity are considered. This focuses the discussion on the polarization, the part of the density operator that is manipulated and observed. The influence of the identity operator on steady-states has been discussed at length elsewhere [26–29].

For systems with two or more spins, describing the evolution using spin operators to treat spin systems independently is a valid approach since most systems treated in NMR are weakly coupled. This approach, valid in the weak coupling regime, is called *product operator formalism*. Product operator formalisms for strongly coupled spins have been described [30].

The density operator can be represented as a linear combination of a set of basis operators $\{\widehat{\mathscr{B}}_k\}$ in Liouville space (as opposed to Hilbert space in the previous section);

$$\hat{\rho}(t) = \sum_{k=1}^{K} b_k(t)\widehat{\mathscr{B}}_k, \tag{28}$$

where the coefficients $b_k(t)$ are time dependent complex numbers and K is the dimension of the Liouville space; the dimension of the Liouville space for N spin-1/2 nuclei is $K = 2^{2N}$, where the corresponding Hilbert space is 2^N-dimensional.

Following Eq. (13), the expectation value of an operator $\widehat{\mathscr{A}}$ can be written as;

$$\left\langle \widehat{\mathscr{A}}(t) \right\rangle = \mathrm{Tr}\{\hat{\rho}(t)\widehat{\mathscr{A}}\} = \sum_{k=1}^{K} b_k(t)\mathrm{Tr}\{\widehat{\mathscr{B}}_k\widehat{\mathscr{A}}\}. \tag{29}$$

The beauty of Eq. (29) is that the time evolution of the density operator and the expectation value of any operator can be found by limited trace operations. The basis operators are normalized as

$$\mathrm{Tr}\{\widehat{\mathscr{B}}_k\widehat{\mathscr{B}}_l\} = \delta_{kl}2^{N-2} \tag{30}$$

where δ_{kl} is the Kronecker delta. The time evolution of the density operator under the effect of a specific time-independent Hamiltonian $\widehat{\mathscr{H}}$ can be described from the integration of Eq. (24) as a rotation of the initial density operator $\hat{\rho}_0 = \hat{\rho}(0)$ to a new operator $\hat{\rho}_t = \hat{\rho}(t)$; this rotation occurs in 'spin-space' as opposed to 'real-space' (compare to the interaction representation of Section 2.2.2 and Appendix A.3):

$$\hat{\rho}_t = e^{-i\widehat{\mathscr{H}}t}\hat{\rho}_0 e^{i\widehat{\mathscr{H}}t}. \tag{31}$$

The most practical basis operators to represent the density operator are the angular-momentum operators, $\mathscr{I}_x, \mathscr{I}_y$ and $\mathscr{I}_z$ (for simplicity we drop the 'hat' from the product operators). For a single-spin (spin-1/2) system, two basis sets can be used: $\{\mathbb{1}, \mathscr{I}_x, \mathscr{I}_y, \mathscr{I}_z\}$ and $\{\mathscr{I}^\alpha, \mathscr{I}^\beta, \mathscr{I}_+, \mathscr{I}_-\}$. These basis sets are related by:

$$\begin{aligned}\mathscr{I}_z &= \frac{1}{2}(\mathscr{I}^\alpha - \mathscr{I}^\beta); \\ \mathscr{I}_y &= \frac{1}{2i}(\mathscr{I}_+ - \mathscr{I}_-); \\ \mathscr{I}_x &= \frac{1}{2}(\mathscr{I}_+ + \mathscr{I}_-);\end{aligned} \tag{32}$$

$$\mathbb{1} = \frac{1}{2}(\mathscr{I}^\alpha + \mathscr{I}^\beta). \tag{33}$$

For one spin-1/2 system with two eigenstates, $|\alpha\rangle$; $(m = +\frac{1}{2})$ and $|\beta\rangle$; $(m = -\frac{1}{2})$, the basis operators can be represented as:

$$\begin{aligned}\mathscr{I}^\alpha &= |\alpha\rangle\langle\alpha|; \\ \mathscr{I}^\beta &= |\beta\rangle\langle\beta|; \\ \mathscr{I}_+ &= |\alpha\rangle\langle\beta|; \\ \mathscr{I}_- &= |\beta\rangle\langle\alpha|,\end{aligned} \tag{34}$$

and

$$\begin{aligned}\mathscr{I}_+|\beta\rangle &= |\alpha\rangle\langle\beta|\beta\rangle = |\alpha\rangle; \\ \mathscr{I}_-|\alpha\rangle &= |\beta\rangle\langle\alpha|\alpha\rangle = |\beta\rangle.\end{aligned} \tag{35}$$

The usefulness of product operators becomes evident when a weakly-coupled system of two spin-1/2 nuclei is considered. This system has *four* eigenstates, $|\alpha\alpha\rangle$, $|\alpha\beta\rangle$, $|\beta\alpha\rangle$, $|\beta\beta\rangle$. There are *four* population terms in single-element operator basis, there are *eight* single-quantum transitions where the state of one spin is unaffected while the state of the other spin changes; *two* double-quantum transitions where both spins change spin states in the same sense; and *two* zero-quantum transitions where both spins change their state in an opposite sense. Instead of manipulating *sixteen* matrix elements to describe the evolution of the density operator one can use *sixteen* simple product operators. The evolution of the spin system in a typical NMR experiment is often limited to a smaller subspace spanned by a few of these product operators. The product operator basis is therefore much more practical.

The sixteen cartesian product operator terms for a two-spin system are

$$\begin{array}{lllllll} \frac{1}{2}\mathbb{1} & \mathscr{I}_x & \mathscr{I}_y & \mathscr{I}_z & \mathscr{S}_x & \mathscr{S}_y & \mathscr{S}_z \\ 2\mathscr{I}_x\mathscr{S}_z & 2\mathscr{I}_y\mathscr{S}_z & 2\mathscr{I}_z\mathscr{S}_z & 2\mathscr{I}_z\mathscr{S}_x & 2\mathscr{I}_z\mathscr{S}_y & & \\ 2\mathscr{I}_x\mathscr{S}_x & 2\mathscr{I}_y\mathscr{S}_y & 2\mathscr{I}_x\mathscr{S}_y & 2\mathscr{I}_y\mathscr{S}_x & & & \end{array}$$

The use of product operators becomes even more favorable for larger spin-systems.

2.2. The master equation of relaxation

2.2.1. The Hamiltonian

Description of the time-evolution of the spin ensemble is given by the Liouville–von Neumann equation (Eq. (24)). In order to use this equation to describe the trajectory of the density operator during an NMR experiment, we have to first define the Hamiltonian of the system during the experiment. Then we solve for the density operator $\hat{\rho}$ at any given time t as it evolves under the influence of this Hamiltonian. The Hamiltonian of a spin system during a generic NMR experiment may be defined as:

$$\widehat{\mathscr{H}}(t) = \widehat{\mathscr{H}}_0 + \widehat{\mathscr{H}}_1(t) + \widehat{\mathscr{H}}_{RF}(t), \tag{36}$$

in the laboratory frame, where $\widehat{\mathscr{H}}_0$ is the main time-independent static Hamiltonian describing the Zeeman interaction of the spins with the external field $\vec{B}_0$, $\widehat{\mathscr{H}}_{RF}(t)$ represents the interaction with time-dependent radio frequency fields, and $\widehat{\mathscr{H}}_1(t)$ is the Hamiltonian for the various interactions leading to relaxation:

$$\widehat{\mathscr{H}}_1(t) = \sum_{\mu} \widehat{\mathscr{H}}_{\mu}(t). \tag{37}$$

The index μ denotes the various spin interactions, e.g. dipolar coupling (DD), chemical shift anisotropy (CSA), etc. The magnitude of $\widehat{\mathscr{H}}_0$ is much larger than that of $\widehat{\mathscr{H}}_1(t)$ for the external field used in normal NMR experiments. In this case, $\vec{B}_0$ defines the axes of quantization and $\widehat{\mathscr{H}}_1(t)$ is taken to be a perturbation to the main Zeeman interaction.

In the laboratory frame, $\widehat{\mathscr{H}}_1(t)$ is a stationary random function of time with zero average. If $\widehat{\mathscr{H}}_1(t)$ does *not* have a vanishing average – i.e. it has some constant offset – then the non-zero, constant part can be added to a redefined static Hamiltonian $\widehat{\mathscr{H}}_0$. The precise form of $\widehat{\mathscr{H}}_1(t)$ will be discussed in Section 3.

2.2.2. The interaction representation and frame transformation

For a system evolving in the absence of RF fields i.e. $\mathscr{H}_{RF}(t) = 0$, the Liouville–von Neumann equation (Eq. (24)) becomes

$$\frac{\partial \hat{\rho}}{\partial t} = -i\left[\widehat{\mathscr{H}}(t), \hat{\rho}\right] = -i\left[\widehat{\mathscr{H}}_0 + \widehat{\mathscr{H}}_1(t), \hat{\rho}\right]. \tag{38}$$

Solving Eq. (38) is simplified by transforming from this Schrödinger representation to the interaction representation, which corresponds to a change of reference frames in classical mechanics. The interaction representation or interaction 'picture', sometimes referred to as the Dirac picture, is an intermediate between the Schrödinger and Heisenberg representations in quantum mechanics [31]. In the Schrödinger picture, operators are assumed to be constant while the wavefunction's state vector evolves with time, whereas in the Heisenberg picture, state vectors are assumed to be constant and it is the operators that carry time dependence. In the interaction picture, the state vectors and the operators each carry part of the time dependence of observables.

For a static Hamiltonian $\widehat{\mathscr{H}}_0$ that contains only the Zeeman interactions, with $\vec{B}_0$, the interaction frame is equivalent to one rotating relative to the laboratory frame such that the effects of the static Hamiltonian $\widehat{\mathscr{H}}_0$ appear to vanish. When $\widehat{\mathscr{H}}_{RF}(t) \neq 0$, during an RF pulse, one may first transform to a rotating frame, so as to make $\widehat{\mathscr{H}}_{\mathrm{RF}}(t)$ time-independent. If the RF field is applied on resonance (i.e. $\omega_{RF} = \omega_0$), the rotating frame coincides with the interaction frame. The interaction representation moves the time dependence of the state vector due to $\widehat{\mathscr{H}}_0$ onto the operator $\widehat{\mathscr{H}}_1(t)$, and thus singles-out the effect of the perturbation $\widehat{\mathscr{H}}_1(t)$.

Transformation to the interaction frame is done by transforming all operators appropriately (see Appendix A.4). Specifically, any arbitrary operator expressed as $\widehat{\mathscr{Q}}$ in the laboratory frame, where $\widehat{\mathscr{Q}} \neq \widehat{\mathscr{H}}_0$, is given in the interaction representation as

$$\widehat{\mathscr{Q}} \rightarrow \tilde{\widehat{\mathscr{Q}}}(t) = e^{i\widehat{\mathscr{H}}_0 t}\,\widehat{\mathscr{Q}}\; e^{-i\widehat{\mathscr{H}}_0 t}. \tag{39}$$

Note that since $\widehat{\mathscr{H}}_0$ is Hermitian, $\widehat{\mathscr{U}} = e^{i\widehat{\mathscr{H}}_0 t}$ is a unitary operator. As mentioned above, operators that have no time dependence in the lab (Schrödinger) frame, may become time dependent in the interaction frame (as should be expected physically since the interaction frame rotates in the lab frame).

In the interaction representation, Eq. (38) transforms to

$$\frac{\partial}{\partial t}\tilde{\hat{\rho}}(t) = -i\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \tilde{\hat{\rho}}(t)\right]. \tag{40}$$

Eq. (40), which represents the Liouville–von Neumann equation in the interaction frame, is derived explicitly in Appendix A.

2.2.3. Derivation of the master equation

2.2.3.1. Solution to the Liouville–von Neumann equation. Eq. (40) is solved by grouping like terms and integrating:

$$\begin{aligned} d\tilde{\hat{\rho}}(t) &= -i\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \tilde{\hat{\rho}}(t)\right]dt, \\ \tilde{\hat{\rho}}(t) &= \tilde{\hat{\rho}}(0) - i\int_0^t \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(t')\right]dt'. \end{aligned} \tag{41}$$

This expression for the density matrix is 'recursive' in the sense that the $\tilde{\hat{\rho}}(t')$ term in the commutator is defined by the formula for $\tilde{\hat{\rho}}(t)$, of which $\tilde{\hat{\rho}}(t')$ itself is a part. In other words, we may write $\tilde{\hat{\rho}}(t')$ as a function of $\tilde{\hat{\rho}}(t'')$, which is a function of $\tilde{\hat{\rho}}(t''')$, and so on. Thus, we may *expand* $\tilde{\hat{\rho}}(t)$ as

$$\tilde{\hat{\rho}}(t) = \tilde{\hat{\rho}}(0) - \int_0^t \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0) - i\int_0^{t'} \left[\widetilde{\widehat{\mathscr{H}}}_1(t''), \tilde{\hat{\rho}}(t'')\right]dt''\right]dt',$$

$$\begin{aligned} \tilde{\hat{\rho}}(t) = \tilde{\hat{\rho}}(0) &- i\int_0^t \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]dt' - \int_0^t dt' \\ &\times \int_0^{t'} \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \left[\widetilde{\widehat{\mathscr{H}}}_1(t''), \tilde{\hat{\rho}}(0)\right]\right]dt'' + \ldots \end{aligned} \tag{42}$$

where we have explicitly written terms up to second order. We may ask, at what order might we truncate the expansion such that our calculations are still acceptably accurate? We consider a short time $t = \Delta t$, during which the density matrix does not evolve significantly from its $t = 0$ value (i.e. that $\tilde{\hat{\rho}}(t) \approx \tilde{\hat{\rho}}(0)$), and in that case, terms higher than second order have negligible contribution (this approach thus qualifies as time-dependent, second order perturbation theory). In the discussion below, we will examine the scope of validity of this second-order approximation. Skinner et al. [3,4] have treated the problem of the relaxation of a two-state system, considering terms up to fourth order in $\widehat{\mathscr{H}}_1(t)$.

Taking the time derivative of Eq. (42) truncated to second order yields:

$$\frac{\partial \tilde{\hat{\rho}}(t)}{\partial t} = -i\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \tilde{\hat{\rho}}(0)\right] - \int_0^t \left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]\right] dt'. \tag{43}$$

2.2.3.2. Ensemble averaging and correlation. Eq. (43) is accurate for an infinitesimally small system. In a large sample, however, remote regions of the ensemble relax independently due to the random nature of $\widehat{\mathscr{H}}_1(t)$. Since $\widehat{\mathscr{H}}_1(t)$ is a random operator, different regions do not in fact evolve under 'identical' Hamiltonians. As a result, even if all regions have identical $\tilde{\hat{\rho}}(0)$, for times $t > 0$, each part of the sample will have a different, randomly-determined $\tilde{\hat{\rho}}(t)$. To describe the macroscopic sample as a whole, we take the ensemble average over all terms, which we denote with an overbar:

$$\frac{\partial\overline{\tilde{\hat{\rho}}}(t)}{\partial t} = -i\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \tilde{\hat{\rho}}(0)\right]} - \int_0^t \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]\right]}\, dt'. \tag{44}$$

Note that for an ensemble-averaged density matrix, the off-diagonal matrix elements $(j \neq k)$ in Eq. (27) – i.e. the coherences – average to zero at equilibrium, which is consistent with the phenomenological description given at the beginning of the article, describing complete precessional dephasing at equilibrium. On the other hand, the diagonal elements $(j = k)$ in Eq. (27) – i.e. the state populations – are unchanged during ensemble averaging. As described, upon perturbation by an RF pulse, the coherences become non-zero, and the populations change, with those matrix elements corresponding to the higher-energy states increasing in magnitude. In terms of the averaged density matrix, relaxation may then be viewed as the process whereby the off-diagonal matrix elements vanish (precessional phase coherence is lost) and the diagonal elements are restored to their equilibrium values, thus indicating the restoration of energy state populations and the equilibrium bulk longitudinal magnetization.

Assuming ergodicity, the instantaneous ensemble average of the Hamiltonian $\widehat{\mathscr{H}}_1(t)$ is equal to its time average, which as noted above is zero. This assumes that $\overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\tilde{\hat{\rho}}(0)} = \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)}\ \overline{\tilde{\hat{\rho}}(0)}$; that is, that averaging over the Hamiltonian and density operator may be done separately. We show this to be true presently in our consideration of the second-order term. Thus, the first term on the right-hand side of Eq. (44) vanishes and we have:

$$\frac{\partial\overline{\tilde{\hat{\rho}}}(t)}{\partial t} = -\int_0^t \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]\right]}\, dt'. \tag{45}$$

Writing the integrand explicitly gives

$$\begin{aligned}
&\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]\right]} \\
&= \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right] - \left[\widetilde{\widehat{\mathscr{H}}}_1(t'), \tilde{\hat{\rho}}(0)\right]\widetilde{\widehat{\mathscr{H}}}_1(t)} \\
&= \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1(t')\tilde{\hat{\rho}}(0) - \widetilde{\widehat{\mathscr{H}}}_1(t)\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t') - \widetilde{\widehat{\mathscr{H}}}_1(t')\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t) + \tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t')\widetilde{\widehat{\mathscr{H}}}_1(t)} \\
&= \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1(t')\tilde{\hat{\rho}}(0)} - \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t')} - \overline{\widetilde{\widehat{\mathscr{H}}}_1(t')\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t)} + \overline{\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t')\widetilde{\widehat{\mathscr{H}}}_1(t)} \\
&= \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1^{\dagger}(t+\tau)\tilde{\hat{\rho}}(0)} - \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1^{\dagger}(t+\tau)} \\
&\quad - \overline{\widetilde{\widehat{\mathscr{H}}}_1^{\dagger}(t+\tau)\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1(t)} + \overline{\tilde{\hat{\rho}}(0)\widetilde{\widehat{\mathscr{H}}}_1^{\dagger}(t+\tau)\widetilde{\widehat{\mathscr{H}}}_1(t)},
\end{aligned} \tag{46}$$

where on the last line we have made use of the fact that all Hamiltonians are Hermitian, $\widehat{\mathscr{H}}(t) = \widehat{\mathscr{H}}^{\dagger}(t)$, and introduced the variable $\tau = t' - t$. We have written Eq. (46) as such to emphasize that each ensemble average is actually a correlation function (see Appendix C): the correlation of the Hamiltonian with itself over time τ on the one hand, and that between the Hamiltonian and the density operator over time t (or $t + \tau$) on the other hand (there is in principle a correlation between the initial value of the density matrix and the Hamiltonian since $\tilde{\hat{\rho}}(0)$ depends on the behavior of $\widehat{\mathscr{H}}(t)$ before $t = 0$).

The correlation of the Hamiltonian with itself is significant for τ on the order of τ_c (the auto-correlation time of the Hamiltonian) or smaller. Similarly, the correlation between the Hamiltonians and $\tilde{\hat{\rho}}(0)$ is negligible for $t \gg \tau_c$. Assuming $t \gg \tau_c$, we may average over $\tilde{\hat{\rho}}(0)$ and $\widehat{\mathscr{H}}(t)\widehat{\mathscr{H}}(t+\tau)$ separately in Eq. (45), since if there is no correlation between these two functions, the ensemble average of the products will be equal to the product of the ensemble averages. This leads to:

$$\frac{d\overline{\tilde{\hat{\rho}}}(t)}{\partial t} = -\int_0^{\infty} \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau), \tilde{\hat{\rho}}(t)\right]\right]} d\tau. \tag{47}$$

2.2.3.3. Approximations and limits of validity. Given that averaging over the Hamiltonians and density operator may be done separately, and based on our assumption that $t = \Delta t$ is small enough that the evolution of the density operator is infinitesimal, we may replace $\tilde{\hat{\rho}}(0)$ with $\tilde{\hat{\rho}}(t)$ in Eq. (47). The fractional variation of the density operator is approximately

$$\frac{\left\|\tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}(0)\right\|}{\left\|\tilde{\hat{\rho}}(0)\right\|} \approx \frac{t}{\left\|\tilde{\hat{\rho}}(0)\right\|}\left\|\frac{d\tilde{\hat{\rho}}(t)}{dt}\right\| \approx \left\|t\int_0^t \overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)}\ d\tau\right\| \tag{48}$$

where $\|\ldots\|$ indicates the magnitude of an operator, which is often measured by the norm. The norm of an operator $\widehat{\mathscr{A}}$ is defined as the square root of the absolute value of the largest-magnitude eigenvalue of $\widehat{\mathscr{A}}^{\dagger}\widehat{\mathscr{A}}$; for a Hermitian operator $\widehat{\mathscr{A}}_H$ such as a Hamiltonian, this is simply the largest absolute value of an eigenvalue of $\widehat{\mathscr{A}}_H$. The trace may similarly be used as a measure of operator 'strength', inasmuch as the trace is frame-independent, and clearly represents the sum of eigenvalues in a representation where the operator is diagonal. Since values of the correlation function for which $\tau \gg \tau_c$ contribute negligibly to the integral, we can justifiably write

$$\frac{\left\|\tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}(0)\right\|}{\left\|\tilde{\hat{\rho}}(0)\right\|} \approx t\overline{\left\|\widehat{\mathscr{H}}_1(t)\right\|^2}\ \tau_c. \tag{49}$$

If the fractional increase is small (i.e. $t\overline{\|\widehat{\mathscr{H}}_1(t)\|^2}\ \tau_c \ll 1$) in addition to the condition $t \gg \tau_c$ being satisfied, then the errors introduced in replacing $\tilde{\hat{\rho}}(0)$ with $\tilde{\hat{\rho}}(t)$ in Eq. (47) are negligible.

Another result of the requirement that $t \gg \tau_c$ is that we may extend the upper limit of integration in Eq. (47) to infinity. As mentioned above, for values of $\tau > \tau_c$, the correlation $\overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)}$ decays rapidly to zero, and thus the contribution to the integral in Eq. (47) at these values of τ is also minuscule. Therefore, extending the upper limit to infinity does not significantly affect the value of the definite integral. Note, however, that while we assume t to be large enough to extend the limits of integration (since it is orders of magnitude larger than τ_c), it must still be small enough that our original assumption $\tilde{\hat{\rho}}(t) \approx \tilde{\hat{\rho}}(0)$ holds as discussed above. Since we are considering $t \gg \tau_c$, $\tilde{\hat{\rho}}(t)$ for individual spins comprising the ensemble would have evolved under the influence of $\widetilde{\widehat{\mathscr{H}}}_1(t)$ over several cycles. This leads to an averaging of the influence of $\widetilde{\widehat{\mathscr{H}}}_1(t)$ on $\tilde{\hat{\rho}}(t)$ for individual members of the ensemble resulting in essentially the same $\tilde{\hat{\rho}}(t)$ for each member. Therefore we can replace $\overline{\tilde{\hat{\rho}}}(t)$ with $\tilde{\hat{\rho}}(t)$ since the individual density operators for each member of the ensemble is approximately the same.

We now have

$$\frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = -\int_0^\infty \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau), \tilde{\hat{\rho}}(t)\right]\right]}\, d\tau, \tag{50}$$

which is known as the master equation of relaxation.

Now we consider more closely our assumption that terms beyond second order may be neglected in our expansion of Eq. (42). This proves to be a useful exercise because it illuminates a relationship between the strength of the Hamiltonians that lead to relaxation and their associated correlation times. Retaining terms beyond second order, Eq. (44) can be written as

$$\frac{d\tilde{\hat{\rho}}(t)}{dt} = \sum_{n=1}^{\infty} A_n, \tag{51}$$

where

$$\begin{aligned} A_1 &= -i\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \tilde{\hat{\rho}}(0)\right]}; \\ A_n &= -i\int_0^t \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), A_{n-1}(t')\right]}\, dt'. \end{aligned} \tag{52}$$

Successive terms contain increasing factors of the Hamiltonian and additional integrals, and thus the relative strengths of successive terms is

$$\frac{\|A_n\|}{\|A_{n-1}\|} \approx \left\|\int_0^t \widehat{\mathscr{H}}_1(t)\ d\tau\right\| \approx \sqrt{\overline{\left\|\widehat{\mathscr{H}}_1(t)\right\|^2}\tau_c^2}. \tag{53}$$

which must be very small for our second-order truncation to be permissible, $\sqrt{\overline{\|\widehat{\mathscr{H}}_1(t)\|^2}\tau_c^2} \ll 1$, and this requirement is satisfied for short τ_c.

Most biomolecular systems currently studied in NMR are constituted by ensembles of spin-1/2 (^{1}H, ^{13}C, ^{15}N and ^{31}P) and have molecular masses below 100 kDa ($\tau_c < 50$ ns) so that the requirement for short τ_c is never a problem. However, we should inspect if this condition holds for one of the most challenging systems that has been studied by liquid-state NMR so far. The strongest dipolar interaction in a biomolecule arises between two protons in a methyl group. These two protons are separated by about 1.8 Å. The amplitude of the dipolar Hamiltonian, scaled by 0.5 due to the rapid methyl rotation, is:

$$\|\mathscr{H}_1\| \approx 6.5 \times 10^4\ \text{s}^{-1}. \tag{54}$$

For example, for [^{13}C, ^{1}H] correlations observed in solution for the protease ClpP at 5 °C [32], τ_c is about 500 ns (5×10^{-7} s). Thus,

$$\|\mathscr{H}_1\|\tau_c \approx 3.25 \times 10^{-2} \ll 1, \tag{55}$$

which agrees with the above requirement.

2.2.3.4. Correction for finite bath temperature. The preceding discussion considers a density matrix that describes only the spins, thereby ignoring the bath and the coupling between the spins and lattice. As a result, the master equation (Eq. (50)) predicts an equal distribution of the spins among all energy states at equilibrium, and thereby *implies* an infinite lattice temperature, which is clearly not physically accurate. To take into account the finite lattice temperature T_L, we make the following replacement

$$\tilde{\hat{\rho}}(t) \rightarrow \tilde{\hat{\rho}}_{\text{c}}(t, T_L) = \tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}_{\text{eq}}(T_L), \tag{56}$$

where $\hat{\rho}_{\text{eq}}(T_L)$ is the thermal equilibrium value of the density operator, determined by the Boltzmann distribution:

$$\tilde{\hat{\rho}}_{\text{eq}}(T_L) = \hat{\rho}_{\text{eq}}(T_L) = \frac{e^{-\widehat{\mathscr{H}}_0/k_B T_L}}{\text{Tr}\left(e^{-\widehat{\mathscr{H}}_0/k_B T_L}\right)}, \tag{57}$$

where k_B is the Boltzmann constant. This is a purely phenomenological, *ad hoc* correction, but it may be confirmed by a rigorous quantum mechanical treatment [1,9,10,33]. Such an approach considers a total Hamiltonian

$$\widehat{\mathscr{H}} = \widehat{\mathscr{H}}_{0,S} + \widehat{\mathscr{H}}_{0,L} + \widehat{\mathscr{H}}_{1,SL}, \tag{58}$$

where $\widehat{\mathscr{H}}_{0,S}$ and $\widehat{\mathscr{H}}_{0,L}$ represent the unperturbed Hamiltonians of the spin system and the lattice, respectively, and $\widehat{\mathscr{H}}_{1,SL}$ represents the coupling between them. Assuming that the thermal equilibrium of the lattice is not significantly altered by spin transitions (weak coupling between spin and lattice i.e. $\hat{\mathscr{H}}_{1,SL}$ is small), then its state may be described by the density operator

$$\hat{\rho}^{(\text{L})} = \frac{e^{-\widehat{\mathscr{H}}_{0,L}/k_B T_L}}{\text{Tr}\left(e^{-\widehat{\mathscr{H}}_{0,L}/k_B T_L}\right)}, \tag{59}$$

and the total density matrix of the spins and lattice is then written as the direct product

$$\hat{\rho}^{(\text{LS})} = \hat{\rho}^{(\text{L})} \otimes\ \hat{\rho}^{(\text{S})}, \tag{60}$$

where $\hat{\rho}^{(S)} = \hat{\rho}$ is the density operator for the spin system. One then proceeds in a manner analogous to that of the preceding semiclassical derivation, considering the evolution of $\hat{\rho}^{(S)}$ in an interaction representation by employing partial traces as described in Section 2.1.1.2 (the mathematics are by necessity significantly more involved). For the case of high temperatures (i.e. large T_L), which is clearly assumed for spins in the solution state, one eventually obtains in place of Eq. (50):

$$\frac{\partial\overline{\tilde{\hat{\rho}}}(t, T_L)}{\partial t} = -\int_0^\infty \left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau), \tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}_{\text{eq}}(T_L)\right]\right] d\tau, \tag{61}$$

thus validating our *ad hoc* correction of Eq. (56).

2.2.4. Summary of semiclassical relaxation theory

The master equation of relaxation is given by

$$\frac{\partial}{\partial t}\tilde{\hat{\rho}}(t, T_L) = -\int_0^\infty \overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t), \left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau), \tilde{\hat{\rho}}_{\text{c}}(t, T_L)\right]\right]}\, d\tau, \tag{62}$$

where:

- The overbar denotes an ensemble average. Averaging of the Hamiltonian and the density operator are done separately.
- Truncation of the expansion of Eq. (42) at second order requires that $\sqrt{\overline{\|\widehat{\mathscr{H}}_1(t)\|^2}\tau_c^2} \ll 1$.
- t must be short enough so that the evolution of $\tilde{\hat{\rho}}$ is negligible, but long as compared to the correlation time. In conjunction with the preceding requirement, this implies that the master equation is valid provided that

$$\tau_c \ll t \ll \left[\overline{\left\|\widehat{\mathscr{H}}_1(t)\right\|^2}\tau_c\right]^{-1}. \tag{63}$$

- The replacement $\tilde{\hat{\rho}}(t) \rightarrow \tilde{\hat{\rho}}_{\text{c}}(t, T_L) = \tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}_{\text{eq}}(T_L)$ is an *ad hoc* correction made to account for the finite lattice temperature, which may be rigorously justified through quantum mechanical treatment of the entire system of bath and spins.

Physically, Eq. (63) implies that under the present framework we may not seek information for timescales on the order of τ_c or shorter, and thus the master equation is only useful for situations in which the relaxation times T_1 and T_2 are much longer that the correlation times τ_c of the processes leading to relaxation (the processes represented by $\widehat{\mathscr{H}}_1(t)$). This makes semi-classical relaxation theory especially well suited to the treatment of spins in the solution state.

2.3. Redfield theory: the master equation in matrix form

2.3.1. Expansion in an eigenbasis

We now transcribe Eq. (50) into matrix form. Let $|\alpha\rangle$ denote one of a set of eigenstates of the unperturbed Hamiltonian $\widehat{\mathscr{H}}_0$, with corresponding eigenvalue (i.e. energy, which takes the form of an angular frequency since we use Dirac units) E_α, not to be confused with the spin eigenstate of the Zeeman term. This is the representation of the master equation in Hilbert Space. The complete set of eigenstates $\{|\alpha\rangle\}$ forms a suitable eigenbasis in which to express $\partial\tilde{\widehat{\rho}}(t)/\partial t$. Using Eq. (46) as a guide, we may express each matrix element of the integrand of Eq. (50) as

$$\begin{aligned}
&\langle\alpha|\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t)\left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau),\tilde{\widehat{\rho}}(t)\right]\right]}|\alpha'\rangle\\
&\quad=\langle\alpha|\overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)\tilde{\widehat{\rho}}(t)}|\alpha'\rangle\\
&\qquad+\langle\alpha|\overline{\tilde{\widehat{\rho}}(t)\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)\widetilde{\widehat{\mathscr{H}}}_1(t)}|\alpha'\rangle\\
&\qquad-\langle\alpha|\overline{\widetilde{\widehat{\mathscr{H}}}_1(t)\tilde{\widehat{\rho}}(t)\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)}|\alpha'\rangle\\
&\qquad-\langle\alpha|\overline{\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)\tilde{\widehat{\rho}}(t)\widetilde{\widehat{\mathscr{H}}}_1(t)}|\alpha'\rangle,
\end{aligned}\tag{64}$$

and through repeated application of the closure theorem (Eq. (3)) we may rewrite this expression as

$$\begin{aligned}
&\langle\alpha|\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t)\left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau),\tilde{\widehat{\rho}}(t)\right]\right]}|\alpha'\rangle\\
&\quad=\sum_{\beta,\beta'}\sum_{\lambda}\overline{\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\lambda\rangle\langle\lambda|\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)|\beta\rangle\langle\beta|\tilde{\widehat{\rho}}(t)|\beta'\rangle\langle\beta'|\alpha'\rangle}\\
&\qquad+\sum_{\beta,\beta'}\sum_{\lambda}\overline{\langle\alpha|\beta\rangle\langle\beta|\tilde{\widehat{\rho}}(t)|\beta'\rangle\langle\beta'|\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)|\lambda\rangle\langle\lambda|\widetilde{\widehat{\mathscr{H}}}_1(t)|\alpha'\rangle}\\
&\qquad-\sum_{\beta,\beta'}\overline{\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\beta\rangle\langle\beta|\tilde{\widehat{\rho}}(t)|\beta'\rangle\langle\beta'|\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)|\alpha'\rangle}\\
&\qquad-\sum_{\beta,\beta'}\overline{\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t+\tau)|\beta\rangle\langle\beta|\tilde{\widehat{\rho}}(t)|\beta'\rangle\langle\beta'|\widetilde{\widehat{\mathscr{H}}}_1(t)|\alpha'\rangle},
\end{aligned}\tag{65}$$

where the summations extend over all eigenstates of $\widehat{\mathscr{H}}_0$.

Next, writing the matrix $\widetilde{\widehat{\mathscr{H}}}_1(t)$ as a function of the Hamiltonians in the laboratory frame, $\widehat{\mathscr{H}}_0$ and $\widehat{\mathscr{H}}_1(t)$ (see Eq. (39)), and employing closure, we see that terms of the form $\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\beta\rangle$ may be written as

$$\begin{aligned}
\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\beta\rangle&=\langle\alpha|e^{i\widehat{\mathscr{H}}_0t}\widehat{\mathscr{H}}_1(t)e^{-i\widehat{\mathscr{H}}_0t}|\beta\rangle\\
&=\sum_{\lambda,\lambda'}\langle\alpha|e^{i\widehat{\mathscr{H}}_0t}|\lambda\rangle\langle\lambda|\widehat{\mathscr{H}}_1(t)|\lambda'\rangle\langle\lambda'|e^{-i\widehat{\mathscr{H}}_0t}|\beta\rangle.
\end{aligned}\tag{66}$$

Recognizing (see Appendix A.1, Eq. (A5)) that

$$e^{\pm i\widehat{\mathscr{H}}_0t}|\lambda\rangle=e^{\pm iE_\lambda t}|\lambda\rangle,\tag{67}$$

we may simplify Eq. (66) to read

$$\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\beta\rangle=\sum_{\lambda,\lambda'}\langle\alpha|e^{iE_\lambda t}|\lambda\rangle\langle\lambda|\widehat{\mathscr{H}}_1(t)|\lambda'\rangle\langle\lambda'|e^{-iE_\beta t}|\beta\rangle.\tag{68}$$

Since $\langle\alpha|\beta\rangle=\delta_{\alpha\beta}$ (where $\delta_{\alpha\beta}$ is the Kronecker delta function), the only non-zero terms in Eq. (68) are those for which $\lambda=\alpha$ and $\lambda'=\beta$, and thus

$$\langle\alpha|\widetilde{\widehat{\mathscr{H}}}_1(t)|\beta\rangle=\langle\alpha|\widehat{\mathscr{H}}_1(t)|\beta\rangle e^{i(E_\alpha-E_\beta)t}.\tag{69}$$

Inserting Eq. (69) into Eq. (65) and writing each matrix element $\langle\beta|\tilde{\widehat{\rho}}(t)|\beta'\rangle$ simply as $\tilde{\rho}_{\beta\beta'}(t)$ we have

$$\begin{aligned}
&\langle\alpha|\overline{\left[\widetilde{\widehat{\mathscr{H}}}_1(t)\left[\widetilde{\widehat{\mathscr{H}}}_1(t+\tau),\tilde{\widehat{\rho}}(t)\right]\right]}|\alpha'\rangle\\
&\quad=\sum_{\beta,\beta'}\sum_{\lambda}\overline{\langle\alpha|\widehat{\mathscr{H}}_1(t)|\lambda\rangle\langle\lambda|\widehat{\mathscr{H}}_1(t+\tau)|\beta\rangle\,\tilde{\rho}_{\beta\beta'}(t)\,\langle\beta'|\alpha'\rangle}\,e^{i(E_\alpha-E_\lambda)t}\,e^{i(E_\lambda-E_\beta)(t+\tau)}\\
&\qquad+\sum_{\beta,\beta'}\sum_{\lambda}\overline{\langle\alpha|\beta\rangle\,\tilde{\rho}_{\beta\beta'}(t)\,\langle\beta'|\widehat{\mathscr{H}}_1(t+\tau)|\lambda\rangle\langle\lambda|\widehat{\mathscr{H}}_1(t)|\alpha'\rangle}\,e^{i(E_{\beta'}-E_\lambda)(t+\tau)}\,e^{i(E_\lambda-E_{\alpha'})t}\\
&\qquad-\sum_{\beta,\beta'}\overline{\langle\alpha|\widehat{\mathscr{H}}_1(t)|\beta\rangle\,\tilde{\rho}_{\beta\beta'}(t)\,\langle\beta'|\widehat{\mathscr{H}}_1(t+\tau)|\alpha'\rangle}\,e^{i(E_\alpha-E_\beta)t}\,e^{i(E_{\beta'}-E_{\alpha'})(t+\tau)}\\
&\qquad-\sum_{\beta,\beta'}\overline{\langle\alpha|\widehat{\mathscr{H}}_1(t+\tau)|\beta\rangle\,\tilde{\rho}_{\beta\beta'}(t)\,\langle\beta'|\widehat{\mathscr{H}}_1(t)|\alpha'\rangle}\,e^{i(E_\alpha-E_\beta)(t+\tau)}\,e^{i(E_{\beta'}-E_{\alpha'})t}.
\end{aligned}\tag{70}$$

2.3.2. Correlation functions and spectral densities

We now introduce the correlation function $G_{\alpha\beta\alpha'\beta'}(\tau)$ and the corresponding spectral density $j_{\alpha\beta\alpha'\beta'}(\omega)$ (see Appendix C), defined by

$$G_{\alpha\beta\alpha'\beta'}(\tau)=\overline{\langle\alpha|\widehat{\mathscr{H}}_1(t)|\beta\rangle\langle\beta'|\widehat{\mathscr{H}}_1(t+\tau)|\alpha'\rangle},\tag{71a}$$

$$j_{\alpha\beta\alpha'\beta'}(\omega)=\int_0^\infty G_{\alpha\beta\alpha'\beta'}(\tau)e^{-i\omega\tau}d\tau.\tag{71b}$$

Since terms of the form $\langle\alpha|\mathscr{A}|\beta\rangle$ in Eq. (70) are scalars we may rearrange them freely in the form of correlation functions. Moreover, since the ensemble averaging of the Hamiltonian and the density operator are done separately, we may write Eq. (62) as

$$\frac{\partial\tilde{\rho}_{\alpha\alpha'}(t)}{\partial t}=-\sum_{\beta,\beta'}\int_0^\infty\left[\begin{array}{c}\delta_{\alpha'\beta'}\sum\limits_{\lambda}G_{\alpha\lambda\beta\lambda}(\tau)e^{-i\left(E_\beta-E_\lambda\right)\tau}e^{i\left(E_\alpha-E_\beta\right)t}\\+\delta_{\alpha\beta}\sum\limits_{\lambda}G_{\lambda\alpha'\lambda\beta'}(\tau)e^{-i\left(E_\lambda-E_{\beta'}\right)\tau}e^{i\left(E_{\beta'}-E_{\alpha'}\right)t}\\-G_{\alpha\beta\alpha'\beta'}(\tau)e^{-i\left(E_{\alpha'}-E_{\beta'}\right)\tau}e^{i\left(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'}\right)t}\\-G_{\beta'\alpha'\beta\alpha}(\tau)e^{-i\left(E_\beta-E_\alpha\right)\tau}e^{i\left(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'}\right)t}\end{array}\right]\tilde{\rho}_{\beta\beta'}(t)d\tau.\tag{72}$$

Recognizing that each term in the bracket is composed of a spectral density multiplied by an exponential,

$$\frac{\partial\tilde{\rho}_{\alpha\alpha'}(t)}{\partial t}=-\sum_{\beta,\beta'}\left[\begin{array}{c}\delta_{\alpha'\beta'}\sum\limits_{\lambda}j_{\alpha\lambda\beta\lambda}(E_\beta-E_\lambda)e^{i\left(E_\alpha-E_\beta\right)t}\\+\delta_{\alpha\beta}\sum\limits_{\lambda}j_{\lambda\alpha'\lambda\beta'}(E_\lambda-E_{\beta'})e^{i\left(E_{\beta'}-E_{\alpha'}\right)t}\\-j_{\alpha\beta\alpha'\beta'}(E_{\alpha'}-E_{\beta'})e^{i\left(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'}\right)t}\\-j_{\beta'\alpha'\beta\alpha}(E_\beta-E_\alpha)e^{i\left(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'}\right)t}\end{array}\right]\tilde{\rho}_{\beta\beta'}(t).\tag{73}$$

Notice that the exponentials in the first two bracketed terms in Eq. (73) may be replaced by $e^{i(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'})t}$ without significantly affecting their values. We may therefore write

$$\frac{\partial\tilde{\rho}_{\alpha\alpha'}(t)}{\partial t}=-\sum_{\beta,\beta'}\left[\begin{array}{c}\delta_{\alpha'\beta'}\sum\limits_{\lambda}j_{\alpha\lambda\beta\lambda}(E_\beta-E_\lambda)\\+\delta_{\alpha\beta}\sum\limits_{\lambda}j_{\lambda\alpha'\lambda\beta'}(E_\lambda-E_{\beta'})\\-j_{\alpha\beta\alpha'\beta'}(E_{\alpha'}-E_{\beta'})\\-j_{\beta'\alpha'\beta\alpha}(E_\beta-E_\alpha)\end{array}\right]\times e^{i\left(E_\alpha-E_\beta+E_{\beta'}-E_{\alpha'}\right)t}\,\tilde{\rho}_{\beta\beta'}(t).\tag{74}$$

2.3.3. The dynamic frequency shift

Since $\widehat{\mathscr{H}}_1(t)$ is a stationary random operator, from Eq. (C24) (see Appendix C) we can write the following expression:

$$j_{\alpha\beta\alpha'\beta'}(\omega) = \frac{1}{2}J_{\alpha\beta\alpha'\beta'}(\omega) - iK_{\alpha\beta\alpha'\beta'}(\omega), \tag{75}$$

where

$$J_{\alpha\beta\alpha'\beta'}(\omega) = \int_{-\infty}^{\infty} G_{\alpha\beta\alpha'\beta'}(\tau)e^{-i\omega\tau}d\tau, \tag{76a}$$

$$K_{\alpha\beta\alpha'\beta'}(\omega) = \int_{0}^{\infty} G_{\alpha\beta\alpha'\beta'}(\tau)\sin(\omega\tau)d\tau. \tag{76b}$$

are both real functions.

The imaginary term $iK_{\alpha\beta\alpha'\beta'}(\omega)$ in Eq. (75) gives rise to a shift in resonance frequency known as the *dynamic frequency shift* [34–36]. This effect is usually small enough to be neglected, although for certain interactions (e.g. quadrupolar) that are comparable in magnitude to the Zeeman interaction $\widehat{\mathscr{H}}_0$, it must be accounted for [37]. This term will be ignored in the present context. Alternatively, one may take the approach mentioned earlier, redefining the static Hamiltonian in such a way that the dynamic frequency shift is included in $\widehat{\mathscr{H}_0}$. Finally, we may remark that only the real part of $j_{\alpha\beta\alpha'\beta'}(\omega)$ contributes to the evolution of the spin system towards equilibrium, that is relaxation.

Considering only the real part, we may simply replace $j_{\alpha\beta\alpha'\beta'}(\omega) \to \frac{1}{2}J_{\alpha\beta\alpha'\beta'}(\omega)$ in Eq. (74).

2.3.4. The Redfield relaxation equation

We now define the rate constants $R_{\alpha\beta,\alpha'\beta'}$, the elements of the so-called *Redfield relaxation matrix*, and rewrite Eq. (74) in an even more compact notation as the *Redfield relaxation equation*:

$$\frac{\partial\tilde{\rho}_{\alpha\alpha'}(t)}{\partial t} = \sum_{\beta,\beta'} R_{\alpha\alpha',\beta\beta'}\; e^{i\left(E_\alpha - E_\beta + E_{\beta'} - E_{\alpha'}\right)t}\; \tilde{\rho}_{\beta\beta'}(t), \tag{77}$$

where

$$R_{\alpha\alpha',\beta\beta'} = \frac{1}{2}\left[\begin{array}{c} J_{\alpha\beta\alpha'\beta'}\left(E_{\alpha'} - E_{\beta'}\right) + J_{\beta'\alpha'\beta\alpha}\left(E_\beta - E_\alpha\right) \\ -\;\delta_{\alpha'\beta'}\sum\limits_\lambda J_{\alpha\lambda\beta\lambda}\left(E_\beta - E_\lambda\right)\; - \;\delta_{\alpha\beta}\sum\limits_\lambda J_{\lambda\alpha'\lambda\beta'}\left(E_\lambda - E_{\beta'}\right)\end{array}\right]. \tag{78}$$

Noting as before that the Redfield Eq. (77) implies an infinite bath temperature, we make the correction, Eq. (56), $\tilde{\rho}(t) \to \tilde{\rho}_c(t, T_L) = \tilde{\rho}(t) - \tilde{\rho}_{eq}(T_L)$. Note that the Redfield formulation makes the implication of infinite temperature somewhat more clearly than did the operator formalism used in the preceding section: because $R_{\alpha\alpha,\beta\beta} = R_{\beta\beta,\alpha\alpha}$ (that is, the probability of transition from $|\,\alpha\rangle$ to $|\,\beta\rangle$ is equal to that of the opposite transition from $|\,\beta\rangle$ to $|\,\alpha\rangle$ – the principle of detailed balance), the (uncorrected) Redfield equation clearly describes an equal distribution of spins among the various energy states at equilibrium.

Finally, we introduce the secular approximation as follows. The terms in Eq. (77) for which $E_\alpha + E_{\beta'} \neq E_\beta + E_{\alpha'}$ will have rapidly fluctuating values, oscillating at frequencies much greater than the rate of evolution of the density operator under the terms $R_{\alpha\alpha,\beta\beta}$. As a result, their contribution will average approximately to zero in the summation. Therefore, we may neglect such terms, keeping only the so-called *secular* terms for which $E_\alpha + E_{\beta'} = E_\beta + E_{\alpha'}$ ('secular' is used here in keeping with its Latin origins, referring to a span of time). In the context of the secular approximation, the oscillations of the secular terms take place on a *secular timescale* as compared to the comparatively-fast fluctuations of the non-secular terms, which are discarded. The exponential for the secular terms will always equal unity, and we may then write the secular approximation of the relaxation equation:

$$\frac{\partial\tilde{\rho}_{\alpha\alpha'}(t, T_L)}{\partial t} = \sum_{\beta,\beta'} R_{\alpha\alpha',\beta\beta'}\,\tilde{\rho}_{\beta\beta'}(t, T_L) \tag{79}$$

Note that the secular approximation may be violated under certain conditions, typically when the difference of energy of two eigenstates is not much larger than the relaxation rates [38]. Eq. (79), which represents the Redfield equation in Hilbert space is rarely used in the context of calculating spin-relaxation rates. Instead the Redfield equation in Liouville space (i.e. in the product operator basis) is widely used. This formalism will be treated in Section 6.

3. The Hamiltonians of relaxation

We now present a systematic approach to represent the Hamiltonians $\widehat{\mathscr{H}}_\mu$ appearing in Eq. (37), in the derivation of the correlation functions (Eq. (71b)), and ultimately the Redfield Relaxation matrix in Eq. (79). The method of presentation of the theory in this part is drawn in large measure from the excellent discussions provided by Mehring [39] and Smith et al. [40–42].

3.1. General treatment of Hamiltonian operators

3.1.1. Tensor representation of Hamiltonian operators

Any scalar may be written as a scalar ('dot') product of vectors or tensors. Thus, the scalar interaction energies represented by the various Hamiltonians $\widehat{\mathscr{H}}_\mu$ that comprise $\widehat{\mathscr{H}}(t)$, Eq. (37), may be written as scalar products, containing terms such as

$$\begin{array}{cc} \vec{\mu}_i \cdot \vec{B}_0 & r^{-3}\left(\vec{\mu}_i \cdot \vec{\mu}_j\right) \\ \text{spin—field interaction} & \text{spin—spin interaction} \end{array} \tag{80}$$

As will be discussed below, all the Hamiltonian operators of interest may be constructed by replacing the classical magnetic dipole moment with its quantum mechanical equivalent, i.e. replacing $\vec{\mu}$ with $\gamma\hbar\vec{\mathscr{I}}$ (or simply $\gamma\vec{\mathscr{I}}$ when working in units of $\hbar$ as in the preceding sections). For simplicity the vector sign is dropped from $\vec{\mathscr{I}}$. $\mathscr{I} = (\mathscr{I}_x, \mathscr{I}_y, \mathscr{I}_z)$ is the spin operator for the given nucleus, and γ is the gyromagnetic ratio. We will limit ourselves to the case of chemical shielding $(\widehat{\mathscr{H}}_\mu = \widehat{\mathscr{H}}_{\mathrm{CS}})$ for spin–field interactions, and to dipolar coupling $(\widehat{\mathscr{H}}_\mu = \widehat{\mathscr{H}}_{\mathrm{DD}})$ for spin–spin interactions.

Employing scalar products, we may develop a formalism in which we cast the single spin–external field interaction Hamiltonian in the form

$$\widehat{\mathscr{H}}^j_{\mathrm{CS}} = C^j_{\mathrm{CS}}\;\mathscr{I}^j \cdot \widehat{A}^j \cdot \vec{B}_0, \tag{81}$$

for the jth spin, where C^j_{CS} is a scalar constant, and $\widehat{A}^j$ is a tensor (the chemical shielding tensor) which we will construct appropriately to describe the given interaction. Explicitly,

$$\widehat{\mathscr{H}}^j_{\mathrm{CS}} = C^j_{\mathrm{CS}}\left(\mathscr{I}^j_x, \mathscr{I}^j_y, \mathscr{I}^j_z\right) \cdot \begin{pmatrix} A^j_{xx} & A^j_{xy} & A^j_{xz} \\ A^j_{yx} & A^j_{yy} & A^j_{yz} \\ A^j_{zx} & A^j_{zy} & A^j_{zz} \end{pmatrix} \cdot \begin{pmatrix} B_{0x} \\ B_{0y} \\ B_{0z} \end{pmatrix}. \tag{82}$$

Similarly, for a spin–spin interaction between the jth and kth spins we may write the Hamiltonian as

$$\widehat{\mathscr{H}}^{jk}_{\mathrm{DD}} = C^{jk}_{\mathrm{DD}}\;\mathscr{I}^j \cdot \widehat{A}^{jk} \cdot \mathscr{I}^k, \tag{83}$$

$$\widehat{\mathscr{H}}^{jk}_{\mathrm{DD}} = C^{jk}_{\mathrm{DD}}\left(\mathscr{I}^j_x, \mathscr{I}^j_y, \mathscr{I}^j_z\right) \cdot \begin{pmatrix} A^{jk}_{xx} & A^{jk}_{xy} & A^{jk}_{xz} \\ A^{jk}_{yx} & A^{jk}_{yy} & A^{jk}_{yz} \\ A^{jk}_{zx} & A^{jk}_{zy} & A^{jk}_{zz} \end{pmatrix} \cdot \begin{pmatrix} \mathscr{I}^k_x \\ \mathscr{I}^k_y \\ \mathscr{I}^k_z \end{pmatrix}. \tag{84}$$

Using a more compact notation we have for the interactions of a spin with the magnetic field:

$$\widehat{\mathscr{H}}^j_{\mathrm{CS}} = C^j_{\mathrm{CS}} \sum_{u,v=\{x,y,z\}} \mathscr{I}^j_u\;A^j_{uv}\;B_{0v}. \tag{85}$$

For the spin–spin interactions,

$$\widehat{\mathscr{H}}^{jk}_{\mathrm{DD}} = C^{jk}_{\mathrm{DD}} \sum_{u,v=\{x,y,z\}} \mathscr{I}^j_u \, A^{jk}_{uv} \, \mathscr{I}^k_v. \tag{86}$$

We may write Eqs. (85) and (86) somewhat more elegantly as

$$\widehat{\mathscr{H}}^{j}_{CS} = C^{j}_{CS} \, \widehat{A}^j \odot \widehat{X}^j, \tag{87a}$$

$$\widehat{\mathscr{H}}^{jk}_{\mathrm{DD}} = C^{jk}_{\mathrm{DD}} \, \widehat{A}^{jk} \odot \widehat{X}^{jk}, \tag{87b}$$

respectively, where $\odot$ denotes the scalar products between two tensors, which, in complete analogy with the vector *dot* product, is defined as

$$\widehat{A} \odot \widehat{X} = \sum_{u,v=\{x,y,z\}} A_{uv} X_{uv}. \tag{88}$$

In writing the Hamiltonians in Eq. (87) we have simply collected the various terms $\mathscr{I}^j_u B^0_v$ and $\mathscr{I}^j_u \mathscr{I}^k_v$ in Eqs. (85) and (86), respectively, organizing them in 3 × 3 matrices $\widehat{X}^j$ and $\widehat{X}^{jk}$:

$$\widehat{X}^j = \begin{pmatrix} \mathscr{I}^j_x \, B_{0x} & \mathscr{I}^j_x \, B_{0y} & \mathscr{I}^j_x \, B_{0z} \\ \mathscr{I}^j_y \, B_{0x} & \mathscr{I}^j_y \, B_{0y} & \mathscr{I}^j_y \, B_{0z} \\ \mathscr{I}^j_z \, B_{0x} & \mathscr{I}^j_z \, B_{0y} & \mathscr{I}^j_z \, B_{0z} \end{pmatrix}, \qquad X^j_{uv} = \mathscr{I}^j_u \, B_{0v}, \tag{89a}$$

$$\widehat{X}^{jk} = \begin{pmatrix} \mathscr{I}^j_x \mathscr{I}^k_x & \mathscr{I}^j_x \mathscr{I}^k_y & \mathscr{I}^j_x \mathscr{I}^k_z \\ \mathscr{I}^j_y \mathscr{I}^k_x & \mathscr{I}^j_y \mathscr{I}^k_y & \mathscr{I}^j_y \mathscr{I}^k_z \\ \mathscr{I}^j_z \mathscr{I}^k_x & \mathscr{I}^j_z \mathscr{I}^k_y & \mathscr{I}^j_z \mathscr{I}^k_z \end{pmatrix}, \qquad X^{jk}_{uv} = \mathscr{I}^j_u \, \mathscr{I}^k_v. \tag{89b}$$

Formally, these matrices represent second-rank tensors formed from Kronecker (i.e. tensorial or dyadic) products between two vectors (i.e. first-rank tensors):

$$\widehat{X}^j = \begin{pmatrix} \mathscr{I}^j_x \\ \mathscr{I}^j_y \\ \mathscr{I}^j_z \end{pmatrix} \otimes (B_{0x}, B_{0y}, B_{0z}) = \vec{\mathscr{I}}^j \otimes \vec{B}_0 \tag{90a}$$

$$\widehat{X}^{jk} = \begin{pmatrix} \mathscr{I}^j_x \\ \mathscr{I}^j_y \\ \mathscr{I}^j_z \end{pmatrix} \otimes (\mathscr{I}^k_x, \mathscr{I}^k_y, \mathscr{I}^k_y) = \vec{\mathscr{I}}^j \otimes \vec{\mathscr{I}}^k \tag{90b}$$

We emphasize at this point that these manipulations are purely mathematical, executed for the purpose of elegance. We have worked with some foresight of our ultimate concern with NMR relaxation and molecular tumbling. In particular, we will usually write the Hamiltonians such that all spin interactions are retained in $\widehat{X}$, while the spatial dependencies (concerned with molecular motion leading to the stochastic time-dependence of $\widehat{\mathscr{H}}_1(t)$) are contained in $\widehat{A}$.

Both $\widehat{A}$ and $\widehat{X}$ are rank-2 tensors and they can in general be written as the sum of three irreducible cartesian tensors of rank-0 (scalar), rank-1 (antisymmetric tensor; $\mathfrak{a}_{ij} = -\mathfrak{a}_{ji}$) and rank-2 (symmetric tensor; $\mathfrak{s}_{ij} = \mathfrak{s}_{ji}$).

$$\widehat{A} = \begin{bmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{yx} & A_{yy} & A_{yz} \\ A_{zx} & A_{zy} & A_{zz} \end{bmatrix} = A_{\mathrm{iso}} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} 0 & \mathfrak{a}_{xy} & \mathfrak{a}_{xz} \\ \mathfrak{a}_{yx} & 0 & \mathfrak{a}_{yz} \\ \mathfrak{a}_{zx} & \mathfrak{a}_{zy} & 0 \end{bmatrix} + \begin{bmatrix} \mathfrak{s}_{xx} & \mathfrak{s}_{xy} & \mathfrak{s}_{xz} \\ \mathfrak{s}_{yx} & \mathfrak{s}_{yy} & \mathfrak{s}_{yz} \\ \mathfrak{s}_{zx} & \mathfrak{s}_{zy} & \mathfrak{s}_{zz} \end{bmatrix}, \tag{91}$$

the ranks of the matrices on the right-hand side are 0, 1 and 2, respectively, and

$$\begin{aligned} A_{\mathrm{iso}} &= \frac{1}{3}(A_{xx} + A_{yy} + A_{zz}) = \frac{1}{3}\mathrm{Tr}(A), \\ \mathfrak{a}_{uv} &= \frac{1}{2}(A_{uv} - A_{vu}), \\ \mathfrak{s}_{uv} &= \frac{1}{2}(A_{uv} + A_{vu} - 2A_{\mathrm{iso}}\delta_{uv}). \end{aligned} \tag{92}$$

The specific elements of the tensors depend on the coordinate system that is used to express the Hamiltonian. In the principal axes frame (PAF) of the spatial tensor, $\widehat{A}$, the rank-2 component is diagonal, thus the PAF will be used to express $\widehat{A}$. Depending on the interaction, the second tensor $\widehat{X}$ contains a dyadic product of spin operators (suitably normalized) or a spin operator with the magnetic field. The ultimate goal is to express each Hamiltonian in the laboratory frame where time dependence comes from the molecular motions.

The various components of the $\widehat{A}$ (spatial) tensor may be written as [13,39,40]:

$$\begin{aligned} A^0_0 &= -\left(\tfrac{1}{\sqrt{3}}\right)(A_{xx} + A_{yy} + A_{zz}) & A^0_0(\mathrm{PAF}) &= -\tfrac{\mathrm{Tr}\{A\}}{3}, \\ A^0_1 &= -\left(\tfrac{i}{\sqrt{2}}\right)(A_{xy} - A_{yx}) & A^0_1(\mathrm{PAF}) &= 0, \\ A^{\pm1}_1 &= -\left(\tfrac{1}{2}\right)(A_{zx} - A_{xz} \pm i(A_{zy} - A_{yz}) & A^{\pm1}_1(\mathrm{PAF}) &= 0, \\ A^0_2 &= \left(\tfrac{1}{\sqrt{6}}\right)[3A_{zz} - (A_{xx} + A_{yy} + A_{zz})] & A^0_2(\mathrm{PAF}) &= \sqrt{\tfrac{3}{2}}\left[A_{zz} - \tfrac{1}{3}\mathrm{Tr}\{A\}\right], \\ A^{\pm1}_2 &= \mp\left(\tfrac{1}{2}\right)[A_{xz} + A_{zx} \pm i(A_{yz} + A_{zy})] & A^{\pm1}_2(\mathrm{PAF}) &= 0, \\ A^{\pm2}_2 &= \left(\tfrac{1}{2}\right)[(A_{xx} - A_{yy} \pm i(A_{xy} + A_{yx})] & A^{\pm2}_2(\mathrm{PAF}) &= \sqrt{\tfrac{1}{2}}(A_{xx} - A_{yy}), \end{aligned} \tag{93}$$

which we have shown in both cartesian and irreducible spherical tensor forms.

In the same manner, the $\widehat{X}$ (spin) tensor can be written in spherical coordinates in the laboratory frame:

$$\begin{aligned} X^0_0(\mathrm{LAB}) &= -\left(\frac{1}{\sqrt{3}}\right)(X_{xx} + X_{yy} + X_{zz}), \\ X^0_1(\mathrm{LAB}) &= \left(\frac{i}{\sqrt{2}}\right)(X_{xy} - X_{yx}), \\ X^{\pm1}_1(\mathrm{LAB}) &= \left(\frac{1}{2}\right)[X_{zx} - X_{xz} \pm i(X_{zy} - X_{yz})], \\ X^0_2(\ \mathrm{LAB}) &= \left(\frac{1}{\sqrt{6}}\right)[3X_{zz} - (X_{xx} + X_{yy} + X_{zz})], \\ X^{\pm1}_1(\mathrm{LAB}) &= \mp\left(\frac{1}{2}\right)[X_{xz} + X_{zx} \pm i(X_{yz} + X_{zy})], \\ X^{\pm2}_2(\mathrm{LAB}) &= \left(\frac{1}{2}\right)[X_{xx} - X_{yy} \pm i(X_{xy} + X_{yx})]. \end{aligned} \tag{94}$$

It is possible to write the spatial tensor $\widehat{A}$ relative to any arbitrary axes system, (AAF), using the Wigner rotation matrices (see Appendix D.5):

$$A^m_l(\mathrm{AAF}) = \sum_{m'=-l}^{l} D^{l*}_{m,m'}(\Omega') A^{m'}_l(\mathrm{PAF}), \tag{95}$$

where l is the rank, m is the order, and Ω is the set of Euler angles defining the orientation of the PAF with respect to an arbitrary axis frame (AAF).

Since the Hamiltonian is time-dependent in the LAB frame, a time-dependent rotation must be performed to express $\widehat{A}$ in this frame:

$$A^m_l(\mathrm{LAB}) = \sum_{m'=-l}^{l} D^{l*}_{m,m'}[\Omega(t)] A^{m'}_l(\mathrm{AAF}). \tag{96}$$

In spherical coordinates, the scalar product of two tensors can be written as:

$$A_l \odot X_l = \sum_{m=-l}^{l} (-1)^m A_l^m X_l^{-m} = \sum_{m=-l}^{l} (-1)^m A_l^{-m} X_l^m. \tag{97}$$

Summing over all the components of the rank-2 tensor we have;

$$\widehat{A} \odot \widehat{X} = \sum_{l=0}^{2} A_l \cdot X_l = \sum_{l=0}^{2} \sum_{m=-l}^{l} (-1)^m A_l^{-m} X_l^m. \tag{98}$$

Combining Eq. (98) with Eq. (81) and Eq. (83), $\mathscr{H}_\mu$ may be expressed as

$$\begin{aligned}
\widehat{\mathscr{H}}_\mu &= C_\mu \sum_u \sum_v A_{uv} X_{uv}, \\
\widehat{\mathscr{H}}_\mu &= C_\mu \widehat{A} \odot \widehat{X}, \\
\widehat{\mathscr{H}}_\mu &= C_\mu \sum_{l=0}^{2} \sum_{m=-l}^{l} (-1)^m A_l^{-m} X_l^m.
\end{aligned} \tag{99}$$

The tensors $\widehat{A}$ and $\widehat{X}$ have nine distinct components (in general).

Any constant (i.e. a, b) can be factored out from the tensor terms, so we define from $\widehat{A}$ and $\widehat{X}$:

$$\begin{aligned}
F_l^m &= \frac{1}{a} A_l^m, \\
T_l^m &= \frac{1}{b} X_l^m, \\
\xi_\mu &= abC_\mu.
\end{aligned} \tag{100}$$

Thus Eq. (37) may be written as:

$$\widehat{\mathscr{H}}_1(t) = \sum_\mu \widehat{\mathscr{H}}_\mu = \sum_\mu \xi_\mu \sum_{l=0}^{2} \sum_{m=-l}^{l} (-1)^m F_l^{-m}(t) T_l^m, \tag{101}$$

$F_l^m(t)$ are time-dependent components in the LAB frame. They will be used to derive the correlation functions and the spectral density function defined in Eq. (71b).

Finally the general form of the Hamiltonian in the LAB frame becomes:

$$\begin{aligned}
\widehat{\mathscr{H}}_\mu(\text{LAB},t) &= \xi \sum_{l=0}^{2} \sum_{m=-l}^{l} (-1)^m F_l^{-m}(\text{LAB},t) T_l^m(\text{LAB}) \\
&= \xi \sum_{l=0}^{2} \sum_{m=-l}^{l} (-1)^m \left[\sum_{m'=-l}^{l} D^{l*}_{-m,m'}[\Omega(t)] F_l^{m'}(\text{AAF}) \right] T_l^m(\text{LAB}).
\end{aligned} \tag{102}$$

We now apply the general procedure we have just developed to two specific interactions of interest for relaxation: chemical shielding and dipolar coupling.

3.1.2. The chemical shift Hamiltonian

In the presence of a strong static field the electrons around the nucleus generate a localized induced magnetic field. Although this induced field is very small when compared to the static field, it depends on the orientation of the molecular orbitals with respect to the static field. The dependence of this interaction upon the orientation of the molecule in space and therefore in the static field makes the chemical shift interaction an important relaxation mechanism. The induced magnetic field can be written as;

$$\vec{B}^i_{\text{ind}} = -\widehat{\sigma}^i \cdot \vec{B}_0, \tag{103}$$

where $\widehat{\sigma}^i$ is the chemical shift tensor (index i refers to a particular spin) and $\vec{B}_0$ is the applied magnetic field. The energy corresponding to this induced field is:

$$E^i_{\text{CS}} = -\vec{\mu}^i \cdot \vec{B}^i_{\text{ind}} = \vec{\mu}^i \cdot \widehat{\sigma}^i \cdot \vec{B}_0. \tag{104}$$

When the quantum mechanical equivalent $(\gamma\hbar\mathscr{I})$ of the magnetic moment vector $\vec{\mu}$ is used while summing over all spins, we obtain:

$$\widehat{\mathscr{H}}_{\text{CS}} = \sum_{i=1}^{N} \widehat{\mathscr{H}}^i_{\text{CS}} = \hbar \sum_{i=1}^{N} \gamma^i \mathscr{I}^i \cdot \widehat{\sigma}^i \cdot \vec{B}_0, \tag{105}$$

where N is the number of spins and $\mathscr{I}$ is transposed as in Eq. (81). From Eq. (104) it is clear that, as the external magnetic field is increased, the interaction energy increases. The direction of the induced magnetic field is not always colinear with the external magnetic field. Eq. (105) can be written in matrix form as:

$$\widehat{\mathscr{H}}_{\text{CS}} = \hbar\gamma^i B_o \left[\mathscr{I}^i_x \mathscr{I}^i_y \mathscr{I}^i_z \right] \cdot \begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} \cdot \begin{bmatrix} B_x \\ B_y \\ B_z \end{bmatrix}, \tag{106}$$

that is,

$$\begin{aligned}
\widehat{\mathscr{H}}^i_{\text{CS}} &= \hbar\gamma^i B_0 \sum_p \sum_q \{ \mathscr{I}^i | p \rangle \langle p | \widehat{\sigma}^i | q \rangle \langle q | \hat{e}_n \} \\
&= \hbar\gamma^i B_0 \sum_p \sum_q \sigma^i_{pq} \mathscr{I}^i_p \vec{B}_q,
\end{aligned} \tag{107}$$

where p and q sum over Cartesian axes, $\hat{e}_n$ is the unit vector in the field direction, and B_q is the projection of $\hat{e}_n$ along the q-axis (in all cases we reserve '^' to denote operators except when denoting unit vectors, e.g. $\hat{e}_n$).

$\widehat{\sigma}$ is a spatial tensor and we can form a spin tensor, $\widehat{X}$, from the dyadic products of the spin angular momentum vector and the static field vector $\vec{B}_n$:

$$\left\langle v \middle| \widehat{X}^i \middle| u \right\rangle = \langle v | \vec{B}_n \mathbb{1} \mathscr{I}^i | u \rangle. \tag{108}$$

We can now write $\widehat{\mathscr{H}}_{\text{CS}}$ as:

$$\widehat{\mathscr{H}}_{\text{CS}} = \hbar\gamma^i B_0 \sum_{p,q=x,y,z} \sigma^i_{pq} X^i_{pq} = C^i \widehat{\sigma}^i \odot \widehat{X}^i, \tag{109}$$

with $C^i_{\text{CS}} = \hbar\gamma^i B_0$. The chemical shift tensor is a rank-2 tensor with 9 components and may be represented by a 3 × 3 matrix.

$$\begin{aligned}
\widehat{\sigma} &= \begin{bmatrix} \sigma'_{xx} & \sigma'_{xy} & \sigma'_{xz} \\ \sigma'_{yx} & \sigma'_{yy} & \sigma'_{yz} \\ \sigma'_{zx} & \sigma'_{zy} & \sigma'_{zz} \end{bmatrix} \\
&= \sigma'_{\text{iso}} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} 0 & \mathfrak{a}'_{xy} & \mathfrak{a}'_{xz} \\ -\mathfrak{a}'_{xy} & 0 & \mathfrak{a}'_{yz} \\ -\mathfrak{a}'_{xz} & -\mathfrak{a}'_{yz} & 0 \end{bmatrix} + \begin{bmatrix} \mathfrak{s}'_{xx} & \mathfrak{s}'_{xy} & \mathfrak{s}'_{xz} \\ \mathfrak{s}'_{yx} & \mathfrak{s}'_{yy} & \mathfrak{s}'_{yz} \\ \mathfrak{s}'_{zx} & \mathfrak{s}'_{zy} & \mathfrak{s}'_{zz} \end{bmatrix}.
\end{aligned} \tag{110}$$

The three tensors on the right-hand side of Eq. (110) are $\widehat{\sigma}_0$, $\widehat{\sigma}_1$ and $\widehat{\sigma}_2$, with ranks 0, 1 and 2, respectively (the primes on the component symbols denote that we have defined this tensor in an arbitrary frame, and distinguish these matrix component values from those in the principal axis frame, which we will write without primes).

For most interactions of interest, the rank-1 component of $\widehat{\sigma}$ is not necessarily zero unless symmetry makes $\mathfrak{a}'_{pq} = \mathfrak{a}'_{qp}$. Under particular circumstances, the contribution of the antisymmetric part of the chemical shift tensor to longitudinal relaxation has been predicted to be non-negligible (up to about 10%) [43]. A detailed treatment of this effect has been described in the literature [43,44]. We will however neglect this component in the present analysis. Under this approximation $\widehat{\sigma}$ is diagonal in the principal axis frame:

$$\widehat{\sigma}(\mathrm{PAF}) = \begin{bmatrix} \sigma_{xx} & 0 & 0 \\ 0 & \sigma_{yy} & 0 \\ 0 & 0 & \sigma_{zz} \end{bmatrix} = \sigma_{\mathrm{iso}} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} \mathfrak{s}_{xx} & 0 & 0 \\ 0 & \mathfrak{s}_{yy} & 0 \\ 0 & 0 & \mathfrak{s}_{zz} \end{bmatrix}, \tag{111}$$

where $\mathfrak{s}_{pp} = \sigma_{pp} - \sigma_{\mathrm{iso}}$ and $\sigma_{\mathrm{iso}} = \frac{1}{3}(\sigma_{xx} + \sigma_{yy} + \sigma_{zz})$.

We can define two parameters here: the chemical shift anisotropy parameter, $\Delta\sigma$, and an asymmetry parameter, η:

$$\begin{aligned} \Delta\sigma &= \sigma_{zz} - \frac{1}{2}(\sigma_{xx} + \sigma_{yy}) = \frac{3}{2}\mathfrak{s}_{zz}, \\ \eta &= \frac{(\mathfrak{s}_{xx} - \mathfrak{s}_{yy})}{\mathfrak{s}_{zz}}. \end{aligned} \tag{112}$$

Using these new parameters $\widehat{\sigma}(\mathrm{PAF})$ can be rewritten as:

$$\widehat{\sigma}(\mathrm{PAF}) = \sigma_{\mathrm{iso}} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \frac{2}{3}\Delta\sigma \begin{bmatrix} -\frac{1}{2}(1-\eta) & 0 & 0 \\ 0 & -\frac{1}{2}(1+\eta) & 0 \\ 0 & 0 & 1 \end{bmatrix}. \tag{113}$$

We can now write the chemical shift tensor in the spherical coordinates in an arbitrary frame (including the rank-1 components):

$$\begin{aligned} \sigma_0^0 &= -\left(\frac{1}{\sqrt{3}}\right)\mathrm{Tr}\{\hat{\sigma}\}, \\ \sigma_1^0 &= -\left(\frac{i}{\sqrt{2}}\right)(\sigma_{xy} - \sigma_{yx}), \\ \sigma_1^{\pm 1} &= -\left(\frac{1}{2}\right)(\sigma_{zx} - \sigma_{xz} \pm i(\sigma_{zy} - \sigma_{yz}), \\ \sigma_2^0 &= \left(\frac{1}{\sqrt{6}}\right)[3\sigma_{zz} - \mathrm{Tr}\{\hat{\sigma}\}], \\ \sigma_2^{\pm 1} &= \mp\left(\frac{1}{2}\right)[\sigma_{xz} + \sigma_{zx} \pm i(\sigma_{yz} + \sigma_{zy})], \\ \sigma_2^{\pm 2} &= \left(\frac{1}{2}\right)[(\sigma_{xx} - \sigma_{yy} \pm i(\sigma_{xy} + \sigma_{yx})]. \end{aligned} \tag{114}$$

Neglecting the antisymmetric components of $\widehat{\sigma}$, i.e. setting $\sigma_1^0 = \sigma_1^{\pm 1} = 0$ we have in the principal axis frame:

$$\begin{aligned} \sigma_0^0(\mathrm{PAF}) &= -\sqrt{3}\sigma_{\mathrm{iso}}, \\ \sigma_2^0(\mathrm{PAF}) &= \sqrt{2/3}\Delta\sigma, \\ \sigma_2^{\pm 1}(\mathrm{PAF}) &= 0, \\ \sigma_2^{\pm 2}(\mathrm{PAF}) &= \frac{1}{3}\Delta\sigma\ \eta. \end{aligned} \tag{115}$$

For an axially symmetric chemical shift tensor, $\eta = 0$, $\sigma_2^{\pm 1}(\mathrm{PAF}) = 0, \textit{and}\ \sigma_2^{\pm 2}(\mathrm{PAF}) = 0$. This is the case treated when calculating relaxation rates in Section 6.

We now expand $\widehat{X}$ into its irreducible spherical components using Eq. (94):

$$\begin{aligned} X_0^0(\mathrm{AAF}) &= -\left(\frac{1}{\sqrt{3}}\right)(B_x\mathscr{I}_x + B_y\mathscr{I}_y + B_z\mathscr{I}_z), \\ X_1^0(\mathrm{AAF}) &= \left(\frac{i}{\sqrt{2}}\right)(B_y\mathscr{I}_x - B_y\mathscr{I}_x), \\ X_1^{\pm 1}(\mathrm{AAF}) &= \left(\frac{1}{2}\right)[B_x\mathscr{I}_z - B_z\mathscr{I}_x \pm i(B_y\mathscr{I}_z - B_z\mathscr{I}_y)], \\ X_2^0(\mathrm{AAF}) &= \left(\frac{1}{\sqrt{6}}\right)[3B_z\mathscr{I}_z - (B_x\mathscr{I}_x + B_y\mathscr{I}_y + B_z\mathscr{I}_z)], \\ X_2^{\pm 1}(\mathrm{AAF}) &= \mp\left(\frac{1}{2}\right)[B_z\mathscr{I}_x + B_x\mathscr{I}_z \pm i(B_z\mathscr{I}_y + B_y\mathscr{I}_z)], \\ X_2^{\pm 2}(\mathrm{AAF}) &= \left(\frac{1}{2}\right)[B_x\mathscr{I}_x - B_y\mathscr{I}_y \pm i(B_y\mathscr{I}_x + B_x\mathscr{I}_y)]. \end{aligned} \tag{116}$$

We can transform $\widehat{X}$ into the laboratory frame. This simplifies the expression of X_l^m since we have chosen the direction of the external magnetic field as the $+z$-axis, thus $\hat{e}_x(\mathrm{LAB}) = \hat{e}_y(\mathrm{LAB}) = 0$ and $\hat{e}_z(\mathrm{LAB}) = 1$:

$$\begin{aligned} X_0^0(\mathrm{LAB}) &= -\left(\frac{1}{\sqrt{3}}\right)\mathscr{I}_z, \\ X_1^0(\mathrm{LAB}) &= 0, \\ X_1^{\pm 1}(\mathrm{LAB}) &= -\frac{1}{2}\mathscr{I}_\pm, \\ X_2^0(\mathrm{LAB}) &= \sqrt{\frac{2}{3}}\mathscr{I}_z, \\ X_2^{\pm 1}(\mathrm{LAB}) &= \mp\frac{1}{2}\mathscr{I}_\pm, \\ X_2^{\pm 2}(\mathrm{LAB}) &= 0. \end{aligned} \tag{117}$$

The chemical shift tensor can be expressed in an arbitrary axis frame (AAF) by rotating each component using a Wigner matrix:

$$\sigma_l^m(\mathrm{AAF}) = \sum_{m'} D_{m,m'}^{l*}(\Omega)\sigma_l^{m'}(\mathrm{PAF}), \tag{118}$$

where $\Omega = (\theta, \phi, \gamma)$ are the Euler angles for the rotation from the PAF to the AAF.

Now the chemical shift Hamiltonian can be expressed in terms of irreducible spherical tensors in the LAB frame:

$$\widehat{\mathscr{H}}_{\mathrm{CS}}^i = C^i\,\widehat{\sigma} \odot \widehat{X} = C^i \sum_{l=0}^{2}\sum_{m=-l}^{l}(-1)^m(\sigma^i)_l^{-m} \cdot (X^i)_l^m. \tag{119}$$

We can substitute Eq. (117), (118) and (110) into Eq. (119). We should keep in mind that we are neglecting the rank-1 component:

$$\widehat{\mathscr{H}}_{\mathrm{CS}}^i = C^i(\sigma^i)_0^0(X^i)_0^0 + C^i\sum_{m=-2}^{2}(-1)^m(\sigma^i)_2^{-m}(X^i)_2^m = \widehat{\mathscr{H}}_{\mathrm{ISO}}^i + \widehat{\mathscr{H}}_{\mathrm{CSA}}^i. \tag{120}$$

$\widehat{\mathscr{H}}_{\mathrm{ISO}}$, the isotropic component of the chemical shift tensor, is rotationally invariant. Thus $\widehat{\mathscr{H}}_{\mathrm{ISO}}$ is time-independent and does not have any contribution to relaxation. It is usually added to the Zeeman Hamiltonian and constitutes a part of $\widehat{\mathscr{H}}_0$. $\widehat{\mathscr{H}}_{\mathrm{CSA}}$ represents the chemical shift anisotropy.

To generalize the final expression of the chemical shift Hamiltonian, we will relate $(\sigma^i)_l^m$ and $(X^i)_l^m$ to new tensors F_l^m and T_l^m, respectively; given by:

$$F_l^m = \sqrt{\frac{5}{6\pi}}\frac{\sigma_l^m}{\mathfrak{s}_{zz}}, \tag{121a}$$

$$T_l^m = -2X_l^m. \tag{121b}$$

Defining a chemical anisotropy interaction constant, $\xi_i^{\mathrm{CSA}} = -\sqrt{\frac{6\pi}{5}}\hbar\gamma^i B_0\mathfrak{s}_{zz}$ we can write the chemical shift anisotropy Hamiltonian for the ith spin in the LAB frame as

$$\widehat{\mathscr{H}}_{\mathrm{CSA}}(\mathrm{LAB},t,i) = \xi_i^{\mathrm{CSA}}\sum_{m=-2}^{2}(-1)^m F_2^{-m}(\mathrm{LAB},t,i)T_2^m(\mathrm{LAB},i). \tag{122}$$

3.1.3. The dipolar Hamiltonian

The classical interaction energy between two dipoles, $\vec{\mu}_i$ and $\vec{\mu}_j$, located at two points in space linked by the vector $\vec{r}$, is given by (see Appendix B):

$$E_{\mathrm{DD}}^{ij} = \frac{\mu_0}{4\pi}\left(\frac{\vec{\mu}_i \cdot \vec{\mu}_j}{r^3} - \frac{3(\vec{\mu}_i \cdot \vec{r}) \cdot (\vec{\mu}_j \cdot \vec{r})}{r^5}\right), \tag{123}$$

where μ_0 is the permeability of free space (not to be confused with the magnetic dipole moment). Summing over all spin pairs and replacing $\vec{\mu}$ with its quantum mechanical equivalent, $\gamma\hbar\vec{\mathscr{I}}$, the dipolar Hamiltonian can be written as:

$$\widehat{\mathscr{H}}_{\mathrm{DD}} = \frac{\mu_0}{4\pi}\sum_i\sum_{j>i}\frac{\gamma_i\gamma_j\hbar^2}{\vec{r}_{ij}^{\,3}}\{\mathscr{I}^i\cdot\mathscr{I}^j - 3[\mathscr{I}^i\cdot\hat{e}_{ij}][\mathscr{I}^j\cdot\hat{e}_{ij}]\}; \tag{124}$$

$\hat{e}_{ij} = \frac{\vec{r}_{ij}}{r_{ij}}$ and $\hat{e}$ is dyadic; $\hat{e} = \hat{e}_{ij}\hat{e}_{ji}^{\dagger}$ so that $\langle u|\hat{e}|v\rangle = e_u e_v$. Eq. (124) can be written as:

$$\widehat{\mathscr{H}}_{\mathrm{DD}}^{ij} = \frac{\gamma_i\gamma_j\hbar^2}{r_{ij}^3}\left\{\mathscr{I}^i\cdot\widehat{D}\cdot\mathscr{I}^j\right\}, \tag{125}$$

where $\widehat{D}$ is a 3×3 matrix (dipolar tensor; note that elsewhere in the article, the symbol $\widehat{D}$ is reserved for the diffusion tensor), the elements of which are given by:

$$\langle u|\widehat{D}^{ij}|v\rangle = \delta_{uv} - 3e_u^j e_v^i, \tag{126}$$

where $(u, v = \{x, y, z\})$. Now the Hamiltonian defined in Eq. (124) can be expanded into combinations of spatial and spin components:

$$\widehat{\mathscr{H}}_{\mathrm{DD}} = \frac{\mu_0}{4\pi}\sum_{i,j;(j>i)}^{N}\frac{\gamma_i\gamma_j\hbar^2}{\vec{r}_{ij}^{\,3}}\left[\mathscr{I}_x^i\ \mathscr{I}_y^i\ \mathscr{I}_z^i\right]\cdot\begin{bmatrix} D_{xx} & D_{xy} & D_{xz}\\ D_{yx} & D_{yy} & D_{yz}\\ D_{zx} & D_{zy} & D_{zz}\end{bmatrix}\cdot\begin{bmatrix}\mathscr{I}_x^j\\ \mathscr{I}_y^j\\ \mathscr{I}_z^j\end{bmatrix}. \tag{127}$$

We can define $\widehat{X}^{ij}$ as the dyadic product of the two spin angular momentum vectors:

$$\langle v|\widehat{X}^{ij}|u\rangle = \left\langle v|\mathscr{I}^j\mathbb{1}\mathscr{I}^i|u\right\rangle \tag{128}$$

then:

$$\widehat{\mathscr{H}}_{\mathrm{DD}} = \frac{\mu_0}{4\pi}\sum_{i,j;(j>i)}^{N}\frac{\gamma_i\gamma_j\hbar^2}{\vec{r}_{ij}^{\,3}}\sum_{u,v}^{\mathrm{axes}}\langle u|\widehat{D}^{ij}|v\rangle\langle v|\widehat{X}^{ij}|u\rangle, \tag{129}$$

$$\widehat{\mathscr{H}}_{\mathrm{DD}} = \frac{\mu_0}{4\pi}\sum_{i,j;(j>i)}^{N} C^{ij}\widehat{D}^{ij}\odot\widehat{X}^{ij}, \tag{130}$$

where, $C_{ij} = \frac{\mu_0}{4\pi}\frac{\gamma_i\gamma_j\hbar^2}{r_{ij}^3}$.

In the principal axis frame (PAF) the z-axis of the Cartesian coordinate system is colinear with the vector joining the two dipoles. We can derive the dipolar matrix from Eq. (126) as

$$\widehat{D}(\mathrm{PAF}) = \begin{bmatrix} 1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & -2\end{bmatrix}. \tag{131}$$

The dipolar tensor is traceless so there is no rank-0 component. This means that, when averaged over all spatial orientations, the dipolar interaction does not change the energy levels of the system. There is no rank-1 component because the dipolar tensor is symmetric.

The ideality of this formulation of the dipolar tensor breaks down when the system is nonlinear (more than two spins). Nonlinear systems require the use of multiple coordinate systems where the dipolar tensor, $\widehat{D}^{ij}$, of each pair is diagonal.

Using an internal (i.e. molecule-fixed) coordinate frame simplifies the representations since only two Euler angles, ϕ and θ, are necessary. The third angle, γ, is arbitrary; an obvious choice is $\gamma = 0$ since the z axes can be aligned with the dipolar PAF.

Before performing any rotations we should represent the rank-2 components (i.e. the only non-zero components) of the dipolar tensor in terms of irreducible spherical tensors:

$$\begin{aligned} D_2^0(\mathrm{PAF}) &= \frac{[3D_{zz} - \mathrm{Tr}\{D\}]}{\sqrt{6}} = -\sqrt{6},\\ D_2^{\pm 1}(\mathrm{PAF}) &= \mp\frac{1}{2}[D_{xz} + D_{zx} \pm i(D_{yz} + D_{zy})] = 0,\\ D_2^{\pm 2}(\mathrm{PAF}) &= \frac{1}{2}[D_{xx} + D_{yy} \pm i(D_{xy} + D_{yx})] = 0. \end{aligned} \tag{132}$$

From the irreducible spherical components of the dipolar tensor expressed in its principal axis frame, we can write $\widehat{D}$ in any coordinate system by using Wigner rotations, i.e. with the set Euler angles $\Omega = (\phi, \theta, 0)$

$$D_l^m(\mathrm{AAF}) = \sum_{m'}\mathscr{D}_{m,m'}^{l*}(\Omega)D_l^{m'}(\mathrm{PAF}), \tag{133}$$

$$D_2^m(\mathrm{AAF}) = \mathscr{D}_{m,0}^{2*}(\Omega)D_2^0 = -\sqrt{6}\mathscr{D}_{m,0}^{2*}(\Omega), \tag{134}$$

with

$$\mathscr{D}_{m,0}^{l*}(\phi,\theta,\gamma) = \left(\frac{4\pi}{2l+1}\right)^{\frac{1}{2}}Y_l^m(\theta,\phi), \tag{135}$$

where $Y_l^m(\theta,\phi)$ are the well known spherical harmonics (see Appendix D). Thus

$$D_2^m(\mathrm{AAF}) = -\sqrt{6}\mathscr{D}_{m,0}^{2*}(\Omega) = -\sqrt{6}\left(\sqrt{\frac{4\pi}{5}}\right)Y_2^m = -\sqrt{\frac{24\pi}{5}}Y_2^m. \tag{136}$$

We can also express the spin tensor, $\widehat{X}$, in terms of irreducible spherical tensors from the Cartesian components, $X_{uv}^{ij} = \mathscr{I}_u^j\mathscr{I}_v^i$, and

$$\begin{aligned} X_0^0(\mathrm{AAF}) &= -\frac{1}{3}[X_{xx}^{ij} + X_{yy}^{ij} + X_{zz}^{ij}] = -\frac{1}{3}[\mathscr{I}^i\cdot\mathscr{I}^j].\\ X_1^0(\mathrm{AAF}) &= \frac{i}{2}[X_{xy}^{ij} - X_{yx}^{ij}] = \frac{i}{2}[\mathscr{I}_x^j\mathscr{I}_y^i - \mathscr{I}_y^j\mathscr{I}_x^i].\\ X_1^{\pm 1}(\mathrm{AAF}) &= \frac{1}{2}\left\{X_{zx}^{ij} - X_{xz}^{ij} \pm i[X_{zy}^{ij} - X_{yz}^{ij}\right\}\\ &= \frac{1}{2}\left\{\mathscr{I}_z^j\mathscr{I}_x^i - \mathscr{I}_x^j\mathscr{I}_z^i \pm i[\mathscr{I}_z^j\mathscr{I}_y^i - \mathscr{I}_y^j\mathscr{I}_z^i]\right\}.\\ X_2^0(\mathrm{AAF}) &= \frac{1}{\sqrt{6}}\left\{3X_{zz} - \left[X_{xx}^{ij} + X_{yy}^{ij} + X_{zz}^{ij}\right]\right\}\\ &= \frac{1}{2\sqrt{6}}\{4\mathscr{I}_z^j\mathscr{I}_z^i - [\mathscr{I}_+^j\mathscr{I}_-^i + \mathscr{I}_-^j\mathscr{I}_+^i]\}.\\ X_2^{\pm 1}(\mathrm{AAF}) &= \mp\frac{1}{2}\left\{X_{xz}^{ij} + X_{zx}^{ij} \pm i[X_{yz}^{ij} + X_{zy}^{ij}\right\} = \mp\frac{1}{2}[\mathscr{I}_z^i\mathscr{I}_\pm^j + \mathscr{I}_z^j\mathscr{I}_\pm^i].\\ X_2^{\pm 2}(\mathrm{AAF}) &= \frac{1}{2}\{X_{xx}^{ij} - X_{yy}^{ij} \pm i[X_{xy}^{ij} + X_{yx}^{ij}\} = \frac{1}{2}\mathscr{I}_\pm^i\mathscr{I}_\pm^j. \end{aligned} \tag{137}$$

No rotations of the spin tensors are required since they have already been expressed in an arbitrary axis frame (AAF).

We now have expressions for the dipolar and spin tensors in an arbitrary axes system. We can express the Hamiltonian in an AAF in terms of irreducible spherical tensors:

$$\begin{aligned} \widehat{\mathscr{H}}_{\mathrm{DD}}^{ij}(\mathrm{AAF}) &= C_{\mathrm{DD}}^{ij}\widehat{D}^{ij}(\mathrm{AAF})\odot\widehat{X}^{ij}(\mathrm{AAF})\\ &= C_{\mathrm{DD}}^{ij}\sum_{l=0}^{2}\sum_{m=-l}^{l}(-1)^m(\mathscr{D}^{ij})_l^{-m}(\mathrm{AAF})(X^{ij})_l^m(\mathrm{AAF}), \end{aligned} \tag{138}$$

which can be simplified since only rank-2 components of $\widehat{D}$ are nonzero:

$$\widehat{\mathscr{H}}_{\mathrm{DD}}^{ij}(\mathrm{AAF}) = C_{\mathrm{DD}}^{ij}\sum_{m=-2}^{2}(-1)^m(\mathscr{D}^{ij})_2^{-m}(\mathrm{AAF})(X^{ij})_2^m(\mathrm{AAF}). \tag{139}$$

We now write explicitly $\widehat{\mathscr{H}}_{\mathrm{DD}}^{ij}(\mathrm{AAF})$ in tensorial form remembering that $\mathscr{D}_2^m = -\sqrt{\frac{24\pi}{5}}Y_2^m(\theta,\phi)$ and defining $(T^{ij})_2^m = -2(X^{ij})_2^m$.

The dipolar Hamiltonian becomes

$$\widehat{\mathscr{H}}^{ij}_{\mathrm{DD}}(\mathrm{AAF}) = C^{ij}_{\mathrm{DD}} \times \sum_{m=-2}^{2} (-1)^m \left\{ -\sqrt{\frac{24\pi}{5}} Y_2^{-m}(\theta,\phi) \right\} \left\{ -\frac{1}{2} (T^{ij})_2^m \right\}, \tag{140}$$

with the dipolar interaction constant $\xi^{ij}_{\mathrm{D}} = C^{ij}_{\mathrm{DD}}\sqrt{\frac{6\pi}{5}}$.

Finally we can write the dipolar Hamiltonian for one spin pair in the laboratory frame:

$$\widehat{\mathscr{H}}^{ij}_{\mathrm{DD}}(\mathrm{LAB},t) = \xi^{ij}_{\mathrm{D}} \sum_{m=-2}^{2} (-1)^m (Y^{ij})_2^{-m}(\mathrm{LAB},t)(T^{ij})_2^m(\mathrm{LAB}), \tag{141}$$

where the spherical harmonics $(Y^{ij})_2^m(\mathrm{LAB},t)$ are derived from Wigner rotation matrices:

$$(Y^{ij})_2^m(\mathrm{LAB},t) = \sum_{m'=-2}^{2} \mathscr{D}^{2*}_{m,m'}[\Omega^{ij}(t)](Y^{ij})_2^{m'}(\mathrm{AAF}). \tag{142}$$

Thus we have defined two of the key terms that constitute $\widehat{\mathscr{H}}_1(t)$ in Eq. (37), i.e. $\widehat{\mathscr{H}}_\mu(t)$. These two components, namely the CSA component and the dipolar component, are defined by Eq. (122) and by Eqs. (141 and 142), respectively. Thus defining both of these Hamiltonians in the LAB frame, we can now proceed to consider molecular rotational diffusion in this frame. This rotational diffusion is what gives rise to the stochastic fluctuations that lead to the time dependence of $\widehat{\mathscr{H}}_1(t)$ in Eq. (37).

4. Rotational diffusion of rigid molecules in randomly-ordered or isotropic solvents

In the following three parts of this article, we assume knowledge of rotational diffusion theory. Detailed derivations are provided in Appendix E.

The simplest diffusive orienting potential is the zero-potential $U(\Omega) = 0$; that is, free diffusion. This is the case for molecular rotational diffusion in an isotropic solvent. Note that while we assume the *solvent ordering* to be isotropic in this section, this does not imply that molecular tumbling is isotropic. As shown below, the nature of molecular rotational diffusion is a function of the geometry of the diffuser.

4.1. The diffusion equation and the rotational diffusion operator ($\widehat{\mathscr{R}}$)

Imagine a 'rigid' molecule tumbling freely in solution. Let Ω represent the set of time-dependent Euler angles (θ,ϕ,γ) that relate the laboratory frame (LAB) to the principal axis frame (PAF) of the molecular rotational diffusion tensor (i.e. molecule-fixed frame) at a given instant.

$\mathscr{P}(\Omega,t)$ denotes the probability of finding the molecule in orientation Ω at some time t. The conditional probability $\mathscr{P}(\Omega,t|\Omega_0)$ is the probability of finding the molecule in orientation Ω at time t, *given that* it was in orientation Ω_0 at a time arbitrarily defined as $t = 0$.

The time-evolution of $\mathscr{P}(\Omega,t|\Omega_0)$ is given by the Fokker-Planck diffusion equation (see Appendix E),

$$\frac{\partial \mathscr{P}(\Omega,t|\Omega_0)}{\partial t} = -\widehat{\mathscr{R}}\mathscr{P}(\Omega,t|\Omega_0) = -\widehat{\mathscr{R}}\mathscr{P}, \tag{143}$$

where $\widehat{\mathscr{R}}$ is the rotational diffusion operator. For free diffusion (i.e. zero ordering potential), $\widehat{\mathscr{R}}$ is given by

$$\widehat{\mathscr{R}} = \widehat{\mathscr{R}}_0 = \sum_{p,q=x,y,z} \widehat{\mathscr{L}}_p D'_{pq} \widehat{\mathscr{L}}_q, \tag{144}$$

where $\widehat{\mathscr{L}}_p$ and $\widehat{\mathscr{L}}_q$ are the p and q components of the dimensionless classical angular momentum (infinitesimal rotation) operator $\vec{\widehat{\mathscr{L}}}$, respectively, and D'_{pq} is the p,q component of the rotational diffusion tensor, $p,q = \{x,y,z\}$ in an arbitrary reference frame (see Appendix E). Both $\vec{\widehat{\mathscr{L}}}$ and $\vec{\widehat{\mathscr{I}}}$ are used to denote the angular momentum but $\vec{\widehat{\mathscr{L}}}$ is the representation of angular momentum in real space whereas $\vec{\widehat{\mathscr{I}}}$ is in spin space. For a rigid molecule, D'_{pq} is time-independent.

4.2. Solving the diffusion equation

To solve the diffusion equation [13], it is most convenient to work in orientational space, i.e. that spanned by the Euler angles (ϕ,θ,γ), rather than in Cartesian space. This enables transformations between reference frames in a simple fashion. Eq. (E61) provides the general solution to the rotational diffusion equation, which is reproduced for convenience below:

$$\mathscr{P} = \sum_\nu \Psi^*_\nu(\Omega_0)\Psi_\nu(\Omega)e^{-b_\nu t}. \tag{145}$$

The $\Psi_\nu(\Omega)$ are eigenfunctions of the rotational diffusion operator $\widehat{\mathscr{R}}$, with corresponding eigenvalues b_ν. The specific forms of these eigenfunctions and eigenvalues are dictated by $\widehat{\mathscr{R}}$, which is in turn determined by the ordering potential $U(\Omega)$. In the remainder of this part of the article, we determine $\Psi_\nu(\Omega)$ and b_ν for the case of the diffusion operator $\widehat{\mathscr{R}}_0$ resulting from an ordering potential $U(\Omega) = 0$ (free diffusion).

4.2.1. Determination of $\Psi_\nu(\Omega)$ and b_ν

4.2.1.1. Expansion of $\Psi_\nu(\Omega)$ in the basis of Wigner rotation functions. We begin by identifying an acceptable basis in which to complete our calculations. The normalized Wigner rotation functions $\mathscr{D}^l_{m,m'}(\Omega)$, introduced earlier in the context of rotations between PAF, LAB and AAF, form a complete orthonormal set and, as such, provide a convenient basis for expanding $\Psi_\nu(\Omega)$. We may expand the $\Psi_\nu(\Omega)$ in the basis of the normalized Wigner rotation functions $\sqrt{\frac{2l+1}{8\pi^2}}\,\mathscr{D}^l_{m,m'}(\Omega)$ as

$$\Psi_\nu(\Omega) = \sum_{l,m,m'} c^l_{\nu,m,m'} \sqrt{\frac{2l+1}{8\pi^2}}\,\mathscr{D}^l_{m,m'}(\Omega), \tag{146}$$

where the $c^l_{\nu,m,m'}$ are the projections of $\Psi_\nu(\Omega)$ onto each of the basis functions $\sqrt{\frac{2l+1}{8\pi^2}}\,\mathscr{D}^l_{m,m'}(\Omega), 0 \leqslant l \leqslant \infty, |\,m\,|, |\,m'\,| \leqslant l$ and $l = 0$ is a scalar and therefore a constant. This is essentially the multipole expansion, used in electromagnetic theory [45].

Substitution of Eq. (146) into (145) yields the general solution for $\mathscr{P}$ in the Wigner basis in the most explicit form:

$$\mathscr{P} = \sum_\nu \left[\sum_{l,m,m'} c^l_{\nu,m,m'} \sqrt{\frac{2l+1}{8\pi^2}}\,\mathscr{D}^{l\,*}_{m,m'}(\Omega_0) \right] \left[\sum_{s,r,r'} c^s_{\nu,r,r'} \sqrt{\frac{2s+1}{8\pi^2}}\,\mathscr{D}^s_{r,r'}(\Omega) \right] e^{-b_\nu t}.$$

$$\mathscr{P} = \frac{1}{8\pi^2} \sum_\nu \sum_{l,m,m'} \sum_{s,r,r'} \times \sqrt{(2l+1)(2s+1)}\,c^l_{\nu,m,m'}\; c^s_{\nu,r,r'}\; \mathscr{D}^{l\,*}_{m,m'}(\Omega_0)\; \mathscr{D}^s_{r,r'}(\Omega)e^{-b_\nu t}. \tag{147}$$

4.2.1.2. Matrix expression of $\widehat{\mathscr{R}}$ in the basis of Wigner rotation functions. Methods of calculation. We will follow the usual approach to obtain the eigenvalues b_ν by solving the characteristic equation $|\widehat{\mathscr{R}} - b_\nu \mathbb{1}| = 0$, where $\mathbb{1}$ is the identity matrix. To do this, we must first express the operator $\widehat{\mathscr{R}}$ as a matrix in the basis of the Wigner rotation functions.

We compute each 'matrix element' of $\widehat{\mathscr{R}}$ is this basis as:

$$\mathscr{R}^{(\mathscr{D})}_{l'l,k'k,j'j} = \langle l',k',j'|\widehat{\mathscr{R}}|l,j,k\rangle, \tag{148}$$

where $|l,k,j\rangle = \sqrt{2l+1/8\pi^2}\mathscr{D}^l_{kj}(\Omega)$. Note that to prevent notational crowdedness due to use of 'double primes', the indexes have been changed to $\{l,j,k\}$ from $\{l,m,m'\}$. To evaluate explicitly the various terms $\mathscr{R}^{(\mathscr{D})}_{l'l,k'k,j'j}$ we must fully understand the operation of $\widehat{\mathscr{R}}$ on each of the basis kets $|\,l,k,j\rangle$. This, in turn, depends on our choice of reference frame (because tensor elements D'_{pq} are frame-dependent). Working in the principal axis frame of the molecular rotational diffusion tensor is a logical choice, especially because it simplifies the expression for $\widehat{\mathscr{R}}$ considerably. In the PAF represented in a Cartesian basis, $\widehat{D}$ is diagonal with principal components D_{xx}, D_{yy}, and D_{zz}. Note that we have removed the primes for the D_{pq} (compare to Eq. (144)) to denote that these are the tensor elements in the diffusion tensor PAF. Note that we have also used D_{pq} where $p,q=\{x,y,z\}$ to represent the components of the dipolar tensor, e.g. in Eq. (127). Since $\widehat{D}$ is diagonal, all elements $D_{p,q\neq p}$ are zero, and using the molecule-fixed Cartesian coordinates, Eq. (144) reduces to:

$$\widehat{\mathscr{R}}(\mathrm{PAF}) = D_{xx}\widehat{\mathscr{L}}^2_x + D_{yy}\widehat{\mathscr{L}}^2_y + D_{zz}\widehat{\mathscr{L}}^2_z. \tag{149}$$

Through fairly straightforward algebraic manipulation, Eq. (149) can be converted into a form that is better suited for an orientational frame:

$$\widehat{\mathscr{R}}(\mathrm{PAF}) = A\widehat{\mathscr{L}}^2 + \frac{1}{2}B(\widehat{\mathscr{L}}^2_+ + \widehat{\mathscr{L}}^2_-) + C\widehat{\mathscr{L}}^2_z, \tag{150}$$

where $\widehat{\mathscr{L}}^2$ is the (dimensionless) total angular momentum operator squared, $\widehat{\mathscr{L}}_\pm$ are the ladder operators,

$$\widehat{\mathscr{L}}^2 = \widehat{\mathscr{L}}^2_x + \widehat{\mathscr{L}}^2_y + \widehat{\mathscr{L}}^2_z \quad \widehat{\mathscr{L}}_\pm = \widehat{\mathscr{L}}_x \pm i\widehat{\mathscr{L}}_y, \tag{151}$$

and the parameters A, B, and C are given by

$$\begin{aligned} A &= \frac{1}{2}(D_{xx}+D_{yy}), \\ B &= \frac{1}{2}(D_{xx}-D_{yy}) \quad C = D_{zz} - A. \end{aligned} \tag{152}$$

The angular momentum operators act on the normalized Wigner Functions, $|\,l,k,j\rangle$, in a manner analogous to their operation on the well-known spherical harmonics, namely

$$\begin{aligned} &\widehat{\mathscr{L}}^2|l,k,j\rangle = l(l+1)|l,k,j\rangle \quad \widehat{\mathscr{L}}_z|l,k,j\rangle = k|l,k,j\rangle, \\ &\widehat{\mathscr{L}}_\pm|l,k,j\rangle = \sqrt{(l\mp k)(l\pm k+1)}\;|l,k\pm 1,j\rangle, \\ &\widehat{\mathscr{L}}^2_\pm|l,k,j\rangle = \sqrt{(l\mp k)(l\pm k+1)(l\mp k-1)(l\pm k+2)}\;|l,k\pm 2,j\rangle. \end{aligned} \tag{153}$$

The Planck's constant $\hbar$ does not appear in Eq. (153) because $\vec{\widehat{\mathscr{L}}}$ is dimensionless.

Note that $|\,l,k,j\rangle$ corresponds to a rotation from the laboratory frame (LAB) to the molecular frame in which the diffusion tensor ($\widehat{D}$) is diagonal (PAF). While k is the eigenvalue of the $\widehat{\mathscr{L}}_z$ operator in the diffusion tensor PAF (see Eq. (153)), j is the eigenvalue of $\widehat{\mathscr{L}}_z$ in the *laboratory* frame (i.e. the projection of the component of angular momentum parallel to the z-axis in the LAB frame). Likewise, the ladder operators have no interaction with j, since we are working in the PAF of the diffusion tensor. While we have omitted frame designation in the notation of our angular momentum operators, an understanding of these properties will become increasingly important in following parts of this article.

We are now in a position to evaluate Eq. (148), using $\widehat{\mathscr{R}} = \widehat{\mathscr{R}}(\mathrm{PAF})$ as expressed in Eq. (150). Defining the constants $\xi^\pm_{lk} \equiv \sqrt{(l\mp k)(l\pm k+1)(l\mp k-1)(l\pm k+2)}$ we can write

$$\begin{aligned} \widehat{\mathscr{R}}|l,k,j\rangle &= A\widehat{\mathscr{L}}^2|l,k,j\rangle + \frac{1}{2}B\Big(\widehat{\mathscr{L}}^2_+|l,k,j\rangle + \widehat{\mathscr{L}}^2_-|l,k,j\rangle\Big) + C\widehat{\mathscr{L}}^2_z|l,k,j\rangle \\ &= Al(l+1)|l,k,j\rangle + \frac{1}{2}B(\xi^+_{lk}|l,k+2,j\rangle + \xi^-_{lk}|l,k-2,j\rangle) \\ &\quad + Ck^2|l,k,j\rangle \end{aligned}$$

$$\begin{aligned} \langle l',k',j'|\widehat{\mathscr{R}}|l,k,j\rangle &= Al(l+1)\langle l',k',j'|l,k,j\rangle \\ &\quad + \frac{1}{2}B(\xi^+_{lk}\langle l',k',j'|l,k+2,j\rangle + \xi^-_{lk}\langle l',k',j'|l,k-2,j\rangle) \\ &\quad + Ck^2\langle l',k',j'|l,k,j\rangle. \end{aligned} \tag{154}$$

We omit the (PAF) notation henceforth for tidiness, but it is understood that we continue to work exclusively in the PAF of the rotational diffusion tensor.

Employing the orthogonality relation in Eq. (154), we have:

$$\begin{aligned} \langle l',k',j'|\widehat{\mathscr{R}}|l,k,j\rangle &= Al(l+1)\delta_{l'l}\delta_{k'k}\delta_{j'j} \\ &\quad + \frac{1}{2}B(\xi^+_{lk}\delta_{l'l}\delta_{k',k+2}\delta_{j'j} + \xi^-_{lk}\delta_{l'l}\delta_{k',k-2}\delta_{j'j}) \\ &\quad + Ck^2\delta_{l'l}\delta_{k'k}\delta_{j'j}, \end{aligned} \tag{155}$$

and finally,

$$\begin{aligned} \mathscr{R}^{(\mathscr{D})}_{l'l,k'k,j'j} &= \langle l',k',j'|\widehat{\mathscr{R}}|l,k,j\rangle \\ &= \delta_{l'l}\delta_{j'j}\left[\delta_{k'k}\Big(Al(l+1)+Ck^2\Big) + \frac{1}{2}B(\xi^+_{lk}\delta_{k',k+2} + \xi^-_{lk}\delta_{k',k-2})\right], \end{aligned} \tag{156}$$

where the superscript $(\mathscr{D})$ implies that we are in the PAF of the diffusion tensor.

Eq. (156) looks rather complicated. However, matters may be simplified considerably upon closer inspection. It is evident that Wigner basis functions with values of $l'\neq l$ do not interact in Eq. (156). In addition, the $\mathscr{D}^l_{kj}(\Omega)$ are defined such that for each value of l, the values of j and k range from $-l$ to l in integer steps; that is j or $k = -l, -l+1, -l+2 \ldots l-1, l$. It is convenient, then, to divide the $l'l, k'k, j'j$-space into l-subspaces, in which we consider only '$\widehat{\mathscr{R}}$-mixing' of basis functions with one value of l at a time. This follows from the fact that two tensors of different rank (i.e. different values of l) do not interact. For the purposes of finding the eigenvalues, then, we may rewrite Eq. (156) in the following way, implicitly assuming $l'=l$:

$$\mathscr{R}^{(\mathscr{D})(l)}_{k'k,j'j} = \delta_{j'j}\left\{\begin{array}{l} \delta_{k'k}\Big(Al(l+1)+Ck^2\Big) \\ +\frac{1}{2}B(\xi^+_{lk}\delta_{k',k+2} + \xi^-_{lk}\delta_{k',k-2}) \end{array}\right\}. \tag{157}$$

It is also clear that $\widehat{\mathscr{R}}^{(\mathscr{D})}(PAF)$ does not mix Wigner basis functions with values of j and $j'\neq j$ (this is expected physically, since $\widehat{\mathscr{R}}^{(\mathscr{D})}(PAF)$ is in the PAF of the molecular rotational diffusion tensor, while j is related to the z-component of angular momentum in the laboratory frame). Moreover, even for $j'=j$, the matrix elements in Eq. (157) have no dependence on j-values whatsoever (whereas they do depend on l,k, and k'). We can then further simplify Eq. (157), writing it as

$$\mathscr{R}^{(\mathscr{D})(l)}_{k'k} = \delta_{k'k}\Big(Al(l+1)+Ck^2\Big) + \frac{1}{2}B(\xi^+_{lk}\delta_{k',k+2} + \xi^-_{lk}\delta_{k',k-2}). \tag{158}$$

Explicit matrix expressions

Using Eq. (158) we may finally write explicit matrix representations for $\mathscr{R}^{(D)(l)}_{k'k}$. Beginning with rank $l=1$, we have

$$\mathscr{R}^{(\mathscr{D})(1)}_{k'k} = \delta_{k'k}\left(2A + Ck^2\right) + \frac{1}{2}B\left(\xi^{+}_{1,k}\delta_{k',k+2} + \xi^{-}_{1,k}\delta_{k',k-2}\right), \tag{159}$$

where

$$\begin{aligned} \xi^{+}_{1,k} &= \sqrt{(1-k)(2+k)(-k)(3+k)} \\ \xi^{-}_{1,k} &= \sqrt{(1+k)(2-k)(k)(3-k)} \end{aligned} \tag{160}$$

and we will compute the matrix $\mathscr{R}^{(\mathscr{D})(1)}$ as follows:

$$\mathscr{R}^{(\mathscr{D})(1)} = \begin{array}{cl} \begin{array}{ccc} k=-1 & k=1 & k=0 \end{array} & \\ \begin{pmatrix} \mathscr{R}^{(\mathscr{D})(1)}_{-1,-1} & \mathscr{R}^{(\mathscr{D})(1)}_{-1,1} & \mathscr{R}^{(\mathscr{D})(1)}_{-1,0} \\ \mathscr{R}^{(\mathscr{D})(1)}_{1,-1} & \mathscr{R}^{(\mathscr{D})(1)}_{1,1} & \mathscr{R}^{(\mathscr{D})(1)}_{1,0} \\ \mathscr{R}^{(\mathscr{D})(1)}_{0,-1} & \mathscr{R}^{(\mathscr{D})(1)}_{0,1} & \mathscr{R}^{(\mathscr{D})(1)}_{0,0} \end{pmatrix} & \begin{array}{l} k'=-1 \\ k'=1 \\ k'=0. \end{array} \end{array} \tag{161}$$

Evaluating Eq. (161) is straightforward and yields:

$$\mathscr{R}^{(\mathscr{D})(1)} = \begin{pmatrix} 2A+C & B & 0 \\ B & 2A+C & 0 \\ 0 & 0 & 2A \end{pmatrix}. \tag{162}$$

By identical methods, for rank $l = 2$

$$\mathscr{R}^{(\mathscr{D})(2)}_{k'k} = \delta_{k'k}\left(6A + Ck^2\right) + \frac{1}{2}B\left(\xi^{+}_{2,k}\delta_{k',k+2} + \xi^{-}_{2,k}\delta_{k',k-2}\right), \tag{163}$$

where

$$\begin{aligned} \xi^{+}_{1,k} &= \sqrt{(2-k)(3+k)(1-k)(4+k)} \\ \xi^{-}_{1,k} &= \sqrt{(2+k)(3-k)(1+k)(4-k)}. \end{aligned} \tag{164}$$

The columns of the matrix representation of $\mathscr{R}^{(\mathscr{D})(2)}$ are reordered as follows:

$$\mathscr{R}^{(\mathscr{D})(2)} = \begin{array}{cl} \begin{array}{ccccc} k=-1; & k=1; & k=-2; & k=0; & k=2 \end{array} & \\ \begin{pmatrix} \mathscr{R}^{(\mathscr{D})(2)}_{-1,-1} & \mathscr{R}^{(\mathscr{D})(2)}_{-1,1} & \cdots\cdots & \cdots\cdots & \mathscr{R}^{(\mathscr{D})(2)}_{-1,2} \\ \mathscr{R}^{(\mathscr{D})(2)}_{1,-1} & \mathscr{R}^{(\mathscr{D})(2)}_{1,1} & \cdots\cdots & \cdots\cdots & \mathscr{R}^{(\mathscr{D})(2)}_{1,2} \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ \mathscr{R}^{(\mathscr{D})(2)}_{2,-1} & \mathscr{R}^{(\mathscr{D})(2)}_{2,1} & \cdots\cdots & \cdots\cdots & \mathscr{R}^{(\mathscr{D})(2)}_{2,2} \end{pmatrix} & \begin{array}{l} k'=-1 \\ k'=1 \\ k'=-2 \\ k'=0 \\ k'=2. \end{array} \end{array} \tag{165}$$

This order yields a block-diagonal matrix form for $\mathscr{R}^{(\mathscr{D})(2)}$, which simplifies further calculations significantly. A straightforward but cumbersome derivation yields

$$\mathscr{R}^{(\mathscr{D})(2)} = \begin{pmatrix} 6A+C & 3B & 0 & 0 & 0 \\ 3B & 6A+C & 0 & 0 & 0 \\ 0 & 0 & 6A+4C & \sqrt{6}B & 0 \\ 0 & 0 & \sqrt{6}B & 6A & \sqrt{6}B \\ 0 & 0 & 0 & \sqrt{6}B & 6A+4C \end{pmatrix}. \tag{166}$$

4.2.1.3. Solving the characteristic equation. Armed with explicit matrix representations, we now seek to determine the eigenvalues $b^{(l)}_{\nu}$ and eigenfunctions $\Psi^{(l)}_{\nu}$ in the Wigner basis. We do this through the usual approach of solving the characteristic equation, $\det(\mathscr{R}^{(\mathscr{D})(l)} - b^{(l)}_{\nu}\mathbb{1}) = 0$.

Rank-1: Let us begin with the simpler case of the rank-1 tensor. The characteristic equation is:

$$\left(2A - b^{(1)}_{\nu}\right)\left[\left(2A + C - b^{(1)}_{\nu}\right)^2 - B^2\right] = 0. \tag{167}$$

Solving Eq. (167) for $b^{(1)}_{\nu}$ yields

$$b^{(1)}_{\nu} = 2A + C \pm B,\ 2A. \tag{168}$$

Entering these results in the eigenvalue Eq. (E52), we can solve for the eigenvectors (eigenfunctions):

$$\begin{gathered} \mathscr{R}^{(\mathscr{D})(1)}\Psi^{(1)}_{\nu} = b^{(1)}_{\nu}\Psi^{(1)}_{\nu} \\ \begin{pmatrix} 2A+C & B & 0 \\ B & 2A+C & 0 \\ 0 & 0 & 2A \end{pmatrix}\begin{pmatrix} c^{(1)}_{\nu,-1} \\ c^{(1)}_{\nu,+1} \\ c^{(1)}_{\nu,0} \end{pmatrix} = b_{\nu}\begin{pmatrix} c^{(1)}_{\nu,-1} \\ c^{(1)}_{\nu,+1} \\ c^{(1)}_{\nu,0} \end{pmatrix}. \end{gathered} \tag{169}$$

As before, the $c^{(l)}_{\nu,k}$ are the components of the eigenfunctions in the Wigner-function basis. Eq. (169) amounts to (yet another) system of linear equations, which may be solved easily for the components $c^{(l)}_{\nu,k}$. The full set of normalized (in the sense that $\Psi^{(1)\top}_{i}\Psi^{(1)}_{j} = \delta_{ij}$, where superscript $\top$ implies the transpose) eigenvectors and eigenvalues for the rank $l = 1$ tensor is given by

$$\begin{array}{lll} \Psi^{(1)}_{-1} = \sqrt{\tfrac{1}{2}}\begin{pmatrix} -1 \\ 1 \\ 0 \end{pmatrix} & \Psi^{(1)}_{+1} = \sqrt{\tfrac{1}{2}}\begin{pmatrix} 1 \\ 1 \\ 0 \end{pmatrix} & \Psi^{(1)}_{0} = \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \\ b^{(1)}_{-1} = 2A + C - B & b^{(1)}_{+1} = 2A + C + B & b^{(1)}_{0} = 2A \\ b^{(1)}_{-1} = D_{yy} + D_{zz} & b^{(1)}_{+1} = D_{xx} + D_{zz} & b^{(1)}_{0} = D_{xx} + D_{yy}. \end{array} \tag{170}$$

In the last line of Eq. (170), we have explicitly computed the eigenvalues b_{ν} in terms of the principal components of the diffusion tensor (see Eq. (152)).

Rank-2: The approach for the rank-2 tensor is identical to that for the rank-1 tensor, although the computations are necessarily somewhat more complicated. The characteristic equation is

$$\det\left(\mathscr{R}^{(\mathscr{D})(2)} - b^{(2)}_{\nu}\mathbb{1}_5\right) = 0, \tag{171}$$

where $\mathbb{1}_5$ is the 5×5 identity matrix.

Since $\mathscr{R}^{(\mathscr{D})(2)}$ is block-diagonal, $(\mathscr{R}^{(\mathscr{D})(2)} - b^{(2)}_{\nu}\mathbb{1}_5)$ is block diagonal as well, and the determinant of the whole matrix is simply the product of the determinants of the individual blocks. It can be shown easily that Eq. (171) evaluates to

$$\begin{aligned} &\left[2(3A + 2C) - b^{(2)}_{\nu}\right]\left[6A + 3B + C - b^{(2)}_{\nu}\right][6A - 3B + C - b_{\nu}] \\ &\quad \times \left[4\left(9A^2 + 6AC - 3B^2 - b^{(2)}_{\nu}(3A + C)\right) + \left(b^{(2)}_{\nu}\right)^2\right], \end{aligned} \tag{172}$$

which when solved for $b^{(2)}_{\nu}$ yields

$$b^{(2)}_{\nu} = 6A + 4C, \quad 6A + C \pm 3B, \quad 2\left(3A + C \pm \sqrt{3B^2 + C^2}\right). \tag{173}$$

As above, we proceed by writing the eigenvalue equation

$$\mathscr{R}^{(\mathscr{D})(2)}\Psi^{(2)}_{\nu} = b^{(2)}_{\nu}\Psi^{(2)}_{\nu} = b^{(2)}_{\nu}\begin{pmatrix} c^{(2)}_{\nu,-1} \\ c^{(2)}_{\nu,+1} \\ c^{(2)}_{\nu,-2} \\ c^{(2)}_{\nu,0} \\ c^{(2)}_{\nu,+2} \end{pmatrix}, \tag{174}$$

which amounts to a system of linear equations that we must solve to determine the components of the eigenvectors. The solutions for three of the five eigenvector/eigenvalue pairs are fairly straightforward:

$$\begin{aligned}
&\Psi_{-2}^{(2)}=\sqrt{\tfrac{1}{2}}\begin{pmatrix}0\\0\\-1\\0\\1\end{pmatrix} \qquad \Psi_{-1}^{(2)}=\sqrt{\tfrac{1}{2}}\begin{pmatrix}-1\\1\\0\\0\\0\end{pmatrix} \qquad \Psi_{+1}^{(2)}=\sqrt{\tfrac{1}{2}}\begin{pmatrix}1\\1\\0\\0\\0\end{pmatrix}\\
&b_{-2}^{(2)}=6A+4C \qquad b_{-1}^{(2)}=6A+C-3B \qquad b_{+1}^{(2)}=6A+C+3B\\
&b_{-2}^{(2)}=D_{xx}+D_{yy}+4D_{zz} \quad b_{-1}^{(2)}=D_{xx}+4D_{yy}+D_{zz} \quad b_{+1}^{(2)}=4D_{xx}+D_{yy}+D_{zz}.
\end{aligned} \tag{175}$$

The other two cases are not so simple, especially when the normalization requirement is imposed. Let us first examine the $v = 2$ case, without imposing any normalization:

$$\begin{aligned}
\psi_{+2}^{(2)} &= \begin{pmatrix}0\\0\\1\\ \frac{-\sqrt{6}\left(C-\sqrt{3B^2+C^2}\right)}{3B}\\1\end{pmatrix}\\
b_{+2}^{(2)} &= 2\left(3A+C+\sqrt{3B^2+C^2}\right),
\end{aligned} \tag{176}$$

where we have used ψ (rather than Ψ) to emphasize that the vector is not normalized. When expressed in terms of the principal components of the diffusion tensor, $b_{+2}^{(2)}$ becomes rather unwieldy. A bit of algebraic manipulation reveals that the expression simplifies significantly by defining the constants

$$\begin{aligned}
\alpha &= \frac{1}{3}\left(D_{xx}+D_{yy}+D_{zz}\right)\\
\beta &= \sqrt{\frac{1}{3}\left(D_{xx}D_{yy}+D_{yy}D_{zz}+D_{zz}D_{xx}\right)}
\end{aligned} \tag{177}$$

whence

$$b_{+2}^{(2)} = 6\left(\alpha+\sqrt{\alpha^2-\beta^2}\right). \tag{178}$$

We now wish to find an analogous simplifying parameterization for $\Psi_{+2}^{(2)}$. Normalization of $\psi_{+2}^{(2)}$ yields

$$\begin{aligned}
&\frac{\psi_{+2}^{(2)}}{\sqrt{\psi_{+2}^{(2)T}\psi_{+2}^{(2)}}} = \Psi_{+2}^{(2)}\\
&= \begin{pmatrix}0\\0\\ \frac{\sqrt{3}B}{2\sqrt{3B^2+C^2-C\sqrt{3B^2+C^2}}}\\ \frac{\sqrt{2}\left(\sqrt{3B^2+C^2}-C\right)}{2\sqrt{3B^2+C^2-C\sqrt{3B^2+C^2}}}\\ \frac{\sqrt{3}B}{2\sqrt{3B^2+C^2-C\sqrt{3B^2+C^2}}}\end{pmatrix} \equiv \begin{pmatrix}0\\0\\X\\Y\\Z\end{pmatrix}.
\end{aligned} \tag{179}$$

Note that $Z = X$ in Eq. (179). We search for a convenient change of variables by taking the ratio X/Y and arbitrarily equating it with the tangent of a new parameter χ_{+2} (which we are about to determine). We add the factor of $1/\sqrt{2}$ with some foresight of the final result, as it makes the expression for our parameter χ_{+2} somewhat simpler:

$$\frac{X}{Y}=\frac{1}{\sqrt{2}}\frac{\sin\chi_{+2}}{\cos\chi_{+2}} \Rightarrow \begin{cases} X=\frac{1}{\sqrt{2}}\sin\chi_{+2}\\ Y=\cos\chi_{+2}. \end{cases} \tag{180}$$

The manipulations to determine χ_{+2} are straightforward:

$$\frac{X}{Y}=\frac{\sqrt{3}B}{\sqrt{2}\left(\sqrt{3B^2+C^2}-C\right)} \;\Rightarrow\; \tan\chi_{+2}=\frac{\sqrt{3}B}{\sqrt{3B^2+C^2}-C},$$

$$\begin{aligned}
\chi_{+2} &= \arctan\left[\frac{\sqrt{3}B}{\sqrt{3B^2+C^2}-C}\right]\\
&= \arctan\left[\frac{\frac{\sqrt{3}}{2}\left(D_{xx}-D_{yy}\right)}{\sqrt{3B^2+C^2}-D_{zz}+\frac{1}{2}\left(D_{xx}+D_{yy}\right)}\right].
\end{aligned} \tag{181}$$

$$\chi_{+2} = \arctan\left[\frac{\sqrt{3}\left(D_{xx}-D_{yy}\right)}{6\sqrt{\alpha^2-\beta^2}-2D_{zz}+D_{xx}+D_{yy}}\right]. \tag{182}$$

Using Eqs. (180) and (182), we can express $\Psi_{+2}^{(2)}$ in a manageable form as

$$\Psi_{+2}^{(2)} = \begin{pmatrix}0\\0\\ \frac{\sin\chi_{+2}}{\sqrt{2}}\\ \cos\chi_{+2}\\ \frac{\sin\chi_{+2}}{\sqrt{2}}\end{pmatrix} = \sqrt{\frac{1}{2}}\begin{pmatrix}0\\0\\ \sin\chi_{+2}\\ \sqrt{2}\cos\chi_{+2}\\ \sin\chi_{+2}\end{pmatrix}. \tag{183}$$

By identical methods to those above, the last rank 2 eigenvector, $\Psi_0^{(2)}$, and its corresponding eigenvalue are found to be

$$\Psi_0^{(2)} = \sqrt{\frac{1}{2}}\begin{pmatrix}0\\0\\ \sin\chi_0\\ \sqrt{2}\cos\chi_0\\ \sin\chi_0\end{pmatrix}, \tag{184}$$

where

$$\begin{aligned}
\chi_0 &= \arctan\left[\frac{\sqrt{3}\left(D_{xx}-D_{yy}\right)}{D_{xx}+D_{yy}-6\sqrt{\alpha^2-\beta^2}-2D_{zz}}\right]\\
b_0^{(2)} &= 6\left(\alpha-\sqrt{\alpha^2-\beta^2}\right)
\end{aligned} \tag{185}$$

4.2.2. Symmetrical molecules

In the preceding sections, we have assumed no molecular symmetry. For an axially symmetric (i.e. a rod, disk, or ellipsoid) or spherically symmetric molecule, the method for solving the master equation is identical to the one followed above, but the calculations are less laborious. In the case of axial symmetry, we take the z-axis of the molecular frame to be along the symmetry axis of the molecule. Due to the symmetry, the diffusion is isotropic in the x and y directions of the diffusion tensor PAF. Accordingly we may write $D_{xx} = D_{yy} = D_\perp$ and $D_{zz} = D_\parallel$, and therefore

$$A = D_\perp \quad B = 0 \quad C = D_\parallel - D_\perp. \tag{186}$$

For spherically symmetric molecules, which diffuse completely isotropically, $D_{xx} = D_{yy} = D_{zz} = D_o$, and

$$A = D_o \quad B = C = 0. \tag{187}$$

Eqs. (186) and (187) may be directly substituted into the characteristic equations to derive the eigenvalues and corresponding eigenvectors.

4.2.2.1. For axially symmetric systems

Rank-1:

$\mathscr{R}^{(\mathscr{D})(1)}$ in Eq. (162) is diagonal, and since $B = 0$, the eigenvalues are:

$$\{2A+C,\quad 2A+C,\quad 2A\} = \{D_\parallel+D_\perp,\ D_\parallel+D_\perp,\ 2D_\perp\}.$$

Rank-2:

Again in this case $\mathscr{R}^{(\mathscr{D})(2)}$ in Eq. (171) is diagonal, with eigenvalues:

$$\begin{aligned}&\{6A+C,\quad 6A+C,\quad 6A+4C,\quad 6A,\quad 6A+4C\}\\&\quad=\{5D_\perp+D_\parallel,\ 5D_\perp+D_\parallel,\ 2D_\perp+4D_\parallel,\quad 6D_\perp,\ 2D_\perp+4D_\parallel\}.\end{aligned}$$

4.2.2.2. For isotropic systems.

$$A=D=D_o,\quad B=C=0.$$

$\mathscr{R}^{(\mathscr{D})(1)}$ is a scalar with a diffusion constant $2D$ (i.e. $\mathscr{R}^{(\mathscr{D})(l)}=2D\mathbb{1}$), $\mathscr{R}^{(\mathscr{D})(2)}$ is also a scalar with a diffusion constant $6D$.

4.2.3. Equilibrium probability distribution

Calculation of the equilibrium probability distribution is straightforward. Direct substitution of $U(\Omega)=0$ into Eq. (E63) yields

$$\begin{aligned}P_{\text{eq}}(\Omega)&=\frac{\exp\left[-U(\Omega)/k_BT\right]}{\int\exp\left[-U(\Omega)/k_BT\right]d\Omega}=\frac{1}{\int d\Omega}\\P_{\text{eq}}(\Omega)&=\frac{1}{\int_0^{2\pi}d\theta\int_0^{\pi}\sin\phi d\phi\int_0^{2\pi}d\gamma}=\frac{1}{8\pi^2}.\end{aligned}\tag{188}$$

Alternatively, considering Eq. (E64),

$$\lim_{t\to\infty}P(\Omega,t|\Omega_0)=P_{\text{eq}}(\Omega).\tag{189}$$

It is evident from inspection of Eq. (147) that in the long time limit, all terms in the summations vanish (because they contain the decaying exponential $e^{-b_\nu t}$), except for the single term arising from the trivial rank $l=0, b_\nu=0$ case. This term is equal to unity, and one therefore arrives at the identical solution $P_{\text{eq}}(\Omega)=1/8\pi^2$ as obtained through consideration of Eq. (E63).

5. Rotational diffusion of rigid molecules in ordered solvents: stationary uniaxial potential

We now turn our attention to diffusion within a non-zero ordering potential $U(\Omega)$ [46,47]. For simplicity, we consider an axially-symmetric or uniaxial potential, the unique axis of which is referred to as the *director*. At present, we assume this frame is fixed relative to the laboratory. We do not treat the more difficult case in which the director is not stationary in the laboratory frame (this phenomenon is commonly referred to as *director fluctuation*). The current description corresponds physically to the diffusion of rigid bodies in a liquid crystal solvent which is aligned at a constant angle with the static magnetic field.

The simplest form for a uniaxial potential, known as the Maier–Saupe potential [48], is given by

$$\mathscr{U}=\frac{U(\Omega)}{k_BT}=\frac{U(\phi)}{k_BT}=-c^2\ \mathscr{D}^{(2)}_{00}(\Omega)=-c^2\ \frac{3\cos^2\phi-1}{2},\tag{190}$$

which may also be written in terms of the second order Legendre polynomial (see Appendix D.2) as $-c^2P_2(\cos\phi)$. The constant c indicates the strength of the potential and ϕ is the angle between the molecular axis and the director.

The solution to this problem is similar to that of the preceding isotropic case. However, several additional steps are necessary as a result of the non-zero ordering potential.

5.1. The diffusion equation and the rotational diffusion operators $\widehat{\mathscr{R}}$ and $\widehat{\Gamma}$

Recall Eq. (143):

$$\frac{\partial\mathscr{P}}{\partial t}=-\widehat{\mathscr{R}}\mathscr{P}.\tag{191}$$

In the presence of the ordering potential, the form of $\widehat{\mathscr{R}}$ is now (see Eqs. (E50) and (E65)):

$$\begin{aligned}\widehat{\mathscr{R}}=\varrho(1+\varepsilon)&\left[\widehat{\mathscr{L}}_x^2+\widehat{\mathscr{L}}_x\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)_{\text{op}}\right]\\+\varrho(1-\varepsilon)&\left[\widehat{\mathscr{L}}_y^2+\widehat{\mathscr{L}}_y\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)_{\text{op}}\right]\\+\varrho\eta&\left[\widehat{\mathscr{L}}_z^2+\widehat{\mathscr{L}}_z\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)_{\text{op}}\right],\end{aligned}\tag{192}$$

where the $(\ldots)_{\text{op}}$ notation is taken to mean that the terms '…' inside parentheses are evaluated and then treated as a single operator, and

$$\begin{aligned}\varrho&\equiv\frac{D_{xx}+D_{yy}}{2},\\\varepsilon&\equiv\frac{D_{xx}-D_{yy}}{D_{xx}+D_{yy}},\\\eta&\equiv\frac{2D_{zz}}{D_{xx}+D_{yy}}.\end{aligned}\tag{193}$$

For the sake of convenience, we define a dimensionless diffusion operator $\widehat{\Gamma}$ as

$$\widehat{\Gamma}=\frac{1}{\varrho}\widehat{\mathscr{R}}.\tag{194}$$

We can now write the diffusion equation as

$$\frac{1}{\varrho}\frac{\partial\mathscr{P}}{\partial t}=-\widehat{\Gamma}\mathscr{P}.\tag{195}$$

5.2. Solving the diffusion equation

5.2.1. General solution

Writing the diffusion equation as Eq. (195) simplifies calculations somewhat, but in essence, the general solution is the same as that for the case of diffusion in an isotropic liquid. The normalized eigenfunctions of $\widehat{\Gamma}$ are obviously the same as those of $\widehat{\mathscr{R}}$, while the eigenvalues of $\widehat{\Gamma}$ are those of $\widehat{\mathscr{R}}$ divided by ϱ. Thus, the solution to the diffusion equation is given by a modified form of Eq. (145):

$$\mathscr{P}=\sum_\nu\Psi^*_\nu(\Omega_0)\Psi_\nu(\Omega)e^{-\varrho a_\nu t},\tag{196}$$

where $\Psi_\nu(\Omega)$ are eigenfunctions of $\widehat{\Gamma}$ (and $\widehat{\mathscr{R}}$), with corresponding eigenvalues $a_\nu=b_\nu/\varrho$.

5.2.2. Finding specific $\Psi^*_\nu(\Omega)$ and a_ν

We proceed again by writing a matrix expression for the diffusion operator $\widehat{\Gamma}$ in the basis of Wigner rotation functions, and solving the characteristic equation $|\widehat{\Gamma}-a_\nu\mathbb{1}|=0$. To simplify calculations, we consider an axially symmetric diffuser such that $D_{xx}=D_{yy}=D_\perp$ and $D_{zz}=D_\parallel$ (see Section 4.2.2.1) and work in the principal axis frame of diffusion tensor.

5.2.2.1. The $\tilde{\widehat{\Gamma}}_{\text{Axial}}$ and ∇^2_{Axial} operators. As explained in detail in Appendix E.4.2, it is convenient to perform calculations using a symmetrized operator, $\tilde{\widehat{\Gamma}}$ (where the 'tilde' $\sim$ above the operator denotes that it has been symmetrized). From Eq. (E95), we have

$$\begin{aligned}&\tilde{\widehat{\Gamma}}_{\text{Axial}}=\nabla^2_{\text{Axial}}+\frac{1}{2}\left(\nabla^2_{\text{Axial}}\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_+\mathscr{U}\right)\left(\widehat{\mathscr{L}}_-\mathscr{U}\right)-\frac{1}{4}\eta\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2,\\&\nabla^2_{\text{Axial}}=\widehat{\mathscr{L}}_x^2+\hat{\mathscr{L}}_y^2+\eta\widehat{\mathscr{L}}_z^2.\end{aligned}\tag{197}$$

The axially-symmetric nabla-squared operator (see Eq. (E92)) may be written more conveniently by recognizing that

$$\begin{aligned}\nabla^2_{\text{Axial}} &= \widehat{\mathscr{L}}^2_x + \hat{\mathscr{L}}^2_y + \widehat{\mathscr{L}}^2_z + (\eta - 1)\widehat{\mathscr{L}}^2_z \\ \nabla^2_{\text{Axial}} &= \widehat{\mathscr{L}}^2 + (\eta - 1)\widehat{\mathscr{L}}^2_z,\end{aligned} \tag{198}$$

Employing the bra-ket notation $|l,k,j\rangle = \sqrt{2l+1/8\pi^2}\mathscr{D}^{(l)}_{kj}(\Omega)$ used previously, we may therefore write (see Eq. (153)):

$$\nabla^2_{\text{Axial}}|l,k,j\rangle = \Big[l(l+1) + k^2(\eta - 1)\Big]|l,k,j\rangle. \tag{199}$$

5.2.2.2. Evaluation of individual $\tilde{\hat{\Gamma}}_{\text{Axial}}$ operator terms. In order to compute the matrix elements of $\hat{\Gamma}_{\text{Axial}}$, we first need to evaluate each term in parentheses in Eq. (197). In our bra-ket notation, $\mathscr{U} = -c^2\mathscr{D}^{(2)}_{00}(\Omega) = -c^2|2,0,0\rangle$, and thus

$$\begin{aligned}&\nabla^2_{\text{Axial}}\mathscr{U} = -c^2[2(3)+0]|2,0,0\rangle = -6c^2|2,0,0\rangle \\ &\widehat{\mathscr{L}}_+\mathscr{U} = -c^2\sqrt{2(3)}|2,1,0\rangle = -\sqrt{6}c^2|2,1,0\rangle \\ &\widehat{\mathscr{L}}_-\mathscr{U} = -c^2\sqrt{2(3)}|2,-1,0\rangle = -\sqrt{6}c^2|2,-1,0\rangle \\ &\widehat{\mathscr{L}}_z\mathscr{U} = 0.\end{aligned} \tag{200}$$

Eq. (197) can be written more explicitly

$$\begin{aligned}\tilde{\hat{\Gamma}}_{\text{Axial}} &= \nabla^2_{\text{Axial}} - \frac{1}{2}\left(-6c^2|2,0,0\rangle\right) \\ &\quad - \frac{1}{4}\left(-\sqrt{6}c^2|2,1,0\rangle\right)\left(-\sqrt{6}c^2|2,-1,0\rangle\right) \\ \tilde{\hat{\Gamma}}_{\text{Axial}} &= \nabla^2_{\text{Axial}} + 3c^2|2,0,0\rangle - \frac{3}{2}c^4|2,1,0\rangle \otimes |2,-1,0\rangle,\end{aligned} \tag{201}$$

we may rewrite the vector product $|2,1,0\rangle \otimes |2,-1,0\rangle$ using the formula

$$\begin{aligned}\left|l_1, m_1', m_1\right\rangle \otimes \left|l_2, m_2', m_2\right\rangle = \sum_{l=|l_1-l_2|}^{|l_1+l_2|} &\left[C(l_1, l_2, l; m_1', m_2', m')\right. \\ &\left.\times C(l_1, l_2, l; m_1, m_2, m)|l, m', m\rangle\right],\end{aligned} \tag{202}$$

where $C(l_1, l_2, l; m_1', m_2', m')$ and $C(l_1, l_2, l; m_1, m_2, m)$ are Clebsch-Gordan coefficients [49–51], and the sum includes all coefficients for which $m_1' + m_2' = m'$, $m_1 + m_2 = m$, $|m'| \leqslant l'$ and $|m| \leqslant l$.

Therefore, we have

$$|2,1,0\rangle \otimes |2,-1,0\rangle = \sum_{l=0}^{4} C(2,2,l;1,-1,0)C(2,2,l;0,0,0)|l,0,0\rangle. \tag{203}$$

The non-zero coefficients $C(2,2,l;0,0,0)$ with l values in the range of the limits of the summation are

$$\begin{aligned}&C(2,2,0;0,0,0) = +\sqrt{1/5} \\ &C(2,2,2;0,0,0) = -\sqrt{2/7} \\ &C(2,2,4;0,0,0) = +\sqrt{18/35},\end{aligned} \tag{204}$$

and thus all terms in the summation for which $l = \{1,\ 3\}$ vanish. Values of $C(2,2,l;1,-1,0)$ for which $l = \{0,\ 2,\ 4\}$ are

$$\begin{aligned}&C(2,2,0;1,-1,0) = -\sqrt{1/5} \\ &C(2,2,2;1,-1,0) = +\sqrt{1/14} \\ &C(2,2,4;1,-1,0) = +\sqrt{8/35}.\end{aligned} \tag{205}$$

Evaluation of Eq. (203) then yields

$$|2,1,0\rangle \otimes |2,-1,0\rangle = -\frac{1}{5}|0,0,0\rangle - \frac{1}{7}|2,0,0\rangle + \frac{12}{35}|4,0,0\rangle. \tag{206}$$

The diffusion operator may then be written as

$$\begin{aligned}\tilde{\hat{\Gamma}}_{\text{Axial}} = \nabla^2_{\text{Axial}} &+ 3c^2|2,0,0\rangle \\ &+ c^4\left(\frac{3}{10}|0,0,0\rangle + \frac{3}{14}|2,0,0\rangle - \frac{18}{35}|4,0,0\rangle\right).\end{aligned} \tag{207}$$

Combining like terms:

$$\tilde{\hat{\Gamma}}_{\text{Axial}} = \nabla^2_{\text{Axial}} + 3c^2\left(1 + \frac{c^2}{14}\right)|2,0,0\rangle + \frac{3c^4}{10}|0,0,0\rangle - \frac{18c^4}{35}|4,0,0\rangle. \tag{208}$$

5.2.2.3. Matrix expression of $\tilde{\hat{\Gamma}}_{\text{Axial}}$ in the basis of Wigner rotation functions. We are now in a position to calculate the individual matrix elements of $\tilde{\hat{\Gamma}}_{\text{Axial}}$:

$$\tilde{\hat{\Gamma}}^{(\mathscr{D})}_{\text{Axial}_{l'l,k'k,j'j}} = \langle l', k', j' | \tilde{\hat{\Gamma}}_{\text{Axial}} | l, k, j\rangle. \tag{209}$$

Note that because of the vector products associated with $\tilde{\hat{\Gamma}}_{\text{Axial}}|l,k,j\rangle$, unlike the diffusion operator for isotropic solvents, the diffusion operator $\tilde{\hat{\Gamma}}_{\text{Axial}}$ *does* mix Wigner basis functions of different rank (i.e. with $l' \neq l$). This would complicate the current problem considerably as compared to the case in which there is no ordering potential, and each l-subspace may be considered independently. However, the absence of any raising or lowering operators in the final form of the axially symmetric rotational diffusion operator prevents mixing in either k or j, as we shall demonstrate shortly. Notice that this is not true for the most general case of fully asymmetric diffusion (see Eq. (E94)), which *does* contain both raising and lowering operators. We do not consider the most general case of the diffusion of a diffuser of arbitrary shape in an arbitrary ordering potential. The reason for using this simplified model is justified due to two reasons: (1) the asymmetry in the rotational diffusion tensor is generally small and ignored in most NMR studies of biomolecules, (2) the liquid crystalline media used for most studies of biomolecules to measure residual dipolar couplings (RDCs) consist of nematic liquid crystals with a unique director [52–54]. Thus, the case considered here is likely to be the most general in the context of biological NMR.

It is easiest to handle the calculations by considering each of the four diffusion operator terms (which we will denote as $\left\{\tilde{\hat{\Gamma}}^{\text{term 1}}_{\text{Axial}} \ldots \tilde{\hat{\Gamma}}^{\text{term 4}}_{\text{Axial}}\right\}$) separately, and adding the results together at the end. We see directly from Eq. (199) that for the first term, $\tilde{\hat{\Gamma}}^{\text{term 1}}_{\text{Axial}} = \nabla^2_{\text{Axial}}$,

$$\langle l', k', j' | \tilde{\hat{\Gamma}}^{\text{term 1}}_{\text{Axial}} | l, k, j\rangle = \Big[l(l+1) + k^2(\eta - 1)\Big]\delta_{l'l}\delta_{k'k}\delta_{j'j}. \tag{210}$$

For the next term, $\tilde{\hat{\Gamma}}^{\text{term 2}}_{\text{Axial}} = 3c^2(1 + c^2/14)|2,0,0\rangle$, the 'matrix element' is:

$$3c^2\left(1 + \frac{c^2}{14}\right)\langle l', k', j' | |2,0,0\rangle \otimes |l,k,j\rangle, \tag{211}$$

where the vector product $|2,0,0\rangle \otimes |l,k,j\rangle$ may be written as

$$|2,0,0\rangle \otimes |l,k,j\rangle = \sum_{L=|2-l|}^{2+l} C(2,l,L;0,k,k)C(2,l,L;0,j,j)|L,k,j\rangle. \tag{212}$$

The element is then

$$\begin{aligned}\langle l,k,j|\tilde{\hat{\Gamma}}^{\text{term 2}}_{\text{Axial}}|l',k',j'\rangle &= 3c^2\left(1 + \frac{c^2}{14}\right) \\ &\quad \times \sum_{L=|2-l|}^{2+l} C(2,l,L;0,k,k)C(2,l,L;0,j,j)\delta_{l'L}\delta_{k'k}\delta_{j'j}.\end{aligned} \tag{213}$$

For the next term, $\tilde{\widehat{\Gamma}}^{\text{term }3}_{\text{Axial}} = \frac{3c^4}{10}|0,0,0\rangle$, the 'matrix element' is

$$\frac{3c^4}{10}\langle l',k',j'||0,0,0\rangle \otimes |l,k,j\rangle, \tag{214}$$

and recognizing that $|0,0,0\rangle = 1$, this element is simply

$$\langle l',k',j'|\tilde{\widehat{\Gamma}}^{\text{term }3}_{\text{Axial}}|l,k,j\rangle = \frac{3c^4}{10}\delta_{l'l}\delta_{k'k}\delta_{j'j}. \tag{215}$$

Finally, for the fourth term, $\tilde{\widehat{\Gamma}}^{\text{term }4}_{\text{Axial}} = \frac{18c^4}{35}|4,0,0\rangle$, the element is

$$-\frac{18c^4}{35}\langle l',k',j'||4,0,0\rangle \otimes |l,k,j\rangle, \tag{216}$$

and we may write the vector product $|4,0,0\rangle \otimes |l,k,j\rangle$ as

$$|4,0,0\rangle \otimes |l,k,j\rangle = \sum_{L=|4-l|}^{4+l} C(4,l,L;0,k,k)C(4,l,L;0,j,j)|L,k,j\rangle. \tag{217}$$

Thus,

$$\begin{aligned}\langle l',k',j'|\tilde{\widehat{\Gamma}}^{\text{term }4}_{\text{Axial}}|l,k,j\rangle = &-\frac{18c^4}{35}\\ &\times \sum_{L=|4-l|}^{4+l} C(4,l,L;0,k,k)C(4,l,L;0,j,j)\delta_{l'L}\delta_{k'k}\delta_{j'j}.\end{aligned} \tag{218}$$

Now that we have evaluated the contribution of each term separately, we may write the full matrix expression for the diffusion operator as

$$\begin{aligned}&\tilde{\widehat{\Gamma}}^{(\mathscr{D})}_{\text{Axial}_{l'l,k'k,j'j}}\\ &= \sum_{n=1}^{4}\langle l',k',j'|\tilde{\widehat{\Gamma}}^{\text{term }n}_{\text{Axial}}|l,k,j\rangle\\ &= \delta_{k'k}\delta_{j'j}\left\{\begin{aligned}&\left[l(l+1)+k^2(\eta-1)\right]\delta_{l'l} + 3c^2\left(1+\tfrac{c^2}{14}\right)\sum_{L=|2-l|}^{2+l} C(2,l,L;0,k,k)C(2,l,L;0,j,j)\delta_{l'L}\\ &+\tfrac{3c^4}{10}\delta_{l'l} - \tfrac{18c^4}{35}\sum_{L=|4-l|}^{4+l} C(4,l,L;0,k,k)C(4,l,L;0,j,j)\delta_{l'L}\end{aligned}\right\}.\end{aligned} \tag{219}$$

This is the equivalent of Eq. (158) for an axially symmetric diffuser in a uniaxial potential. However, the explicit evaluation of matrix elements of $\tilde{\widehat{\Gamma}}^{(\mathscr{D})}_{\text{Axial}}$ is far more complex. Thus, obtaining the eigenvectors and eigenvalues is best done numerically, rather than analytically as in the simpler case of $\widehat{\mathscr{R}}^{(\mathscr{D})}_{\text{Axial}}$ in Section 4.

6. Calculation of relaxation rates

6.1. Relaxation rates in Liouville basis

Following the derivation of the Redfield equation of relaxation (Section 2), the presentation of the Hamiltonian operators of interactions contributing to relaxation (Section 3), and the treatment of rotational diffusion (Sections 4 and 5), the calculation of relaxation rates in the Liouville basis is now straightforward.

Although the calculation of the Redfield equation of relaxation (Section 2.3) was useful for the introduction of concepts, it will now be more convenient to derive relaxation rates while employing the product operator formalism (Section 2.1.3). Our starting point will be Eq. (62) and the expressions of the Hamiltonian operators of interactions contributing to relaxation found in Section 3.

We use Eq. (101) to describe each contribution to $\widehat{\mathscr{H}}(t)$. Assuming as before that the time dependence lies in spatial operators, we have

$$\widehat{\mathscr{H}}_{\mu}(t) = \xi_{\mu}\sum_{l=0}^{2}\sum_{m=-l}^{+l}(-1)^m F_l^{-m}(t)T_l^m, \tag{220}$$

where $F^l_m(t)$ is a function of spatial variables, T_l^m is a tensor spin operator. They satisfy the properties:

$$T_l^{-m} = (T_l^m)^*, \quad F_l^{-m} = (F_l^m)^*. \tag{221}$$

It is possible to expand T_l^m in a basis of the commutation superoperator $\widehat{\widehat{\mathscr{H}}}_0$ (a superoperator is an operator that acts in a linear vector space formed by a set of operators; see for example reference [24]), where

$$T_l^m = \sum_p T_l^{mp} = \sum_p c_p^{(l)}\widehat{\mathscr{H}}_p \tag{222}$$

$$[\widehat{\mathscr{H}}_0, \widehat{\mathscr{H}}_p] = \widehat{\widehat{\mathscr{H}}}_0\widehat{\mathscr{H}}_p = \omega_p\widehat{\mathscr{H}}_p. \tag{223}$$

The ω_p are the eigenfrequencies of the Hamiltonian $\widehat{\mathscr{H}}_0$. Eq. (223) implies:

$$\exp(-i\widehat{\mathscr{H}}_0 t)\widehat{\mathscr{H}}_p\exp(i\widehat{\mathscr{H}}_0 t) = \exp(-i\omega_p t)\widehat{\mathscr{H}}_p. \tag{224}$$

When Eq. (224) is applied in the interaction frame one obtains

$$\begin{aligned}T_l^m &= \exp\{i\widehat{\mathscr{H}}_0 t\}T_l^m\exp\{-i\widehat{\mathscr{H}}_0 t\}\\ &= \sum_p \exp\{i\widehat{\mathscr{H}}_0 t\}T_l^{mp}\exp\{-i\widehat{\mathscr{H}}_0 t\} = \sum_p T_l^{mp}\exp\{i\omega_p t\}.\end{aligned} \tag{225}$$

$$\begin{aligned}T_l^{-m} &= \exp\{i\widehat{\mathscr{H}}_0 t\}T_l^{-m}\exp\{-i\widehat{\mathscr{H}}_0 t\}\\ &= \sum_p \exp\{i\widehat{\mathscr{H}}_0 t\}T_l^{-mp}\exp\{-i\widehat{\mathscr{H}}_0 t\}\\ &= \sum_p T_l^{-mp}\exp\{-i\omega_p t\}.\end{aligned} \tag{226}$$

Using Eqs. (220), (225) and (226) combined with Eq. (62) one obtains (where we have written $\rho_{eq}(T_L)$ as ρ_{eq} for notational simplicity):

$$\begin{aligned}\frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = &-\xi^2\sum_{l=0}^{2}\sum_{m,m'}\sum_{p,p'}\exp\{i(-\omega_{p'}+\omega_p)t\}\left[T_l^{m'p'},\left[T_l^{mp},\tilde{\hat{\rho}}(t)-\tilde{\hat{\rho}}_{\text{eq}}\right]\right]\\ &\times\int_0^{\infty}\overline{F_l^{-m'}(t)F_l^m(t+\tau)\exp\{-i\omega_p\tau\}}d\tau,\end{aligned} \tag{227}$$

where we assume, for the sake of clarity, that only one interaction contributes to relaxation. More complete expressions are provided below. The imaginary parts of Eq. (227), which are also called *dynamic frequency shift* (see Section 2.3.3), are the second-order frequency shifts of resonance lines that are included in $\widehat{\mathscr{H}}_0$.

The real part of Eq. (227) can be written as:

$$\begin{aligned}\frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = &-\xi^2\sum_{l=0}^{2}\sum_{m,m'}\sum_{p,p'}\exp\{i(-\omega_{p'}+\omega_p)t\}\\ &\times\left[T_l^{m'p'},\left[T_l^{mp},\tilde{\hat{\rho}}(t)-\tilde{\hat{\rho}}_{\text{eq}}\right]\right]j_l^m(\omega_p),\end{aligned} \tag{228}$$

where the power spectral density function $j_l^m(\omega_p)$ is:

$$\begin{aligned}j_l^m(\omega_p) &= \text{Re}\int_{-\infty}^{\infty}\overline{F_l^{-m}(t)F_l^m(t-\tau)\exp\{-i\omega_p\tau\}}d\tau,\\ j_l^m(\omega_p) &= \text{Re}\int_{-\infty}^{\infty}\overline{F_l^m(t)F_l^{-m}(t+\tau)\exp\{-i\omega_p\tau\}}d\tau.\end{aligned} \tag{229}$$

Note that:

$$j_l^m(\omega) = (-1)^m j_l^0(\omega_p) = \frac{1}{2}(-1)^m J_l(\omega). \tag{230}$$

Thus we only need to calculate the spectral density function for $m = 0$ [55].

The time dependence of $F_l^m(t)$ for a rigid molecule comes only from the transformation from an arbitrary molecular basis frame to the laboratory frame, which is to say from molecular tumbling. Making use of Eqs. (96) and (100), we can write:

$$j_l^m(\omega_p) = \mathrm{Re}\int_{-\infty}^{+\infty} \overline{\sum_{m'=-l}^{l}\sum_{m''=-l}^{l} \mathscr{D}^{l*}_{m,m'}(\Omega(t))F_l^{m'}(\mathrm{AAF})\mathscr{D}^{l*}_{-m,m''}(\Omega(t+\tau))F_l^{m''}(\mathrm{AAF})\exp(-i\omega_p\tau)}\,d\tau. \tag{231}$$

We now use Eq. (C12) to link the correlation functions to the orientation probability of the molecule:

$$\begin{aligned} j_l^m(\omega_p) = {} & \mathrm{Re}\int_{-\infty}^{+\infty}\sum_{m'=-l}^{l}\sum_{m''=-l}^{l}(-1)^{m-m'} \\ & \times \int_{\Omega}\int_{\Omega_0}\mathscr{D}^{l}_{m,m'}(\Omega(t))\mathscr{D}^{l*}_{-m,m''}(\Omega(t+\tau))\mathscr{P}_{\mathrm{eq}}(\Omega_0)\mathscr{P}(\Omega,\tau|\Omega_0) \\ & \times F_l^{m'}(\mathrm{AAF})F_l^{m''}(\mathrm{AAF})\exp(-i\omega_p\tau)\,d\tau, \end{aligned} \tag{232}$$

where the orientations $\Omega,\ \Omega_0$ have been defined in Eqs. (C7)–(C9).

The probability $\mathscr{P}(\Omega,\ \tau|\Omega)$ is expressed in Eq. (147) and the equilibrium probability can be found in Eq. (188):

$$\begin{aligned} j_l^m(\omega_p) = {} & \mathrm{Re}\int_{-\infty}^{+\infty}\sum_{v}\sum_{m',m''}\sum_{s,r,r'}\sum_{u,v,v'}\frac{(-1)^{m-m'}}{(8\pi^2)^2} \\ & \times\sqrt{(2s+1)(2u+1)}c^{s}_{v,r,r'}c^{u}_{v,v,v'}e^{-b_v\tau}e^{-i\omega_p\tau} \\ & \times\int_{\Omega}\mathscr{D}^{l*}_{-m,m''}(\Omega)\mathscr{D}^{u}_{v,v'}(\Omega)\,d\Omega\int_{\Omega_0}\mathscr{D}^{l}_{-m,m'}(\Omega_0)\mathscr{D}^{s*}_{r,r'}(\Omega_0)\,d\Omega_0 \\ & \times F_l^{m'}(\mathrm{AAF})F_l^{m''}(\mathrm{AAF})\,d\tau. \end{aligned} \tag{233}$$

We now use the orthogonality relationship for Wigner functions Eq. (D87):

$$\begin{aligned} j_l^m(\omega_p) = {} & \mathrm{Re}\int_{-\infty}^{+\infty}\sum_{v}\sum_{m',m''}\sum_{s,r,r'}\sum_{u,v,v'}(-1)^{m-m'} \\ & \times\frac{\sqrt{(2s+1)(2u+1)}}{(2s+1)(2u+1)}c^{s}_{v,r,r'}c^{u}_{v,v,v'}e^{-(b_v+i\omega_p)\tau} \\ & \times\delta_{-m,v}\delta_{m'',v'}\delta_{l,u}\delta_{-m,r}\delta_{m',r'}\delta_{l,s}F_l^{m'}(\mathrm{AAF})F_l^{m''}(\mathrm{AAF})\,d\tau, \end{aligned} \tag{234}$$

so that

$$j_l^m(\omega_p) = \mathrm{Re}\int_{-\infty}^{+\infty}\sum_{v}\sum_{m',m''}\frac{(-1)^{m-m'}}{2l+1}c^{l}_{v,-m,m'}c^{l}_{-m,m''}e^{-(b_v+i\omega_p)\tau}F_l^{m'}(\mathrm{AAF})F_l^{m''}(\mathrm{AAF})\,d\tau. \tag{235}$$

Performing the Fourier transform, we finally obtain:

$$j_l^m(\omega_p) = \sum_{v}\sum_{m',m''}\frac{(-1)^{m-m'}}{2l+1}c^{l}_{v,-m,m'}c^{l}_{v,-m,m''}F_l^{m'}(\mathrm{AAF})F_l^{m''}(\mathrm{AAF})\,2\,\frac{b_v^{(l)}}{(b_v^{(l)})^2+\omega_p^2}. \tag{236}$$

It has been assumed that the random processes $F_l^m(t)$ and $F_l^{m'}(t)$ are statistically independent unless $m' = -m$, which results in a vanishing ensemble average in Eq. (227). Thus we can use a single index $c^{(l)}_{v,m}$ for the coefficients. The $b_v^{(l)}$ and $c^{(l)}_{v,m}$ have been defined in Section 4.2.1.3.

Terms in Eq. (228) for which $\omega_p - \omega_{p'} \neq 0$ are nonsecular (with few unusual exceptions) and they do not affect the long-term behavior of $\tilde{\hat{\rho}}(t)$. When none of the eigenfrequencies are degenerate, the terms in Eq. (228) are secular and nonzero only if $p = p'$, which yields:

$$\begin{aligned} \frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = {} & -\xi^2\sum_{l=0}^{2}\sum_{m} \\ & \times\sum_{p}\left[T_l^{-mp},\left[T_l^{mp},\tilde{\hat{\rho}}(t)-\tilde{\hat{\rho}}_{\mathrm{eq}}\right]\right](-1)^m j_l^m(\omega_p). \end{aligned} \tag{237}$$

Now, the isotropic $l = 0$ terms do not contribute to relaxation; the $l = 1$ are non-zero for CSA (see Section 3.1.2) but we have chosen to neglect them. The only relevant terms are the $l = 2$ terms in Eq. (237). Thus we have:

$$\frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = -\xi^2\sum_{m}\sum_{p}\left[T_2^{-mp},\left[T_2^{mp},\tilde{\hat{\rho}}(t)-\tilde{\hat{\rho}}_{\mathrm{eq}}\right]\right](-1)^m j_2^m(\omega_p). \tag{238}$$

Using Eq. (230), replacing $j_2(\omega)$ by $J(\omega_p)$, and dropping the subscript in $J_2(\omega_p)$ since $l = 2$ is assumed:

$$\frac{\partial\tilde{\hat{\rho}}(t)}{\partial t} = -\frac{1}{2}\xi^2\sum_{m}\sum_{p}\left[T_2^{-mp},\left[T_2^{mp},\tilde{\hat{\rho}}(t)-\tilde{\hat{\rho}}_{\mathrm{eq}}\right]\right]J(\omega_p). \tag{239}$$

This equation can be transformed back into the laboratory frame to obtain a modified version of the Liouville-von Neuman equation taking into account relaxation.

$$\frac{\partial\hat{\rho}(t)}{\partial t} = -i[\widehat{\mathscr{H}}_0,\hat{\rho}(t)] - \hat{\hat{R}}(\hat{\rho}(t)-\hat{\rho}_{\mathrm{eq}}). \tag{240}$$

The relaxation superoperator $\hat{\hat{R}}$ is given by

$$\hat{\hat{R}} = \frac{1}{2}\xi^2\sum_{m}\sum_{p}[(T_2^{-mp}),[(T_2^{mp}),]]J(\omega_p). \tag{241}$$

The stochastic Hamiltonian will contribute to relaxation under two conditions as can be seen in Eq. (240): (1) the double commutator cannot be zero and (2) the spectral density function must have a significant value at the characteristic frequencies ω_p of the spin system.

Using the basis of product operators (see Eq. (28)), we have the matrix form of the master equation in Liouville space:

$$\frac{\partial b_r(t)}{\partial t} = \sum_{s}\left\{-i\omega_{rs}b_s(t) - R_{B_r,B_s}\left[b_s(t)-b_s^0\right]\right\}, \tag{242}$$

with the frequency ω_{rs}:

$$\omega_{rs} = \frac{\left\langle\widehat{\mathscr{B}}_r\middle|\left[\widehat{\mathscr{H}}_0,\widehat{\mathscr{B}}_s\right]\right\rangle}{\left\langle\widehat{\mathscr{B}}_r\middle|\widehat{\mathscr{B}}_r\right\rangle}. \tag{243}$$

The relaxation rate R_{B_r,B_s} between the operators $\widehat{\mathscr{B}}_r$ and $\widehat{\mathscr{B}}_s$ can be calculated as:

$$R_{B_r,B_s} = \frac{\left\langle\widehat{\mathscr{B}}_r|\hat{\hat{R}}|\widehat{\mathscr{B}}_s\right\rangle}{\left\langle\widehat{\mathscr{B}}_r||\widehat{\mathscr{B}}_r\right\rangle},$$

$$R_{B_r,B_s} = \frac{(-1)^m}{2}\xi^2\sum_{m}\sum_{p}\left(\frac{\left\langle\widehat{\mathscr{B}}_r\middle|\left[T_{2p}^{-m},\left[T_{2p}^{m},\widehat{\mathscr{B}}_s\right]\right]\right\rangle}{\left\langle\widehat{\mathscr{B}}_r\middle|\widehat{\mathscr{B}}_r\right\rangle}\right)J(\omega_p). \tag{244}$$

When basis operators are normalized, $\mathrm{Tr}\{\mathscr{B}_r^2\} = \mathrm{Tr}\{\mathscr{B}_s^2\}$. When $r = s$, the diagonal element R_{B_r,B_r} is called the auto-relaxation rate of $\mathscr{B}_r$, whereas for $r \neq s$, the off diagonal element R_{B_r,B_s} is called the cross-relaxation rate between $\hat{\mathscr{B}}_r$ and $\hat{\mathscr{B}}_s$.

Eq. (240) has been derived assuming that all terms appear from the same interaction μ. However, as seen from Eq. (101) interference terms may occur when for two different sets of interactions μ and μ' (with $\mu \neq \mu'$) take place. In such a case Eq. (240) transforms to:

$$\frac{d\tilde{\hat{\rho}}(t)}{dt} = -\frac{1}{2}\sum_{\mu,\mu'}\xi_\mu\xi_{\mu'}\sum_m \times \sum_p \left[(T_2^{-mp})_{\mu'}, \left[(T_2^{mp})_{\mu'}, \tilde{\hat{\rho}}(t) - \tilde{\hat{\rho}}_{\mathrm{eq}}\right]\right](-1)^m J^{\mu\mu'}(\omega_p), \tag{245}$$

when $\mu \neq \mu', J^{\mu\mu'}(\omega_p)$ is the cross-correlation spectral density function.

Following similar steps as before we have the equivalent of Eq. (244)

$$R^{\mu\mu'}_{B_r,B_s} = \frac{1}{2}\xi_\mu\xi_{\mu'}\sum_m \times \sum_p \left(\frac{\left\langle \widehat{\mathscr{B}}_r \middle| \left[(T_2^{-mp})_{\mu}, \left[(T_2^{mp})_{\mu'}, \widehat{\mathscr{B}}_s\right]\right]\right\rangle}{\left\langle \widehat{\mathscr{B}}_r \middle| \widehat{\mathscr{B}}_r\right\rangle}\right)(-1)^m J^{\mu\mu'}(\omega_p). \tag{246}$$

$R^{\mu\mu'}_{rs}$ is the cross-correlated cross-relaxation rate between $\widehat{\mathscr{B}}_r$ and $\widehat{\mathscr{B}}_s$. Thus transforming back into the LAB frame (see Eq. (240)), in general we have:

$$\frac{d\hat{\rho}(t)}{dt} = -i[\mathscr{H}_0, \hat{\rho}(t)] - \sum_{\mu,\mu'}\hat{\hat{R}}^{\mu\mu'}(\hat{\rho}(t) - \hat{\rho}_{\mathrm{eq}}), \tag{247}$$

where the matrix elements $R^{\mu\mu'}_{B_r,B_s}$ of $\hat{\hat{R}}^{\mu\mu'}$ are given by Eq. (246).

6.2. Relaxation for a two-spin system

For a two-spin system $(\mathscr{I}, \mathscr{S})$ the 16-dimensional Liouville space leads to a 256-element relaxation superoperator. If the normalized identity basis vector, $\frac{1}{2}\hat{1}$, were to be ignored the resultant 15×15 matrix representation of $\hat{\hat{R}}$ is symmetric, i.e. $R_{B_r,B_s} = R_{B_s,B_r}$. While we neglect the identity basis vector in the current discussion, its inclusion makes the relaxation superoperator singular, but is required to predict the correct steady state. Several publications have discussed the so-called homogeneous superoperator that includes the identity [26–29]. Thus, one needs to calculate 15 diagonal and 105 off-diagonal elements. However, many off-diagonal terms are nonsecular, e.g. double-quantum terms cross-relax with double-quantum terms only, so that $\hat{\hat{R}}$ is block-diagonal: the so-called Redfield kite [24]. For the non-zero terms we present explicit calculations for three representative terms.

Remembering the definitions of the spin tensors derived in Section 3, we can calculate the double commutators $[T_2^{-mp}, [T_2^{mp}, \mathscr{I}_z]]$. These terms T_2^{mp} can be obtained from Eq. (137), realizing $T_2^m = -2X_2^m$.

Looking at Table 1, it is clear why each term T_2^m was split into constituent T_2^{mp}. The T_2^m term, for example, contains the so-called longitudinal two-spin order component, $\mathscr{I}_z\mathscr{S}_z$, which has an eigenvalue of zero under the static Hamiltonian $\widehat{\mathscr{H}}_0$, and also the zero-quantum 'flip-flop' terms T_2^{01} and $(T_2^{01})^*$ that have eigenvalues $\pm(\omega_I - \omega_S)$.

Similarly, we can obtain T_2^{mp} for the CSA interaction by using Eq. (117). These are shown in Table 2.

Table 1
Tensor operators for the spin part of the dipole-dipole interaction.

m	p	T_l^{mp}	$T_l^{-mp} = T_l^{mp*}$	ω_p
0	0	$\left(\frac{-4}{\sqrt{6}}\right)\mathscr{I}_z\mathscr{S}_z$	$\left(\frac{-4}{\sqrt{6}}\right)\mathscr{I}_z\mathscr{S}_z$	0
0	1	$\frac{1}{\sqrt{6}}\mathscr{I}_+\mathscr{S}_-$	$\frac{1}{\sqrt{6}}\mathscr{I}_-\mathscr{S}_+$	$\omega_{\mathscr{I}} - \omega_{\mathscr{S}}$
1	0	$\mathscr{I}_z\mathscr{S}_+$	$-\mathscr{I}_z\mathscr{S}_-$	$\omega_{\mathscr{S}}$
1	1	$\mathscr{I}_+\mathscr{S}_z$	$-\mathscr{I}_-\mathscr{S}_z$	$\omega_{\mathscr{I}}$
2	0	$-\mathscr{I}_+\mathscr{S}_+$	$-\mathscr{I}_-\mathscr{S}_-$	$\omega_{\mathscr{I}} + \omega_{\mathscr{S}}$

Table 2
Tensor operators for the spin part of the chemical shift anisotropy (CSA).

m	p	T_l^{mp}	$T_l^{-mp} = T_l^{mp*}$
0	0	$-\frac{4}{\sqrt{6}}\mathscr{I}_z$	$-\frac{4}{\sqrt{6}}\mathscr{I}_z$
1	0	$\mathscr{I}_+$	$-\mathscr{I}_-$
2	0	–	–

Having written the T_2^{mp} for the major interactions, we are now ready to derive the matrix elements of the relaxation superoperator $\hat{\hat{R}}$. Other excellent treatises [2] are available which provide expressions for most matrix elements of $\hat{\hat{R}}$. This review is designed to provide a general method to calculate relaxation rates, so we will only present three representative examples.

6.2.1. Auto-correlated relaxation

We first present the derivation of R_{I_+,I_+}, referred to as the spin-spin (or transverse) relaxation rate, R_2, which is an auto-relaxation rate. In Eq. (246):

$$\left|\widehat{\mathscr{B}}_s\right\rangle = \mathscr{I}_+; \qquad \left\langle\widehat{\mathscr{B}}_r\right| = \widehat{\mathscr{B}}_r^\dagger = (\mathscr{I}_+)^\dagger = \mathscr{I}_-. \tag{248}$$

6.2.1.1. DD contribution. For the auto-correlated contribution, i.e. $\mu = \mu' = \mathrm{DD}$ in Eq. (246), we first consider the relevant commutation operations term-by-term.

$$\left[(T_2^{-mp})_{\mathrm{DD}}, \left[(T_2^{mp})_{\mathrm{DD}}, \mathscr{I}_+\right]\right]. \tag{249}$$

Term 1: T_2^{00}

$$\left[T_2^{00}, \left[T_2^{00}, \mathscr{I}_+\right]\right] = \left(\frac{4}{\sqrt{6}}\right)^2 [\mathscr{I}_z\mathscr{S}_z, [\mathscr{I}_z\mathscr{S}_z, \mathscr{I}_+]] = \frac{8}{3} \times \frac{1}{4}\mathscr{I}_+ = \frac{2}{3}\mathscr{I}_+. \tag{250}$$

Taking the trace of the right-hand side and dividing by the normalization term, with $(T^+)^+ = T^-$ we have for term 1:

$$\frac{2}{3}\frac{\mathrm{Tr}\{\mathscr{I}_-\mathscr{I}_+\}}{\mathrm{Tr}\{\mathscr{I}_-\mathscr{I}_+\}} = \frac{2}{3}. \tag{251}$$

Thus, multiplying by the corresponding $J(\omega_p)$, we have the contribution of term 1:

$$(-1)^0\frac{2}{3}\,J(0) = \frac{2}{3}J(0). \tag{252}$$

Now consider the other terms of Table 1 one-by-one:

$$\begin{aligned}
&\left[T_2^{-01}, \left[T_2^{01}, \mathscr{I}_+\right]\right] = 0 \ \text{Term 2} \rightarrow 0,\\
&\left[T_2^{01}, \left[T_2^{-01}, \mathscr{I}_+\right]\right] = \frac{1}{6}\mathscr{I}_+ \ \text{Term 3} \rightarrow (-1)^0 J(\omega_I - \omega_S) \times \frac{1}{6} = \frac{1}{6}J(\omega_I - \omega_S),\\
&\left[T_2^{-10}, \left[T_2^{10}, \mathscr{I}_+\right]\right] = -\frac{1}{2}\mathscr{I}_+ \ \text{Term 4} \rightarrow (-1)^1 J(\omega_S) \times \left(-\frac{1}{2}\right) = \frac{1}{2}J(\omega_S),\\
&\left[T_2^{10}, \left[T_2^{-10}, \mathscr{I}_+\right]\right] = -\frac{1}{2}\mathscr{I}_+ \ \text{Term 5} \rightarrow (-1)^{-1} J(\omega_S) \times \left(-\frac{1}{2}\right) = \frac{1}{2}J(\omega_S),\\
&\left[T_2^{-11}, \left[T_2^{11}, \mathscr{I}_+\right]\right] = 0 \ \text{Term 6} \rightarrow 0,\\
&\left[T_2^{11}, \left[T_2^{-11}, \mathscr{I}_+\right]\right] = -\frac{1}{2}\mathscr{I}_+ \ \text{Term 7} \rightarrow (-1)^{-1} J(\omega_I) \times \left(-\frac{1}{2}\right) = \frac{1}{2}J(\omega_I),\\
&\left[T_2^{-20}, \left[T_2^{20}, \mathscr{I}_+\right]\right] = 0 \ \text{Term 8} \rightarrow 0,\\
&\left[T_2^{20}, \left[T_2^{-20}, \mathscr{I}_+\right]\right] = \mathscr{I}_+ \ \text{Term 9} \rightarrow (-1)^{-2} J(\omega_I + \omega_S) \times 1 = J(\omega_I + \omega_S).
\end{aligned} \tag{253}$$

Summing all terms, we find the contribution of dipole-dipole auto-correlation to the transverse relaxation rate to be:

$$\frac{2}{3}J(0)+\frac{1}{6}J(\omega_I-\omega_S)+2\frac{1}{2}J(\omega_S)+\frac{1}{2}J(\omega_I)+J(\omega_I+\omega_S)$$
$$=\frac{1}{6}(4J(0)+J(\omega_I-\omega_S)+6J(\omega_S)+3J(\omega_I)+6J(\omega_I+\omega_S)). \tag{254}$$

The dipole–dipole contribution to R_{I_+,I_+} becomes:

$$R^{\mathrm{DD}}_{I_+,I_+}=\frac{1}{2}\xi'^2_{DD}\frac{1}{6}(4J(0)+J(\omega_I-\omega_S)+6J(\omega_S)+3J(\omega_I)+6J(\omega_I+\omega_S)), \tag{255}$$

where for constant r_{IS}

$$\xi'_{\mathrm{DD}}=\left(\frac{\mu_0}{4\pi}\right)\sqrt{\frac{3}{2}}\frac{\gamma_I\gamma_S\hbar}{r^3_{IS}}, \tag{256}$$

and thus, we have:

$$R^{\mathrm{DD}}_{I_+,I_+}=\frac{1}{8}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\gamma_I^2\gamma_S^2\hbar^2}{r^6_{IS}}(4J(0)+J(\omega_I-\omega_S)+6J(\omega_S)+3J(\omega_I)$$
$$+6J(\omega_I+\omega_S)). \tag{257}$$

6.2.1.2. CSA contribution. Next we consider the CSA of spin $\mathscr{I}$ to be finite and axially symmetric. Using Table 2 we obtain:

Term 1: T_2^{00}

$$\left[T_2^{00},\left[T_2^{00},\mathscr{I}_+\right]\right]=\frac{8}{3}[\mathscr{I}_z,[\mathscr{I}_z,\mathscr{I}_+]]=\frac{8}{3}\mathscr{I}_+. \tag{258}$$

Leading to a contribution of $(-1)^0\,J(0)\times\frac{8}{3}=\frac{8}{3}J(0)$.

$$\left[T_2^{-00},\left[T_2^{00},\mathscr{I}_+\right]\right]=0\ \text{Term2}\rightarrow 0,$$
$$\left[T_2^{00},\left[T_2^{-00},\mathscr{I}_+\right]\right]=2\mathscr{I}_+\ \text{Term3}\rightarrow(-1)^0J(\omega_I)\times 2=2J(\omega_I). \tag{259}$$

Thus the total contribution from the CSA becomes:

$$R^{\mathrm{CSA}}_{I_+,I_+}=\frac{1}{2}\xi'^2_{\mathrm{CSA,I}}\frac{2}{3}(4J(0)+3J(\omega_I)). \tag{260}$$

with

$$\xi'_{\mathrm{CSA,I}}=\frac{\Delta\sigma_I\gamma_I B_0}{\sqrt{6}}, \tag{261}$$

thus we have:

$$R^{\mathrm{CSA,I}}_{I_+,I_+}=\frac{\Delta\sigma_I^2\gamma_I^2B_0^2}{18}(4J(0)+3J(\omega_I)). \tag{262}$$

Finally, we have:

$$R_{I_+,I_+}=R^{\mathrm{DD}}_{I_+,I_+}+R^{\mathrm{CSA,I}}_{I_+,I_+} \tag{263}$$

thus

$$R_{I_+,I_+}=\frac{1}{8}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\gamma_I^2\gamma_S^2\hbar^2}{r^6_{IS}}(4J(0)+J(\omega_I-\omega_S)+6J(\omega_S)+3J(\omega_I)$$
$$+6J(\omega_I+\omega_S))+\frac{\Delta\sigma_I^2\gamma_I^2B_0^2}{18}(4J(0)+3J(\omega_I)). \tag{264}$$

Following the derivation of an auto-correlated auto-relaxation rate, we now provide an example of auto-correlated cross-relaxation, choosing the operators $\widehat{\mathscr{B}}_r$ and $\widehat{\mathscr{B}}_s$ to be $\mathscr{S}_z$ and $\mathscr{I}_z$, respectively. We evaluate each term in Eq. (246) and find that non-zero commutators arise from the term T_2^{01} and its complex conjugate, thus

$$\left[T_2^{-01},\left[T_2^{01},\mathscr{I}_z\right]\right]=\frac{1}{6}(\mathscr{I}_z-\mathscr{S}_z) \tag{265}$$

and

$$\frac{\left\langle\mathscr{S}_z\middle|\left[T_2^{-01},\left[T_2^{01},\mathscr{I}_z\right]\right]\right\rangle}{\langle\mathscr{S}_z|\mathscr{S}_z\rangle}=\frac{1}{6}\frac{\langle\mathscr{S}_z|\mathscr{I}_z-\mathscr{S}_z\rangle}{\langle\mathscr{S}_z|\mathscr{S}_z\rangle}=-\frac{1}{6}. \tag{266}$$

The term, T_2^{01}, contributes $(-1)^0\,J(\omega_I-\omega_S)\times(-\frac{1}{6})=-\frac{1}{6}J(\omega_I-\omega_S)$. A similar contribution comes from the corresponding complex conjugate making the total contribution $-\frac{1}{3}J(\omega_I-\omega_S)$. The only other contributions come from terms corresponding to row 5 of Table 1. This contribution is $2J(\omega_I+\omega_S)$. Thus we have:

$$R_{S_z,I_z}=\frac{1}{2}\xi'^2_{DD}\frac{1}{3}(-J(\omega_I-\omega_S)+6J(\omega_I+\omega_S)) \tag{267}$$

which for constant intermolecular distance r_{IS}:

$$R_{S_z,I_z}=\frac{1}{4}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\gamma_I^2\gamma_S^2\hbar^2}{r^6_{IS}}(-J(\omega_I-\omega_S)+6J(\omega_I+\omega_S)). \tag{268}$$

R_{S_z,I_z} is related to the so-called steady-state NOE in the following way:

$$NOE=1+\frac{R_{S_z,I_z}}{R_{I_z,I_z}}\frac{\gamma_S}{\gamma_I}. \tag{269}$$

6.2.2. Cross-correlated relaxation

Finally, we derive the cross-correlated cross-relaxation rate, due to the interference between the dipolar interactions of the $\mathscr{I}$ and $\mathscr{S}$ spins ($\mu=\mathrm{DD}$) and CSA ($\mu'=\mathrm{CSA}$) interactions of the $\mathscr{I}$ spin [56,57]. From the secular approximation, the only non-zero contribution to $\Gamma_{I_z,2I_zS_z}$ corresponds to the contributions of row 4 in Table 1 and row 2 in Table 2:

$$\left[(T_2^{-10})_{\mathrm{DD}},\left[(T_2^{11})_{\mathrm{CSA}},2\mathscr{I}_z\mathscr{S}_z\right]\right]=-[\mathscr{I}_-\mathscr{S}_z,[\mathscr{I}_+,2\mathscr{I}_z\mathscr{S}_z]]$$
$$=-[\mathscr{I}_-\mathscr{S}_z,2\mathscr{I}_+\mathscr{S}_z]$$
$$=-2\mathscr{S}_z^2[\mathscr{I}_-,\mathscr{I}_+]=4\mathscr{S}_z^2\mathscr{I}_z=\mathscr{I}_z. \tag{270}$$

Taking the trace with $\mathscr{I}_z$ and multiplying by the corresponding spectral density term, we obtain a contribution of $(-1)^1J^{\mu\mu'}(\omega_I)$.

Considering the three other combinations of $(T_2^{-10})_{\mathrm{DD}}$, $(T_2^{11})_{\mathrm{CSA}}$, $(T_2^{10})_{\mathrm{DD}}$ and $(T_2^{-11})_{\mathrm{CSA}}$ we have a total contribution of $-4J(\omega_I)$. In the limit of isotropic overall tumbling and an axially symmetric CSA tensor for $\mathscr{I}, R_{I_z,2I_{zz}}$ is given by

$$R_{I_z,2I_zS_z}=-\frac{1}{2}\xi'_{\mathrm{DD}}\xi'_{\ \mathrm{CSA}}4J^{\mu\mu'}(\omega_I)$$
$$=-\left(\frac{\mu_0}{4\pi}\right)\frac{\gamma_I^2\gamma_S\hbar}{r^3_{IS}}B_0\Delta\sigma_I\frac{(3cos^2\theta-1)}{2}J(\omega_I), \tag{271}$$

where

$$J^{\mu\mu'}(\omega_I)=\frac{(3cos^2\theta-1)}{2}J(\omega_I), \tag{272}$$

and θ is the angle between the $\mathscr{I}\mathscr{S}$ dipolar vector and the unique axis of the CSA tensor of spin $\mathscr{I}$.

7. Conclusions

We have provided a unified, self-consistent description of the microscopic (quantum) interactions that influence dynamics in spin-space for an ensemble of spin-1/2 particles, as well as the real-space effects of the macroscopic (classical) global rotational diffusion determined both by molecular shape and the nature of the solvent, and finally the combined effects of the two on the spin-relaxation rates measured by NMR spectroscopists. The measurement of amide ^{15}N spin-lattice (R_1), spin–spin

(R_2) and the steady-state NOE with the attached hydrogen has become routine for practitioners of biomolecular NMR spectroscopy, both expert as well as non-expert [58–60]. These rates can be used to determine the underlying spectral density functions and to interpret them using the Lipari-Szabo formalism (the so-called 'model-free' approach) that relies on the separation of the global rotational diffusion and local dynamics on single [61,62] or multiple timescales [63,64]. This separation is formally possible only for isotropic overall diffusion in an isotropic medium and is thus not covered here. Good approximations can be used for auto-correlated relaxation in the case of weakly anisotropic diffusion. All spectral density functions in this review have been derived assuming that the spin-system under consideration is rigidly attached to the biomolecule and that the only motion results from the overall rotational diffusion. The reader is referred to the original papers [61,62] or pedagogical treatises [2,65] on the topic for further details. It is to be mentioned here that alternative approaches that do not require such a separation have also been proposed, but have not yet been widely applied [66,67].

In this review, we have chosen not to derive detailed expressions for all possible matrix elements of the 16-component relaxation superoperator for a simple two spin-1/2 system, providing three illustrative calculations instead. The general expressions provided here should allow the reader to calculate the relaxation rates for the remaining elements. In recent years, a wide array of sophisticated pulse sequences have been developed to measure a large number of these matrix elements, i.e. auto-relaxation and cross-relaxation rates of different sets of coherences. The reader is referred to the excellent book by Cavanagh et al. [2] and the references therein for examples.

Most results presented here are available, in varying levels of detail, throughout dispersed literature. It is hoped that our detailed derivations and presentation in a consistent formalism will be helpful for a more general understanding of the origins, approximations, and theoretical underpinnings of spin-relaxation in isotropic and anisotropic media.

Acknowledgements

This work has been partially suppoted by a grant MCB0843141 from the National Science Foundation. The NMR facility at the City College of New York is partially supported by a grant 5G12 RR003060 from the National Institutes of Health.

Appendix A. Miscellaneous theorems

We present here some theorems that will be of use in deriving some of the expressions provided in the text.

A.1. Operator exponentials

The exponential $e^{k\widehat{\mathscr{A}}t}$ of an operator $\widehat{\mathscr{A}}$ can be written as a Taylor series,

$$e^{k\widehat{\mathscr{A}}t} = \sum_{n=0}^{\infty} \frac{(kt)^n \widehat{\mathscr{A}}^n}{n!}. \tag{A1}$$

The time derivative is given by

$$\frac{\partial}{\partial t} e^{k\widehat{\mathscr{A}}t} = \sum_{n=1}^{\infty} \frac{k^n t^{n-1} \widehat{\mathscr{A}}^n}{n!} \tag{A2}$$

so that:

$$\frac{\partial}{\partial t} e^{k\widehat{\mathscr{A}}t} = k\widehat{\mathscr{A}} e^{k\widehat{\mathscr{A}}t} = e^{k\widehat{\mathscr{A}}t} k\widehat{\mathscr{A}}. \tag{A3}$$

If $|\lambda\rangle$ is the eigenstate and E is the eigenvalue of an operator, i.e.

$$\widehat{\mathscr{A}}|\lambda\rangle = E|\lambda\rangle \tag{A4}$$

by using Eq. (A1) one can show:

$$e^{ik\widehat{\mathscr{A}}}|\lambda\rangle = e^{ikE}|\lambda\rangle. \tag{A5}$$

A.2. Properties of the commutator

A.2.1. Unitary operator–commutator product

Let $\widehat{\mathscr{U}}$ be an unitary operator ($\widehat{\mathscr{U}}^\dagger \widehat{\mathscr{U}} = \widehat{\mathscr{U}}\widehat{\mathscr{U}}^\dagger = \widehat{\mathbb{1}}$), and $\widehat{\mathscr{A}}$ and $\widehat{\mathscr{B}}$ denote arbitrary operators. Then we may write:

$$\widehat{\mathscr{U}}\left[\widehat{\mathscr{A}}, \widehat{\mathscr{B}}\right]\widehat{\mathscr{U}}^\dagger = \left[\widehat{\mathscr{U}}\widehat{\mathscr{A}}\widehat{\mathscr{U}}^\dagger, \widehat{\mathscr{U}}\widehat{\mathscr{B}}\widehat{\mathscr{U}}^\dagger\right]. \tag{A6}$$

A.2.2. 'Distributivity' of the commutator

We employ the following in Section A.5. For any three operators $\widehat{\mathscr{A}}$, $\widehat{\mathscr{B}}$, and $\widehat{\mathscr{C}}$

$$\left[\widehat{\mathscr{A}} + \widehat{\mathscr{B}}, \widehat{\mathscr{C}}\right] = \left[\widehat{\mathscr{A}}, \widehat{\mathscr{C}}\right] + \left[\widehat{\mathscr{B}}, \widehat{\mathscr{C}}\right]. \tag{A7}$$

A.3. Interaction representation for $\widehat{\mathscr{H}}_1(t)$

The Hamiltonian for relaxation interactions is given by the following in the interaction representation:

$$\begin{aligned}\widetilde{\widehat{\mathscr{H}}}_1(t) &= e^{i\widehat{\mathscr{H}}_0 t}\widehat{\mathscr{H}}_1(t)e^{-i\widehat{\mathscr{H}}_0 t} = e^{i\widehat{\mathscr{H}}_0 t}\sum_\mu \widehat{\mathscr{H}}_\mu(t)e^{-i\widehat{\mathscr{H}}_0 t} \\ &= \sum_\mu e^{i\widehat{\mathscr{H}}_0 t}\widehat{\mathscr{H}}_\mu(t)e^{-i\widehat{\mathscr{H}}_0 t} = \sum_\mu \widetilde{\widehat{\mathscr{H}}}_\mu(t).\end{aligned} \tag{A8}$$

A.4. Change of representation: similarity and unitary transformations

A.4.1. Change of basis by a linear transformation

Let $\widehat{\mathscr{S}}$ denote a linear, invertible (non-singular, i.e. $\det(\mathscr{S}) \neq 0$) operation that transforms one basis set $\mathfrak{B} = \{|i_{\mathfrak{B}}\rangle\}$ spanning an n-dimensional Hilbert space $\mathbb{H}$ into another set of n vectors $\mathfrak{C} = \{|i_{\mathfrak{C}}\rangle\}$ that are also in $\mathbb{H}$. For all the vectors in each basis set, we have

$$\widehat{\mathscr{S}}|i_{\mathfrak{B}}\rangle = |i_{\mathfrak{C}}\rangle \quad \widehat{\mathscr{S}}^{-1}|i_{\mathfrak{C}}\rangle = |i_{\mathfrak{B}}\rangle. \tag{A9}$$

Any vector $|v\rangle$ in $\mathbb{H}$ may be written in the basis $\mathfrak{B}$ as an expansion $|v\rangle = \sum_{i=1}^n v_i^{(\mathfrak{B})}|i_{\mathfrak{B}}\rangle$ where $v_i^{(\mathfrak{B})}$ is the ith component of $|v\rangle$ in the basis $\mathfrak{B}$ (analogous expressions hold for any other basis). Since $\widehat{\mathscr{S}}$ is linear, $|w\rangle = \widehat{\mathscr{S}}^{-1}|v\rangle$ is an element of $\mathbb{H}$, and it follows that

$$\begin{aligned}|w\rangle &= \widehat{\mathscr{S}}^{-1}|v\rangle = \sum_{i=1}^n w_i^{(\mathfrak{B})}|i_{\mathfrak{B}}\rangle, \\ |v\rangle &= \widehat{\mathscr{S}}|w\rangle = \sum_{i=1}^n w_i^{(\mathfrak{B})}\widehat{\mathscr{S}}|i_{\mathfrak{B}}\rangle = \sum_{i=1}^n w_i^{(\mathfrak{B})}|i_{\mathfrak{C}},\rangle\end{aligned} \tag{A10}$$

where the last expression has the same form as the expansion of a vector in a basis set. Thus, since $|v\rangle$ is an arbitrary vector, $\mathfrak{C}$ forms a basis for $\mathbb{H}$, and any linear, invertible transformation may be regarded simply as a change of basis.

Given that $\mathfrak{B}$ and $\mathfrak{C}$ form bases for $\mathbb{H}$, we may write

$$\begin{aligned}|v\rangle^{(\mathfrak{B})} &= \mathscr{S}^{(\mathfrak{B})}|v\rangle^{(\mathfrak{C})}, \\ |v\rangle^{(\mathfrak{C})} &= \mathscr{S}^{(\mathfrak{B})^{-1}}|v\rangle^{(\mathfrak{B})},\end{aligned} \tag{A11}$$

where $\mathscr{S}^{(\mathfrak{B})}$ denotes the matrix representation of $\widehat{\mathscr{S}}$ in the basis $\mathfrak{B}$, and $|v\rangle^{(\mathfrak{B})}$ and $|v\rangle^{(\mathfrak{C})}$ denote the column-vector representations (i.e. the list of components) of the vector $|v\rangle$ in bases $\mathfrak{B}$ and

$\mathfrak{C}$, respectively. We thus have clear rules for how vector components transform under a change of basis.

A.4.2. Transformation of operators under a change of basis: similarity transformations

We now determine how operator elements transform under a change of basis. Consider the general operator (basis-independent) equation $|u\rangle = \widehat{\mathscr{A}}|v\rangle$, where $\widehat{\mathscr{A}}$ is an arbitrary operator. We may write in each of the two bases $\mathfrak{B}$ and $\mathfrak{C}$

$$|u\rangle^{(\mathfrak{B})} = \mathscr{A}^{(\mathfrak{B})}|v\rangle^{(\mathfrak{B})} \tag{A12}$$

and

$$|u\rangle^{(\mathfrak{C})} = \mathscr{A}^{(\mathfrak{C})}|v\rangle^{(\mathfrak{C})}. \tag{A13}$$

Using the first of Eqs. (A11), we may write Eq. (A12) as

$$\begin{aligned} \mathscr{S}^{(\mathfrak{B})}|u\rangle^{(\mathfrak{C})} &= \mathscr{A}^{(\mathfrak{B})}\mathscr{S}^{(\mathfrak{B})}|v\rangle^{(\mathfrak{C})}, \\ |u\rangle^{(\mathfrak{C})} &= \mathscr{S}^{(\mathfrak{B})^{-1}}\mathscr{A}^{(\mathfrak{B})}\mathscr{S}^{(\mathfrak{B})}|v\rangle^{(\mathfrak{C})}. \end{aligned} \tag{A14}$$

Comparing Eqs. (A14) and (A13), we see that

$$\mathscr{A}^{(\mathfrak{C})} = \mathscr{S}^{(\mathfrak{B})^{-1}}\mathscr{A}^{(\mathfrak{B})}\mathscr{S}^{(\mathfrak{B})}, \tag{A15}$$

and through application of analogous logic to Eq. (A13) and comparison to Eq. (A12)

$$\mathscr{A}^{(\mathfrak{B})} = \mathscr{S}^{(\mathfrak{B})}\mathscr{A}^{(\mathfrak{C})}\mathscr{S}^{(\mathfrak{B})^{-1}}. \tag{A16}$$

Eqs. (A15) and (A16) are called *similarity transformations*, and are mathematical formulations of a result that is intuitively obvious: the action of an operator in a given (arbitrary) basis may be divided into the following steps: (1) transform the vector (operand) into a basis where the matrix representation of the operator is known, (2) operate on the transformed vector using the matrix representation of the operator in that basis, (3) transform the vector (modified by the operator) back into the original basis.

Similarity transformations are useful when converting matrices into convenient forms for computation (e.g. changing to a basis in which the matrix representation of a given operator is diagonal, as in the the principal axis frame of the diffusion tensor). As should be expected from a change of representation, basis-independent operator properties are constant among the various matrix representations produced through similarity transformations. Of particular interest, similarity transformations conserve the value of the determinant

$$\left|\mathscr{A}^{(\mathfrak{C})}\right| = \left|\mathscr{S}^{(\mathfrak{B})^{-1}}\right|\left|\mathscr{A}^{(\mathfrak{B})}\right|\left|\mathscr{S}^{(\mathfrak{B})}\right| = \left|\mathscr{S}^{(\mathfrak{B})^{-1}}\mathscr{S}^{(\mathfrak{B})}\right|\left|\mathscr{A}^{(\mathfrak{B})}\right| = \left|\mathscr{A}^{(\mathfrak{B})}\right|, \tag{A17}$$

where we have employed the relation $|\mathscr{A}\mathscr{B}| = |\mathscr{A}||\mathscr{B}|$. Therefore, a similarity transformation leaves the characteristic polynomial unchanged

$$\left|\mathscr{A}^{(\mathfrak{C})} - \lambda\mathbb{1}^{(\mathfrak{C})}\right| = \left|\mathscr{S}^{(\mathfrak{B})^{-1}}\mathscr{A}^{(\mathfrak{B})}\mathscr{S}^{(\mathfrak{B})} - \mathscr{S}^{(\mathfrak{B})^{-1}}\lambda\mathbb{1}^{(\mathfrak{B})}\mathscr{S}^{(\mathfrak{B})}\right| = \left|\mathscr{A}^{(\mathfrak{B})} - \lambda\mathbb{1}^{(\mathfrak{B})}\right| \tag{A18}$$

and thus the eigenvalues of $\mathscr{A}^{(\mathfrak{B})}$ and $\mathscr{A}^{(\mathfrak{C})}$ are the same (though the column eigenvectors generally are not). This feature allows us to represent operators (or tensors) in an arbitrary interaction frame (AAF), and then transform into other frames (PAF, LAB, etc.), while preserving eigenvalues, norms, etc. Finally, the trace is preserved

$$\begin{aligned} \mathrm{Tr}\left(\mathscr{A}^{(\mathfrak{C})}\right) &= \sum_{i=1}^{n}\mathscr{A}_{ii}^{(C)} = \sum_{i,j,k=1}^{n}\left(\mathscr{S}^{(\mathfrak{B})^{-1}}\right)_{ij}\mathscr{A}_{jk}^{(\mathfrak{B})}\mathscr{S}_{ki}^{(\mathfrak{B})} \\ &= \sum_{j,k=1}^{n}\delta_{jk}\mathscr{A}_{jk}^{(\mathfrak{B})} = \sum_{k=1}^{n}\mathscr{A}_{kk}^{(\mathfrak{B})} = \mathrm{Tr}\left(\mathscr{A}^{(\mathfrak{B})}\right). \end{aligned} \tag{A19}$$

A.4.3. Unitary transformations: rotations

A special class of similarity transformation is the unitary transformation, for which $\widehat{\mathscr{S}} = \widehat{\mathscr{U}}$, with $\widehat{\mathscr{U}}^{\dagger}\widehat{\mathscr{U}} = \widehat{\mathscr{U}}\widehat{\mathscr{U}}^{\dagger} = \widehat{\mathbb{1}}$ (that is, $\widehat{\mathscr{U}}^{-1} = \widehat{\mathscr{U}}^{\dagger}$). We may write

$$\begin{aligned} &|i_{\mathfrak{C}}\rangle = \widehat{\mathscr{U}}|i_{\mathfrak{B}}\rangle, \\ &\langle i_{\mathfrak{C}} \mid j_{\mathfrak{C}}\rangle = \langle i_{\mathfrak{B}}|\widehat{\mathscr{U}}^{\dagger}\widehat{\mathscr{U}}|j_{\mathfrak{B}}\rangle = \langle i_{\mathfrak{B}} \mid j_{\mathfrak{B}}\rangle, \end{aligned} \tag{A20}$$

from which we see that under a unitary transformation of a basis set, the magnitudes of the basis vectors are maintained (the $i = j$ cases), and the projections of each basis vector on to every other one also remain constant (the $i \neq j$ cases). Geometrically, this implies that the lengths of the basis vectors and the 'angles' between all of them are preserved under unitary transformations. Such transformations therefore describe simple rotations, like the transformation from the laboratory (LAB) to the principal axes frame (PAF) of the various interaction tensors. Calculations involving the CSA and the dipolar tensors shown in Section 3, and those involving the diffusion tensor in Section 4 all make use of unitary transformations.

A.4.4. Active and passive transformations

Notice that the components of $|v\rangle$ in Eq. (A11) transform inversely to the way the basis vectors themselves transform (compare to Eq. (A9)). This is because, under a change of basis, the vector $|v\rangle$ is in fact unchanged; it is only the coordinate system that is modified. For example, consider the case where $\widehat{\mathscr{S}}$ produces a simple rotation in real, three-dimensional space: the coordinate axes are rotated by some finite angle about a given axis, and the vector components transform in the opposite sense (by an equal and opposite angle of rotation about the same axis), so as to maintain the correct specification of the abstract vector. Because the vector (i.e. the physical system) itself remains unchanged, a change-of-basis operation is classified as a *passive transformation*.

It is clear from this description that a mathematically-equivalent description is obtained by performing an *active transformation* that leaves the coordinate frame constant (i.e. leaves the basis vectors unchanged), but transforms all of the vectors in the opposite sense to that in which the basis vectors are modified in a passive transformation. In this case, however, the operation of an arbitrary operator $\widehat{\mathscr{A}}$ on the basis vectors remains unchanged (because the basis itself is unchanged), and therefore, the matrix elements of $\widehat{\mathscr{A}}$ are constant under an active transformation. Notice that the designation of active versus passive transformations is referenced to the vectors rather than the operators. Vectors are changed in active transformations, and left untouched in passive ones. The operators are constant in active transformations, and undergo similarity transformation in passive ones.

A.5. Density matrix evolution in the interaction frame

We now consider the transformation of a system evolving under a Hamiltonian $\widehat{\mathscr{H}} = \widehat{\mathscr{H}}_0 + \widehat{\mathscr{H}}_1(t)$, where $\widehat{\mathscr{H}}_0$ is time-independent, with the time evolution described by Eq. (38). Using the unitary operators $\widehat{\mathscr{U}} = e^{i\widehat{\mathscr{H}}_0 t}$ and $\widehat{\mathscr{U}}^{\dagger} = e^{-i\widehat{\mathscr{H}}_0 t}$, where $\widehat{\mathscr{H}}_0 t$ is time-independent, we have

$$\begin{aligned} \frac{\partial}{\partial t}\tilde{\hat{\rho}} &= \frac{\partial}{\partial t}\left[\widehat{\mathscr{U}}\hat{\rho}\widehat{\mathscr{U}}^{\dagger}\right] = \frac{\partial\widehat{\mathscr{U}}}{\partial t}\hat{\rho}\widehat{\mathscr{U}}^{\dagger} + \widehat{\mathscr{U}}\frac{\partial\hat{\rho}}{\partial t}\widehat{\mathscr{U}}^{\dagger} + \widehat{\mathscr{U}}\hat{\rho}\frac{\partial\widehat{\mathscr{U}}^{\dagger}}{\partial t} \\ &= i\widehat{\mathscr{H}}_0\widehat{\mathscr{U}}\hat{\rho}\widehat{\mathscr{U}}^{\dagger} + \widehat{\mathscr{U}}\left(-i\left[\widehat{\mathscr{H}}(t),\hat{\rho}\right]\right)\widehat{\mathscr{U}}^{\dagger} + \widehat{\mathscr{U}}\hat{\rho}\widehat{\mathscr{U}}^{\dagger}\left(-i\widehat{\mathscr{H}}_0\right) \\ &= i\widehat{\mathscr{H}}_0\tilde{\hat{\rho}} - i\widehat{\mathscr{U}}\left[\widehat{\mathscr{H}}(t),\hat{\rho}\right]\widehat{\mathscr{U}}^{\dagger} - i\tilde{\hat{\rho}}\widehat{\mathscr{H}}_0 \\ &= i\left[\widehat{\mathscr{H}}_0,\tilde{\hat{\rho}}\right] - i\widehat{\mathscr{U}}\left[\widehat{\mathscr{H}}(t),\hat{\rho}\right]\widehat{\mathscr{U}}^{\dagger}. \end{aligned} \tag{A21}$$

Using Eq. (A6), the last term is:

$$\begin{aligned} i\widehat{\mathscr{U}}\left[\widehat{\mathscr{H}}(t),\hat{\rho}\right]\widehat{\mathscr{U}}^{\dagger} &= i\left[\widehat{\mathscr{U}}\widehat{\mathscr{H}}\widehat{\mathscr{U}}^{\dagger},\widehat{\mathscr{U}}\hat{\rho}\widehat{\mathscr{U}}^{\dagger}\right] \\ &= i\left[\widehat{\mathscr{U}}\left(\widehat{\mathscr{H}}_0+\widehat{\mathscr{H}}_1(t)\right)\widehat{\mathscr{U}}^{\dagger},\tilde{\hat{\rho}}\right] \\ &= i\left[\widehat{\mathscr{U}}\widehat{\mathscr{H}}_0\widehat{\mathscr{U}}^{\dagger}+\widehat{\mathscr{U}}\widehat{\mathscr{H}}_1(t)\widehat{\mathscr{U}}^{\dagger},\tilde{\hat{\rho}}\right] \\ &= i\left[\widehat{\mathscr{H}}_0\widehat{\mathscr{U}}\widehat{\mathscr{U}}^{\dagger}+\widetilde{\widehat{\mathscr{H}}}_1(t),\tilde{\hat{\rho}}\right] \\ &= i\left[\widehat{\mathscr{H}}_0+\widetilde{\widehat{\mathscr{H}}}_1(t),\tilde{\hat{\rho}}\right]. \end{aligned} \tag{A22}$$

Therefore, using Eq. (A7) we obtain,

$$\frac{\partial}{\partial t}\tilde{\hat{\rho}} = -i\left[\widetilde{\widehat{\mathscr{H}}}_1(t),\tilde{\hat{\rho}}\right], \tag{A23}$$

where the effects of the static component $\widehat{\mathscr{H}}_0$ have been removed.

Appendix B. Treatment of NMR interactions

B.1. Dipole–dipole interaction energy

The quantum mechanical Hamiltonian for dipolar coupling is justified by the analogous formula for interaction energy of two magnetic dipoles obtained through classical electromagnetic theory. The relevant calculation is presented below.

B.1.1. Magnetic field due to a point dipole

Consider a magnetic dipole moment (i.e. an infinitesimal current loop), the location of which we take to define the origin of our coordinate system. In SI units, the magnetic vector potential at a location described by the position vector $\vec{r} = r\hat{e}_r$ due to this magnetic dipole is given by

$$\vec{A}_{\mathrm{D}} = \frac{\mu_0}{4\pi}\frac{\vec{\mu}\times\vec{r}}{r^3}, \tag{B1}$$

where × denotes the vector cross product, $\vec{\mu} = \mu\hat{e}_z$ is the magnetic dipole moment, $\hat{e}_z$ is a unit vector pointing along the z-axis of a right-handed Cartesian coordinate system, and $\mu_0 = 4\pi\times 10^{-7}\ \mathrm{kg\ m\ s^{-2}\ A^{-2}}$ is the permeability of free space (not to be confused with the magnetic dipole moment). In spherical polar coordinates (r,θ,ϕ)(not to be confused with Euler angles), where θ and ϕ are the polar and azimuthal angles, respectively (following the convention most often used in physics [49]).

$$\hat{e}_z = \cos\theta\ \hat{e}_r - \sin\theta\ \hat{e}_\theta \tag{B2}$$

and we have

$$\vec{\mu}\times\vec{r} = \mu(\cos\theta\ \hat{e}_r - \sin\theta\ \hat{e}_\theta)\times r\ \hat{e}_r \tag{B3}$$

and since $\hat{e}_r\times\hat{e}_r = 0$ and $\hat{e}_\theta\times\hat{e}_r = -\hat{e}_\phi$

$$\vec{\mu}\times\vec{r} = \mu r\sin\theta\ \hat{e}_\phi. \tag{B4}$$

The magnetic field $\vec{B}_{\mathrm{D}}$ produced by the magnetic dipole is given by the curl of $\vec{A}_{\mathrm{D}}$:

$$\vec{B}_{\mathrm{D}} = \vec{\nabla}\times\vec{A}_{\mathrm{D}}, \tag{B5}$$

where in spherical coordinates the curl of an arbitrary function V is defined as:

$$\vec{\nabla}\times\vec{V} = \frac{1}{r^2\sin\theta}\begin{vmatrix} \hat{e}_r & r\ \hat{e}_\theta & r\sin\theta\ \hat{e}_\phi \\ \frac{\partial}{\partial r} & \frac{\partial}{\partial\theta} & \frac{\partial}{\partial\phi} \\ V_r & rV_\theta & r\sin\theta V_\phi \end{vmatrix}. \tag{B6}$$

Since $\vec{A}_{\mathrm{D}}$ has neither $\hat{e}_r$ nor $\hat{e}_\theta$ components ($A_{\mathrm{D}_r} = A_{\mathrm{D}_\theta} = 0$), and

$$A_{\mathrm{D}_\phi} = \frac{\mu_0}{4\pi}\frac{\mu\sin\theta}{r^2}, \tag{B7}$$

we have

$$\begin{aligned} \vec{B}_{\mathrm{D}} &= \frac{1}{r^2\sin\theta}\begin{vmatrix} \hat{e}_r & r\ \hat{e}_\theta & r\sin\theta\ \hat{e}_\phi \\ \frac{\partial}{\partial r} & \frac{\partial}{\partial\theta} & \frac{\partial}{\partial\phi} \\ 0 & 0 & r\sin\theta A_{\mathrm{D}_\phi} \end{vmatrix} \\ &= \frac{\mu_0}{4\pi}\frac{1}{r^2\sin\theta}\left[\frac{\partial}{\partial\theta}\left(\frac{\mu\sin^2\theta}{r}\right)\hat{e}_r - \frac{\partial}{\partial r}\left(\frac{\mu\sin^2\theta}{r}\right)r\ \hat{e}_\theta\right] \\ &= \frac{\mu_0}{4\pi}\frac{2\mu\cos\theta\ \hat{e}_r\ +\ \mu\sin\theta\ \hat{e}_\theta}{r^3}. \end{aligned} \tag{B8}$$

Employing Eq. (B2) once more

$$\vec{B}_{\mathrm{D}} = \frac{\mu_0}{4\pi}\frac{2\mu\cos\theta\hat{e}_r + \mu(\cos\theta\hat{e}_r - \hat{e}_z)}{r^3} = \frac{\mu_0}{4\pi}\left[\frac{3\mu\cos\theta\hat{e}_r}{r^3} - \frac{\vec{\mu}}{r^3}\right] \tag{B9}$$

and using the definition of the scalar dot product:

$$\vec{B}_{\mathrm{D}} = \frac{\mu_0}{4\pi}\left[\frac{3(\vec{\mu}\cdot\vec{r})\hat{e}_r}{r^4} - \frac{\vec{\mu}}{r^3}\right]. \tag{B10}$$

or somewhat more elegantly

$$\vec{B}_{\mathrm{D}} = \frac{\mu_0}{4\pi}\left[\frac{3(\vec{\mu}\cdot\vec{r})\ \vec{r}}{r^5} - \frac{\vec{\mu}}{r^3}\right]. \tag{B11}$$

B.1.2. Interaction energy between two point dipoles

The potential energy, E, of a magnetic dipole placed in a magnetic field $\vec{B}$ is given by

$$E = -\vec{\mu}\cdot\vec{B} \tag{B12}$$

Thus, the interaction energy, $E_{\mathrm{D_1D_2}}$, between two magnetic dipoles $\vec{\mu}_1$ and $\vec{\mu}_2$ is given by

$$E_{\mathrm{D_1D_2}} = -\vec{\mu}_1\cdot\vec{B}_{\mathrm{D}_2} = \frac{\mu_0}{4\pi}\left[\frac{\vec{\mu}_1\cdot\vec{\mu}_2}{r^3} - \frac{3(\vec{\mu}_1\cdot\vec{r})(\vec{\mu}_2\cdot\vec{r})}{r^5}\right] \tag{B13}$$

which is Eq. (123).

B.2. Chemical shielding

The presence of an applied magnetic field induces an electrical current in the electron cloud surrounding a nucleus, thereby generating an additional magnetic field. As a result, the total magnetic field at nucleus is changed. This effect can enhance (de-shielding) or decrease (shielding) the strength of the magnetic field at the nucleus and may also change the effective orientation of the magnetic field such that the applied and the total magnetic fields at the nucleus are not colinear. The difference can be inferred by the perturbation of the vector potential ($\vec{A}$) by the electron cloud. It is also correct to say that the external magnetic field creates a magnetic dipole moment at the nucleus, which creates a perturbed vector potential.

The shielding effect depends on the orientation of the external field; hence it should be described by a tensor rather than a scalar number. The orientational dependence of the chemical shielding on the external magnetic field can be observed in solid-state NMR [68].

For a nucleus with a magnetic moment $\vec{\mu}$ in an external magnetic field $\vec{B}$, the energy change ΔE is given by [69]

$$\Delta E = -\vec{\mu}\cdot\vec{B} + \vec{\mu}\cdot\hat{\sigma}\ \vec{B}, \tag{B14}$$

where the first term is the direct interaction of the nucleus with the field (the so-called Zeeman interaction) while the second term is the electron-coupled interaction described by the shielding tensor $\widehat{\sigma}$.

Before starting the actual description of the perturbation effects we should note the differences between the terms "chemical shift" and "chemical shielding". The chemical shielding, as described above, is an orientation-dependent tensor quantity that describes the change in the local magnetic field (i.e. the field sensed by the nucleus) due to the interaction of the electron cloud with the external field, whereas the chemical shift is the change of the resonance frequency of a nucleus relative to a given standard [68].

The relation between chemical shift, $\widehat{\delta}$, and chemical shielding tensor can be expressed as:

$$\widehat{\delta} = \widehat{\mathbb{1}}\,\sigma_{\text{iso}} - \widehat{\sigma}, \tag{B15}$$

where $\widehat{\mathbb{1}}$ is the unit rank-2 tensor, σ_{iso} is the isotropic value of the given standard and $\widehat{\sigma}$ is the chemical shielding tensor.

The chemical shielding tensor is a 3×3 matrix with nine non-zero components (in general). The tensor itself is asymmetric, but the number of independent non-zero components can be reduced by molecular symmetry. One can define each term of the matrix representation of $\widehat{\sigma}$ as:

$$\sigma_{ik} = \frac{\partial^2 E}{\partial \mu_i \partial B_k}, \tag{B16}$$

where E is the total electronic energy of the molecule, $i, k = x, y, z$, and B_k are the components of the external magnetic field in the direction k.

The energy E is determined by using second-order perturbation theory. Excellent reviews are available on the calculation of chemical shift tensor elements. We refer the reader to these reviews without reproducing the results here [70–73].

Appendix C. Correlation functions and spectral densities

C.1. The auto-correlation function

Consider any function $\Omega(t)$ that takes a random value at each point in time, governed by the probability $P(\Omega, t)$. That is, $P(\Omega, t)$ gives the probability that $\Omega(t)$ will take the value Ω at time t. Such a function $\Omega(t)$ can define, for example, the orientation of a body undergoing rotational diffusion, in time.

The average value of $\Omega(t)$, i.e. the average orientation, is given by integrating over all possible orientations, Ω, at a given time:

$$\overline{\Omega(t)} = \int \Omega(t) P(\Omega, t) d\Omega. \tag{C1}$$

A function $f(t) = f(\Omega(t))$ will likewise be random in time, with an average value

$$\overline{f(t)} = \int f(\Omega) P(\Omega, t) d\Omega. \tag{C2}$$

The averages in Eqs. (C1) and (C2) may be interpreted physically in a similar way as the average in Eq. (44); that is, as ensemble averages over an ensemble of particles undergoing independent rotational diffusion. In the case of relaxation, Hamiltonians for interactions such as the dipolar coupling and chemical shift anisotropy satisfy the requirements for the function $f(\Omega(t))$: spatial functions that are constant in the molecular diffusion frame are stochastic functions in the lab frame, due to the effect of rotational diffusion that constantly reorients the molecule with respect to the external field.

Now, we may consider that while $\Omega(t)$ is random, for short times τ the values $\Omega(t)$ and $\Omega(t+\tau)$ will not be completely independent random variables, but will instead show a correlation. Physically, this must be the case for rotational diffusion, since the diffuser cannot instantaneously 'jump' from one orientation to another that is significantly different. Defining $t' = t + \tau$, we can define the function $P(\Omega', t'; \Omega, t)$ as the probability that $\Omega(t) = \Omega$ and $\Omega(t') = \Omega'$. We define the conditional probability $P(\Omega', t' | \Omega, t)$ as the probability that $\Omega(t') = \Omega'$ *given that we know* $\Omega(t) = \Omega$ at the earlier time t. We may thus interpret $P(\Omega', t' | \Omega, t)$ as a probability of 'transition' from orientation Ω to Ω' over the time $\tau = t' - t$.

$P(\Omega', t'; \Omega, t)$ depends on the probability that the diffuser is in state Ω at time t to begin with (which has a probability $P(\Omega, t)$ of occurring), and then on the probability of the transition to state Ω' over time τ (which has probability $P(\Omega', t' | \Omega, t)$ of occurring). Then we may write:

$$P(\Omega', t'; \Omega, t) = P(\Omega, t) P(\Omega', t' | \Omega, t). \tag{C3}$$

The *auto-correlation* function $G_a(t, t')$, of a random function $f_a(t)$ with itself relative to times t and t', is defined as

$$G_a(t, t') = \overline{f_a(t) f_a^*(t')}, \tag{C4}$$

where the overbar denotes an ensemble average.

In the same vein as Eq. (C2), we may rewrite the auto-correlation function as

$$G_a(t, t') = \int\int f_a(\Omega) f_a^*(\Omega') P\big(\Omega', t'; \Omega, t\big) d\Omega d\Omega' \tag{C5}$$

and employing Eq. (C3),

$$G_a(t, t') = \int\int P(\Omega, t) P\big(\Omega', t' | \Omega, t\big) f_a(\Omega) f_a^*(\Omega') d\Omega d\Omega'. \tag{C6}$$

We assume rotational diffusion to be a Markovian process, which is to say that the future state of the system depends only on the present state, and not upon how it arrived there (i.e. the system has no 'memory'). This implies that the statistical properties of $\Omega(t)$ – that is, the functions $P(\Omega, t)$ – are in fact independent of time (i.e. $\Omega(t)$ are *stationary* random functions). Furthermore, the functions $P(\Omega', t' | \Omega, t)$ and $P(\Omega', t'; \Omega, t)$ do not depend specifically on the times t and t', but rather on their difference τ. Thus, it does not matter *when* we start measuring the auto-correlation function; what matters is only the period of time over which we measured it (i.e. how *long* we measure it for). Simply stated, all the probability functions are independent of the origin of time, which implies ergodicity. As a result, we may arbitrarily set $t = 0$, yielding:

$$\begin{aligned}
&t' = \tau, \\
&G_a(t, t') \to G_a(\tau), \\
&P(\Omega, t) \to P(\Omega_0), \\
&P(\Omega', t' | \Omega, t) \to P(\Omega, \tau | \Omega_0),
\end{aligned} \tag{C7}$$

where Ω_0 denotes the value of $\Omega(t)$ at time $t = 0$. The auto-correlation function is then

$$G_a(\tau) = \int\int f_a(\Omega_0) f_a^*(\Omega) P(\Omega_0) P(\Omega, \tau | \Omega_0) d\Omega d\Omega_0. \tag{C8}$$

In the case of rotational diffusion, we assume that the system is at equilibrium at $t = 0$, and denote the equilibrium probability distribution function as $P(\Omega_0) = P_{\text{eq}}(\Omega_0)$. The auto-correlation function can be written as [74]:

$$G_a(\tau) = \int\int f_a(\Omega_0) f_a^*(\Omega) P_{\text{eq}}(\Omega_0) P(\Omega, \tau | \Omega_0, 0) d\Omega d\Omega_0. \tag{C9}$$

C.2. The cross-correlation function

The *cross-correlation* of two random functions $f_a(\Omega)$ and $f_b(\Omega)$ is defined using the same reasoning as above for the auto-correlation, yielding

$$G_{ab}(\tau) = \overline{f_a(t) f_b^*(t')} \tag{C10}$$

and

$$G_{ab}(t,t') = \int\int f_a(\Omega) f_b^*(\Omega') P(\Omega', t'; \Omega, t) d\Omega d\Omega'. \tag{C11}$$

Taking $t = 0$ and assuming the system to be at equilibrium initially,

$$G_{ab}(\tau) = \int\int f_a(\Omega_0) f_b^*(\Omega) P_{\mathrm{eq}}(\Omega_0) P(\Omega, \tau|\Omega_0) d\Omega d\Omega_0. \tag{C12}$$

It may of course be considered that the auto-correlation function is simply a special case of the cross-correlation function for which $b = a$.

C.3. Properties of correlation functions

As discussed above, for ergodic processes $f_a(t)$, we may arbitrarily move the origin of time without affecting the value of the correlation function. We may therefore write

$$G_{ab}(\tau) = \overline{f_a(0) f_b^*(\tau)} = \overline{f_a(-\tau) f_b^*(0)}, \tag{C13}$$

which is to say

$$G_{ab}(\tau) = G_{ba}^*(-\tau). \tag{C14}$$

Consider the auto-correlation function $G_a(\tau)$. If $f_a(\tau)$ is a real function, then $G_a^*(\tau) = G_a(\tau)$ and $G_a(\tau)$ is thus both real and even:

$$G_a(\tau) = G_a(-\tau). \tag{C15}$$

For real functions $f_a(t)$ and $f_b(t)$, the correlation function is a maximum at the origin (this is plain to see for auto-correlation: at $\tau = 0$ a function is perfectly correlated with itself):

$$|G_{ab}(\tau)| \leqslant G_{ab}(0). \tag{C16}$$

C.4. Operator correlation functions

The concept of correlation is not restricted to scalar functions. We may just as easily define correlation between stochastic operators $\widehat{\mathscr{A}}_a(t)$ and $\widehat{\mathscr{A}}_b(t)$, simply replacing complex conjugate operations with the adjoint, and considering an operator and its Hermitian conjugate in place of real and complex scalar functions:

$$G^{(ab)}_{iji'j'} = \overline{\langle i|\mathscr{A}_a(t)|j\rangle\langle j'|\mathscr{A}_b^\dagger(t+\tau)|i'\rangle}, \tag{C17}$$

where the various kets are basis kets. Since Hamiltonians are Hermitian, $\widehat{\mathscr{H}}_a = \widehat{\mathscr{H}}_a^\dagger$, their correlation is given simply by

$$G^{(ab)}_{iji'j'} = \overline{\langle i|\mathscr{H}_a(t)|j\rangle\langle j'|\mathscr{H}_b(t+\tau)|i'\rangle}. \tag{C18}$$

C.5. The spectral density functions

The *spectral density* function $J_{ab}(\omega)$ (often referred to as the *power spectrum*) is defined simply as the Fourier transform of the correlation function:

$$J_{ab}(\omega) = \int_{-\infty}^{\infty} G_{ab}(\tau) e^{-i\omega\tau} d\tau = J_{ba}^*(\omega) \tag{C19}$$

Thus, the auto-correlated spectral density function $J_a(\omega)$ is real. Employing the Euler identity $e^{i\theta} = \cos\theta + i\sin\theta$, we may write,

$$\begin{aligned} J_{ab}(\omega) &= \int_{-\infty}^{\infty} G_{ab}(\tau)[\cos(-\omega\tau) + i\sin(-\omega\tau)]d\tau \\ &= \int_{-\infty}^{\infty} G_{ab}(\tau)[\cos(\omega\tau) - i\sin(\omega\tau)]d\tau. \end{aligned} \tag{C20}$$

Since for a real, ergodic function $f_a(t)$, the auto-correlation $G_a(\tau)$ is an even function, it follows that:

$$J_a(\omega) = 2\int_0^{\infty} G_a(\tau)\cos(\omega\tau)d\tau \tag{C21}$$

and in this case $J_a(\omega)$ is also a real and even function: $J_a(\omega) = J_a(-\omega)$. In addition, we note without proof that the auto-correlated spectral density function of an ergodic process is non-negative for all ω.

Eq. (C21) facilitates the definition of two other auto-correlated spectral density functions of ergodic processes which appear often in the main text, $j_a(\omega)$ and $K_a(\omega)$. Rewriting Eq. (C21) and employing the Euler identity in the opposite sense as in Eq. (C20), we have

$$\begin{aligned} \frac{1}{2}J_a(\omega) &= \int_0^{\infty} G_a(\tau)[\cos(\omega\tau) - i\sin(\omega\tau) + i\sin(\omega\tau)]d\tau \\ &= \int_0^{\infty} G_a(\tau)e^{-i\omega\tau}d\tau + i\int_0^{\infty} G_a(\tau)\sin(\omega\tau)d\tau \end{aligned} \tag{C22}$$

and defining

$$\begin{aligned} j_a(\omega) &= \int_0^{\infty} G_a(\tau)e^{-i\omega\tau}d\tau, \\ K_a(\omega) &= \int_0^{\infty} G_a(\tau)\sin(\omega\tau)d\tau, \end{aligned} \tag{C23}$$

we have

$$j_a(\omega) = \frac{1}{2}J_a(\omega) - iK_a(\omega). \tag{C24}$$

Thus the real and imaginary parts of $j_a(\omega)$, respectively, are given by

$$\begin{aligned} \mathrm{Re}\{j_a(\omega)\} &= \frac{1}{2}J_a(\omega), \\ \mathrm{Im}\{j_a(\omega)\} &= -K_a(\omega). \end{aligned} \tag{C25}$$

The correlation function is written in terms of the spectral density $J_{ab}(\omega)$ as

$$G_{ab}(\tau) = \frac{1}{2\pi}\int_{-\infty}^{\infty} J_{ab}(\omega)e^{i\omega\tau}d\omega. \tag{C26}$$

For $\tau = 0$, Eq. (C26) becomes

$$G_{ab}(0) = \frac{1}{2\pi}\int_{-\infty}^{\infty} J_{ab}(\omega)d\omega. \tag{C27}$$

Likewise,

$$G_a(0) = \overline{f_a(t)^2} = \frac{1}{2\pi}\int_{-\infty}^{\infty} J_{ab}(\omega)d\omega. \tag{C28}$$

In the event that $f_a(t)$ represents a component of a fluctuating magnetic field (e.g. one of the various mechanisms leading to relaxation), the quantity in Eq. (C28) represents an expansion in the frequency spectrum of the power dissipated by the process.

C.6. Correlation times

A *correlation time* is defined somewhat loosely as a time interval τ_c such that $G(\tau_c)$ is large. Correlation does not exist for significantly longer intervals: $|\tau| \gg \tau_c$, and $G(\tau)$ decays rapidly for times longer than τ_c. Various definitions for τ_c are appropriate depending on the interaction in question. For example, one option is to use the total area under the $G(\tau)$ curve as a metric of the length of the effective correlation time:

$$\tau_c = \int_0^{\infty} |G(\tau)|d\tau. \tag{C29}$$

Alternatively, one might choose a differential definition of the effective τ_c that measures the 'decay' slope of $G(\tau)$:

$$\tau_c = \left|\frac{d}{d\tau}G(\tau)\Big|_{\tau=0}\right|^{-1}. \tag{C30}$$

Several factors affect the correlation time of the rotation of a given rigid molecule, including molecular size, molecular shape, solvent viscosity, and temperature. In water, τ_c is typically on the order of hundreds of picoseconds for small molecules, and on the order of nanoseconds for macromolecules [2].

Appendix D. Fundamental theory of angular momentum and rotations

In this appendix, we present the fundamental results of angular momentum theory. Much of this material is covered in standard quantum mechanics texts [19,50,51], and Brink and Satchler [75], Zare [76], and Rose [77] have written excellent books devoted to the topic of angular momentum and rotations (we follow arguments from both of these latter two books below). In addition, Silver [78] provides a thorough yet accessible treatment of irreducible tensor methods.

The physical and mathematical tools developed in this appendix are central to this article, and must be fully understood in order to appreciate the details of both relaxation theory and rotational diffusion theory.

D.1. Orbital angular momentum operators

D.1.1. Operator definitions

Classically, a particle of mass m travelling with velocity $\vec{v}$ at position $\vec{r}$ has linear momentum $\vec{p} = m\vec{v}$ and angular momentum

$$\vec{L} = \vec{r} \times \vec{p}, \tag{D1}$$

where $\times$ denotes the vector cross product. $\vec{\widehat{\mathscr{L}}}$, the quantum mechanical counterpart of $\vec{L}$ in Eq. (D1), is obtained by replacing $\vec{p}$ with the operator $\hat{p} = \frac{\hbar}{i}\nabla$ where ∇ is the gradient 'del' operator $\nabla = \frac{\partial}{\partial x}\hat{e}_x + \frac{\partial}{\partial y}\hat{e}_y + \frac{\partial}{\partial z}\hat{e}_z$ (and $\hat{e}_x, \hat{e}_y$, and $\hat{e}_z$ are unit vectors in a right-handed Cartesian coordinate system). The form of $\hat{p}$ may be justified according to its role as the generator of infinitesimal translation (see Appendix D.3.1). The $\hat{p}$ operator is clearly Hermitian. For notational convenience, we shall proceed using so-called Planck's units in which $\hbar = 1$, as in the main text. The operator components of the quantum mechanical angular momentum vector operator $\widehat{\mathscr{L}}$ are then

$$\widehat{\mathscr{L}}_j = -i\left(k\frac{\partial}{\partial l} - l\frac{\partial}{\partial k}\right), \tag{D2}$$

where $\{j,k,l\} = \{x,y,z\}$ and cyclic permutations; that is, $\{j,k,l\} = \{\{x,y,z\},\{y,z,x\},\{z,x,y\}\}$. In spherical polar coordinates (r,θ,ϕ), where θ and ϕ are the polar and azimuthal angles, respectively,

$$\begin{aligned}
\widehat{\mathscr{L}}_x &= i\left(\sin\phi\frac{\partial}{\partial\theta} + \cot\theta\cos\phi\frac{\partial}{\partial\phi}\right),\\
\widehat{\mathscr{L}}_y &= i\left(-\cos\phi\frac{\partial}{\partial\theta} + \cot\theta\sin\phi\frac{\partial}{\partial\phi}\right),\\
\widehat{\mathscr{L}}_z &= -i\frac{\partial}{\partial\phi}.
\end{aligned} \tag{D3}$$

By writing their matrix representations in a suitable basis of eigenfunctions (see below), it can be verified that these operators are Hermitian (they thus have strictly real eigenvalues corresponding to quantum mechanical observables, namely, the projection of total angular momentum onto each axis). These operators correspond to the *orbital* angular momentum of a particle, due to the motion of its center of mass about an external point.

The angular momentum operators obey commutation relations of the form

$$\left[\widehat{\mathscr{L}}_j, \widehat{\mathscr{L}}_k\right] = i\widehat{\mathscr{L}}_l, \tag{D4}$$

where, again, $\{j,k,l\} = \{x,y,z\}$ and cyclic permutations.

These relationships may be easily verified through the application of the various operators to test functions (i.e. confirming that $[\widehat{\mathscr{L}}_j, \widehat{\mathscr{L}}_k]f = \widehat{\mathscr{L}}_j\widehat{\mathscr{L}}_k f - \widehat{\mathscr{L}}_k\widehat{\mathscr{L}}_j f = \widehat{\mathscr{L}}_l f$ for any function f). The commutation relation (D4) is also frequently expressed in the literature using the equivalent equation, $[\widehat{\mathscr{L}}_j, \widehat{\mathscr{L}}_k] = i\epsilon_{jkl}\widehat{\mathscr{L}}_l$, where ϵ_{jkl} is known as the Levi-Civita symbol or asymmetric unit (pseudo)tensor, and is defined by $\epsilon_{xyz} = \epsilon_{yzx} = \epsilon_{zxy} = 1$, $\epsilon_{xzy} = \epsilon_{yxz} = \epsilon_{zyx} = -1$, and all other $\epsilon_{jkl} = 0$. The commutation relation is also occasionally given as $\vec{\widehat{\mathscr{L}}} \times \vec{\widehat{\mathscr{L}}} = i\vec{\widehat{\mathscr{L}}}$, which is indeed quite elegant, if less immediately informative than the other expressions.

The total angular momentum squared operator $\widehat{\mathscr{L}}^2$ is defined as

$$\widehat{\mathscr{L}}^2 = \vec{\widehat{\mathscr{L}}} \cdot \vec{\widehat{\mathscr{L}}} = \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + \widehat{\mathscr{L}}_z^2, \tag{D5}$$

which can be expressed in spherical polar coordinates as

$$\widehat{\mathscr{L}}^2 = -\left[\frac{1}{\sin^2\theta}\frac{\partial^2}{\partial\phi^2} + \frac{1}{\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial}{\partial\theta}\right)\right]. \tag{D6}$$

The operator obeys the commutation relations

$$\left[\widehat{\mathscr{L}}^2, \widehat{\mathscr{L}}_x\right] = \left[\widehat{\mathscr{L}}^2, \widehat{\mathscr{L}}_y\right] = \left[\widehat{\mathscr{L}}^2, \widehat{\mathscr{L}}_z\right] = 0, \tag{D7}$$

which, like Eq. (D4), may be verified through application of the operators to arbitrary test functions. Since the orientation of the coordinate system may be chosen arbitrarily, Eq. (D7) shows that $\widehat{\mathscr{L}}^2$ commutes with the projection of the orbital angular momentum on *any* Cartesian axis.

D.1.2. Eigenfunctions and eigenvalues

Two quantum mechanical variables are 'compatible' – that is, they may be measured/observed simultaneously and without uncertainty – if states exist that have well-defined eigenvalues for the operators corresponding to *both* variables. That is, two variables are simultaneously observable if there is a complete, simultaneous set of eigenfunctions of both corresponding operators (any arbitrary state vector may be expanded in such a basis). The existence of such eigenfunctions implies that the operators corresponding to such variables commute. This is readily seen by considering two operators $\widehat{\mathscr{A}}$ and $\widehat{\mathscr{B}}$ with simultaneous eigenfunctions $|a,b\rangle$. For all eigenfunctions $|a,b\rangle$:

$$\begin{aligned}
&\widehat{\mathscr{A}}|a,b\rangle = a|a,b\rangle,\\
&\widehat{\mathscr{B}}|a,b\rangle = b|a,b\rangle,\\
&\widehat{\mathscr{A}}\widehat{\mathscr{B}}|a,b\rangle = b\widehat{\mathscr{A}}|a,b\rangle = ba|a,b\rangle,\\
&\widehat{\mathscr{B}}\widehat{\mathscr{A}}|a,b\rangle = a\widehat{\mathscr{B}}|a,b\rangle = ba|a,b\rangle,\\
&\quad\Rightarrow \widehat{\mathscr{A}}\widehat{\mathscr{B}} - \widehat{\mathscr{B}}\widehat{\mathscr{A}} = [\widehat{\mathscr{A}}, \widehat{\mathscr{B}}] = 0.
\end{aligned} \tag{D8}$$

Because the various $\widehat{\mathscr{L}}_j$ do not commute with each other, while each commutes with $\widehat{\mathscr{L}}^2$, we may know only the total angular momentum (squared) and *one* of the components with simultaneous certainty. In other words, the eigenfunctions of $\widehat{\mathscr{L}}^2$ are simultaneous eigenfunctions of one of the $\widehat{\mathscr{L}}_j$, the identity of which depends on how we choose our coordinate system. By convention, we take this to be $\widehat{\mathscr{L}}_z$, though we could have chosen another axis just as easily. Thus we may choose normalized states $|\lambda_l, m\rangle$ such that

$$\begin{aligned}
&\widehat{\mathscr{L}}^2|\lambda_l, m\rangle = \lambda_l|\lambda_l, m\rangle,\\
&\widehat{\mathscr{L}}_z|\lambda_l, m\rangle = m|\lambda_l, m\rangle,
\end{aligned} \tag{D9}$$

so that λ_l is proportional to the square of the total angular momentum, and m is proportional to the projection of the total angular momentum onto the laboratory z-axis.

Consider the operator $\widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 = \widehat{\mathscr{L}}^2 - \widehat{\mathscr{L}}_z^2$, which is diagonal in the $\{|\lambda_l, m\rangle\}$ basis since all $|\lambda_l, m\rangle$ are eigenfunction of both $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$

$$\left(\widehat{\mathscr{L}}^2 - \widehat{\mathscr{L}}_z^2\right)|\lambda_l, m\rangle = \left(\lambda_l - m^2\right)|\lambda_l, m\rangle. \tag{D10}$$

The quantity $\lambda_l - m^2$ is clearly greater than or equal to zero since each term is the square of a real scalar, and the total angular momentum is larger in magnitude than its projection onto the z-axis. We then have $\lambda_l \geqslant m^2$, implying that the values of m for a given λ_l are bounded between some $m = m_{\max}$ and $m = m_{\min}$. Let us denote these extreme values of m more succinctly, as l and l':

$$l \equiv m_{\max} \leqslant m \leqslant m_{\min} \equiv l'. \tag{D11}$$

In the following sections, we will define the nature of these eigenfunctions and eigenvalues more precisely.

D.1.3. Definition of ladder operators

We define two operators $\widehat{\mathscr{L}}_+$ and $\widehat{\mathscr{L}}_-$

$$\widehat{\mathscr{L}}_\pm \equiv \widehat{\mathscr{L}}_x \pm i\widehat{\mathscr{L}}_y \tag{D12}$$

or in spherical polar coordinates,

$$\widehat{\mathscr{L}}_\pm = e^{\pm i\phi}\left(\pm\frac{\partial}{\partial\theta} + i\cot\theta\frac{\partial}{\partial\phi}\right), \tag{D13}$$

which are non-Hermitian (in fact, $\widehat{\mathscr{L}}_\pm^\dagger = \widehat{\mathscr{L}}_\mp$), and therefore do not have real eigenvalues that correspond to observables. That is to say, there is no simple correspondence between these operators and any physical quantity or measurement. They are nevertheless quite useful in examining the nature of wave functions.

It is readily obtained from Eqs. (D4) and (D7) that

$$\begin{gathered}\left[\widehat{\mathscr{L}}^2, \widehat{\mathscr{L}}_\pm\right] = 0 \quad \left[\widehat{\mathscr{L}}_z, \widehat{\mathscr{L}}_\pm\right] = \pm\widehat{\mathscr{L}}_\pm, \\ \left[\widehat{\mathscr{L}}_+, \widehat{\mathscr{L}}_-\right] = 2\widehat{\mathscr{L}}_z.\end{gathered} \tag{D14}$$

Let us examine the second of the commutation relations (D14) by application to an eigenfunction $|\lambda_l, m\rangle$:

$$\begin{aligned}\left[\widehat{\mathscr{L}}_z, \widehat{\mathscr{L}}_\pm\right]|\lambda_l, m\rangle &= \pm\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle \\ &= \widehat{\mathscr{L}}_z\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle - \widehat{\mathscr{L}}_\pm\widehat{\mathscr{L}}_z|\lambda_l, m\rangle \\ &= \widehat{\mathscr{L}}_z\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle - m\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle, \\ \widehat{\mathscr{L}}_z\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle &= \left(m\widehat{\mathscr{L}}_\pm \pm \widehat{\mathscr{L}}_\pm\right)|\lambda_l, m\rangle, \\ \widehat{\mathscr{L}}_z\left(\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle\right) &= (m \pm 1)\left(\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle\right).\end{aligned} \tag{D15}$$

According to Eq. (D9), this implies that

$$\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle = \lambda_\pm|\lambda_l, m \pm 1\rangle, \tag{D16}$$

where the constants λ_+ and λ_- have yet to be determined. Thus, $\widehat{\mathscr{L}}_+$ and $\widehat{\mathscr{L}}_-$, aptly referred to as the raising and lowering operators, respectively (or ladder operators as a pair), operate on the eigenstates $|\lambda_l, m\rangle$ so as to alter m by ± 1 while preserving the value of λ_l, producing 'new' states that are also eigenstates of $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$. Because the value of m is strictly bounded between l and l' (see Eq. (D11)), $\widehat{\mathscr{L}}_+$ and $\widehat{\mathscr{L}}_-$ act at the top and bottom of the state 'ladder', respectively, to annihilate the state rather than transform it (they are therefore also called creation and annihilation operators). That is:

$$\widehat{\mathscr{L}}_+|\lambda_l, l\rangle = \widehat{\mathscr{L}}_-|\lambda_l, l'\rangle = 0. \tag{D17}$$

Notice that beginning with any single eigenstate for a given value of λ_l, one could use the ladder operators to determine every other possible state of equivalent λ_l-value.

D.1.4. Determination of eigenvalues using ladder operators

With an understanding of the ladder operators, consider the operator $\widehat{\mathscr{L}}_-\widehat{\mathscr{L}}_+$, which we now use to determine the form of the eigenvalues λ_l and m. Using Eq. (D12), we have

$$\begin{aligned}\widehat{\mathscr{L}}_-\widehat{\mathscr{L}}_+ &= (\widehat{\mathscr{L}}_x - i\widehat{\mathscr{L}}_y)(\widehat{\mathscr{L}}_x + i\widehat{\mathscr{L}}_y) \\ &= \widehat{\mathscr{L}}_x^2 + i\widehat{\mathscr{L}}_x\widehat{\mathscr{L}}_y - i\widehat{\mathscr{L}}_y\widehat{\mathscr{L}}_x + \widehat{\mathscr{L}}_y^2 \\ &= \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + i(\widehat{\mathscr{L}}_x\widehat{\mathscr{L}}_y - \widehat{\mathscr{L}}_y\widehat{\mathscr{L}}_x) \\ &= \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + i\left[\widehat{\mathscr{L}}_x, \widehat{\mathscr{L}}_y\right] = \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + i^2\widehat{\mathscr{L}}_z \\ &= \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 - \widehat{\mathscr{L}}_z = \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + (\widehat{\mathscr{L}}_z^2 - \widehat{\mathscr{L}}_z^2) - \widehat{\mathscr{L}}_z \\ &= \widehat{\mathscr{L}}^2 - \widehat{\mathscr{L}}_z^2 - \widehat{\mathscr{L}}_z.\end{aligned} \tag{D18}$$

Applying this operator to an eigenfunction with maximal $m = l$,

$$\begin{aligned}&\widehat{\mathscr{L}}_-\widehat{\mathscr{L}}_+|\lambda_l, l\rangle = \widehat{\mathscr{L}}_-(0) = 0, \\ &\left(\widehat{\mathscr{L}}^2 - \widehat{\mathscr{L}}_z^2 - \widehat{\mathscr{L}}_z\right)|\lambda_l, l\rangle = (\lambda_l - l^2 - l)|\lambda_l, l\rangle = 0,\end{aligned} \tag{D19}$$

which implies

$$\lambda_l = l(l+1). \tag{D20}$$

Using identical reasoning for the operator $\widehat{\mathscr{L}}_+\widehat{\mathscr{L}}_- = \widehat{\mathscr{L}}^2 - \mathscr{L}_z^2 + \mathscr{L}_z$ and applying it to an eigenfunction $|\lambda_l, l'\rangle$ with minimal $m = l'$, one obtains

$$\lambda_l = l'(l' - 1), \tag{D21}$$

which in consideration of Eq. (D20) indicates

$$\begin{aligned}&l(l+1) = l'(l'-1) \\ &(l + l')((l+1) - l') = 0 \\ &\quad\Rightarrow l' = -l, l+1.\end{aligned} \tag{D22}$$

The solution $l' = l + 1$ is inadmissible, since it violates our definition of $l = m_{\max}$ and implies $l' > l$. Thus we conclude that $l' = -l$, and m may thus take any of the $2l + 1$ values from l to $-l$, in integer steps:

$$m = l, l-1, \ldots -l+1, -l. \tag{D23}$$

One may see this easily by starting at the top $(m = l)$ of the of the eigenstate 'ladder' and working down to the bottom $(m = -l)$ by repeated application of $\widehat{\mathscr{L}}_-$.

As for l, consider that, starting on either end of the eigenstate ladder, one can reach the other end in n steps, where n is some integer; but we know that the number of necessary steps is just $2l$ (i.e. $2l$ is an integer)

$$2l = n \quad \Rightarrow \quad l = n/2. \tag{D24}$$

Since n is an integer, this implies that l may take on integral (even n) or half-integral (odd n) values. As it happens, only integral values of l are permissible for orbital angular momentum. There are many justifications of this constraint; the simplest is to consider somewhat more concretely the action of $\widehat{\mathscr{L}}_z$ on an eigenfunction expressed in spherical coordinates. Using the last line in Eq. (D3), we have:

$$\widehat{\mathscr{L}}_z|\lambda_l, m\rangle = m|\lambda_l, m\rangle = -i\frac{\partial}{\partial\phi}|\lambda_l, m\rangle, \tag{D25}$$

from which we infer that $|\lambda_l, m\rangle$ behaves like $e^{im\phi}$,

$$-i\frac{\partial}{\partial\phi}\left[e^{im\phi}\right] = -i(im)e^{im\phi} = m\ e^{im\phi}. \tag{D26}$$

However, if half-integer l – and therefore half-integer m – were allowed, the wave function would not be single-valued under a 2π rotation (which *should* leave the system invariant):

$$e^{im(2\pi)} = \begin{cases} +1, & m = \text{integer}, \\ -1, & m = \text{half integer}, \end{cases} \tag{D27}$$

This confirms that l and consequently m take only integer values.

D.1.5. Determination of $\lambda_\pm$

In the preceding treatment, it was unnecessary to determine the actual values of the constants λ_+ and λ_- appearing in Eq. (D16). However, because the ladder operators appear throughout the main text and in many practical applications, it is worth determining the values $\lambda_\pm$, as we shall do presently. As noted earlier, we have $\widehat{\mathscr{L}}_\pm^\dagger = \widehat{\mathscr{L}}_\mp$. Therefore, we may take the adjoint of Eq. (D16) as follows:

$$\begin{aligned} &\left(\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle\right)^\dagger = \left(\lambda_\pm|\lambda_l, m\pm 1\rangle\right)^\dagger, \\ &\langle\lambda_l, m|\widehat{\mathscr{L}}_\mp = \langle\lambda_l, m\pm 1|\lambda_\pm^*. \end{aligned} \tag{D28}$$

Using this result, we may calculate the expectation value $\langle\lambda_l, m|\widehat{\mathscr{L}}_\mp\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle$ as follows:

$$\begin{aligned} \langle\lambda_l, m|\widehat{\mathscr{L}}_\mp\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle &= \langle\lambda_l, m\pm 1|\lambda_\pm^*\lambda_\pm|\lambda_l, m\pm 1\rangle \\ &= \lambda_\pm^*\lambda_\pm\langle\lambda_l, m\pm 1|\lambda_l, m\pm 1\rangle = |\lambda_\pm|^2. \end{aligned} \tag{D29}$$

However, we can calculate the same entity using Eq. (D18):

$$\begin{aligned} \langle\lambda_l, m|\widehat{\mathscr{L}}_\mp\widehat{\mathscr{L}}_\pm|\lambda_l, m\rangle &= \langle\lambda_l, m|(\widehat{\mathscr{L}}^2 - \widehat{\mathscr{L}}_z^2 \pm \widehat{\mathscr{L}}_z)|\lambda_l, m\rangle \\ &= \langle\lambda_l, m|(\lambda_l - m^2 \pm m)|\lambda_l, m\rangle \\ &= (\lambda_l - m^2 \pm m)\langle\lambda_l, m|\lambda_l, m\rangle \\ &= \lambda_l - m^2 \pm m = l(l+1) - m(m\pm 1). \end{aligned} \tag{D30}$$

Using the previous two equations, we may then write,

$$|\lambda_\pm|^2 = l(l+1) - m(m\pm 1), \tag{D31}$$

which is to say,

$$\lambda_\pm = \sqrt{l(l+1) - m(m\pm 1)} \tag{D32}$$

or alternatively,

$$\lambda_\pm = \sqrt{(l\mp m)(l\pm m+1)}. \tag{D33}$$

Both expressions appear often in the literature, and are equivalent.

D.1.6. Summary

Given the extensive use of angular momentum operators in Section 4, it is worth summarizing the results obtained in this section. We have defined the orbital angular momentum, the related operators, and the eigenfunctions and calculated the corresponding eigenvalues. Here we review the key results.

The quantum mechanical vector operator $\vec{\widehat{\mathscr{L}}}$ has components (which are themselves operators)

$$\widehat{\mathscr{L}}_j = -i\left(k\frac{\partial}{\partial l} - l\frac{\partial}{\partial k}\right), \tag{D34}$$

where $\{j, k, l\} = \{x, y, z\}$ and cyclic permutations. These operators obey commutation relations of the form

$$\left[\widehat{\mathscr{L}}_j, \widehat{\mathscr{L}}_k\right] = i\widehat{\mathscr{L}}_l, \tag{D35}$$

where again $\{j, k, l\} = \{x, y, z\}$ and cyclic permutations.

The total angular momentum squared operator $\widehat{\mathscr{L}}^2$ is defined as

$$\widehat{\mathscr{L}}^2 = \vec{\widehat{\mathscr{L}}}\cdot\vec{\widehat{\mathscr{L}}} = \widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + \widehat{\mathscr{L}}_z^2 \tag{D36}$$

and commutes with each of the components of $\vec{\widehat{\mathscr{L}}}$. We may choose functions that are simultaneously eigenfunctions of $\widehat{\mathscr{L}}^2$ and only one of the components of $\widehat{\mathscr{L}}$, which we choose by convention to be $\widehat{\mathscr{L}}_z$. We label each of these eigenfunctions $|\lambda_l, m\rangle$ according to the eigenvalues λ_l and m, of $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$, respectively. In fact, it is more practical to label the eigenfunctions as $|l, m\rangle$, where l is related to λ_l according to $\lambda_l = l(l+1)$. Thus

$$\begin{aligned} &\widehat{\mathscr{L}}^2|l, m\rangle = l(l+1)|l, m\rangle, \\ &\widehat{\mathscr{L}}_z|l, m\rangle = m|l, m\rangle. \end{aligned} \tag{D37}$$

The label l is related to the system's total angular momentum (squared), and is called the *orbital angular momentum quantum number* or *azimuthal quantum number*, while m (which is related to the component of the angular momentum in the z direction) is known as the *magnetic quantum number*. l may take only positive integer values (i.e. $l = 0, 1, 2, 3, 4\ldots$). Given a particular value of l, m may take any of the values between l and $-l$, in integer steps:

$$m = l, l-1, \ldots, 0, \ldots -l+1, -l. \tag{D38}$$

Finally, we note the so-called ladder operators,

$$\widehat{\mathscr{L}}_\pm \equiv \widehat{\mathscr{L}}_x \pm i\widehat{\mathscr{L}}_y. \tag{D39}$$

which are non-Hermitian, $\widehat{\mathscr{L}}_\pm^\dagger = \widehat{\mathscr{L}}_\mp$, and obey the relations

$$\begin{aligned} &\left[\widehat{\mathscr{L}}^2, \widehat{\mathscr{L}}_\pm\right] = 0 \quad \left[\widehat{\mathscr{L}}_z, \widehat{\mathscr{L}}_\pm\right] = \pm\widehat{\mathscr{L}}_\pm, \\ &\left[\widehat{\mathscr{L}}_+, \widehat{\mathscr{L}}_-\right] = 2\widehat{\mathscr{L}}_z. \end{aligned} \tag{D40}$$

The ladder operators act on the simultaneous eigenfunctions of $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$ according to

$$\begin{aligned} \widehat{\mathscr{L}}_\pm|l, m\rangle &= \sqrt{l(l+1) - m(m\pm 1)}\ |l, m\pm 1\rangle \\ &= \sqrt{(l\mp m)(l\pm m+1)}\ |l, m\pm 1\rangle. \end{aligned} \tag{D41}$$

For eigenfunctions labeled by maximal or minimal values of m ($m = +l$ and $m = -l$, respectively), the ladder operators act to annihilate the state

$$\widehat{\mathscr{L}}_+|l, l\rangle = \widehat{\mathscr{L}}_-|l, -l\rangle = 0. \tag{D42}$$

Note that all the results derived in this section are equally applicable to the spin angular momentum operator $\vec{\widehat{\mathscr{I}}}$. In this case, however, l and consequently m can take half-integer values. For example, for a spin-1/2 system $l = \frac{1}{2}$ and $m = \pm\frac{1}{2}$.

D.2. Spherical harmonics

D.2.1. Definition

When considering orbital angular momentum, spherical polar coordinates provide a logical and natural representation in which to perform explicit calculations. In this coordinate system, the eigenfunctions $|l, m\rangle$ of $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$ are given by the well-known spherical harmonic functions:

$$|l, m\rangle \to Y_l^m(\theta, \phi). \tag{D43}$$

The $Y_l^m(\theta, \phi)$ for $m \geqslant 0$ are given by

$$\begin{aligned} Y_l^m(\theta, \phi) = (-1)^l\left[\frac{(2l+1)!}{4\pi}\right]^{1/2} \\ \times\frac{1}{2^1 l!}\left[\frac{(l+m)!}{(2l)!(l-m)!}\right]^{1/2} e^{im\phi}(\sin\theta)^{-m}\frac{d^{l-m}}{d(\cos\theta)^{l-m}}(\sin\theta)^{2l}. \end{aligned} \tag{D44}$$

Forms for $m < 0$ may be obtained by successive application of the lowering operator $\widehat{\mathscr{L}}_-$ to $Y_l^0(\theta,\phi)$, or more simply through the relation

$$Y_l^{-m}(\theta,\phi) = (-1)^m Y_l^{m*}(\theta,\phi). \tag{D45}$$

Note that for $m = 0$, the spherical harmonics have no ϕ-dependence whatsoever.

The spherical harmonics may also be expressed in terms of the so-called *associated* Legendre polynomials $P_l^m(\cos\theta)$ (again with $0 \leqslant m \leqslant l$):

$$Y_l^m(\theta,\phi) = (-1)^m \left[\frac{(2l+1)(l-m)!}{4\pi(l+m)!}\right]^{1/2} e^{im\phi} P_l^m(\cos\theta), \tag{D46}$$

where

$$P_l^m(\cos\theta) = \sin^m\theta \frac{d^m}{d(\cos\theta)^m} P_l(\cos\theta) \tag{D47}$$

and the ordinary Legendre polynomials $P_l(\cos\theta)$ are given by

$$P_l(\cos\theta) = \frac{1}{2^l l!}\frac{d^l}{d(\cos\theta)^l}\left(\cos^2\theta - 1\right)^l. \tag{D48}$$

The spherical harmonics may naturally be thought of in terms of $(2l+1)$-member groups sharing the same value of l. Functions $Y_l^m(\theta,\phi)$ of the same l-value are said to be of the same *rank*.

D.2.2. Orthonormalization

The $Y_l^m(\theta,\phi)$ are orthogonal and normalized in the sense that

$$\int_0^{2\pi}\int_0^{\pi} Y_l^{m*}(\theta,\phi) Y_{l'}^{m'}(\theta,\phi)\sin\theta\, d\theta\, d\phi = \delta_{ll'}\delta_{mm'}, \tag{D49}$$

where $\delta_{nn'}$ is the Kronecker delta.

D.2.3. Addition theorem

The $Y_l^m(\theta,\phi)$ obey the so-called addition theorem:

$$\begin{aligned}\left(\frac{2l+1}{4\pi}\right)^{1/2} Y_l^0(\theta,0) &= P_l(\cos\theta)\\ &= \sum_{m=-l}^{l} Y_l^{m*}(\theta_1,\phi_1) Y_l^m(\theta_2,\phi_2).\end{aligned} \tag{D50}$$

D.2.4. Explicit expressions for $l \leqslant 2$

For reference, we list the first several spherical harmonics:

$$\begin{aligned}
Y_0^0 &= (4\pi)^{-1/2}\\
Y_1^{\pm 1} &= \mp(3/8\pi)^{1/2}\sin\theta e^{\pm i\phi}\\
Y_1^0 &= (3/4\pi)^{1/2}\cos\theta\\
Y_2^{\pm 2} &= (15/32\pi)^{1/2}\sin^2\theta e^{\pm 2i\phi}\\
Y_2^{\pm 1} &= \mp(15/8\pi)^{1/2}\sin\theta\cos\theta e^{\pm i\phi}\\
Y_2^0 &= (5/16\pi)^{1/2}\left(3\cos^2\theta - 1\right).
\end{aligned} \tag{D51}$$

D.3. Orbital angular momentum operators as generators of infinitesimal rotations

D.3.1. Unitary transformations and generators of infinitesimal transformations

Suppose $\widehat{\mathscr{U}}(\delta\Theta)$ is a unitary operator defined as

$$\widehat{\mathscr{U}}(\delta\Theta) = \hat{\mathbb{1}} + i\delta\Theta\widehat{\mathscr{T}}, \tag{D52}$$

where $\delta\Theta$ is an infinitesimal, real quantity, and the operator $\widehat{\mathscr{T}}$ is Hermitian, $\widehat{\mathscr{T}}^\dagger = \widehat{\mathscr{T}}$ ($\widehat{\mathscr{T}}$ must be Hermitian for $\widehat{\mathscr{U}}$ to be unitary). Thus, $\widehat{\mathscr{U}}$ is very nearly equal to the identity operator, but creates an infinitesimal transformation due to $\widehat{\mathscr{T}}$, which is therefore called the *generator of infinitesimal transformation*.

Repeated unitary transformations constitute a single 'net' unitary transformation; a repeated change of basis is equivalent to a single change of basis from the original to the final representation (see Appendix A.4.1). We may then regard a finite unitary transformation as the sum of infinitesimal ones, dividing the finite 'step size' Θ into n smaller steps of size Θ/n and considering the limit as $n \to \infty$. We write:

$$\widehat{\mathscr{U}}(\Theta) = \lim_{n\to\infty}\left(\hat{\mathbb{1}} + i\frac{\Theta}{n}\widehat{\mathscr{T}}\right)^n = \exp\left(i\Theta\widehat{\mathscr{T}}\right), \tag{D53}$$

and we may alternatively interpret the operator exponential on the right-hand side of Eq. (D53) as the power series expansion.

D.3.2. Rotations

As discussed in Appendix A.4.3, rotations are unitary transformations, and we therefore expect to write a rotation operator in the form of Eq. (D53). We define a positive angle of rotation as one for which turning a right-handed screw about its axis through the specified angle would advance the screw forward along the axis, *away* from the origin. We specify a given rotation $\widehat{\mathscr{D}}_n(\Theta)$ using a unit vector $\hat{e}_n$ lying along the axis of rotation, and a (positive or negative) angle of rotation Θ. That is, $\widehat{\mathscr{D}}_n(\Theta)$ rotates a state vector $|\Phi_0\rangle$ around $\hat{e}_n$ through an angle Θ, transforming it into $|\Phi\rangle \equiv |\Phi_0 + \Theta\rangle$

$$\widehat{\mathscr{D}}_n(\Theta)|\Phi_0\rangle = |\Phi\rangle. \tag{D54}$$

Note that this is an active transformation, operating on the physical system. An equivalent passive transformation would rotate the *coordinate system* in the opposite sense, that is, through an angle $-\Theta$ (see Appendix A.4.4).

For convenience, consider a rotation around the z-axis (that is $\hat{e}_n = \hat{e}_z$) by an angle ϕ. As $\phi \to 0$, $\widehat{\mathscr{D}}_n(\phi) \to \hat{\mathbb{1}}$, and therefore $|\Phi\rangle \to |\Phi_0\rangle$. Then for very small ϕ, we may replace $|\Phi\rangle$ with it a Maclaurin series expansion of $|\Phi_0\rangle$

$$|\Phi\rangle = \sum_{n=0}^{\infty}\frac{(-\phi)^n}{n!}\frac{\partial^n}{\partial\phi^n}|\Phi_0\rangle = \exp\left(-\phi\frac{\partial}{\partial\phi}\right)|\Phi_0\rangle \Rightarrow \widehat{\mathscr{D}}_z(\phi) = \exp\left(-\phi\frac{\partial}{\partial\phi}\right) \tag{D55}$$

or making use of Eq. (D3)

$$\widehat{\mathscr{D}}_z(\phi) = \exp\left(-i\phi\widehat{\mathscr{L}}_z\right). \tag{D56}$$

Thus, comparing Eqs. (D56) and (D53), we see that the angular momentum operator $\widehat{\mathscr{L}}_z$ is the generator of infinitesimal rotation about the z-axis (alternatively, some authors use Eq. (D56) to *define* $\widehat{\mathscr{L}}_z$). Generalizing this illustrative result to an arbitrary axis of rotation is straightforward, and yields

$$\widehat{\mathscr{D}}_n(\Theta) = \exp\left(-i\Theta\,\vec{\widehat{\mathscr{L}}}\cdot\hat{e}_n\right), \tag{D57}$$

where $\cdot$ denotes the dot product, and $\vec{\widehat{\mathscr{L}}}$ is the angular momentum vector operator with components $\widehat{\mathscr{L}}_x$, $\widehat{\mathscr{L}}_y$, and $\widehat{\mathscr{L}}_z$.

D.4. Euler rotations

D.4.1. Definitions

As mentioned in Appendix D.3.1, successive unitary transformations constitute a single 'net' unitary transformation. Thus, one may specify the total reorientation achieved by repeated rotations as a *single* rotation through a proper angle Θ, about an appropriate axis defined by the vector $\hat{e}_n$. Therefore, any reorientation in three-dimensional space may be specified by just three parameters: two to define the orientation of $\hat{e}_n$, and one to indicate Θ. Euler first

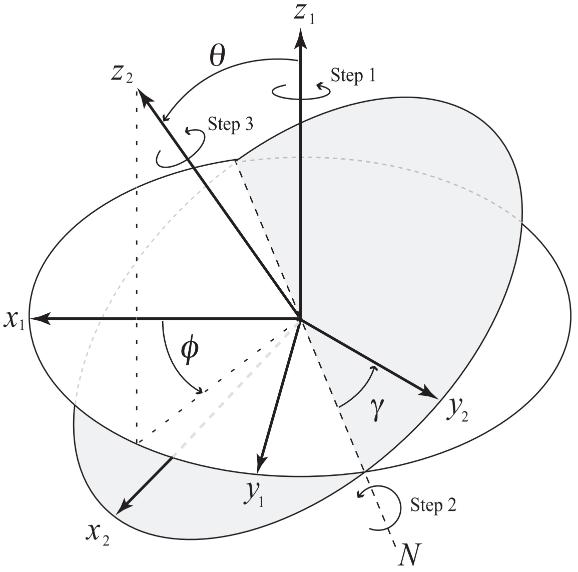

Fig. 1. The Euler angles ϕ, θ, and γ describing transformation from the initial $F_1 = (x_1, y_1, z_1)$ frame to the final $F_2 = (x_2, y_2, z_2)$ frame. The three Euler rotations are made in order about specific axes as denoted in the figure. The line of nodes N marks the intersection between the x_1y_1- and x_2y_2-planes (shown as white and gray discs, respectively), which are tilted relative to one another by an angle θ.

proved this property of rotations, and the so-called *Euler angles* $\Omega = (\phi, \theta, \gamma)$ (we also use θ and ϕ for spherical polar coordinates; see Appendix D.4.3 for a discussion on conventions) and associated rotations that bear his name comprise a convenient means for specifying reorientations.

Euler angles are used to describe the transformation whereby a set of axes $F = (x, y, z)$ initially coinciding with $F_1 = (x_1, y_1, z_1)$ is made to coincide with another set $F_2 = (x_2, y_2, z_2)$ sharing a common origin. For example, consider the passive transformation (see Appendix A.4.4) from the 'space-fixed' coordinates of the laboratory (LAB) to the 'body-fixed' coordinates of a diffusion tensor or interaction tensor principal axis frame (PAF). Similarly, Euler angles may be used to specify the active rotation of functions, tensors, or rigid bodies within a fixed coordinate system. The prescription [50,76–79] for Euler rotations is as follows (Fig. 1).

> *Step 1.* Assume two stationary axis systems F_1 and F_2, and one axis system F which rotates. Initially, F and F_1 coincide. Rotate the axis system F counterclockwise about the positive z_1-axis by an angle ϕ. This carries the y-axis into the so-called line of nodes N along the intersection between the x_1y_1- and x_2y_2-planes.
>
> *Step 2.* Looking along the line of nodes N towards the rotated positive y-axis, rotate the F axis system counterclockwise about N by an angle θ. The z- and z_2-axes now coincide, and the x-axis now lies in the x_2y_2-plane.
>
> *Step 3.* Finally, rotate the F axis system counterclockwise about the z_2-axis by an angle γ. The F axis system now coincides with F_2.

Note that the angles ϕ and θ are equivalent to the identically-named spherical polar coordinates; the former fix the axis of the final Euler rotation just as the azimuthal and polar coordinates fix $\hat{e}_r$. Thus, ϕ and θ fix $\hat{e}_n$, while $\gamma = \Theta$.

To avoid redundancy, the Euler angles, like the spherical polar coordinates, are confined to the particular ranges:

$$0 \leqslant \phi \leqslant 2\pi \quad 0 \leqslant \theta \leqslant \pi \quad 0 \leqslant \gamma \leqslant 2\pi. \tag{D58}$$

D.4.2. Rotation operators parameterized by Euler angles

D.4.2.1. Active rotations. Making repeated use of Eq. (D57), we may write the active rotation of a state vector $|\Phi_0\rangle$ to $|\Phi\rangle$ as specified by Euler angles

$$\widehat{\mathscr{D}}(\Omega)|\Phi_0\rangle = \widehat{\mathscr{D}}(\phi, \theta, \gamma)|\Phi_0\rangle = |\Phi\rangle, \tag{D59}$$

where

$$\begin{aligned}\widehat{\mathscr{D}}(\Omega) &= \widehat{\mathscr{D}}(\phi, \theta, \gamma) = \widehat{\mathscr{D}}_{z_2}(\gamma)\widehat{\mathscr{D}}_N(\theta)\widehat{\mathscr{D}}_{z_1}(\phi) \\ &= \exp(-i\gamma\widehat{\mathscr{L}}_{z_2})\exp(-i\theta\widehat{\mathscr{L}}_N)\exp(-i\phi\widehat{\mathscr{L}}_{z_1}).\end{aligned} \tag{D60}$$

Eq. (D60) is somewhat cumbersome because it contains angular momentum operators referenced to both the F_1 and F_2 coordinate systems. In fact, we may write the rotation operator referenced entirely to the F_1 coordinates, by proceeding as follows.

$\widehat{\mathscr{D}}_N(\theta)$ may be regarded as a rotation about the y_1 axis under the transformation $\widehat{\mathscr{D}}_{z_1}(\phi)$; that is, as a rotation about the y-axis of a coordinate system rotated relative to F_1 by ϕ about the z_1-axis. According to Eq. (A16), we may write this transformation in the original F_1 frame as

$$\widehat{\mathscr{D}}_N(\theta) = \widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta)\widehat{\mathscr{D}}_{z_1}(-\phi). \tag{D61}$$

In similar fashion, $\widehat{\mathscr{D}}_{z_2}(\gamma)$ is equivalent the rotation $\widehat{\mathscr{D}}_{z_1}(\gamma)$ under the transformation $\widehat{\mathscr{D}}_N(\theta)$

$$\widehat{\mathscr{D}}_{z_2}(\gamma) = \widehat{\mathscr{D}}_N(\theta)\widehat{\mathscr{D}}_{z_1}(\gamma)\widehat{\mathscr{D}}_N(-\theta) \tag{D62}$$

or employing Eq. (D61),

$$\widehat{\mathscr{D}}_{z_2}(\gamma) = \widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta)\widehat{\mathscr{D}}_{z_1}(-\phi)\widehat{\mathscr{D}}_{z_1}(\gamma)\widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(-\theta)\widehat{\mathscr{D}}_{z_1}(-\phi). \tag{D63}$$

Since rotations about the same axis obviously commute, we may write

$$\widehat{\mathscr{D}}_{z_2}(\gamma) = \widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta)\widehat{\mathscr{D}}_{z_1}(\gamma)\widehat{\mathscr{D}}_{y_1}(-\theta)\widehat{\mathscr{D}}_{z_1}(-\phi) \tag{D64}$$

Inserting Eqs. (D61) and (D64) into Eq. (D60), we have

$$\begin{aligned}\widehat{\mathscr{D}}(\phi, \theta, \gamma) = {} & \widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta)\widehat{\mathscr{D}}_{z_1}(\gamma)\widehat{\mathscr{D}}_{y_1}(-\theta) \\ & \widehat{\mathscr{D}}_{z_1}(-\phi)\widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta) \\ & \widehat{\mathscr{D}}_{z_1}(-\phi)\widehat{\mathscr{D}}_{z_1}(\phi)\end{aligned} \tag{D65}$$

$$\begin{aligned}\widehat{\mathscr{D}}(\phi, \theta, \gamma) &= \widehat{\mathscr{D}}_{z_1}(\phi)\widehat{\mathscr{D}}_{y_1}(\theta)\widehat{\mathscr{D}}_{z_1}(\gamma) \\ &= \exp(-i\phi\widehat{\mathscr{L}}_{z_1})\exp(-i\theta\widehat{\mathscr{L}}_{y_1})\exp(-i\gamma\widehat{\mathscr{L}}_{z_1}).\end{aligned} \tag{D66}$$

Eq. (D66) expresses the rather unexpected, yet highly useful result that the Euler rotations may all be carried out in the *same* frame F_1, with the order of the rotations reversed.

D.4.2.2. Passive rotations. A passive rotation affecting the coordinate system rather than the state vectors is equivalent to an active rotation of the state vectors in the opposite direction with the coordinates fixed, as described in Appendix A.4.4. Thus, if we desire a passive transformation between bases, we subject each basis vector to a transformation of the form of Eq. (D66), and the coordinates of the state vectors transform as if the vectors had undergone the inverse rotation.

It is clear from geometrical arguments that the inverse rotation is achieved by reversing the order of the Euler rotations, and rotating through negative angles:

$$\begin{aligned}\widehat{\mathscr{D}}^{-1}(\phi, \theta, \gamma) &= \widehat{\mathscr{D}}(-\gamma, -\theta, -\phi) \\ &= \exp(i\gamma\widehat{\mathscr{L}}_{z_1})\exp(i\theta\widehat{\mathscr{L}}_{y_1})\exp(i\phi\widehat{\mathscr{L}}_{z_1}).\end{aligned} \tag{D67}$$

Thus, in performing a change of frame from F_1 to F_2 (see Appendix A.4.1), state vector components transform according to

$$|\Phi\rangle^{(F_2)} = \exp(i\gamma\widehat{\mathscr{L}}_{z_1})\exp(i\theta\widehat{\mathscr{L}}_{y_1}) \exp(i\phi\widehat{\mathscr{L}}_{z_1})|\Phi\rangle^{(F_1)}. \tag{D68}$$

D.4.3. Conventions and notation

The prescription given above for Euler rotations is the one most commonly adopted throughout physics and NMR literature. However, as with spherical coordinates, multiple conventions exist, and one must pay careful attention to conventions when consulting any reference. See p. 108 of Ref. [79] for a helpful survey of conventions.

The Euler angles frequently appear in the literature as α, β, and γ. We prefer to use the symbols ϕ and θ for the first two angles because of their equivalence to the spherical polar coordinates, as mentioned above. Note, however, the reversal of the order of appearance of ϕ and θ in spherical polar coordinates vs. Euler angle specifications.

Euler angles are sets of angles, but *not* vectors, and therefore no simple rules of addition, subtraction, or commutation apply (this is a result of the non-commutivity of rotations about different axes). For example, since Euler rotations involve multiple rotations in prescribed order, reorientations specified by the angles Ω are in general *not undone* by rotations through the angles $-\Omega = (-\phi, -\theta, -\gamma)$; that is to say, $-\Omega$ does not specify the inverse of the transformation specified by Ω, and vice versa. In fact, as noted earlier, the inverse of the transformation specified by Ω is accomplished by rotating through the negative angles $-\Omega$, but performing the rotations in the opposite order, i.e. $\Omega^{-1} = (-\gamma, -\theta, -\phi)$. Some authors do use $-\Omega$ to specify the inverse of the transformation specified by Ω, which is indeed tempting, for it appeals to the intuitive notion that rotation through a negative angle should generate an apposite configuration compared to a rotation through a positive angle. However, such notation obscures the fact that Ω represents a *set* of angles and that these Euler angles are not in fact a symmetric set of parameters. We avoid potential confusion by using the notation Ω^{-1} instead.

$$\widehat{\mathscr{D}}^{-1}(\Omega) = \widehat{\mathscr{D}}(\Omega^{-1}) \neq \widehat{\mathscr{D}}(-\Omega) \tag{D69}$$

Likewise, performing the rotation specified by Ω_{12} (e.g. from frame F_1 to F_2) followed by the rotation specified by Ω_{23} is *not* equivalent to the rotation specified by $\Omega_{12} + \Omega_{23} = (\phi_{12} + \phi_{23}, \theta_{12} + \theta_{23}, \gamma_{12} + \gamma_{23})$. We prefer instead the notation $\Omega_{13} = \Omega_{12\to 23}$ to specify the total resulting transformation.

$$\widehat{\mathscr{D}}(\Omega_{13}) = \widehat{\mathscr{D}}(\Omega_{23})\widehat{\mathscr{D}}(\Omega_{12}) = \widehat{\mathscr{D}}(\Omega_{12\to 23}) \neq \widehat{\mathscr{D}}(\Omega_{12} + \Omega_{23}) \tag{D70}$$

Different authors adopt different points of view regarding how the rotation operator is to be applied, i.e. whether it is an active transformation on the state vectors (the physical system), or a passive transformation that rotates the coordinate axes. Section 1.15 of Ref. [78] provides a helpful account of the conventions adopted by various authors of standard texts, as well as making note of some inconsistencies. Wolf [80] offers a particularly enlightening and detailed discussion of these matters.

D.5. Wigner rotation matrices

D.5.1. Definition

Matrix representations of rotation operators in the basis of $\widehat{\mathscr{L}}^2$ and $\widehat{\mathscr{L}}_z$ eigenfunctions $Y_l^m(\theta, \phi) = |l, m\rangle$ are known as *Wigner matrices* [81], which we introduce now.

The arbitrary rotation operator $\widehat{\mathscr{D}}_n(\Theta) = \exp(-i\Theta\, \vec{\widehat{\mathscr{L}}} \cdot \hat{e}_n)$ commutes with $\widehat{\mathscr{L}}^2$,

$$\left[\exp\left(-i\Theta\, \vec{\widehat{\mathscr{L}}} \cdot \hat{e}_n\right), \widehat{\mathscr{L}}^2\right] = \sum_v \frac{1}{v!}(-i\Theta)^v \left[\left(\vec{\widehat{\mathscr{L}}} \cdot \hat{e}_n\right)^v, \widehat{\mathscr{L}}^2\right] = 0. \tag{D71}$$

$\widehat{\mathscr{L}}^2$ commutes with the angular momentum operator $\vec{\widehat{\mathscr{L}}} \cdot \hat{e}_n$ referenced to any axis n (see Eq. (D7)). Thus, the rotated eigenfunction $\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle$ is still an eigenfunction of $\widehat{\mathscr{L}}^2$, and its eigenvalue is unchanged:

$$\widehat{\mathscr{L}}^2\left(\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle\right) = \widehat{\mathscr{D}}_n(\Theta)\left(\widehat{\mathscr{L}}^2|l, m\rangle\right) = l(l+1)\left(\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle\right). \tag{D72}$$

This is fairly intuitive: the total angular momentum (squared) does not depend on a particular orientation or choice of coordinates. The *projection* of the total angular momentum onto a the z-axis, however, does depend on orientation and choice of coordinates, and the eigenvalue m of $\widehat{\mathscr{L}}_z$ is therefore not preserved under rotation. Rather, the rotated function $\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle$ is a superposition of eigenfunctions $|l, k\rangle$ with different eigenvalues k but the same l. We may write this rotated eigenfunction, then, as a linear combination of the complete set of $2l + 1$ eigenfunctions $|l, k\rangle$, each weighted by $\langle l, k|\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle$, its projection onto the rotated state vector

$$\begin{aligned}\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle &= \sum_{k=-l}^{l} \langle l, k|\widehat{\mathscr{D}}_n(\Theta)|l, m\rangle|l, k\rangle \\ &= \sum_{k=-l}^{l} \langle l, k|\widehat{\mathscr{D}}(\phi, \theta, \gamma)|l, m\rangle|l, k\rangle \\ &= \sum_{k=-l}^{l} \mathscr{D}^l_{km}(\phi, \theta, \gamma)|l, k\rangle\end{aligned} \tag{D73}$$

D.5.2. Evaluation of matrix elements

The coefficients $\mathscr{D}^l_{km}(\phi, \theta, \gamma) = \mathscr{D}^l_{km}(\Omega)$ of the expansion in Eq. (D73) are simply the matrix elements of the rotation operator expanded in the basis of eigenfunctions $|l, m\rangle$, that is, elements of the Wigner rotation matrices. Like the spherical harmonics, the Wigner elements (also commonly referred to as *Wigner functions*), are naturally grouped by l-value, and functions with equivalent values of l are said to be of the same *rank*. By convention, the matrices are arranged with k decreasing from top to bottom and m decreasing from left to right. For example, for $l = 1$ (i.e. rank 1) Wigner functions, we have

$$\mathscr{D}^1(\Omega) = \begin{pmatrix} \mathscr{D}^1_{11}(\Omega) & \mathscr{D}^1_{10}(\Omega) & \mathscr{D}^1_{1-1}(\Omega) \\ \mathscr{D}^1_{01}(\Omega) & \mathscr{D}^1_{00}(\Omega) & \mathscr{D}^1_{0-1}(\Omega) \\ \mathscr{D}^1_{-11}(\Omega) & \mathscr{D}^1_{-10}(\Omega) & \mathscr{D}^1_{-1-1}(\Omega) \end{pmatrix} \tag{D74}$$

Computation of the matrix elements is relatively straightforward. First, we note (by analogy to Eq. (67)) that

$$\exp(-i\Theta\widehat{\mathscr{L}}_z)|l, m\rangle = \exp(-im\Theta)|l, m\rangle. \tag{D75}$$

Then we may write the matrix elements as

$$\begin{aligned}\mathscr{D}^l_{km}(\phi, \theta, \gamma) &= \langle l, k|\widehat{\mathscr{D}}(\phi, \theta, \gamma)|l, m\rangle \\ &= \langle l, k|\exp(-i\phi\widehat{\mathscr{L}}_z)\exp(-i\theta\widehat{\mathscr{L}}_y)\exp(-i\gamma\widehat{\mathscr{L}}_z)|l, m\rangle \\ &= \exp(-ik\phi)\exp(-im\gamma)\langle l, k|\exp(-i\theta\widehat{\mathscr{L}}_y)|l, m\rangle\end{aligned} \tag{D76}$$

and therefore

$$\mathscr{D}^l_{km}(\phi, \theta, \gamma) = \exp(-ik\phi)\exp(-im\gamma)d^l_{km}(\theta) \tag{D77}$$

where

$$d^l_{km}(\theta) \equiv \langle l, k|\exp(-i\theta\widehat{\mathscr{L}}_y)|l, m\rangle \tag{D78}$$

Table 3
Rank-1 reduced Wigner functions, $d^1_{km}(\theta)$.

k	m		
	1	0	−1
1	$\cos^2\left(\frac{\theta}{2}\right)$	$\frac{-1}{\sqrt{2}}\sin\theta$	$\sin^2\left(\frac{\theta}{2}\right)$
0	$\frac{1}{\sqrt{2}}\sin\theta$	$\cos\theta$	$\frac{-1}{\sqrt{2}}\sin\theta$
−1	$\sin^2\left(\frac{\theta}{2}\right)$	$\frac{1}{\sqrt{2}}\sin\theta$	$\cos^2\left(\frac{\theta}{2}\right)$

is referred to as the *reduced* Wigner rotation function/matrix element. The derivation of closed expressions for $d^l_{km}(\theta)$ (of which several are available, the first given by Wigner [81]) is somewhat laborious, and we therefore make note only of the result:

$$d^l_{km}(\phi) = \sqrt{(l+k)!(l-k)!(l+m)!(l-m)!}\sum_s \times \frac{(-1)^{k-m+s}\left(\cos\frac{\theta}{2}\right)^{2l+m-k-2s}\left(\sin\frac{\theta}{2}\right)^{k-m+2s}}{(l+m-s)!(k-m+s)!(l-k-s)!s!}. \tag{D79}$$

The summation in Eq. (D79) extends over all positive values of s for which none of the arguments of the factorial terms in the denominator is negative. Clearly, $d^0_{00}(\theta) = 1$. Tables 3 and 4 provide complete expressions for the first- and second-rank reduced Wigner functions.

D.5.3. Properties

Wigner functions of rank l may be used to rotate spherical harmonics of the same rank. More generally, any irreducible spherical tensor T_l of rank l with components T^k_l may be rotated according to Eq. (D73),

$$T^m_l = \sum_{k=-l}^{l} \mathscr{D}^l_{km}(\Omega_{AB})T^k_l \tag{D80}$$

That is, in general, when rotating a tensor from an 'orientation A' where it has components T^k_l to another 'orientation B' in which the components are T^m_l (connected by the Euler angles Ω_{AB}), each component T^m_l of the rotated tensor may be calculated using Eq. (D80).

Note that Eqs. (D77) and (D79) define the Wigner functions for *active* rotations, which we have chosen because we find the preceding explanations somewhat more intuitive from this point of view. Expressions for passive rotations (i.e. coordinate transformations) may be easily obtained by making use of Eq. (D67) (that is, by changing the sign of all Euler angles, and interchanging ϕ and γ) or more simply, by noting that Wigner matrices are unitary

$$\mathscr{D}^{l^{-1}}_{km}(\Omega) = \mathscr{D}^l_{km}(-\gamma, -\theta, -\phi) = \mathscr{D}^{l*}_{mk}(\Omega). \tag{D81}$$

Then to perform a coordinate transformation from the F_1 initial frame (typically an interaction frame) to the F_2 final frame (typically the laboratory frame) on the tensor T_l, one simply subjects its components to the inverse of the transformation in Eq. (D80). Then

$$T^m_l(F_2) = \sum_{k=-l}^{l} \mathscr{D}^{l*}_{mk}(\Omega_{12})T^k_l(F_1), \tag{D82}$$

where Ω_{12} is the set of Euler angles describing the rotation of the F_1 coordinate frame into the F_2 coordinate frame. Note that some references define the Wigner functions to produce passive rotations, in which case the usage of Eqs. (D80) and (D82) would be reversed.

The reduced Winger functions obey the relationships,

$$d^l_{nk}(\theta) = d^l_{kn}(-\theta) = d^l_{-k,-n}(\theta) = (-1)^{n-k}d^l_{kn}(\theta) = (-1)^{n-k}d^l_{-n,-k}(\theta) \tag{D83}$$

from which it is straightforward to see from the definition in Eq. (D77):

$$\mathscr{D}^l_{km}(\Omega) = (-1)^{k-m}\mathscr{D}^{l*}_{-k-m}(\Omega). \tag{D84}$$

A well-known property of unitary matrices is that their columns, when treated as vectors, are orthonormal to one another, with an identical relationship holding for the rows. Since the Wigner matrices are unitary, we may therefore write the orthogonality relationship

$$\sum_{k=-l}^{l} \mathscr{D}^{l*}_{km}(\Omega)\mathscr{D}^l_{kn}(\Omega) = \delta_{mn}, \tag{D85}$$

for the columns and

$$\sum_{k=-l}^{l} \mathscr{D}^{l*}_{mk}(\Omega)\mathscr{D}^l_{nk}(\Omega) = \delta_{mn}, \tag{D86}$$

for the rows.

It is easily shown [76] that Wigner functions are also orthogonal in the sense that

$$\int \mathscr{D}^{l'*}_{k'm'}(\Omega)\mathscr{D}^l_{km}(\Omega)d\Omega = \frac{8\pi^2}{2l+1}\delta_{l'l}\delta_{k'k}\delta_{m'm}, \tag{D87}$$

where

$$\int d\Omega = \int_0^{2\pi} d\phi \int_0^{\pi} d\theta \sin\theta \int_0^{2\pi} d\gamma. \tag{D88}$$

This orthogonality makes the *normalized* Wigner functions

$$\mathfrak{D} = \left\{ \sqrt{\frac{2l+1}{8\pi^2}}\mathscr{D}^l_{km}(\Omega) \right\}, \tag{D89}$$

an ideal basis set in which to expand other scalar functions.

For the rotation specified by $\Omega_{13} = \Omega_{12\to 23}$, the following 'addition theorem' applies:

$$\mathscr{D}^l_{km}(\Omega_{13}) = \sum_{n=-l}^{l} \mathscr{D}^l_{kn}(\Omega_{12})\mathscr{D}^l_{nm}(\Omega_{23}). \tag{D90}$$

Finally, we note that the normalized spherical harmonics may be easily expressed in terms of Wigner functions,

Table 4
Rank-2 reduced Wigner functions, $d^2_{km}(\theta)$.

k	m				
	2	1	0	−1	−2
2	$\cos^4\left(\frac{\theta}{2}\right)$	$-\frac{1+\cos\theta}{2}\sin\theta$	$\sqrt{\frac{3}{8}}\sin^2\theta$	$-\frac{1-\cos\theta}{2}\sin\theta$	$\sin^4\left(\frac{\theta}{2}\right)$
1	$\frac{1+\cos\theta}{2}\sin\theta$	$\cos^2\theta - \frac{1-\cos\theta}{2}$	$-\sqrt{\frac{3}{8}}\sin(2\theta)$	$\frac{1+\cos\theta}{2} - \cos^2\theta$	$-\frac{1-\cos\theta}{2}\sin\theta$
0	$\sqrt{\frac{3}{8}}\sin^2\theta$	$\sqrt{\frac{3}{8}}\sin(2\theta)$	$\frac{1+3\cos(2\theta)}{4}$	$-\sqrt{\frac{3}{8}}\sin(2\theta)$	$\sqrt{\frac{3}{8}}\sin^2\theta$
−1	$\frac{1-\cos\theta}{2}\sin\theta$	$\frac{1+\cos\theta}{2} - \cos^2\theta$	$\sqrt{\frac{3}{8}}\sin(2\theta)$	$\cos^2\theta - \frac{1-\cos\theta}{2}$	$-\frac{1+\cos\theta}{2}\sin\theta$
−2	$\sin^4\left(\frac{\theta}{2}\right)$	$\frac{1-\cos\theta}{2}\sin\theta$	$\sqrt{\frac{3}{8}}\sin^2\theta$	$\frac{1+\cos\theta}{2}\sin\theta$	$\cos^4\left(\frac{\theta}{2}\right)$

$$Y_l^m(\theta,\phi) = \sqrt{\frac{2l+1}{4\pi}}\mathscr{D}^{l*}_{m0}(\phi,\theta,\gamma), \tag{D91}$$

$$Y_l^{-m}(\theta,\gamma) = \sqrt{\frac{2l+1}{4\pi}}\mathscr{D}^{l}_{0m}(\phi,\theta,\gamma), \tag{D92}$$

and likewise the associated Legendre polynomials are given by

$$\mathscr{D}^{l}_{00}(\phi,\theta,\gamma) = P_l(\cos\theta). \tag{D93}$$

Appendix E. Diffusion equations and operators

E.1. The diffusion equation

E.1.1. Derivation

In this section we derive the rotational diffusion equation [82–85] from first principles, employing arguments from Newtonian and statistical mechanics [86].

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t} = &-\widehat{\mathscr{L}}\cdot\left[\left(\widehat{D}\cdot\widehat{\mathscr{L}}\frac{U(\Omega)}{k_BT}\right)P(\Omega,t|\Omega_0)\right]\\ &-\widehat{\mathscr{L}}\cdot\widehat{D}\cdot\widehat{\mathscr{L}}P(\Omega,t|\Omega_0).\end{aligned} \tag{E1}$$

Bulk materials such as liquids, membranes or proteins are many-body systems (i.e. systems of N interacting particles), and the motional processes in these systems can be defined by Newton's equation:

$$m_i\frac{\partial^2}{\partial t^2}\vec{r}_i = -\frac{\partial}{\partial\vec{r}_i}U(\vec{r}_1,\vec{r}_2,\ldots,\vec{r}_N), \tag{E2}$$

where the position of ith particle is described by $\vec{r}_i$. This equation becomes unwieldy to solve exactly when the system is large, i.e. the number of particles, N, is large. However, some processes can be described with only a few degrees of freedom: instead of using the positions of all particles, the position of the center of mass is sufficient to describe motional properties (e.g. translational or rotational diffusion).

For a set of N particles of mass m let us consider a small subset of three degrees of freedom, with generalized coordinates $q_1,\ q_2,\ q_3$. The evolution of these coordinates can be described by a Langevin equation [87]:

$$m\frac{d^2}{dt^2}q_j = -\frac{\partial}{\partial q_j}U(q_1,q_2,q_3) - \gamma\frac{\partial}{\partial t}q_j + \sigma\epsilon_j(t), \tag{E3}$$

with $j = 1,2,3$.

The first derivative on the right-hand side is the force derived from the effective potential $U(q_1,q_2,q_3)$. The second term is a friction force exerted by surrounding molecules (i.e. elements outside the subspace spanned by the three degrees of freedom under consideration). Note that, in this case, the projection of the friction force along one dimension does not depend on the coordinates in other dimensions. The friction coefficient γ is in general a tensor quantity. We treat it as a scalar in the present discussion for simplicity. The last term in the above equation is a stochastic force due to the collisions with surrounding molecules. The sum of the last two terms is the so-called Langevin force [88], where σ represents the amplitude of the stochastic force.

Let us consider Eq. (E3) along one of the three dimensions.

We define a 'vector' $\vec{r} = \begin{bmatrix} r_1 \\ r_2 \end{bmatrix}$ with $r_1 = m\dfrac{dq_j}{dt}$ and $r_2 = mq_j$.

The process of interest here is stochastic and can be described with a stochastic differential equation (SDE):

$$\frac{\partial\vec{r}(t)}{\partial t} = \vec{A}[\vec{r}(t),t] + \widehat{B}[\vec{r}(t),t]\cdot\vec{h}(t); \tag{E4}$$

$\vec{A}[\vec{r}(t),t]$ is the drift term and $\widehat{B}[\vec{r}(t),t]$ is the noise term. When the fluctuation term $\vec{h}(t)$ is set to zero, Eq. (E4) describes the deterministic drift of particles due to the force $\vec{A}[\vec{r}(t),t]$ [83].

We have:

$$\begin{aligned}\vec{A}[\vec{r}(t),t] &= \begin{bmatrix} F(r_2/m) - \gamma r_1/m \\ r_1 \end{bmatrix}\\ \widehat{B}[\vec{r}(t),t] &= \begin{bmatrix} \sigma & 0 \\ 0 & 0 \end{bmatrix}\\ \vec{h}(t) &= \begin{bmatrix} \epsilon_j(t) \\ 0 \end{bmatrix}\end{aligned} \tag{E5}$$

with $F(q_j) = -\dfrac{\partial}{\partial q_j}U(q_1,q_2,q_3)$.

The stochastic term $\epsilon_j(t)$ averages to zero:

$$\overline{\epsilon_j(t)} = 0. \tag{E6}$$

It corresponds to events (collisions) that can be considered instantaneous and uncorrelated, so that

$$\overline{\epsilon_i(t_1)\epsilon_j(t_0)} = \delta_{ij}\delta(t_1 - t_0). \tag{E7}$$

At this point we make use of Itō's formula to write the SDE for a distribution function $f[\vec{r}(t)]$. The derivation of Itō's formula is beyond the scope of this review, and a detailed discussion can be found elsewhere [89].

$$\begin{aligned}df[\vec{r}(t)] = &\sum_i A_i(\partial_i f[\vec{r}(t)])dt + \sum_{ij} B_{ij}(\partial_i f[\vec{r}(t)])dw_j(t)\\ &+\frac{1}{2}\sum_{ijk} B_{ik}B_{jk}(\partial_i\partial_j f[\vec{r}(t)])dt,\end{aligned} \tag{E8}$$

where

$$\partial_i = \frac{\partial}{\partial q_i}, \quad i,j,k = 1,2,3. \tag{E9}$$

Taking the average, $\overline{df[\vec{r}(t)]}$, of $df[\vec{r}(t)]$, the second sum vanishes because B_{ij} and $\partial_i f[\vec{r}(t)]$ are statistically independent of $dw_j(t)$, and $dw_j(t) = h(t)dt$.

Finally we can write the average of the time derivative of the distribution function as:

$$\overline{\frac{d}{dt}f[\vec{r}(t)]} = \sum_i \overline{A_i(\partial_i f[\vec{r}(t)])} + \frac{1}{2}\sum_{ij}\overline{[\hat{B}\cdot\hat{B}^{\mathsf{T}}]_{ij}(\partial_i\partial_j f[\vec{r}(t)])}, \tag{E10}$$

where $\widehat{B}^{\mathsf{T}}$ is the transpose of $\widehat{B}$. The term $\overline{\frac{d}{dt}f[\vec{r}(t)]}$ can be written in terms of the sum of all possible jumps with probabilities $P(\vec{r},t|\vec{r}_0,t_0)$:

$$\overline{\frac{d}{dt}f[\vec{r}(t)]} = \int f[\vec{r}(t)]P(\vec{r},t|\vec{r}_0,t_0)d\vec{r}\,. \tag{E11}$$

Eqs. (E10) and (E11) yield

$$\begin{aligned}&\int f[r(t)]P(\vec{r},t|\vec{r}_0,t_0)d\vec{r}\\ &\quad = \int dr\begin{pmatrix}\sum_i A_i(\partial_i f[\vec{r}(t)])\\ +\frac{1}{2}\sum_{ij}[\widehat{B}\cdot\widehat{B}^{\mathsf{T}}]_{ij}(\partial_i\partial_j f[\vec{r}(t)])\end{pmatrix}P(\vec{r},t|\vec{r}_0,t_0).\end{aligned} \tag{E12}$$

Eq. (E12) can be simplified by changing the order of the partial differential operators. For further simplification we can assume that there is a subspace, S, with a surface ∂s on which the result of integration is a good approximation. Then the first sum in Eq. (E12) becomes:

$$\begin{aligned}\int_S d\vec{r}\,\textstyle\sum_i \vec{A}_i(\partial_i f[\vec{r}(t)])P(\vec{r},t|\vec{r}_0,t_0) \\ = -\int_S d\vec{r}\, f[\vec{r}]\sum_i \partial_i \vec{A}_i P(\vec{r},t|\vec{r}_0,t_0) \\ + \int_S d\vec{r}\left(\sum_i \partial_i \vec{A}_i f[\vec{r}]P(\vec{r},t|\vec{r}_0,t_0)\right);\end{aligned} \tag{E13}$$

$$\begin{aligned}\int_S d\vec{r}\,\sum_i \vec{A}_i(\partial_i f[\vec{r}(t)])P(\vec{r},t|\vec{r}_0,t_0) \\ = -\int_S d\vec{r}\, f[\vec{r}]\sum_i \partial_i \vec{A}_i P(\vec{r},t|\vec{r}_0,t_0) \\ + \int_{\partial S} d\vec{a}\cdot\vec{A} f[\vec{r}]P(\vec{r},t|\vec{r}_0,t_0).\end{aligned} \tag{E14}$$

The second integral on the right-hand side is the surface term. Assuming that $P(\vec{r},t|\vec{r}_0,t_0)$ is of finite spatial extent in a way that it vanishes on the boundary, ∂s, the surface term can be neglected.

The same calculation can be applied to the second sum of Eq. (E12) which then leads to

$$\begin{aligned}\int f[\vec{r}]P(\vec{r},t|\vec{r}_0,t_0)d\vec{r} \\ = -\int_S d\vec{r}\, f[\vec{r}]\begin{pmatrix}\sum_i \partial_i A_i P(\vec{r},t|\vec{r}_0,t_0) \\ +\frac{1}{2}\sum_{ij}\partial_i\partial_j[\widehat{B}\cdot\widehat{B}^{\mathrm{T}}]_{ij}P(\vec{r},t|\vec{r}_0,t_0)\end{pmatrix}.\end{aligned} \tag{E15}$$

Since $f[\vec{r}]$ is an arbitrary function we can rewrite Eq. (E15) as

$$\begin{aligned}\frac{\partial}{\partial t}P(\vec{r},t|\vec{r}_0,t_0) \\ = -\sum_i \partial_i A_i P(\vec{r},t|\vec{r}_0,t_0) + \frac{1}{2}\sum_{ij}\partial_i\partial_j[\widehat{B}\cdot\widehat{B}^T]_{ij}P(\vec{r},t|\vec{r}_0,t_0).\end{aligned} \tag{E16}$$

Eq. (E16) is the Fokker–Planck (FP) Equation. It holds for the SDE Eq. (E4) in the Itō framework. Thus, a Langevin process, i.e. Eq. (E3), can be described by the Fokker–Planck equation, the explicit form of which can be written as:

$$\frac{\partial}{\partial t}P(\vec{r},t|\vec{r}_0,t_0) = \left(-\vec{\nabla}\cdot\frac{\vec{F}(r)}{\gamma} + \nabla^2\frac{\sigma^2}{2\gamma^2}\right)P(\vec{r},t|\vec{r}_0,t_0) \tag{E17}$$

with $r = q_j$.

In the case of a scalar potential $U(\vec{r})$ such that $\vec{F}(\vec{r}) = -\vec{\nabla}U(\vec{r})$ one expects the Boltzmann distribution to be a stationary solution. The Boltzmann distribution is:

$$P_B(\vec{r}\,|\vec{r}_0) = \frac{1}{Z}\exp\left(\frac{-U(\vec{r})}{k_B T}\right), \tag{E18}$$

with

$$\frac{\partial}{\partial t}P_B(\vec{r}\,|\vec{r}_0) = 0. \tag{E19}$$

and

$$Z = \int \exp\left(\frac{-U(\vec{r})}{k_B T}\right)d\vec{r}, \tag{E20}$$

where Z is the partition function that ensures $P_B(\vec{r}\,|\vec{r}_0)$ is normalized. An alternate form for Z has been defined following Eq. (E63).

Defining a diffusion term $D = \sigma^2/2\gamma^2$ (note that diffusion along q_1, q_2 and q_3 directions are assumed to be same, due to the friction coefficient γ being a scalar; D is in reality a rank-2 tensor, $\widehat{D}$, as described below), writing $\beta = 1/k_B T$ and using Eqs. (E18) and (E19) as the stationary solution to the FP equation we obtain

$$\left(\vec{\nabla}\cdot\vec{\nabla}D - \vec{\nabla}\cdot\frac{\vec{F}(\vec{r})}{\gamma}\right)e^{-\beta U(\vec{r})} = 0, \tag{E21}$$

and Eq. (E17) becomes

$$\frac{\partial}{\partial t}P(\vec{r},t|\vec{r}_0,t_0) = \vec{\nabla}\cdot\left(\vec{\nabla}D - \frac{\vec{F}(\vec{r})}{\gamma}\right)P(\vec{r},t|\vec{r}_0,t_0). \tag{E22}$$

We integrate Eq. (E22) over the subspace S with a number of particles N_S to give

$$N_S(t|\vec{r}_0,t_0) = \int_S d\vec{r}\,P(\vec{r},t|\vec{r}_0,t_0). \tag{E23}$$

We now take the partial differential with respect to time t and use Eq. (E22) to obtain:

$$\frac{\partial}{\partial t}N_S(t|\vec{r}_0,t_0) = \int_S d\vec{r}\;\vec{\nabla}\cdot\left(\vec{\nabla}D - \frac{\vec{F}(\vec{r})}{\gamma}\right)P(\vec{r},t|\vec{r}_0,t_0). \tag{E24}$$

We can apply Gauss' Theorem to give:

$$\frac{\partial}{\partial t}N_S(t|\vec{r}_0,t_0) = \int_{\partial S} d\vec{a}\cdot\left(\vec{\nabla}D - \frac{\vec{F}(\vec{r})}{\gamma}\right)P(\vec{r},t|\vec{r}_0,t_0). \tag{E25}$$

The left side of the equation defines the rate of change of the number of particles, N_S. The right side contains a surface integral summing the scalar products between the surface element $d\vec{a}$ of ∂S and $j(\vec{r},t|\vec{r}_0,t_0)$, the particle flux at the boundary ∂S. Essentially Eq. (E25) is the *continuity equation* where:

$$j(\vec{r},t|\vec{r}_0,t_0) = \left(\vec{\nabla}D - \frac{\vec{F}(\vec{r})}{\gamma}\right)P(\vec{r},t|\vec{r}_0,t_0). \tag{E26}$$

Using the stationary solution of the FP equation (the Boltzmann distribution) with boundary conditions such that at equilibrium the flux vanishes:

$$j_0(\vec{r}) = \left(\vec{\nabla}D - \frac{\vec{F}(\vec{r})}{\gamma}\right)Ne^{-\beta U(\vec{r})} = 0. \tag{E27}$$

Noting that

$$\vec{\nabla}De^{-\beta U(\vec{r})} = e^{-\beta U(\vec{r})}\left(\vec{\nabla}D + \beta D\vec{F}(\vec{r})\right), \tag{E28}$$

one can rewrite Eq. (E27) as:

$$e^{\beta U(\vec{r})}\left(D\beta\vec{F}(\vec{r}) + \nabla D - \frac{\vec{F}(\vec{r})}{\gamma}\right) = 0 \tag{E29}$$

from which one obtains

$$\vec{\nabla}D = \vec{F}(\vec{r})(\gamma^{-1} - D\beta). \tag{E30}$$

Eq. (E30) is known as the *fluctuation dissipation theorem* (FD). The FD theorem is better known for the case of a uniform diffusion constant D, when

$$D\beta\gamma = 1 \iff \sigma^2 = 2k_B T\gamma. \tag{E31}$$

The friction coefficient γ depends on the physical properties of the particle and the environment as $\gamma = 6\pi\eta a$, where a is the radius of the particle (the particle is assumed to be spherical) and η is the viscosity. Then

$$D = \frac{1}{\beta\gamma} = \frac{k_B T}{6\pi\eta a}. \tag{E32}$$

Eq. (E32) is the Stokes–Einstein relation for the diffusion constant.

Eq. (E31) is important since it implies a relationship between the amplitude of the fluctuating forces σ and the amplitude of the dissipative forces γ. The FD theorem states that for a system to attain thermodynamic equilibrium, the amplitudes of fluctuating and dissipative forces have to obey a temperature dependent relationship.

We now use Eq. (E30) in the following identity, which holds for any function $f(r)$:

$$\vec{\nabla}\cdot\vec{\nabla}Df(r)=\vec{\nabla}\cdot D\vec{\nabla}f(r)+\vec{\nabla}\cdot f(r)\vec{\nabla}D, \tag{E33}$$

$$\vec{\nabla}\cdot\vec{\nabla}Df(r)=\vec{\nabla}\cdot D\vec{\nabla}f(r)+\vec{\nabla}\cdot\vec{F}\left(\frac{1}{\gamma}-D\beta\right), \tag{E34}$$

and using Eq. (E34) for the first term on the right-hand side of Eq. (E22) one obtains the Smoluchowski equation. The Smoluchowski equation is also called the *Diffusion Equation*, and is

$$\frac{\partial P(\vec{r},t|\vec{r}_0,t_0)}{\partial t}=-\vec{\nabla}\cdot\left[D\vec{\nabla}+\beta D\vec{\nabla}U(\vec{r})\right]P(\vec{r},t|\vec{r}_0,t_0). \tag{E35}$$

Eq. (E35) was constructed assuming a scalar γ and therefore a scalar D, but it can be generalized by replacing the scalar D by the corresponding rank-2 tensor $\overset{\frown}{D}$ with principal values (D_1,D_2,D_3) and by substituting r_0 by $\{q_1^0,q_2^0,q_3^0\}$ where q_j^0 is the value of q_j at time t_0. In the PAF of the diffusion tensor:

$$\overset{\frown}{D}=\begin{bmatrix}D_1&0&0\\0&D_2&0\\0&0&D_3\end{bmatrix}. \tag{E36}$$

We obtain:

$$\frac{\partial P(q_1,q_2,q_3,t|q_1^0,q_2^0,q_3^0,t_0)}{\partial t}$$
$$=-\vec{\nabla}\cdot\left[\overset{\frown}{D}\,\vec{\nabla}+\beta\overset{\frown}{D}\,\vec{\nabla}U(q_1,q_2,q_3)\right]P(q_1,q_2,q_3,t|q_1^0,q_2^0,q_3^0,t_0). \tag{E37}$$

When $(q_1,q_2,q_3)=(x,y,z)$, Eq. (E37) describes translational diffusion in a three-dimensional space. Rotational and translational diffusion come from the same molecular processes. They often have to be considered as coupled. However this coupling does not affect relaxation in solution, except perhaps when intermolecular effects become important, e.g. in solutions with paramagnetic ions [1,90,91]. From this fundamental similarity, we derive the equation of rotational diffusion from that of translational diffusion. This can be achieved by forcing translational diffusion to take place on a sphere of radius r_0 and using spherical polar coordinates $\Omega=(r,\theta,\phi)$.

We now consider the simple case of isotropic diffusion with a scalar diffusion constant D. We have for any function f:

$$\vec{\nabla}\cdot D\vec{\nabla}f=D\frac{1}{r_0^2}\left[\frac{\partial^2 f}{\partial\theta^2}+\frac{1}{\tan\theta}\frac{\partial f}{\partial\theta}+\frac{1}{\sin^2\theta}\frac{\partial^2 f}{\partial\theta^2}\right]. \tag{E38}$$

Defining $D'=D/r_0^2$ and introducing the angular momentum operator $\widehat{\mathscr{L}}$, we also have:

$$\vec{\widehat{\mathscr{L}}}\cdot D'\vec{\widehat{\mathscr{L}}}f=D'\widehat{\mathscr{L}}^2 f=-D'\left[\frac{\partial^2 f}{\partial\theta^2}+\frac{1}{\tan\theta}\frac{\partial f}{\partial\theta}+\frac{1}{\sin^2\theta}\frac{\partial^2 f}{\partial\theta^2}\right]. \tag{E39}$$

The expressions of Eqs. (E38) and (E39) are equal. This property can be used twice in Eq. (E37) to give:

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t}&=-\vec{\widehat{\mathscr{L}}}\cdot D\vec{\widehat{\mathscr{L}}}P(\Omega,t|\Omega_0)\\&\quad-\vec{\widehat{\mathscr{L}}}\cdot\left[D\vec{\widehat{\mathscr{L}}}\beta U(\Omega)\right]P(\Omega,t|\Omega_0,t_0),\end{aligned} \tag{E40}$$

where Ω describes the orientation of the diffusing particle.

A similar development can be used when the diffusion is anisotropic, with a diffusion tensor $\overset{\frown}{D}$, leading to:

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t}&=-\vec{\widehat{\mathscr{L}}}\cdot\overset{\frown}{D}\,\vec{\widehat{\mathscr{L}}}P(\Omega,t|\Omega_0,t_0)\\&\quad-\vec{\widehat{\mathscr{L}}}\cdot\left[\overset{\frown}{D}\,\vec{\widehat{\mathscr{L}}}\frac{U(\Omega)}{k_BT}\right]P(\Omega,t|\Omega_0,t_0).\end{aligned} \tag{E41}$$

where we have written β explicitly as $1/k_BT$. In general, we will use the Euler angles (see Appendix D.4) to specify the orientation Ω.

E.1.2. Explicit notation

It is convenient to rewrite the diffusion equation, Eq. (E41), by explicitly evaluating the terms element-by-element. Making the substitutions

$$\begin{aligned}\mathscr{U}&=\frac{U(\Omega)}{k_BT},\\\mathscr{P}&=P(\Omega,t|\Omega_0),\end{aligned} \tag{E42}$$

we can write:

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t}&=-\vec{\widehat{\mathscr{L}}}\cdot\left[\left(\overset{\frown}{D}\cdot\vec{\widehat{\mathscr{L}}}\frac{U(\Omega)}{k_BT}\right)P(\Omega,t|\Omega_0)\right]-\vec{\widehat{\mathscr{L}}}\cdot\overset{\frown}{D}\cdot\vec{\widehat{\mathscr{L}}}P(\Omega,t|\Omega_0)\\
&=-\vec{\widehat{\mathscr{L}}}\cdot\left[\left(\overset{\frown}{D}\cdot\vec{\widehat{\mathscr{L}}}\mathscr{U}\right)\mathscr{P}\right]-\vec{\widehat{\mathscr{L}}}\cdot\overset{\frown}{D}\cdot\vec{\widehat{\mathscr{L}}}\mathscr{P}\\
&=-\vec{\widehat{\mathscr{L}}}\cdot\overset{\frown}{D}\cdot\left[\vec{\widehat{\mathscr{L}}}\mathscr{P}+\left(\vec{\widehat{\mathscr{L}}}\mathscr{U}\right)\mathscr{P}\right]\\
&=-\vec{\widehat{\mathscr{L}}}\cdot\begin{pmatrix}D_{xx}&D_{xy}&D_{xz}\\D_{yx}&D_{yy}&D_{yz}\\D_{zx}&D_{zy}&D_{zz}\end{pmatrix}\left[\begin{pmatrix}\widehat{\mathscr{L}}_x\mathscr{P}\\\widehat{\mathscr{L}}_y\mathscr{P}\\\widehat{\mathscr{L}}_y\mathscr{P}\end{pmatrix}+\begin{pmatrix}\widehat{\mathscr{L}}_x\mathscr{U}\\\widehat{\mathscr{L}}_y\mathscr{U}\\\widehat{\mathscr{L}}_y\mathscr{U}\end{pmatrix}\mathscr{P}\right]\\
&=-\vec{\widehat{\mathscr{L}}}\cdot\left[\begin{pmatrix}D_{xx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{xy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{xz}\widehat{\mathscr{L}}_z\mathscr{P}\\D_{yx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{yy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{yz}\widehat{\mathscr{L}}_z\mathscr{P}\\D_{zx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{zy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{zz}\widehat{\mathscr{L}}_z\mathscr{P}\end{pmatrix}\right.\\
&\qquad\left.+\begin{pmatrix}D_{xx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{xy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{xz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\\D_{yx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{yy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{yz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\\D_{zx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{zy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{zz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\end{pmatrix}\right].\end{aligned} \tag{E43}$$

Expanding the dot product, we have:

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t}=&-\widehat{\mathscr{L}}_x\left[\begin{array}{l}\left(D_{xx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{xy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{xz}\widehat{\mathscr{L}}_z\mathscr{P}\right)\\+\left(D_{xx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{xy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{xz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\right)\end{array}\right]\\
&-\widehat{\mathscr{L}}_y\left[\begin{array}{l}\left(D_{yx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{yy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{yz}\widehat{\mathscr{L}}_z\mathscr{P}\right)\\+\left(D_{yx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{yy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{yz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\right)\end{array}\right]\\
&-\widehat{\mathscr{L}}_z\left[\begin{array}{l}\left(D_{zx}\widehat{\mathscr{L}}_x\mathscr{P}+D_{zy}\widehat{\mathscr{L}}_y\mathscr{P}+D_{zz}\widehat{\mathscr{L}}_z\mathscr{P}\right)\\+\left(D_{zx}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\mathscr{P}+D_{zy}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\mathscr{P}+D_{zz}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)\mathscr{P}\right)\end{array}\right].\end{aligned} \tag{E44}$$

Which can be written more succinctly with the use of index notation:

$$\begin{aligned}\frac{\partial P(\Omega,t|\Omega_0)}{\partial t}&=-\sum_i\widehat{\mathscr{L}}_i\left[\sum_j D_{ij}\widehat{\mathscr{L}}_j\mathscr{P}+D_{ij}\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)\mathscr{P}\right]\\&=-\sum_{i,j}\widehat{\mathscr{L}}_i\left[D_{ij}\widehat{\mathscr{L}}_j\mathscr{P}+D_{ij}\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)\mathscr{P}\right].\end{aligned} \tag{E45}$$

Since the terms D_{ij} are scalar constants and the angular momentum operators are purely differentiation operators, we can factor the D_{ij} terms out of the expression in Eq. (E45), yielding a useful expression for the diffusion equation in index notation:

$$\frac{\partial\mathscr{P}}{\partial t} = -\sum_{i,j} D_{ij}\widehat{\mathscr{L}}_i\left[\widehat{\mathscr{L}}_j\mathscr{P} + \left(\widehat{\mathscr{L}}_j\mathscr{U}\right)\mathscr{P}\right]. \tag{E46}$$

The diffusion equation simplifies considerably if we work in the principal axis frame (PAF) of the rotational diffusion tensor, for this frame is fixed to the rotation of the molecule, and the elements of the diffusion tensor are therefore constant. Further, in this frame, the rotational diffusion tensor is by definition diagonal. Thus, all terms for which $j \neq i$ vanish:

$$\begin{aligned}\frac{\partial\mathscr{P}}{\partial t} &= -\sum_{i} D_{ii}\widehat{\mathscr{L}}_i\left[\widehat{\mathscr{L}}_i\mathscr{P} + \left(\widehat{\mathscr{L}}_i\mathscr{U}\right)\mathscr{P}\right]\\ &= -\sum_{i} D_{ii}\left[\widehat{\mathscr{L}}_i^2\mathscr{P} + \widehat{\mathscr{L}}_i\left(\widehat{\mathscr{L}}_i\mathscr{U}\right)\mathscr{P}\right].\end{aligned} \tag{E47}$$

Many authors write Eq. (E46) with the $\mathscr{P}$ terms factored-out on the right side. Indeed, this is convenient, since it facilitates the definition of a diffusion operator $\widehat{\mathscr{R}}$, i.e.

$$\frac{\partial\mathscr{P}}{\partial t} = -\widehat{\mathscr{R}}\mathscr{P}, \tag{E48}$$

with:

$$\widehat{\mathscr{R}} = \sum_{i} D_{ii}\left[\widehat{\mathscr{L}}_i^2 + \widehat{\mathscr{L}}_i\left(\widehat{\mathscr{L}}_i\mathscr{U}\right)\right]. \tag{E49}$$

However, it is worth noting that Eq. (E48) is at least somewhat misleading if one evaluates the operator expression rigorously. This is because the term $\widehat{\mathscr{L}}_i(\widehat{\mathscr{L}}_i\mathscr{U})$ would appear to operate on $\mathscr{P}$ as a scalar, i.e. as $(\widehat{\mathscr{L}}_i^2\mathscr{U})\mathscr{P}$ rather than $\widehat{\mathscr{L}}_i((\widehat{\mathscr{L}}_i\mathscr{U})\mathscr{P})$. To avoid confusion, we therefore prefer to write the diffusion operator as

$$\widehat{\mathscr{R}} = -\sum_{i} D_{ii}\left[\widehat{\mathscr{L}}_i^2 + \widehat{\mathscr{L}}_i\left(\widehat{\mathscr{L}}_i\mathscr{U}\right)_{\text{op}}\right], \tag{E50}$$

where the $(\ldots)_{\text{op}}$ notation is taken to mean that the terms '...' inside parentheses are evaluated and then treated as a single operator.

E.2. Solution to the diffusion equation

To solve the diffusion equation for $\mathscr{P} = P(\Omega, t|\Omega_0)$, let us use the separation of variables approach, and assume a solution in which $P(\Omega, t|\Omega_0)$ is the product of two functions, $f_v(t)$, which is a function of time only, and $\Psi_v(\Omega)$, which is a function of orientation only:

$$P(\Omega, t|\Omega_0) = f_v(t)\Psi_v(\Omega). \tag{E51}$$

Further, let us assume that $\Psi_v(\Omega)$ is the v^{th} eigenfunction of the operator $\widehat{\mathscr{R}}$, with corresponding eigenvalue b_v

$$\widehat{\mathscr{R}}\Psi_v(\Omega) = b_v\Psi_v(\Omega) \tag{E52}$$

and that $\Psi_v(\Omega)$ is normalized, in the sense that

$$\int \Psi_v^*(\Omega)\Psi_v(\Omega)d\Omega = 1. \tag{E53}$$

Inserting Eq. (E51) into Eq. (E48), we have

$$\begin{aligned}&\frac{\partial}{\partial t}(f_v\Psi_v) = -\widehat{\mathscr{R}}f_v\Psi_v = -b_vf_v\Psi_v,\\ &\Psi_v\frac{\partial f_v}{\partial t} = -b_vf_v\Psi_v\end{aligned} \tag{E54}$$

since $\widehat{\mathscr{R}}$ acts only on the spatial function Ψ_v, and $\frac{\partial\Psi_v}{\partial t} = 0$. We temporarily omit the argument of each function for the sake of tidiness, but the temporal dependence of $f_v(t)$ and the spatial dependence of $\Psi_v(\Omega)$ are understood and utilized in the work below. We proceed by multiplying both sides of Eq. (E54) by the complex conjugate Ψ_v^*, and integrating over all Ω-space, making use of the normalization of Ψ_v (Eq. (E53)) in the second line below:

$$\begin{aligned}&\int \Psi_v^*\Psi_v\frac{\partial f_v}{\partial t}d\Omega = -\int \Psi_v^*b_vf_v\Psi_vd\Omega,\\ &\frac{\partial f_v}{\partial t}\int \Psi_v^*\Psi_vd\Omega = -b_vf_v\int \Psi_v^*\Psi_vd\Omega,\\ &\frac{\partial f_v}{\partial t} = -b_vf_v.\end{aligned} \tag{E55}$$

Eq. (E55) is an ordinary differential equation that is quite easy to solve by grouping like terms and integrating:

$$\tfrac{\partial f_v}{f_v} = -b_v\partial t \qquad\Rightarrow\quad f_v = e^{-b_vt}e^{C_0}, \tag{E56}$$

where C_0 is simply an arbitrary constant of integration. It is plain to see that $e^{C_0} = f_v(0)$, and thus

$$f_v(t) = f_v(0)e^{-b_vt}. \tag{E57}$$

The next step in solving the diffusion equation is to find $f_v(0)$. We do this by multiplying both sides of Eq. (E51) by $\Psi_v^*(\Omega)$ and integrating over all orientations:

$$\begin{aligned}&\int \Psi_v^*(\Omega)P(\Omega, t|\Omega_0)d\Omega = \int \Psi_v^*(\Omega)f_v(t)\Psi_v(\Omega)d\Omega\\ &\quad = f_v(t)\int \Psi_v^*(\Omega)\Psi_v(\Omega)d\Omega,\\ &\int \Psi_v^*(\Omega)P(\Omega, t|\Omega_0)d\Omega = f_v(t),\\ &f_v(0) = \int \Psi_v^*(\Omega)P(\Omega, 0|\Omega_0)d\Omega.\end{aligned} \tag{E58}$$

Now, by definition of probability, $\int P(\Omega, 0|\Omega_0)d\Omega = 1$, and the *conditional* probability $P(\Omega, 0|\Omega_0)$ must be zero for $\Omega \neq \Omega_0$ (the molecule can only have one orientation at $t = 0$, and we have already defined this to be Ω_0). The function $P(\Omega, 0|\Omega_0)$ thus qualifies as a Dirac delta function $\delta(\Omega - \Omega_0)$. Thus, we can solve explicitly for $f_v(0)$:

$$f_v(0) = \int \Psi_v^*(\Omega)\delta(\Omega - \Omega_0)d\Omega = \Psi_v^*(\Omega_0). \tag{E59}$$

This 'completes' our solution to the diffusion equation, giving

$$P(\Omega, t|\Omega_0) = \Psi_v^*(\Omega_0)\Psi_v(\Omega)e^{-b_vt}. \tag{E60}$$

Up to this point, our arguments have been completely general: our choice of the eigenfunctions of $\widehat{\mathscr{R}}$, $\Psi_v(\Omega)$, was completely arbitrary. That is, Eq. (E60) is valid for any eigenfunction/eigenvalue pair $\Psi_v(\Omega)/b_v$. By the principle of superposition, a linear combination of the independent solutions must also itself be a solution to the diffusion equation. Thus, a more general solution to the diffusion equation than the one in Eq. (E60) is given by

$$P(\Omega, t|\Omega_0, 0) = \sum_{v} \Psi_v^*(\Omega_0)\Psi_v(\Omega)e^{-b_vt}. \tag{E61}$$

E.3. Equilibrium probability distribution

The thermal equilibrium probability distribution function $P_{\text{eq}}(\Omega)$ satisfies the condition

$$\frac{dP_{\text{eq}}(\Omega)}{dt} = 0 = -\widehat{\mathscr{R}}P_{\text{eq}}(\Omega), \tag{E62}$$

and is related to the ordering potential $U(\Omega)$ as the Boltzmann distribution:

$$P_{\mathrm{eq}}(\Omega)=\frac{\exp\left[-U(\Omega)/k_BT\right]}{\int\exp\left[-U(\Omega)/k_BT\right]d\Omega}=\frac{\exp\left[-U(\Omega)/k_BT\right]}{Z},\tag{E63}$$

where T is the temperature, k_B is the Boltzmann constant, and $Z=\int\exp[-U(\Omega)/k_BT]d\Omega$ is the partition function.

Alternatively, one may consider that the equilibrium probability distribution $P_{\mathrm{eq}}(\Omega)$ is equivalent to the long time behavior of the conditional probability $P(\Omega,t|\Omega_0)$:

$$\lim_{t\to\infty}P(\Omega,t|\Omega_0)=P_{\mathrm{eq}}(\Omega).\tag{E64}$$

E.4. The diffusion operator

In the principal axis frame of the rotational diffusion tensor, the rotational diffusion operator is given by Eq. (E50). Note that in the absence of any ordering potential (i.e. $\mathscr{U}=0$), Eq. (E50) reduces to the rotational diffusion operator encountered in the discussion of rigid molecules tumbling in isotropic solvents (Section 4).

E.4.1. Change of variables

When explicitly writing every term of the rotational diffusion operator, it is helpful to rewrite the diffusion tensor in its principal axis frame as

$$\begin{aligned}&\widehat{D}(\mathrm{PAF})=\begin{pmatrix}D_{xx}&0&0\\0&D_{yy}&0\\0&0&D_{zz}\end{pmatrix}=\varrho\begin{pmatrix}1+\varepsilon&0&0\\0&1-\varepsilon&0\\0&0&\eta\end{pmatrix};\\&\varrho=\frac{D_{xx}+D_{yy}}{2};\quad\varepsilon=\frac{D_{xx}-D_{yy}}{D_{xx}+D_{yy}};\\&\eta=\frac{2D_{zz}}{D_{xx}+D_{yy}}.\end{aligned}\tag{E65}$$

This is simply a change of variables employed for mathematical convenience, and has no physical significance. Nevertheless, it may be useful to interpret ε as an asymmetry parameter of the diffusion tensor. η is the ratio of the diffusion constant around the molecular z-axis ('spinning', which is measured by ϱ) relative to the diffusion constant of the molecular z-axis itself ('tumbling', which is measured by D_{zz}). In other words, η characterizes the anisotropy of the diffusion tensor. These interpretations will become especially clear at the end of the following section; see Eqs. (E94)–(E96).

It is convenient to define a 'new' diffusion operator as

$$\widehat{\Gamma}\equiv\frac{1}{\varrho}\widehat{\mathscr{R}}.\tag{E66}$$

We can now write the diffusion equation as

$$\frac{1}{\varrho}\frac{\partial\mathscr{P}}{\partial t}=-\widehat{\Gamma}\mathscr{P}.\tag{E67}$$

E.4.2. Symmetrization

E.4.2.1. The symmetrizing transformation. The diffusion operator $\widehat{\Gamma}$ is not self-adjoint; that is, its matrix representation in a basis of Wigner functions is not Hermitian. For computational convenience (i.e. because fewer calculations are necessary to solve for the eigenvalues and eigenvectors of a symmetrical matrix), it is convenient to apply a 'symmetrizing' similarity transformation (see Appendix A.4.2) to $\widehat{\Gamma}$. The transformation is of the form

$$\widetilde{\widehat{\Gamma}}=\widehat{P}_{\mathrm{eq}}^{-1/2}\,\widehat{\Gamma}\,\widehat{P}_{\mathrm{eq}}^{1/2},\tag{E68}$$

where $\widehat{P}_{\mathrm{eq}}^{\pm1/2}=P_{\mathrm{eq}}^{\pm1/2}(\Omega)$ are regarded as operators, and $\widetilde{\widehat{\Gamma}}$ is the resulting symmetrized diffusion operator. A corresponding transformation will be carried out on $\mathscr{P}$, which we treat as a vector.

The symmetrizing transformation amounts to a change in basis. Consider $\widehat{P}_{\mathrm{eq}}^{-1/2}$ to be simply an operator that changes the representation of vectors from one basis to another

$$\widehat{P}_{\mathrm{eq}}^{-1/2}|v\rangle=|v'\rangle;\quad\widehat{P}_{\mathrm{eq}}^{1/2}|v'\rangle=|v\rangle\tag{E69}$$

with $\widehat{\Gamma}$ acting on $|v\rangle$ and $\widetilde{\widehat{\Gamma}}$ acting on $|v'\rangle$

$$\widehat{\Gamma}|v_1\rangle=|v_2\rangle;\quad\widetilde{\widehat{\Gamma}}\left|v_1'\right\rangle=\left|v_2'\right\rangle.\tag{E70}$$

Under the symmetrizing transformation, the eigenvalues of the diffusion operator remain unchanged, while the eigenvectors of $\widetilde{\widehat{\Gamma}}$ are those of $\widehat{\Gamma}$ multiplied by $P_{\mathrm{eq}}^{-1/2}$:

$$\widehat{\Gamma}|m\rangle=\lambda|m\rangle;\quad\widetilde{\widehat{\Gamma}}|m'\rangle=\lambda|m'\rangle=\lambda\widehat{P}_{\mathrm{eq}}^{-1/2}|m\rangle.\tag{E71}$$

Regarding $\mathscr{P}$ as vector (expanded, for example, as a sum of Wigner rotation functions), the application of the symmetrizing transformation to $\mathscr{P}$ within the above framework is straightforward. Explicitly, from Eq. (E69), we have

$$\begin{aligned}&\widetilde{\mathscr{P}}=\widehat{P}_{\mathrm{eq}}^{-1/2}\mathscr{P},\\&\widetilde{P}(\Omega,t|\Omega_0)=\widehat{P}_{\mathrm{eq}}^{-1/2}(\Omega)P(\Omega,t|\Omega_0)\end{aligned}\tag{E72}$$

and the diffusion equation (E67) becomes:

$$\frac{1}{\varrho}\frac{\partial\widetilde{\mathscr{P}}}{\partial t}=-\widetilde{\widehat{\Gamma}}\widetilde{\mathscr{P}}.\tag{E73}$$

One should avoid becoming overly-concerned with this vector formalism, however: both $\mathscr{P}$ and $\widetilde{\mathscr{P}}$, no matter how they are written, are in fact scalars (as is $\widehat{P}_{\mathrm{eq}}^{-1/2}$, for that matter), and therefore all the commutation rules of scalar algebra continue to apply. For example, a separate transformation of the following form may be convenient:

$$\widetilde{P}'(\Omega,t|\Omega_0)=\widehat{P}_{\mathrm{eq}}^{-1/2}(\Omega)P(\Omega,t|\Omega_0)P_{\mathrm{eq}}^{1/2}(\Omega_0)\tag{E74}$$

and the following diffusion equation is no less valid than Eq. (E73):

$$\frac{1}{\varrho}\frac{\partial\widetilde{\mathscr{P}'}}{\partial t}=-\widetilde{\widehat{\Gamma}}\widetilde{\mathscr{P}'}.\tag{E75}$$

E.4.2.2. Evaluation of the symmetrized diffusion operator. The evaluation of the symmetrized operator $\widetilde{\widehat{\Gamma}}$ is quite laborious. This can be done by defining expressions for each of the three terms

$$\widehat{P}_{\mathrm{eq}}^{-1/2}\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]\widehat{P}_{\mathrm{eq}}^{1/2},\quad j=\{x,y,z\}.\tag{E76}$$

Explicitly, we have

$$\begin{aligned}&\frac{\exp\left[\mathscr{U}/2\right]}{Z^{-1/2}}\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]\frac{\exp\left[-\mathscr{U}/2\right]}{Z^{1/2}}\\&\quad=\exp\left[\mathscr{U}/2\right]\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]\exp\left[-\mathscr{U}/2\right].\end{aligned}\tag{E77}$$

Applying the operator in Eq. (E77) on a test function f, we have

$$\begin{aligned}&e^{\mathscr{U}/2}\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]e^{-\mathscr{U}/2}f\\&\quad=e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j^2\left(e^{-\mathscr{U}/2}f\right)+e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\left(e^{-\mathscr{U}/2}f\right).\end{aligned}\tag{E78}$$

The explicit expression for the angular momentum operator $\widehat{\mathscr{L}}_j$ is

$$\widehat{\mathscr{L}}_j=-i\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right),\tag{E79}$$

where the coordinates $\{j,k,l\}=\{x,y,z\}$ and cyclic permutations thereof.

We now explicitly calculate each term in Eq. (E78). To begin,

$$\begin{aligned}\widehat{\mathscr{L}}_j^2(e^{-\mathscr{U}/2}f) &= \left[-i\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)\right]^2(e^{-\mathscr{U}/2}f)\\ &= -\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)(e^{-\mathscr{U}/2}f)\\ &= \left(l\frac{\partial}{\partial k}-k\frac{\partial}{\partial l}\right)\left[k\left(e^{-\mathscr{U}/2}\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}e^{-\mathscr{U}/2}f\right)\right.\\ &\quad\left.-l\left(e^{-\mathscr{U}/2}\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}e^{-\mathscr{U}/2}f\right)\right]\\ &= \left(l\frac{\partial}{\partial k}-k\frac{\partial}{\partial l}\right)e^{-\mathscr{U}/2}\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ &= l\frac{\partial}{\partial k}\left[e^{-\mathscr{U}/2}\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\right]\\ &\quad -k\frac{\partial}{\partial l}\left[e^{-\mathscr{U}/2}\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\right].\end{aligned}\tag{E80}$$

Therefore

$$\begin{aligned}&e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j^2(e^{-\mathscr{U}/2}f)\\ &= l\left\{\begin{array}{c}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ +\left[\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)+k\left(\frac{\partial^2 f}{\partial l\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial l\partial k}f\right)-l\left(\frac{\partial^2 f}{\partial k^2}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial k^2}f\right)\right]\end{array}\right\}\\ &\quad -k\left\{\begin{array}{c}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ +\left[k\left(\frac{\partial^2 f}{\partial l^2}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial l^2}f\right)-\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)-l\left(\frac{\partial^2 f}{\partial k\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial k\partial l}f\right)\right]\end{array}\right\}\\ &= \frac{1}{2}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ &\quad +l\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)+kl\left(\frac{\partial^2 f}{\partial l\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial l\partial k}f\right)\\ &\quad -l^2\left(\frac{\partial^2 f}{\partial k^2}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial k^2}f\right)-k^2\left(\frac{\partial^2 f}{\partial l^2}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial l^2}f\right)\\ &\quad +k\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)+kl\left(\frac{\partial^2 f}{\partial k\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial^2\mathscr{U}}{\partial k\partial l}f\right).\end{aligned}\tag{E81}$$

Expanding all terms but the first, we may write the right-hand side as

$$\begin{aligned}&\frac{1}{2}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ &\quad +l\frac{\partial f}{\partial l}-\frac{1}{2}l\frac{\partial\mathscr{U}}{\partial l}f+kl\frac{\partial^2 f}{\partial l\partial k}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}-\frac{1}{2}kl\frac{\partial^2\mathscr{U}}{\partial l\partial k}f-l^2\frac{\partial^2 f}{\partial k^2}\\ &\quad +\frac{1}{2}l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}+\frac{1}{2}l^2\frac{\partial^2\mathscr{U}}{\partial k^2}f-k^2\frac{\partial^2 f}{\partial l^2}+\frac{1}{2}k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}+\frac{1}{2}k^2\frac{\partial^2\mathscr{U}}{\partial l^2}f\\ &\quad +k\frac{\partial f}{\partial k}-\frac{1}{2}k\frac{\partial\mathscr{U}}{\partial k}f+kl\frac{\partial^2 f}{\partial k\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial^2\mathscr{U}}{\partial k\partial l}f\\ &= \frac{1}{2}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ &\quad +\left\{l\frac{\partial f}{\partial l}+k\frac{\partial f}{\partial k}-l^2\frac{\partial^2 f}{\partial k^2}-k^2\frac{\partial^2 f}{\partial l^2}+2kl\frac{\partial^2 f}{\partial k\partial l}\right\}\\ &\quad -\left\{\frac{1}{2}l\frac{\partial\mathscr{U}}{\partial l}f+\frac{1}{2}k\frac{\partial\mathscr{U}}{\partial k}f-\frac{1}{2}l^2\frac{\partial^2\mathscr{U}}{\partial k^2}f-\frac{1}{2}k^2\frac{\partial^2\mathscr{U}}{\partial l^2}f+kl\frac{\partial^2\mathscr{U}}{\partial l\partial k}f\right\}\\ &\quad +\frac{1}{2}l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}+\frac{1}{2}k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}.\end{aligned}\tag{E82}$$

Recognizing that

$$\begin{aligned}\widehat{\mathscr{L}}_j^2 f &= (-i)^2\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)f\\ &= \left(l\frac{\partial}{\partial k}-k\frac{\partial}{\partial l}\right)\left(k\frac{\partial f}{\partial l}-l\frac{\partial f}{\partial k}\right)\\ &= l\left(\frac{\partial f}{\partial l}+k\frac{\partial^2 f}{\partial l\partial k}-l\frac{\partial^2 f}{\partial k^2}\right)-k\left(k\frac{\partial^2 f}{\partial l^2}-\frac{\partial f}{\partial k}-l\frac{\partial^2 f}{\partial k\partial l}\right)\\ &= l\frac{\partial f}{\partial l}-l^2\frac{\partial^2 f}{\partial k^2}-k^2\frac{\partial^2 f}{\partial l^2}+k\frac{\partial f}{\partial k}+2kl\frac{\partial^2 f}{\partial k\partial l},\end{aligned}\tag{E83}$$

we may write the left-hand side of Eq. (E82) as

$$\begin{aligned}&\frac{1}{2}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)\left[k\left(\frac{\partial f}{\partial l}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}f\right)-l\left(\frac{\partial f}{\partial k}-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}f\right)\right]\\ &\quad +\widehat{\mathscr{L}}_j^2 f-\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+\frac{1}{2}l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}+\frac{1}{2}k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}\\ &\quad -\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}\\ &= \widehat{\mathscr{L}}_j^2 f-\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+\frac{1}{2}k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}-\frac{1}{4}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2 f\\ &\quad -\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}+\frac{1}{4}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}\\ &\quad +\frac{1}{4}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial\mathscr{U}}{\partial l}f+\frac{1}{2}l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{4}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2 f\\ &\quad +\frac{1}{2}l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}+\frac{1}{2}k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}.\end{aligned}\tag{E84}$$

Thus

$$\begin{aligned}e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j^2(e^{-\mathscr{U}/2}f) &= \widehat{\mathscr{L}}_j^2 f-\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}\\ &\quad -\frac{1}{4}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2 f-kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}+\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f\\ &\quad -kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}+l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{4}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2 f.\end{aligned}\tag{E85}$$

Proceeding to the next term in Eq. (E78), we note that

$$\begin{aligned}&\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}e^{-\mathscr{U}/2}f\\ &= -i\widehat{\mathscr{L}}_j\left[\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right]\\ &= -\left(k\frac{\partial}{\partial l}-l\frac{\partial}{\partial k}\right)\left[\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right]\\ &= \left(l\frac{\partial}{\partial k}-k\frac{\partial}{\partial l}\right)\left[\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right]\\ &= l\frac{\partial}{\partial k}\left[\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right]-k\frac{\partial}{\partial l}\left[\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right]\\ &= l\left[\left(\frac{\partial\mathscr{U}}{\partial l}+k\frac{\partial^2\mathscr{U}}{\partial l\partial k}-l\frac{\partial^2\mathscr{U}}{\partial k^2}\right)e^{-\mathscr{U}/2}f-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f\right.\\ &\quad\left.+\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}\frac{\partial f}{\partial k}\right]-k\left[\left(k\frac{\partial^2\mathscr{U}}{\partial l^2}-\frac{\partial\mathscr{U}}{\partial k}-l\frac{\partial^2\mathscr{U}}{\partial k\partial l}\right)e^{-\mathscr{U}/2}f\right.\\ &\quad\left.-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}f+\left(k\frac{\partial\mathscr{U}}{\partial l}-l\frac{\partial\mathscr{U}}{\partial k}\right)e^{-\mathscr{U}/2}\frac{\partial f}{\partial l}\right].\end{aligned}\tag{E86}$$

Therefore,

$$
\begin{aligned}
&e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}e^{-\mathscr{U}/2}f\\
&=\left[\left(l\frac{\partial\mathscr{U}}{\partial l}+kl\frac{\partial^2\mathscr{U}}{\partial l\partial k}-l^2\frac{\partial^2\mathscr{U}}{\partial k^2}\right)f-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\left(kl\frac{\partial\mathscr{U}}{\partial l}-l^2\frac{\partial\mathscr{U}}{\partial k}\right)f\right.\\
&\quad\left.+\left(kl\frac{\partial\mathscr{U}}{\partial l}-l^2\frac{\partial\mathscr{U}}{\partial k}\right)\frac{\partial f}{\partial k}\right]-\left[\left(k^2\frac{\partial^2\mathscr{U}}{\partial l^2}-k\frac{\partial\mathscr{U}}{\partial k}-kl\frac{\partial^2\mathscr{U}}{\partial k\partial l}\right)f\right.\\
&\quad\left.-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\left(k^2\frac{\partial\mathscr{U}}{\partial l}-kl\frac{\partial\mathscr{U}}{\partial k}\right)f+\left(k^2\frac{\partial\mathscr{U}}{\partial l}-kl\frac{\partial\mathscr{U}}{\partial k}\right)\frac{\partial f}{\partial l}\right]\\
&=\left(l\frac{\partial\mathscr{U}}{\partial l}+kl\frac{\partial^2\mathscr{U}}{\partial l\partial k}-l^2\frac{\partial^2\mathscr{U}}{\partial k^2}\right)f-\frac{1}{2}\frac{\partial\mathscr{U}}{\partial k}\left(kl\frac{\partial\mathscr{U}}{\partial l}-l^2\frac{\partial\mathscr{U}}{\partial k}\right)f\\
&\quad+\left(kl\frac{\partial\mathscr{U}}{\partial l}-l^2\frac{\partial\mathscr{U}}{\partial k}\right)\frac{\partial f}{\partial k}-\left(k^2\frac{\partial^2\mathscr{U}}{\partial l^2}-k\frac{\partial\mathscr{U}}{\partial k}-kl\frac{\partial^2\mathscr{U}}{\partial k\partial l}\right)f\\
&\quad+\frac{1}{2}\frac{\partial\mathscr{U}}{\partial l}\left(k^2\frac{\partial\mathscr{U}}{\partial l}-kl\frac{\partial\mathscr{U}}{\partial k}\right)f-\left(k^2\frac{\partial\mathscr{U}}{\partial l}-kl\frac{\partial\mathscr{U}}{\partial k}\right)\frac{\partial f}{\partial l}\\
&=l\frac{\partial\mathscr{U}}{\partial l}f+kl\frac{\partial^2\mathscr{U}}{\partial l\partial k}f-l^2\frac{\partial^2\mathscr{U}}{\partial k^2}f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial\mathscr{U}}{\partial l}f+\frac{1}{2}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f\\
&\quad+kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}-l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-k^2\frac{\partial^2\mathscr{U}}{\partial l^2}f+k\frac{\partial\mathscr{U}}{\partial k}f+kl\frac{\partial^2\mathscr{U}}{\partial k\partial l}f\\
&\quad+\frac{1}{2}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}+kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}.
\end{aligned}
\tag{E87}
$$

Grouping terms and again making use of Eq. (E83), we may write this as

$$
\begin{aligned}
&e^{\mathscr{U}/2}\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}e^{-\mathscr{U}/2}f\\
&=\left\{l\frac{\partial\mathscr{U}}{\partial l}f+k\frac{\partial\mathscr{U}}{\partial k}f-l^2\frac{\partial^2\mathscr{U}}{\partial k^2}f-k^2\frac{\partial^2\mathscr{U}}{\partial l^2}f+2kl\frac{\partial^2\mathscr{U}}{\partial k\partial l}f\right\}\\
&\quad+\frac{1}{2}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f+\frac{1}{2}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial\mathscr{U}}{\partial l}f+kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}\\
&\quad-l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}+kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}=\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f\\
&\quad+\frac{1}{2}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f+\frac{1}{2}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial\mathscr{U}}{\partial l}f+kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}\\
&\quad-l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}+kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}.
\end{aligned}
\tag{E88}
$$

Adding together the terms in Eqs. (E85) and (E88), the whole operator applied to *f* becomes:

$$
\begin{aligned}
&e^{\mathscr{U}/2}\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]e^{-\mathscr{U}/2}f\\
&=\widehat{\mathscr{L}}_j^2f-\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+\frac{1}{2}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f\\
&\quad+\frac{1}{2}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial\mathscr{U}}{\partial l}f+kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}-l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}\\
&\quad-\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}+kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}+k^2\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial l}\\
&\quad-\frac{1}{4}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial f}{\partial k}+\frac{1}{2}kl\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f-kl\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial l}\\
&\quad+l^2\frac{\partial\mathscr{U}}{\partial k}\frac{\partial f}{\partial k}-\frac{1}{4}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f\\
&=\widehat{\mathscr{L}}_j^2f+\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f+\frac{1}{4}l^2\left(\frac{\partial\mathscr{U}}{\partial k}\right)^2f+\frac{1}{4}k^2\left(\frac{\partial\mathscr{U}}{\partial l}\right)^2f-\frac{1}{2}kl\\
&\quad\times\frac{\partial\mathscr{U}}{\partial l}\frac{\partial\mathscr{U}}{\partial k}f\\
&=\widehat{\mathscr{L}}_j^2f+\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)f-\frac{1}{4}\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)^2f.
\end{aligned}
\tag{E89}
$$

We have finally

$$
e^{\mathscr{U}/2}\left[\widehat{\mathscr{L}}_j^2+\widehat{\mathscr{L}}_j\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)_{\mathrm{op}}\right]e^{-\mathscr{U}/2}=\widehat{\mathscr{L}}_j^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_j^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_j\mathscr{U}\right)^2.
\tag{E90}
$$

Now, using Eqs. (E66) and (E90), we may write

$$
\begin{aligned}
\widetilde{\widehat{\Gamma}}&=\left(\widehat{\mathscr{L}}_x^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_x^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2\right)\\
&\quad+\left(\widehat{\mathscr{L}}_y^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_y^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\right)\\
&\quad+\eta\left(\widehat{\mathscr{L}}_z^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_z^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right)\\
&\quad+\varepsilon\left(\widehat{\mathscr{L}}_x^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_x^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2\right)\\
&\quad-\varepsilon\left(\widehat{\mathscr{L}}_y^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_y^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\right),
\end{aligned}
$$

$$
\begin{aligned}
\widetilde{\widehat{\Gamma}}&=\left(\widehat{\mathscr{L}}_x^2+\widehat{\mathscr{L}}_y^2+\eta\widehat{\mathscr{L}}_z^2\right)+\frac{1}{2}\left(\widehat{\mathscr{L}}_x^2\mathscr{U}+\widehat{\mathscr{L}}_y^2\mathscr{U}+\eta\widehat{\mathscr{L}}_z^2\mathscr{U}\right)\\
&\quad-\frac{1}{4}\left(\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2+\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2+\eta\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right)\\
&\quad+\varepsilon\left(\widehat{\mathscr{L}}_x^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_x^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2\right)\\
&\quad-\varepsilon\left(\widehat{\mathscr{L}}_y^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_y^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\right),
\end{aligned}
$$

$$
\begin{aligned}
\widetilde{\widehat{\Gamma}}&=\nabla^2+\frac{1}{2}\left(\nabla^2\mathscr{U}\right)\\
&\quad-\frac{1}{4}\left(\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2+\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2+\eta\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right)\\
&\quad+\varepsilon\left(\widehat{\mathscr{L}}_x^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_x^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2\right)\\
&\quad-\varepsilon\left(\widehat{\mathscr{L}}_y^2+\frac{1}{2}\left(\widehat{\mathscr{L}}_y^2\mathscr{U}\right)-\frac{1}{4}\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\right),
\end{aligned}
\tag{E91}
$$

where we have defined the nabla-squared operator as

$$
\nabla^2=\widehat{\mathscr{L}}_x^2+\widehat{\mathscr{L}}_y^2+\eta\widehat{\mathscr{L}}_z^2.
\tag{E92}
$$

Note that this ∇^2 operator is *not* equivalent to the Laplacian (which is typically represented by the same symbol) unless $\eta=1$. It is convenient to replace the operators $\widehat{\mathscr{L}}_x$ and $\widehat{\mathscr{L}}_y$ with the ladder operators $\widehat{\mathscr{L}}_\pm$, since the Wigner functions are eigenfunctions of the ladder operators, and this makes computations using ladder operators quite straightforward. With some foresight, we calculate the following quantities,

$$
\begin{aligned}
\left(\widehat{\mathscr{L}}_+\mathscr{U}\right)\left(\widehat{\mathscr{L}}_-\mathscr{U}\right)&=\left[\left(\widehat{\mathscr{L}}_x+i\widehat{\mathscr{L}}_y\right)\mathscr{U}\right]\cdot\left[\left(\widehat{\mathscr{L}}_x-i\widehat{\mathscr{L}}_y\right)\mathscr{U}\right]\\
&=\left[\widehat{\mathscr{L}}_x\mathscr{U}+i\widehat{\mathscr{L}}_y\mathscr{U}\right]\cdot\left[\widehat{\mathscr{L}}_x\mathscr{U}-i\widehat{\mathscr{L}}_y\mathscr{U}\right]\\
&=\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2+\left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2,
\end{aligned}
$$

$$
\begin{aligned}
&-\frac{1}{2}\left(\widehat{\mathscr{L}}_+^2+\widehat{\mathscr{L}}_-^2\right)\\
&=-\frac{1}{2}\left[\left(\widehat{\mathscr{L}}_x+i\widehat{\mathscr{L}}_y\right)^2+\left(\widehat{\mathscr{L}}_x-i\widehat{\mathscr{L}}_y\right)^2\right]\\
&=-\frac{1}{2}\left[\widehat{\mathscr{L}}_x^2-\widehat{\mathscr{L}}_x^2+i\widehat{\mathscr{L}}_x\widehat{\mathscr{L}}_y+i\widehat{\mathscr{L}}_y\widehat{\mathscr{L}}_x\widehat{\mathscr{L}}_x^2-\widehat{\mathscr{L}}_x^2-i\widehat{\mathscr{L}}_x\widehat{\mathscr{L}}_y-i\widehat{\mathscr{L}}_y\widehat{\mathscr{L}}_x\right],
\end{aligned}
\tag{E93}
$$

$$
-\frac{1}{2}\left(\widehat{\mathscr{L}}_+^2+\widehat{\mathscr{L}}_-^2\right)=\widehat{\mathscr{L}}_y^2-\widehat{\mathscr{L}}_x^2,
$$

$$\begin{aligned}\left(\widehat{\mathscr{L}}_{\pm}\mathscr{U}\right)^2 &= \left[\left(\widehat{\mathscr{L}}_x \pm i\widehat{\mathscr{L}}_y\right)\mathscr{U}\right]^2 = \left[\widehat{\mathscr{L}}_x\mathscr{U} \pm i\widehat{\mathscr{L}}_y\mathscr{U}\right]^2\\ &= \left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2 \mp \left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\\ &\quad \pm i\left(\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\left(\widehat{\mathscr{L}}_y\mathscr{U}\right) + \left(\widehat{\mathscr{L}}_y\mathscr{U}\right)\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)\right),\end{aligned}$$

$$\left(\widehat{\mathscr{L}}_{+}\mathscr{U}\right)^2 + \left(\widehat{\mathscr{L}}_{-}\mathscr{U}\right)^2 = 2\left(\left(\widehat{\mathscr{L}}_x\mathscr{U}\right)^2 - \left(\widehat{\mathscr{L}}_y\mathscr{U}\right)^2\right).$$

The direct substitution into Eq. (E91) yields

$$\begin{aligned}\widetilde{\widehat{\Gamma}} = &\left[\nabla^2 + \frac{1}{2}\left(\nabla^2\mathscr{U}\right) - \frac{1}{4}\left(\widehat{\mathscr{L}}_{+}\mathscr{U}\right)\left(\widehat{\mathscr{L}}_{-}\mathscr{U}\right) - \frac{1}{4}\eta\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right]\\ &+ \varepsilon\left[\frac{1}{2}\left(\widehat{\mathscr{L}}^2_{+} + \widehat{\mathscr{L}}^2_{-}\right) + \frac{1}{4}\left[\left(\widehat{\mathscr{L}}^2_{+} + \widehat{\mathscr{L}}^2_{-}\right)\mathscr{U}\right] - \frac{1}{8}\left[\left(\widehat{\mathscr{L}}_{+}\mathscr{U}\right)^2 + \left(\widehat{\mathscr{L}}_{-}\mathscr{U}\right)^2\right]\right].\end{aligned} \tag{E94}$$

This expression for the fully-symmetrized diffusion operator is completely general. When the diffuser has axially or spherical symmetry, the expression becomes simpler. For axial symmetry, $D_{xx} = D_{yy} = D_{\perp}$. Then, $\varrho = D_{\perp}, \varepsilon = 0$, and $\eta = D_{\parallel}/D_{\perp}$. The symmetrized rotational diffusion operator then simplifies to

$$\begin{aligned}&\widetilde{\widehat{\Gamma}}_{(\mathrm{Axial})} = \left[\nabla^2_{(\mathrm{Axial})} + \frac{1}{2}\left(\nabla^2_{(\mathrm{Axial})}\mathscr{U}\right) - \frac{1}{4}\left(\widehat{\mathscr{L}}_{+}\mathscr{U}\right)\left(\widehat{\mathscr{L}}_{-}\mathscr{U}\right) - \frac{1}{4}\eta\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right],\\ &\nabla^2_{(\mathrm{Axial})} = \widehat{\mathscr{L}}^2_x + \widehat{\mathscr{L}}^2_y + \eta\widehat{\mathscr{L}}^2_z.\end{aligned} \tag{E95}$$

For a spherical diffuser, $D_{xx} = D_{yy} = D_{zz} = D_o$, and therefore $\rho = D_o, \varepsilon = 0$, and $\eta = 1$:

$$\begin{aligned}&\widetilde{\widehat{\Gamma}}_{(\mathrm{Spherical})} = \left[\nabla^2_{(\mathrm{Spherical})} + \frac{1}{2}\left(\nabla^2_{(\mathrm{Spherical})}\mathscr{U}\right) - \frac{1}{4}\left(\widehat{\mathscr{L}}_{+}\mathscr{U}\right)\left(\widehat{\mathscr{L}}_{-}\mathscr{U}\right) - \frac{1}{4}\left(\widehat{\mathscr{L}}_z\mathscr{U}\right)^2\right],\\ &\nabla^2_{(\mathrm{Spherical})} = \widehat{\mathscr{L}}^2_x + \widehat{\mathscr{L}}^2_y + \widehat{\mathscr{L}}^2_z.\end{aligned} \tag{E96}$$

Appendix F. Nomenclature

$\dagger$	adjoint (transpose conjugate)
T	transpose
$*$	complex conjugate
$\times$	scalar multiplication or vector cross product, as appropriate to the operands
$\cdot$	vector dot (inner) product
$\otimes$	direct (tensorial) product
$\odot$	tensorial scalar product
$\hat{}$	operator (i.e. 'hats' above symbols denote they are operators, e.g. $\widehat{\mathscr{A}}$)

$\hat{\mathbb{1}}$	identity operator
$\mathbb{1}_l$	$l \times l$ identity matrix

α	constant equal to $\frac{1}{3}(D_{xx} + D_{yy} + D_{zz})$ (also used as an index in various equations)
$\mid \alpha\rangle$	eigenstate of a spin-1/2 particle with $m = 1/2$
β	constant equal to $\sqrt{\frac{1}{3}(D_{xx}D_{yy} + D_{yy}D_{zz} + D_{zz}D_{xx})}$ (also used as an index, and in Appendix E, a constant equal to $\frac{1}{k_BT}$)
$\mid \beta\rangle$	eigenstate of a spin-1/2 particle with $m = -1/2$
χ_0	notation-simplifying constant (see Eq. (185))
χ_{+2}	notation-simplifying constant (see Eq. (182))

δ_{ij}	Kronecker delta function
$\delta(x - x_0)$	Dirac delta function, centered at x_0
ε	constant equal to $(D_{xx} - D_{yy})/(D_{xx} + D_{yy})$
η	constant equal to $2D_{zz}/(D_{xx} + D_{yy})$
γ	third Euler angle of the set $\Omega = (\theta, \phi, \gamma)$ (also used to denote the gyromagnetic ratio, and in Appendix E, a friction coefficient)
$\underset{\sim}{\widehat{\Gamma}}$	rotational diffusion operator equal to $1/\rho\,\widehat{\mathscr{R}}$
$\widehat{\Gamma}$	symmetrized rotational diffusion operator
$\Gamma^{(\mathscr{D})(l)}$	l-ranked matrix representation of $\widehat{\Gamma}$ in the basis of the Wigner functions $\mathscr{D}^{(l)}_{nm}(\Omega)$. (Note that the matrix derived here is in the PAF of the global rotational diffusion tensor $\widehat{D}$.)

$\vec{\mu}$	magnetic dipole moment
μ_0	permeability of free space, equal to $4\pi \times 10^{-7}\mathrm{kg\ m\ s^{-2}A^{-2}}$
$\vec{\nabla}$	gradient 'del' operator, equal to $\frac{\partial}{\partial x}\hat{e}_x + \frac{\partial}{\partial y}\hat{e}_y + \frac{\partial}{\partial z}\hat{e}_z$ in Cartesian coordinates
∇^2	nabla-squared operator, defined as $\widehat{\mathscr{L}}^2_x + \widehat{\mathscr{L}}^2_y + \eta\widehat{\mathscr{L}}^2_z$
Ω	set of Euler angles (θ, ϕ, γ) that specify a given Euler/Wigner rotation; for example from the laboratory frame to some other frame
ω_0	Larmor frequency
ϕ	second Euler angle of the set $\Omega = (\theta, \phi, \gamma)$ (also used to denote the azimuthal angle in spherical polar coordinates)
$\lvert\Phi_k\rangle$	wave function of the kth particle in an ensemble
$\Psi_v(\Omega)$	normalized eigenfunction of the rotational diffusion operators $\widehat{\mathscr{R}}$ and $\widehat{\Gamma}$, with corresponding eigenvalues b_v and a_v, respectively
$\Psi^{(l)}_v(\Omega)$	eigenfunction of the $\mathscr{R}^{(\mathscr{D})(l)}$ and $\Gamma^{(\mathscr{D})(l)}$ matrices of rank l (see $\Psi_v(\Omega)$)
$\psi_v(\Omega)$	eigenfunction of the rotational diffusion operator $\widehat{\mathscr{R}}$
$\hat{\rho}$	density operator
$\hat{\rho}_{\beta\beta}$	matrix element of density operator
$\widetilde{\hat{\rho}}$	density operator in the interaction frame
$\underset{\sim}{\rho}$	constant equal to $\frac{1}{2}(D_{xx} + D_{yy})$
$\widehat{\sigma}$	chemical shift tensor
$\Delta\sigma$	chemical shift anisotropy parameter, $\Delta\sigma = \sigma_{\parallel} - \sigma_{\perp}$
$\sigma_{\parallel}$	component of the chemical shift tensor parallel to the unique axis
$\sigma_{\perp}$	component of the chemical shift tensor perpendicular to the unique axis
τ	time (Used in the change of variables $t' = t + \tau$ in Sections 2.2.3.2 and C.1.)
τ_c	correlation time
θ	first Euler angle of the set $\Omega = (\theta, \phi, \gamma)$ (also used to denote the polar angle in spherical polar coordinates)

$[a, b]$	commutator between a and b, equal to $ab - ba$
$\underset{\sim}{A}$	notation-simplifying constant equal to $\frac{1}{2}(D_{xx} + D_{yy})$
$\widehat{A}$	tensor containing spatial dependencies of an interaction (e.g. dipolar coupling) leading to relaxation
$\widehat{A}^j$	tensor containing spatial dependencies of chemical shielding interaction for spin j
$\vec{A}$	magnetic vector potential (Appendix B) or a drift term (Appendix E)
$\widehat{\mathscr{A}}$	some arbitrary, general operator
$\overline{\widehat{\mathscr{A}}}$	average value of $\widehat{\mathscr{A}}$
$\langle\widehat{\mathscr{A}}\rangle$	(quantum mechanical) expectation value of $\widehat{\mathscr{A}}$
$\mathscr{A}^{(\mathfrak{R})}$	matrix representation of $\widehat{\mathscr{A}}$ in the basis $\mathfrak{R}$
$\mathscr{A}$	matrix representation of $\widehat{\mathscr{A}}$
A_{iso}	diagonal component of the rank-0 (isotropic) Cartesian tensor $A_{\mathrm{iso}}\mathbb{1}_3$
a_v	eigenvalue corresponding to the $\Psi_v(\Omega)$ eigenfunction of the rotational diffusion operator $\widehat{\Gamma}$, equal to b_v/ρ
$a^{(l)}_v$	eigenvalue of the $\Gamma^{(\mathscr{D})(l)}$ matrix of rank l (see b_v)
$\mathfrak{a}_{uv}$	u, v component of a rank-1 antisymmetric Cartesian tensor
$\underset{\sim}{B}$	constant equal to $\frac{1}{2}(D_{xx} - D_{yy})$
$\vec{B}_0$	static external magnetic field, which defines the z-axis in the laboratory frame
b_v	eigenvalue corresponding to the $\Psi_v(\Omega)$ eigenfunction of the rotational diffusion operator $\widehat{\mathscr{R}}$

$b_v^{(l)}$	eigenvalue of the $\mathscr{R}^{(\mathscr{D})(l)}$ matrix of rank l (see b_v)
C	notation-simplifying constant equal to $D_{zz} - \frac{1}{2}(D_{xx} + D_{yy}) = D_{zz} - A$

$C(l_1, l_2, l; m_1, m_2, m)$	Clebsch–Gordan coefficients
D'_{pq}	p, q element of a body's global rotational diffusion tensor, in an arbitrary frame of reference
D_{pq}	p, q element of a body's global rotational diffusion tensor, in its principal axis frame (PAF)
D_o	isotropic global rotational diffusion constant (For isotropic diffusers $D_{xx} = D_{yy} = D_{zz} \equiv D_o$.)
$D_\perp$	principal global rotational diffusion component perpendicular to principal axis of symmetry for axially symmetric diffusers (The principal axis of symmetry is taken to be the z-axis, So $D_{xx} = D_{yy} = D_\perp$.)
$\widehat{\mathscr{D}}_n(\theta)$	operator representing a rotation of θ about an axis n represented by the unit vector $\hat{e}_n$
$D_\parallel$	principal global rotational diffusion component parallel to the principal axis of symmetry for axially symmetric diffusers (The principal axis of symmetry is taken to be the z-axis, so $D_{zz} = D_\parallel$.)
$\mathscr{D}^l(\Omega)$	Wigner rotation matrix of rank l
$\mathscr{D}^l_{km}(\Omega)$	k, m element of the Wigner rotation matrix of rank l; the l-rank n, m Wigner function
$d^l_{km}(\phi)$	k, m reduced Wigner rotation function of rank l
$\widehat{D}$	global rotational diffusion tensor. The same symbol has also been used to represent the dipolar tensor in Section 3.1.3
E	eigenvalue of a linear quantum mechanical operator, i.e. $\widehat{\mathscr{H}}$
e	exponential (also denoted exp(…))
$\hat{e}_p$	unit vector in the p direction (e.g. $\hat{e}_x$ for a unit vector pointing along the x-axis)
$\hat{e}_{ij}$	unit vector pointing along a vector $\vec{r}_{ij}$

$G(\tau)$	correlation function (see Appendix C)
$G_{\alpha\beta\alpha'\beta'}(\tau)$	correlation function (see Section 2.3.2)
$\widehat{\mathscr{H}}$	total Hamiltonian
$\widehat{\mathscr{H}}_0$	Zeemann Hamiltonian resulting from the external applied field, $\vec{B}_0$
$\widehat{\mathscr{H}}_1(t)$	total Hamiltonian for interactions leading to relaxation, equal to $\sum_\mu \widehat{\mathscr{H}}_\mu(t)$
$\widehat{\mathscr{H}}_\mu(t)$	Hamiltonian for a single interaction leading to relaxation (e.g. $\widehat{\mathscr{H}}_{DD}$ for dipole–dipole coupling)
$\widehat{\mathscr{H}}_{RF}(t)$	Hamiltonian for radio frequency (RF) pulses

$\hbar$	(reduced) Planck's constant, equal to $h/2\pi = 1.0545 \times 10^{-34}$ J s
i	$\sqrt{-1}$ (also used as an index)
$\overrightarrow{\widehat{\mathscr{I}}}$	spin angular momentum operator
$\widehat{\mathscr{I}}_p$	p component of the spin angular momentum operator $\overrightarrow{\widehat{\mathscr{I}}}$
$\mathscr{I}$	spin quantum number ($\mathscr{I}$ = 1/2 for spin-1/2 particles; also denoted by m)
$j_{\alpha\beta\alpha'\beta'}(\omega)$	spectral density function
$\lvert k\rangle$	ket in bra-ket (Dirac) notation, denoting the vector or state with the label k
$\langle k\rvert$	bra in bra-ket (Dirac) notation, equal to $\lvert k\rangle^\dagger$
$\langle k \vert j\rangle$	inner product between kets $\lvert k\rangle$ and $\lvert j\rangle$
k_B	Boltzmann constant $= 1.3806503 \times 10^{-23}$ m^2 kg s^{-2} K^{-1}
$\vec{L}$	dimensionless infinitesimal rotation (classical angular momentum) vector
$\overrightarrow{\widehat{\mathscr{L}}}$	dimensionless infinitesimal rotation (angular momentum) operator
$\widehat{\mathscr{L}}^2$	dimensionless angular momentum squared operator, equal to $\widehat{\mathscr{L}}_x^2 + \widehat{\mathscr{L}}_y^2 + \widehat{\mathscr{L}}_z^2$
$\widehat{\mathscr{L}}_p$	p component of the dimensionless infinitesimal rotation operator $\overrightarrow{\widehat{\mathscr{L}}}$
$\widehat{\mathscr{L}}_\pm$	angular momentum raising and lowering operators (a.k.a ladder/creation-annihilation operators)
$\vec{M}$	total bulk magnetization of the NMR sample
M_p	p component of the total magnetization $\vec{M}$
M_0	magnitude of the magnetization of the NMR sample at thermal equilibrium
$P(\Omega, t)$	probability of finding a body in the orientation specified by Ω at time t
$\mathscr{P} = P(\Omega, t \vert \Omega_0)$	conditional probability of finding a body in orientation Ω at time t, given an orientation Ω_0 at $t = 0$
$R_{\alpha\beta,\alpha'\beta'}$	the elements of the so-called Redfield relaxation matrix (see Section 2.3.4)
$\widehat{\widehat{R}}$	relaxation superoperator
R_{B_r,B_s}	matrix element for the relaxation superoperator, $\widehat{\widehat{R}}$, in the $\widehat{\mathscr{B}}_r, \widehat{\mathscr{B}}_s$ basis (see Eq. (244))
R_1	longitudinal relaxation rate, equal to $1/T_1$
R_2	transverse relaxation rate, equal to $1/T_2$
$\widehat{\mathscr{R}}$	rotational diffusion operator
$\mathscr{R}^{(\mathscr{D})(l)}$	l-ranked matrix representation of $\widehat{\mathscr{R}}$ in the basis of the Wigner functions $\mathscr{D}^l_{km}(\Omega)$ (Note that the matrix derived here is in the PAF of the global rotational diffusion tensor $\widehat{D}$.)
$\overrightarrow{\widehat{\mathscr{S}}}$	spin angular momentum operator (see $\overrightarrow{\widehat{\mathscr{I}}}$, $\widehat{\mathscr{I}}_p$, and $\mathscr{I}$)
$\mathfrak{s}_{uv}$	u, v component of a rank-2 symmetric Cartesian tensor
t	time
T	absolute temperature in Kelvins
T_L	lattice temperature in Kelvins
$\mathrm{Tr}(\mathscr{A})$	trace (sum of diagonal elements $\mathscr{A}_{ii}$) of the arbitrary matrix $\mathscr{A}$
$\mathrm{Tr}_b(\mathscr{A})$	partial trace of the arbitrary matrix $\mathscr{A}$ over the b variables

T_1	longitudinal relaxation time constant
T_2	transverse relaxation time constant
T_l^m	tensorial spin operator of rank l
$U(\Omega)$	diffusive ordering potential, e.g. the potential that orders diffusers within a liquid crystal solvent
$\mathscr{U}$	'reduced' diffusive ordering potential, equal to $U(\Omega)/k_BT$
$\vec{v}$	a vector with Cartesian coordinates v_x, v_y, and v_z
$\widehat{X}$	tensor containing spin dependencies of an interaction (e.g. dipolar coupling) leading to relaxation
$Y_l^m(\theta, \phi)$	spherical harmonic of rank l
Z	partition function (see Eq. (E63))

PAF	principal axis frame, in which the matrix of an operator is diagonal (and its principal components/eigenvalues are the diagonal matrix elements)
AAF	arbitrary axis frame
LAB	laboratory frame

References

[1] A. Abragam, The Principles of Nuclear Magnetism, Clarendon Press, Oxford, 1996.

[2] J. Cavanagh, W.J. Fairbrother, A.G. Palmer III, N.J. Skelton, M. Rance, Protein NMR Spectroscopy: Principles and Practice, second ed., Academic Press, New York, 2007.

[3] J. Budimir, J.L. Skinner, On the relationship between T_1 and T_2 for stochastic relaxation models, J. Stat. Phys. 49 (1987) 1029–1042.

[4] B.B. Laird, J.L. Skinner, T_2 can be greater than $2T_1$ even at finite temperature, J. Chem. Phys. 94 (1991) 4405–4410.

[5] F. Bloch, Nuclear induction, Phys. Rev. 70 (1946) 460–474.

[6] F. Bloch, Dynamical theory of nuclear induction. II, Phys. Rev. 102 (1956) 104–135.

[7] F. Bloch, Generalized theory of relaxation, Phys. Rev. 105 (1957) 1206–1222.

[8] R.K. Wangsness, F. Bloch, The dynamical theory of nuclear induction, Phys. Rev. 89 (1953) 728–739.

[9] A.G. Redfield, On the theory of relaxation processes, IBM J. Res. Dev. 1 (1957) 19–31.

[10] A.G. Redfield, The theory of relaxation processes, in: J. Waugh (Ed.), Advances in Magnetic Resonance, vol. 1, Academic Press, New York, 1965, pp. 1–32.

[11] J. McConnell, The Theory of Nuclear Magnetic Relaxation in Liquids, first ed., Cambridge University Press, New York, 1987.

[12] C.P. Slitcher, Principles of Magnetic Resonance, third ed., Springer-Verlag, New York, 1992.

[13] D.M. Grant, R.A. Brown, Relaxation of coupled spins from rotational diffusion, in: D.M. Grant, R. Harris (Eds.), Encyclopedia of Nuclear Magnetic Resonance, Wiley, Chichester, 1996, pp. 4003–4018.

[14] N. Murali, V. Krishnan, A primer for nuclear magnetic relaxation in liquids, Concepts Magn. Reson. A 17A (2003) 86–116.

[15] M. Goldman, Quantum Description of High-Resolution NMR in Liquids, Clarendon Press, Oxford, 1991.

[16] G.M. Clore, A.M. Gronenborn, A. Szabo, N. Tjandra, Determining the magnitude of the fully asymmetric diffusion tensor from heteronuclear relaxation data in the absence of structural information, J. Am. Chem. Soc. 120 (1998) 4889–4890.

[17] D. Fushman, R. Xu, D. Cowburn, Direct determination of changes of interdomain orientation on ligation: use of the orientational dependence of ^{15}N NMR relaxation in abl SH(32), Biochemistry 38 (1999) 10225–10230.

[18] R. Ghose, D. Fushman, D. Cowburn, Determination of the rotational diffusion tensor of macromolecules in solution from NMR relaxation data with a combination of exact and approximate methods–application to the determination of interdomain orientation in multidomain proteins, J. Magn. Reson. 149 (2001) 204–217.

[19] C. Cohen-Tannoudji, B. Diu, F. Laloë, Quantum Mechanics, first ed., vol. 1, Wiley, New York, 1977.

[20] U. Fano, Description of states in quantum mechanics by density matrix and operator techniques, Rev. Mod. Phys. 29 (1957) 74–93.

[21] D.T. Haar, Theory and applications of the density matrix, Rep. Progr. Phys. 24 (1961) 304–362.

[22] P.S. Hubbard, Quantum-mechanical and semiclassical forms of the density operator theory of relaxation, Rev. Mod. Phys. 33 (1961) 249–264.

[23] R.M. Lynden-Bell, The calculation of line shapes by density matrix methods, Prog. NMR Spectrosc. 2 (1967) 163–204.

[24] R.R. Ernst, G. Bodenhausen, A. Wokaun, Principles of Nuclear Magnetic Resonance in One and Two Dimensions, Oxford University Press, 1990.

[25] O. Sørensen, G. Eich, M. Levitt, G. Bodenhausen, R. Ernst, Product operator formalism for the description of NMR pulse experiments, Prog. NMR Spectrosc. 16 (1984) 163–192.

[26] R. Ghose, Average Liouvillian theory in nuclear magnetic resonance – principles, properties, and applications, Concepts Magn. Reson. 12 (2000) 152–172.

[27] T.O. Levante, R.R. Ernst, Homogeneous versus inhomogeneous quantum-mechanical master equations, Chem. Phys. Lett. 241 (1995) 73–78.

[28] M.H. Levitt, L.D. Bari, Steady state in magnetic resonance pulse experiments, Phys. Rev. Lett. 69 (1992) 3124–3127.

[29] M.H. Levitt, L.D. Bari, The homogeneous master equation and the manipulation of relaxation networks, Bull. Magn. Reson. 16 (1994) 94–114.

[30] L.E. Kay, R.E.D. McClung, A product operator description of AB and ABX spin systems, J. Magn. Reson. 77 (1988) 258–273.

[31] F. Schwabl, Advanced Quantum Mechanics, fourth ed., Springer-Verlag, Berlin, 2007.

[32] V. Tugarinov, P.M. Hwang, J.E. Ollerenshaw, L.E. Kay, Cross-correlated relaxation enhanced ^{1}H–^{13}C NMR spectroscopy of methyl groups in very high molecular weight proteins and protein complexes, J. Am. Chem. Soc. 125 (2003) 10420–10428.

[33] M. Goldman, Formal theory of spin–lattice relaxation, J. Magn. Reson. 149 (2001) 160–187.

[34] L. Werbelow, R.E. London, Dynamic frequency shift, Concepts Magn. Reson. 8 (1996) 325–338.

[35] L.G. Werbelow, NMR dynamic frequency shifts and the quadrupolar interaction, J. Chem. Phys. 70 (1979) 5381–5383.

[36] L.G. Werbelow, R.E. London, Dynamic nuclear magnetic resonance frequency shifts for spin 1/2 nuclei coupled to efficiently relaxed spin >1/2 nuclei, J. Chem. Phys. 102 (1995) 5181–5189.

[37] R. Ghose, J.H. Prestegard, Electron spin–nuclear spin cross-correlation effects on multiplet splittings in paramagnetic proteins, J. Magn. Reson. 128 (1997) 138–143.

[38] F. Ferrage, T.R. Eykyn, G. Bodenhausen, Coherence transfer by single-transition cross-polarization: quantitation of cross-correlation effects in nuclear magnetic resonance, J. Chem. Phys. 113 (2000) 1081–1087.

[39] M. Mehring, High Resolution NMR Spectroscopy in Solids, Springer-Verlag, New York, 1976.

[40] S.A. Smith, W.E. Palke, J.T. Gerig, The Hamiltonians of NMR part I, Concepts Magn. Reson. 4 (1992) 107–144.

[41] S.A. Smith, W.E. Palke, J.T. Gerig, The Hamiltonians of NMR part II, Concepts Magn. Reson. 4 (1992) 181–204.

[42] S.A. Smith, W.E. Palke, J.T. Gerig, The Hamiltonians of NMR part III, Concepts Magn. Reson. 5 (1993) 151–177.

[43] J. Kowalewski, L. Werbelow, Evaluation of spin relaxation induced by chemical shielding anisotropy: a comment on the importance of the antisymmetric component, J. Magn. Reson. 128 (1997) 144–148.

[44] F.A.L. Anet, D.J. O'leary, The shielding tensor part II: understanding its strange effects on relaxation, Concepts Magn. Reson. 4 (1992) 35–52.

[45] J.D. Jackson, Classical Electrodynamics, third ed., Wiley, New York, 1998.

[46] R.Y. Dong, Nuclear Magnetic Resonance of Liquid Crystals, second ed., Springer, New York, 1997.

[47] R. Tarroni, C. Zannoni, On the rotational diffusion of asymmetric molecules in liquid crystals, J. Chem. Phys. 95 (1991) 4550–4564.

[48] W. Maier, A. Saupe, Eine einfache molekulare theorie des nematischen kristallinflussigen zustandes, Z. Naturforsch. A 13 (1958) 564–566.

[49] G.B. Arfken, H.J. Weber, Mathematical Methods for Physicists: A Comprehensive Guide, sixth ed., Academic Press, Burlington, MA, 2005.

[50] J.J. Sakurai, Modern Quantum Mechanics, Revised ed., Addison Wesley, Reading, MA, 1993.

[51] R. Shankar, Principles of Quantum Mechanics, second ed., Plenum, New York, 1994.

[52] A. Bax, Weak alignment offers new NMR opportunities to study protein structure and dynamics, Protein Sci. 12 (2003) 1–16.

[53] J.H. Prestegard, C.M. Bougault, A.I. Kishore, Residual dipolar couplings in structure determination of biomolecules, Chem. Rev. 104 (2004) 3519–3540.

[54] M. Zweckstetter, NMR: prediction of molecular alignment from structure using the PALES software, Nat. Protoc. 3 (2008) 679–690.

[55] P.S. Hubbard, Some properties of correlation functions of irreducible tensor operators, Phys. Rev. 180 (1969) 319–326.

[56] M. Goldman, Interference effects in the relaxation of a pair of unlike spin-1/2 nuclei, J. Magn. Reson. 60 (1984) 437–452.

[57] A. Kumar, R.C.R. Grace, P.K. Madhu, Cross-correlations in NMR, Prog. NMR Spectrosc. 37 (2000) 191–319.

[58] A.G. Palmer III, NMR probes of molecular dynamics: overview and comparison with other techniques, Annu. Rev. Biophys. Biomol. Struct. 30 (2001) 129–155.

[59] D.A. Case, Molecular dynamics and NMR spin relaxation in proteins, Acc. Chem. Res. 35 (2002) 325–331.

[60] L.E. Kay, NMR studies of protein structure and dynamics, J. Magn. Reson. 173 (2005) 193–207.

[61] G. Lipari, A. Szabo, Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. 1. Theory and range of validity, J. Am. Chem. Soc. 104 (1982) 4546–4559.

[62] G. Lipari, A. Szabo, Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. 2. Analysis of experimental results, J. Am. Chem. Soc. 104 (1982) 4559–4570.

[63] G.M. Clore, A. Szabo, A. Bax, L.E. Kay, P.C. Driscoll, A.M. Gronenborn, Deviations from the simple two-parameter model-free approach to the interpretation of nitrogen-15 nuclear magnetic relaxation of proteins, J. Am. Chem. Soc. 112 (1990) 4989–4991.

[64] J.L. Baber, A. Szabo, N. Tjandra, Analysis of slow interdomain motion of macromolecules using NMR relaxation data, J. Am. Chem. Soc. 123 (2001) 3953–3959.

[65] G. Nodet, D. Abergel, An overview of recent developments in the interpretation and prediction of fast internal protein dynamics, Eur. Biophys. J. 36 (2007) 985–993.

[66] V. Tugarinov, Z. Liang, Y.E. Shapiro, J.H. Freed, E. Meirovitch, A structural mode-coupling approach to ^{15}N NMR relaxation in proteins, J. Am. Chem. Soc. 123 (2001) 3055–3063.

[67] V. Tugarinov, Y.E. Shapiro, Z. Liang, J.H. Freed, E. Meirovitch, A novel view of domain flexibility in *E. coli* adenylate kinase based on structural mode-coupling ^{15}N NMR relaxation, J. Mol. Biol. 315 (2002) 155–170.

[68] J.C. Facelli, Calculations of chemical shieldings: theory and applications, Concepts Magn. Reson. 20A (2004) 42–69.

[69] W. Lipscomb, The chemical shift and other second-order magnetic and electric properties of small molecules, in: J. Waugh (Ed.), Advances in Magnetic Resonance, vol. 2, Academic Press, New York, 1966, pp. 137–176.

[70] L.B. Casabianca, A.C. de Dios, Ab initio calculations of NMR chemical shifts, J. Chem. Phys. 128 (2008) 052201–052210.

[71] W. Kutzelnigg, U. Fleischer, M. Schindler, The IGLO-method: ab initio calculation and interpretation of NMR chemical shifts and magnetic susceptibilities, in: P. Diehl, H. Günther, R. Kosfield, J. Seelig (Eds.), NMR: Basic Principles and Progress, vol. 23, Springer-Verlag, Berlin, 1990, pp. 165–262.

[72] E. Oldfield, Chemical shifts in amino acids, peptides, and proteins: from quantum chemistry to drug design, Annu. Rev. Phys. Chem. 53 (2002) 349–378.

[73] J.A. Tossell (Ed.), Nuclear Magnetic Shielding and Molecular Structure, first ed., Kluwer Academic, Dordrecht, 1993.

[74] D.T. Gillespie, Markov Processes: An Introduction for Physical Scientists, Academic Press, San Diego, 1991.

[75] D.M. Brink, G.R. Satchler, Angular Momentum, third ed., Oxford University Press, USA, 1994.

[76] R.N. Zare, Angular Momentum: Understanding Spatial Aspects in Chemistry and Physics, first ed., Wiley, New York, 1988.

[77] M. Rose, Elementary Theory of Angular Momentum, Wiley, New York, 1957.

[78] B.L. Silver, Irreducible Tensor Methods: An Introduction for Chemists, Academic Press, New York, 1976.

[79] H. Goldstein, C.P. Poole, J.L. Safko, Classical Mechanics, third ed., Addison-Wesley, Reading, MA, 2001.

[80] A.A. Wolf, Rotation operators, Am. J. Phys. 37 (1969) 531–536.

[81] E.P. Wigner, Group Theory and its Application to the Quantum Mechanics of Atomic Spectra, Academic Press, New York, 1959.

[82] L.D. Favro, Theory of the rotational Brownian motion of a free rigid body, Phys. Rev. 119 (1960) 53–62.

[83] L.D. Favro, Rotational Brownian motion, in: R. Burgess (Ed.), Fluctuation Phenomena in Solids, Academic Press, New York, 1965, pp. 79–101.

[84] W.H. Furry, Isotropic rotational Brownian motion, Phys. Rev. 107 (1957) 7–13.

[85] A. Ferrarini, P. Nordio, G. Moro, Diffusion models for molecular motion in uniaxial mesophases, in: G.R. Luckhurst, C.A. Veracini (Eds.), The Molecular Dynamics of Liquid Crystals, Springer, New York, 1994, pp. 41–69.

[86] I. Kosztin, K. Schulten, Course Syllabus for 'Physics 8101: Non-Equilibrium Statistical Mechanics', University of Missouri-Columbia. Available from: <http://www.ks.uiuc.edu/kosztin/PHYCS498NSM/LectureNotes.html>, 2008.

[87] W. Coffey, Y.P. Kalmykov, J.T. Waldron, The Langevin Equation: With Applications to Stochastic Problems in Physics, Chemistry, and Electrical Engineering, second ed., World Scientific, River Edge, NJ, 2004.

[88] N.V. Kampen, Stochastic Processes in Physics and Chemistry, third ed., Elsevier, Amsterdam, 2007.

[89] C. Gardiner, Handbook of Stochastic Methods: For Physics, Chemistry and the Natural Sciences, third ed., Springer, New York, 2004.

[90] I. Beloborodov, V. Orekhov, A. Arseniev, Effect of coupling between rotational and translational Brownian motions on NMR spin relaxation: consideration using green function of rigid body diffusion, J. Magn. Reson. 132 (1998) 328–329.

[91] L. Hwang, J.H. Freed, Dynamic effects of pair correlation functions on spin relaxation by translational diffusion in liquids, J. Chem. Phys. 63 (1975) 4017–4025.