

Residual Dipolar Coupling Constants: An Elementary Derivation of Key Equations

F. KRAMER, M.V. DESHMUKH, H. KESSLER, S.J. GLASER

Institut für Organische Chemie und Biochemie, Technische Universität München, Lichtenbergstraße 4, 85747, Garching, Germany

ABSTRACT: Residual dipolar couplings have recently found a wide range of applications in high-resolution NMR of biomolecules in the liquid state. A nonisotropic orientational distribution of a molecule of interest results in nonzero average dipolar coupling constants. Here, we present an intuitive introduction to the alignment tensor and an elementary derivation of key equations. © 2004 Wiley Periodicals, Inc. Concepts Magn Reson Part A 21A: 10–21, 2004

KEY WORDS: alignment tensor; coupling constant; dipole coupling; dipolar Hamiltonian; order matrix; probability matrix; residual dipolar coupling; Saupe matrix

INTRODUCTION

Although dipolar couplings are the dominant interactions in solid state NMR of spin- $\frac{1}{2}$ nuclei, they are averaged to zero for isotropically reorienting molecules in the liquid state. This makes it possible to achieve high-resolution spectra with relative ease in liquid state NMR. On the other hand, a wealth of structural information is lost if dipolar couplings vanish. However, even in liquid state NMR, molecules can be partially aligned, e.g., by external fields (mag-

netic or electric) or by anisotropic solvents (1–8). For example, in liquid crystalline solvents, the dissolved molecules are partially aligned through steric and anisotropic interactions with the solvent molecules, and dipolar couplings can be observed (9, 10). The recent success and wide use of such residual dipolar couplings is due to the development and characterization of several new alignment media such as bicelles (5), filamentous phage Pf1 (11), and polyacrylamide gels (12, 13), which make it possible to create a relatively small, tunable degree of alignment. This allows the spectroscopist to adjust the alignment in such a way, that the size of the average dipolar coupling is on the order of the J couplings. In this case, the resulting spectra are still simple, and dipolar coupling constants can be measured relatively easy by comparing line splittings in isotropic and in aligned samples. Techniques to measure residual dipolar couplings and a

Received 25 September 2003; revised 10 December 2003; accepted 12 December 2003

Correspondence to: Steffen Glaser; E-mail: Glaser@ch.tum.de
Concepts in Magnetic Resonance Part A, Vol. 21A(1) 10–21 (2004)
Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/cmra.20003
© 2004 Wiley Periodicals, Inc.

wide range of applications have been discussed in a number of articles and reviews (2–8).

Here, we revisit the fundamental question of how to calculate the expected residual dipolar coupling constant for a homonuclear (e.g., ^1H – ^1H) or heteronuclear (e.g., ^{15}N – ^1H) spin pair. This turns out to be a surprisingly simple calculation if we know the orientation and the three principal components of the so-called *alignment tensor*. This alignment tensor is a key concept that is crucial to understand residual dipolar couplings. However, in our experience, many students and even seasoned practitioners in the field of NMR have conceptual difficulties to fully understand the physical meaning of the alignment tensor which sometimes lead to serious misconceptions (*vide infra*). This may result in part from the common practice in literature, to derive the alignment tensor using mathematically elegant, but not very intuitive approaches based on spherical harmonics, their addition theorems, Legendre polynomials, Wigner rotation matrices, and a confusing number of angles between various axes.

In contrast, we here use a streamlined geometric approach similar to the original derivation by Saupe (9, 10), which is based on the Cartesian representation of vectors. Except for the most basic rules of matrix and vector multiplication, only elementary mathematics is needed to derive the alignment tensor. As a didactical aid on the way to understanding the alignment tensor, we discuss the related *probability tensor*. Numerical examples and illustrating figures are used to convey the physical meaning of these tensors. In the Appendix, various expressions for the residual dipolar coupling constants commonly found in literature are derived from the presented key results.

STATIC DIPOLAR COUPLING HAMILTONIAN

We consider two spins I and S with an internuclear vector \vec{R} (see Fig. 1). This vector can be expressed in the form

$$\vec{R} = R\vec{r}, \quad [1]$$

where R is the distance between the two nuclei and \vec{r} is a unit vector pointing in the direction of \vec{R} . Similarly, the vector representing the external magnetic field \vec{B} can be expressed in the form

$$\vec{B} = B\vec{b}, \quad [2]$$

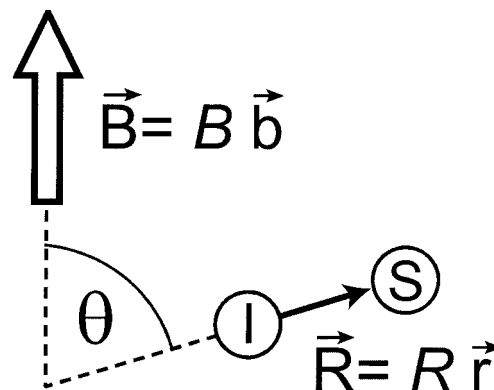


Figure 1 Definition of the angle θ between the internuclear vector \vec{R} (connecting spins I and S) and the magnetic field vector \vec{B} . The unit vectors \vec{r} and \vec{b} point in the direction of \vec{R} and \vec{B} , respectively.

where B is the magnitude of the static magnetic field, and \vec{b} is a unit vector pointing in the direction of the magnetic field. In the lab frame (x^L, y^L, z^L), where by convention the magnetic field points along the z^L axis, the (truncated) dipolar coupling Hamiltonian has the form (14):

$$\mathcal{H}_D = 2\pi D \left\{ I_{z^L} S_{z^L} - \frac{1}{2} I_{x^L} S_{x^L} - \frac{1}{2} I_{y^L} S_{y^L} \right\}. \quad [3]$$

If the spins I and S are heteronuclear, the second and third term in the bracket can be neglected, resulting in the simpler weak dipolar coupling Hamiltonian:

$$\mathcal{H}_D = 2\pi D I_{z^L} S_{z^L} \quad [4]$$

(which has the same form as the weak heteronuclear J coupling Hamiltonian). In both cases, the dipolar coupling constant (which in the weak coupling limit corresponds directly to the experimentally observed line splittings in units of Hz) is given by (14):

$$D = \frac{\kappa}{R^3} \left(\cos^2\theta - \frac{1}{3} \right), \quad [5]$$

where θ is the angle between the internuclear vector and the magnetic field (see Fig. 1). The term

$$\kappa = -\frac{3}{8\pi^2} \gamma_I \gamma_S \mu_0 \hbar \quad [6]$$

only depends on physical constants (14): the gyromagnetic ratios γ_I and γ_S of spin I and S , respectively, the Planck constant $\hbar = h/2\pi$ and the perme-

ability of vacuum μ_0 . For example, for ^1H - ^1H , ^{13}C - ^1H , and ^{15}N - ^1H spin pairs, $\kappa = -360.3$, -90.6 , and $36.5 \text{ kHz } \text{\AA}^3$, respectively. The maximum possible value of $\cos^2\theta$ is 1 (for $\theta = 0$ or π), and hence, according to Eq. [5], the maximum possible dipolar coupling constant is

$$D_{\max} = \kappa/R^3(1 - 1/3) = (2/3)\kappa/R^3, \quad [7]$$

which corresponds, e.g., to 21.7 kHz for a ^{15}N - ^1H spin pair with distance $R = 1.04 \text{ \AA}$.

Remember that the scalar product between two unit vectors is identical to the cosine of the angle θ between the two vectors. Hence, the term $\cos\theta$ in Eq. [5] can always be expressed in the form

$$\cos\theta = \vec{b}^T \vec{r}. \quad [8]$$

Here, \vec{b}^T is a row vector (the transpose of the column vector \vec{b}) that allows us to write the scalar product of the two vectors as a usual matrix product between the 1×3 matrix \vec{b}^T and the 3×1 matrix \vec{r} (*vide infra*).

TIME-DEPENDENT AND AVERAGE DIPOLAR COUPLING HAMILTONIAN

Now we consider the two spins I and S to be part of a molecule in solution. In the lab frame, the magnetic field vector \vec{B} is constant (pointing along the z^L axis), but the internuclear vector \vec{R} is now time-dependent [see Fig. 2(A)]. For simplicity, we assume that the molecule is rigid (no internal dynamics and constant distance R), such that the time dependence of \vec{R} is solely due to the rotational tumbling motion of the molecule. Hence, the term $\cos\theta$ (and as a result also the dipolar coupling constant D and the dipolar coupling Hamiltonian) is time-dependent. For proteins, the rotational correlation time is on the order of nanoseconds and on the time scale of the NMR experiment, only the time-averaged dipolar Hamiltonian $\overline{\mathcal{H}}_D$ gives rise to splittings in the spectrum (relaxation effects caused by the fluctuations of the dipolar Hamiltonian will not be considered here). The time-averaged dipolar coupling constant

$$\bar{D} = \frac{\kappa}{R^3} \left(\overline{\cos^2\theta} - \frac{1}{3} \right) \quad [9]$$

represents the so-called *residual dipolar coupling constant*, which depends on the average alignment of the molecule.

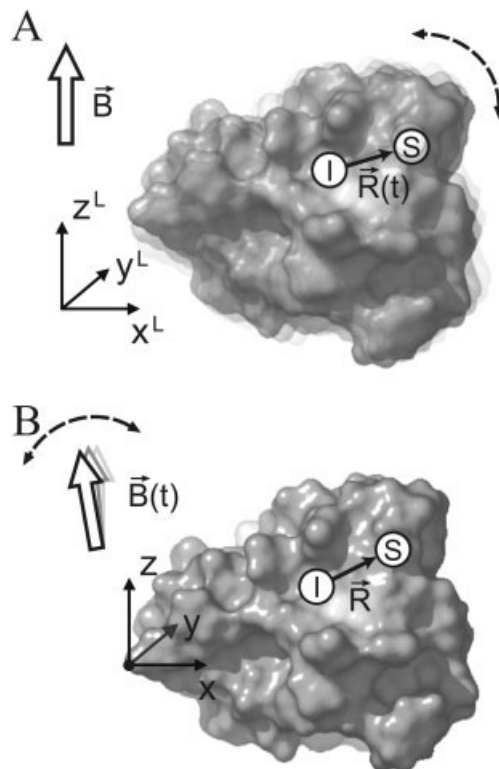


Figure 2 Effect of molecular tumbling of a rigid molecule as seen (A) from the lab frame of reference (with axes x^L , y^L , z^L) and (B) from an arbitrary molecular frame of reference (with axes x , y , z). In the lab frame (A), the magnetic field \vec{B} is constant and points by definition along the z^L axis, whereas the internuclear vector \vec{R} keeps changing its direction. In a molecular frame (B), the situation is reversed: here, any given internuclear vector is constant, whereas the orientation of the magnetic field is time-dependent.

OUTLINE AND KEY RESULTS

The goal of this manuscript is to derive a general approach for the calculation of \bar{D} for any pair of spins if the “alignment properties” of the molecule are known. Before we go into the formal derivation, we give a brief outline of the steps and state the final result. First, we move from the lab frame (x^L , y^L , z^L) [cf. Fig. 2(A)] to a frame of reference (x , y , z) that is fixed to the molecule [cf. Fig. 2(B)]. In this frame of reference, the term $\cos^2\theta$ can be conveniently expressed with the help of a probability tensor \mathbf{P} , which is a second order approximation of the orientational probability distribution of the direction of the external magnetic field in the molecular fixed frame of reference (6, 15). This probability tensor \mathbf{P} can be represented by an ellipsoid [cf. Fig. 3(A)] with a fixed orientation in the chosen molecular frame (x , y , z).

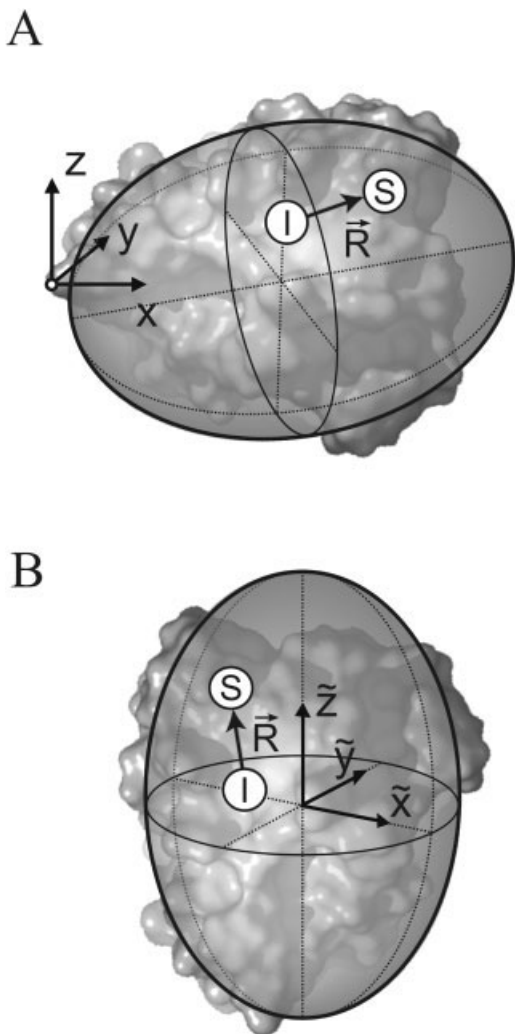


Figure 3 The molecule, a given internuclear vector \vec{R} and the probability ellipsoid (a graphical representation of the probability tensor \mathbf{P} , cf. Eq. [25]) are shown (A) in an arbitrarily chosen molecular frame [cf. Fig. 2(B)] and (B) in the special coordinate system (with axes \tilde{x} , \tilde{y} , \tilde{z}) defined by the principal axes of the probability ellipsoid.

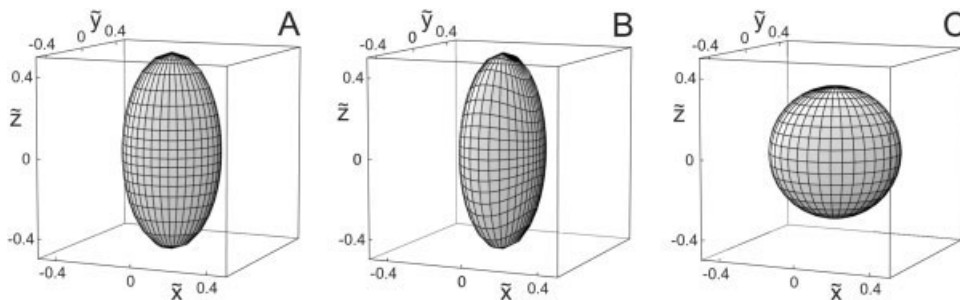


Figure 4 Examples of three characteristic probability ellipsoids (graphical representations of the probability tensor \mathbf{P} , cf. Eq. [25]) as seen from the principal axis system with axes \tilde{x} , \tilde{y} , \tilde{z} [cf. Fig. 3(B)]. (A) An axially symmetric probability ellipsoid with $P_{\tilde{x}} = P_{\tilde{y}} = 0.25$ and $P_{\tilde{z}} = 0.5$. (B) A rhombic probability ellipsoid with $P_{\tilde{x}} = 0.2$, $P_{\tilde{y}} = 0.3$, and $P_{\tilde{z}} = 0.5$. (C) An isotropic probability ellipsoid with $P_{\tilde{x}} = P_{\tilde{y}} = P_{\tilde{z}} = 1/3$.

The principal values $P_{\tilde{x}}$, $P_{\tilde{y}}$, and $P_{\tilde{z}}$ of the probability tensor (i.e., the lengths of the half axes of the *probability ellipsoid*) are the probabilities to find the magnetic field along the corresponding principal axes of the probability ellipsoid, and hence $P_{\tilde{x}} + P_{\tilde{y}} + P_{\tilde{z}} = 1$.

For example, for an isotropically reorienting molecule, $P_{\tilde{x}} = P_{\tilde{y}} = P_{\tilde{z}} = 1/3$, and the probability ellipsoid is reduced to a sphere [see Fig. 4(C)]. On the other hand, if a molecule is fully aligned, $P_{\tilde{x}} = P_{\tilde{y}} = 0$ and $P_{\tilde{z}} = 1$ (by convention, the principal elements are ordered with increasing magnitude), i.e., the probability tensor is reduced to a single line in the direction of the magnetic field.

In general, the principal axes of the probability ellipsoid define a special molecular fixed axis system (\tilde{x} , \tilde{y} , \tilde{z}), in which the calculation of residual dipolar coupling constants is especially simple [see Fig. 3(B)]: If we know the three Cartesian components $r_{\tilde{x}}$, $r_{\tilde{y}}$, and $r_{\tilde{z}}$ of any given internuclear unit vector \vec{r} in this principal axis system, the term $\cos^2\theta$ in Eq. [8] is simply given by

$$\overline{\cos^2\theta} = P_{\tilde{x}}r_{\tilde{x}}^2 + P_{\tilde{y}}r_{\tilde{y}}^2 + P_{\tilde{z}}r_{\tilde{z}}^2. \quad [10]$$

If this simple equation (derived below) is inserted into Eq. [9], the residual coupling constant can be predicted for any arbitrary spin pair in a molecule, as long as the orientation and principal values of the probability tensor are known.

With this key result, we can calculate everything, and we could stop here, except that residual dipolar coupling constants are commonly not expressed in terms of the introduced probability tensor \mathbf{P} (corresponding in general to a real symmetric 3×3 matrix with trace 1) but in terms of its traceless part (its “resolvent”) $\mathbf{P} - 1/3 \mathbf{I}$, which is called the *alignment tensor A* (5):

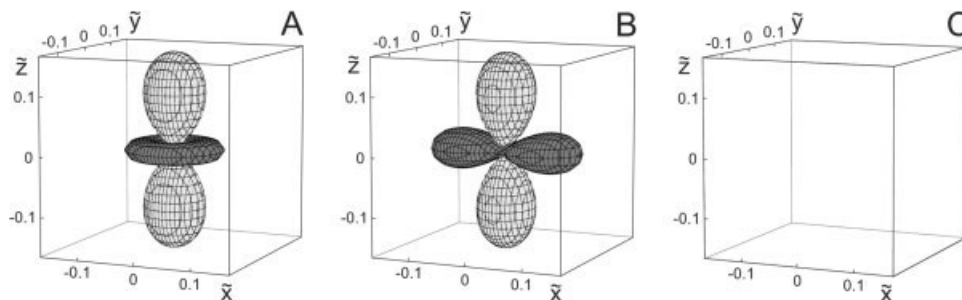


Figure 5 Graphical representations of the alignment tensors, which correspond to the three probability tensors shown in Figure 4(A–C). The principal components of the alignment tensor are (A) $A_{\bar{x}} = A_{\bar{y}} = 0.25 - 1/3 = -1/12$, $A_{\bar{z}} = 0.5 - 1/3 = -1/6$, (B) $A_{\bar{x}} = 0.2 - 1/3 = -2/15$, $A_{\bar{y}} = 0.3 - 1/3 = -1/30$, $A_{\bar{z}} = 0.5 - 1/3 = 1/6$, and (C) $A_{\bar{x}} = A_{\bar{y}} = A_{\bar{z}} = 1/3 - 1/3 = 0$. The plots show the surfaces where $(\vec{r}^T \mathbf{A} \vec{r})/R^3 = 1 \text{ \AA}^{-3}$ (light gray) or -1 \AA^{-3} (dark gray) if the \bar{x} , \bar{y} , and \bar{z} axes are labeled in units of \AA .

$$\mathbf{A} = \mathbf{P} - \frac{1}{3} \mathbf{1}. \quad [11]$$

The three principal components $A_{\bar{x}}$, $A_{\bar{y}}$, and $A_{\bar{z}}$ of the alignment tensor \mathbf{A} are simply given by

$$A_{\bar{x}} = P_{\bar{x}} - \frac{1}{3}, \quad A_{\bar{y}} = P_{\bar{y}} - \frac{1}{3}, \quad A_{\bar{z}} = P_{\bar{z}} - \frac{1}{3}, \quad [12]$$

and the principal axes of \mathbf{A} and \mathbf{P} are identical.

Note that in contrast to the probability tensor \mathbf{P} (see Figs. 3 and 4), the alignment tensor \mathbf{A} cannot be represented as an ellipsoid, because one or two of the principal components $A_{\bar{x}}$, $A_{\bar{y}}$, and $A_{\bar{z}}$ of the alignment tensor are negative if any of the three components is nonzero due to $A_{\bar{x}} + A_{\bar{y}} + A_{\bar{z}} = 0$. Alternative graphical representations of the effects of the alignment tensor are shown in Figures 5 and 6 (*vide infra*).

In terms of the principal components of the alignment tensor, the term $(\overline{\cos^2\theta} - 1/3)$ in the equation for the residual dipolar coupling constant (Eq. [9]) can be expressed as

$$\left(\overline{\cos^2\theta} - \frac{1}{3}\right) = A_{\bar{x}} r_{\bar{x}}^2 + A_{\bar{y}} r_{\bar{y}}^2 + A_{\bar{z}} r_{\bar{z}}^2. \quad [13]$$

If this equation is inserted into Eq. [9], it is again possible to predict the residual coupling constant for any arbitrary spin pair in a molecule, provided that the orientation and principal values of the alignment tensor are known.

Conversely, the alignment tensor \mathbf{A} (or the probability tensor \mathbf{P}) can be determined if a sufficient number of experimental dipolar coupling constants are measured for a given molecule (16). As will be shown below, the alignment tensor \mathbf{A} (and the probability tensor \mathbf{P}) is characterized by five independent

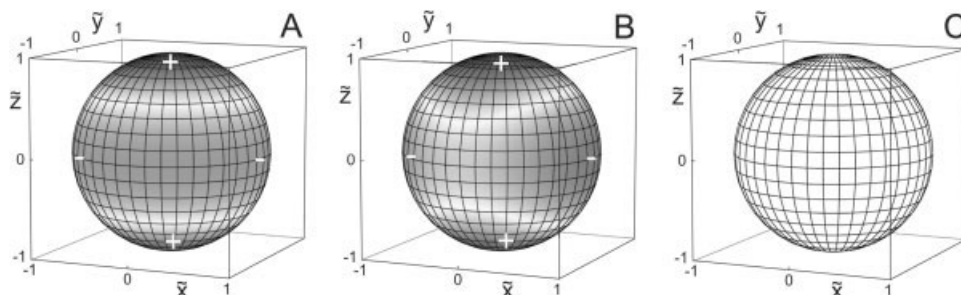


Figure 6 For the three cases shown in Figures 4 and 5 with (A) $A_{\bar{x}} = A_{\bar{y}} = -1/12$, $A_{\bar{z}} = -1/6$, (B) $A_{\bar{x}} = -2/15$, $A_{\bar{y}} = -1/30$, $A_{\bar{z}} = 1/6$, and (C) $A_{\bar{x}} = A_{\bar{y}} = A_{\bar{z}} = 0$, the magnitude of the scaling factor $(\overline{\cos^2\theta} - 1/3)$ is coded on a unit sphere as a function of the orientation of the internuclear vector \vec{R} (white: vanishing scaling factor). Positive and negative scaling factors are denoted by the respective sign.

parameters. Therefore, at least five dipolar coupling constants need to be measured in order to determine the five unknown parameters (16). In many cases, it is also possible to accurately predict the alignment tensor \mathbf{A} (17) or the probability tensor, \mathbf{P} for a given molecule in a given liquid crystalline solvent, and hence to predict the expected dipolar coupling constants for a proposed molecular structure from first principles.

DERIVATION OF THE PROBABILITY AND ALIGNMENT TENSORS

In an arbitrarily chosen molecular frame with axes (x , y , z) [see Fig. 2(B)], a given internuclear vector \vec{R} is constant (still assuming a rigid molecule without internal dynamics):

$$\vec{R} = R\vec{r} = R \begin{pmatrix} r_x \\ r_y \\ r_z \end{pmatrix}. \quad [14]$$

However, in this frame of reference, the direction of the magnetic field vector \vec{B} is time-dependent if the molecule tumbles in solution:

$$\vec{B} = B\vec{b} = B \begin{pmatrix} b_x(t) \\ b_y(t) \\ b_z(t) \end{pmatrix}. \quad [15]$$

The definition of $\cos \theta$ via the scalar product of the unit vectors \vec{b} and \vec{r} (cf. Eq. [8]) is valid in any frame of reference. Hence, we can express $\cos \theta$ in the molecular frame as a function of the components of the unit vectors \vec{b} and \vec{r} , which point in the (varying) direction of the magnetic field \vec{B} and of the (constant) internuclear vector \vec{R} , respectively:

$$\begin{aligned} \cos \theta &= \vec{b}^T \cdot \vec{r} = (b_x(t) \quad b_y(t) \quad b_z(t)) \begin{pmatrix} r_x \\ r_y \\ r_z \end{pmatrix} \\ &= b_x(t)r_x + b_y(t)r_y + b_z(t)r_z, \end{aligned} \quad [16]$$

and

$$\begin{aligned} \cos^2 \theta &= (b_x(t)r_x + b_y(t)r_y + b_z(t)r_z)^2 \\ &= b_x^2(t)r_x^2 + b_x(t)b_y(t)r_xr_y + b_x(t)b_z(t)r_xr_z \\ &\quad + b_y(t)b_x(t)r_yr_x + b_y^2(t)r_y^2 + b_y(t)b_z(t)r_yr_z \\ &\quad + b_z(t)b_x(t)r_zr_x + b_z(t)b_y(t)r_zr_y + b_z^2(t)r_z^2. \end{aligned} \quad [17]$$

Note that Eq. [17] can also be expressed in the form

$$\begin{aligned} \cos^2 \theta &= (r_x \quad r_y \quad r_z) \begin{pmatrix} b_x^2(t) & b_x(t)b_y(t) & b_x(t)b_z(t) \\ b_x(t)b_y(t) & b_y^2(t) & b_y(t)b_z(t) \\ b_x(t)b_z(t) & b_y(t)b_z(t) & b_z^2(t) \end{pmatrix} \begin{pmatrix} r_x \\ r_y \\ r_z \end{pmatrix}. \end{aligned} \quad [18]$$

Hence, the time average of $\cos^2 \theta$ is given by

$$\begin{aligned} \overline{\cos^2 \theta} &= (r_x \quad r_y \quad r_z) \begin{pmatrix} \overline{b_x^2(t)} & \overline{b_x(t)b_y(t)} & \overline{b_x(t)b_z(t)} \\ \overline{b_x(t)b_y(t)} & \overline{b_y^2(t)} & \overline{b_y(t)b_z(t)} \\ \overline{b_x(t)b_z(t)} & \overline{b_y(t)b_z(t)} & \overline{b_z^2(t)} \end{pmatrix} \begin{pmatrix} r_x \\ r_y \\ r_z \end{pmatrix} \\ &= \vec{r}^T \mathbf{P} \vec{r}. \end{aligned} \quad [19]$$

We call the matrix

$$\mathbf{P} = \begin{pmatrix} \overline{b_x^2(t)} & \overline{b_x(t)b_y(t)} & \overline{b_x(t)b_z(t)} \\ \overline{b_x(t)b_y(t)} & \overline{b_y^2(t)} & \overline{b_y(t)b_z(t)} \\ \overline{b_x(t)b_z(t)} & \overline{b_y(t)b_z(t)} & \overline{b_z^2(t)} \end{pmatrix} \quad [20]$$

the *probability matrix*. For a known probability matrix, \mathbf{P} , the residual dipolar coupling constant (Eq. [9]) is given by

$$\bar{D} = \frac{\kappa}{R^3} \left(\vec{r}^T \mathbf{P} \vec{r} - \frac{1}{3} \right). \quad [21]$$

The matrix \mathbf{P} is real, symmetric, and has a trace of 1 because

$$\begin{aligned} \text{tr}\{\mathbf{P}\} &= P_{xx} + P_{yy} + P_{zz} = \overline{b_x^2(t)} + \overline{b_y^2(t)} + \overline{b_z^2(t)} \\ &= \overline{(b_x^2(t) + b_y^2(t) + b_z^2(t))} = 1, \end{aligned} \quad [22]$$

since by definition, \vec{b} is a unit vector, and hence, $b_x^2(t) + b_y^2(t) + b_z^2(t) = 1$ for all times t . Therefore, \mathbf{P} is fully specified by only five independent parameters. The matrix \mathbf{P} can be represented graphically as an ellipsoid (see Figs. 3 and 4). The three principal axes \vec{x} , \vec{y} , and \vec{z} of this ellipsoid are defined by the three eigenvectors of the matrix \mathbf{P} and the lengths of the three half axes are defined by the eigenvalues $P_{\vec{x}}$, $P_{\vec{y}}$, and $P_{\vec{z}}$ [see Fig. 3(A)].

In the special frame of reference defined by this principal axis system [see Fig. 3(B)], the matrix \mathbf{P} is diagonal:

$$\mathbf{P} = \begin{pmatrix} P_{\bar{x}} & 0 & 0 \\ 0 & P_{\bar{y}} & 0 \\ 0 & 0 & P_{\bar{z}} \end{pmatrix}. \quad [23]$$

In this case the eigenvalues (principal values) $P_{\bar{x}} = \overline{b_{\bar{x}}^2}$, $P_{\bar{y}} = \overline{b_{\bar{y}}^2}$, and $P_{\bar{z}} = \overline{b_{\bar{z}}^2}$ are the probabilities to find the magnetic field along the principal axes \bar{x} , \bar{y} , and \bar{z} , respectively. Therefore we call \mathbf{P} simply the probability tensor. [Rigorously, \mathbf{P} corresponds to the sum of the zero and second-order term of a spherical harmonics expansion of the probability distribution function describing the orientation of a reference vector relative to a rigid body (4, 15).]

In the principal axis system, Eq. [21] for the calculation of the residual dipolar coupling reduces simply to

$$\bar{D} = \frac{\kappa}{R^3} \left(P_{\bar{x}} r_{\bar{x}}^2 + P_{\bar{y}} r_{\bar{y}}^2 + P_{\bar{z}} r_{\bar{z}}^2 - \frac{1}{3} \right). \quad [24]$$

For example, in the static case,

$$\bar{\mathbf{b}} = \begin{pmatrix} b_x \\ b_y \\ b_z \end{pmatrix}$$

is constant, and hence,

$$\mathbf{P} = \begin{pmatrix} b_x^2 & b_x b_y & b_x b_z \\ b_x b_y & b_y^2 & b_y b_z \\ b_x b_z & b_y b_z & b_z^2 \end{pmatrix}. \quad [25]$$

The matrix has a much simpler form in the principal axis frame (\bar{x} , \bar{y} , \bar{z}), where the \bar{z} axis is parallel to the vector $\bar{\mathbf{b}}$. In this reference frame,

$$\bar{\mathbf{b}} = \begin{pmatrix} b_{\bar{x}} \\ b_{\bar{y}} \\ b_{\bar{z}} \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix} \quad \text{and} \quad \mathbf{P} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix}. \quad [26]$$

In this case, the probability ellipsoid is reduced to a line along the \bar{z} axis and the dipolar coupling constant is

$$\bar{D} = D = \frac{\kappa}{R^3} \left(r_{\bar{z}}^2 - \frac{1}{3} \right). \quad [27]$$

For a completely isotropically reorienting molecule, the averages $\overline{b_x(t)b_y(t)}$, $\overline{b_x(t)b_z(t)}$, $\overline{b_y(t)b_z(t)}$ are zero, and $P_{\bar{x}} = P_{\bar{y}} = P_{\bar{z}} = 1/3$, i.e., the probability matrix:

$$\mathbf{P} = \begin{pmatrix} \frac{1}{3} & 0 & 0 \\ 0 & \frac{1}{3} & 0 \\ 0 & 0 & \frac{1}{3} \end{pmatrix} \quad [28]$$

is diagonal in any molecular fixed frame of reference. Hence, there is an equal probability of 1/3 for the magnetic field direction to point along all three axes of reference. The corresponding probability ellipsoid is a sphere with radius 1/3 [see Fig. 4(C)], and the residual dipolar coupling constant is

$$\bar{D} = \frac{\kappa}{R^3} \left(\frac{1}{3} (r_{\bar{x}}^2 + r_{\bar{y}}^2 + r_{\bar{z}}^2) - \frac{1}{3} \right) = 0. \quad [29]$$

Figure 4(A) shows an example of an axially symmetric probability ellipsoid with the principal values $P_{\bar{x}} = P_{\bar{y}} = 0.25$ and $P_{\bar{z}} = 0.5$. Figure 4(B) shows an example without axial symmetry, where $P_{\bar{x}} = 0.2$, $P_{\bar{y}} = 0.3$, and $P_{\bar{z}} = 0.5$. Note that the lack of axial symmetry simply means that there are two different probabilities $P_{\bar{x}} \neq P_{\bar{y}}$ for the magnetic field to point along the principal axes \bar{x} and \bar{y} of the molecular-fixed probability tensor. However, this does by no means imply that in the lab frame there are different probabilities for the molecule to be aligned along the x^L or y^L direction. For example in the case shown in Figure 4(B), $P_{\bar{x}} = 0.2$, $P_{\bar{y}} = 0.3$, and $P_{\bar{z}} = 0.5$ are the probabilities that the \bar{x} , \bar{y} , and \bar{z} axes are aligned parallel to B_0 .

In the NMR literature, it is not customary to consider the probability tensor \mathbf{P} (which can be nicely depicted as an ellipsoid), but to use its traceless part which is called the alignment tensor

$$\mathbf{A} = \mathbf{P} - \frac{1}{3} \mathbf{1}. \quad [30]$$

If we multiply \mathbf{A} from the left with the unit row vector $\bar{\mathbf{r}}^T$ and from the right with the column vector $\bar{\mathbf{r}}$ and using Eq. [19] and Eq. [30], we get

$$\begin{aligned} \bar{\mathbf{r}}^T \mathbf{A} \bar{\mathbf{r}} &= \bar{\mathbf{r}}^T \left(\mathbf{P} - \frac{1}{3} \mathbf{1} \right) \bar{\mathbf{r}} \\ &= \bar{\mathbf{r}}^T \mathbf{P} \bar{\mathbf{r}} - \frac{1}{3} \bar{\mathbf{r}}^T \bar{\mathbf{r}} \\ &= \overline{\cos^2 \theta} - \frac{1}{3}, \end{aligned} \quad [31]$$

which can also be used to calculate the residual dipolar coupling constant in Eq. [9] or [21]:

$$\bar{D} = \frac{\kappa}{R^3} (\bar{r}^T \mathbf{A} \bar{r}). \quad [32]$$

\mathbf{P} and \mathbf{A} have the same principal axis system (\tilde{x} , \tilde{y} , \tilde{z}) (except for a possible reordering of the axis labels if the convention is used that $|P_{\tilde{x}}| \leq |P_{\tilde{y}}| \leq |P_{\tilde{z}}|$ and $|A_{\tilde{x}}| \leq |A_{\tilde{y}}| \leq |A_{\tilde{z}}|$), and the principal values are related by

$$A_{\tilde{x}} = P_{\tilde{x}} - \frac{1}{3}, \quad A_{\tilde{y}} = P_{\tilde{y}} - \frac{1}{3},$$

and

$$A_{\tilde{z}} = P_{\tilde{z}} - \frac{1}{3}, \quad [33]$$

with $A_{\tilde{x}} + A_{\tilde{y}} + A_{\tilde{z}} = 0$.

In the principal axis system

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = A_{\tilde{x}} r_{\tilde{x}}^2 + A_{\tilde{y}} r_{\tilde{y}}^2 + A_{\tilde{z}} r_{\tilde{z}}^2, \quad [34]$$

and hence, the residual dipolar coupling constant is given by

$$\bar{D} = \frac{\kappa}{R^3} (A_{\tilde{x}} r_{\tilde{x}}^2 + A_{\tilde{y}} r_{\tilde{y}}^2 + A_{\tilde{z}} r_{\tilde{z}}^2). \quad [35]$$

The alignment tensor cannot be represented as an ellipsoid, because at least one of the principal values is always negative if $\mathbf{A} \neq 0$.

In Figure 5, we show a graphical representation of the \mathbf{A} tensors which corresponds to the \mathbf{P} tensors shown in Figure 4. The plots show the surfaces where the term $|\bar{r}^T \mathbf{A} \bar{r} / R^3|$ is constant. Hence, if spin I is assumed to be located in the origin, the plots show the possible locations of spin S for which the residual dipolar coupling constants has the same magnitude. For the case of an isotropically reorienting molecule (spherical probability tensor), the residual dipolar coupling is always zero, and no such surface exists.

The dependence of the scaling factor $(\overline{\cos^2 \theta} - 1/3)$ on the orientation of the internuclear vector is sometimes shown by the color of a unit sphere. For the three cases shown in Figure 4 and 5, the corresponding grayscale coded surface representations of the alignment tensors are shown in Figure 6. The grayscale intensity represents the scaling factor of a residual dipolar coupling constant if spin I is located at the

origin and spin S is moved over the surface, i.e., assuming a constant internuclear distance.

For example, in the axially symmetric case shown in Figure 6(A) with $A_{\tilde{x}} = A_{\tilde{y}} = -1/12$ and $A_{\tilde{z}} = 1/6$, the scaling factor $(\overline{\cos^2 \theta} - 1/3)$ is zero if the \tilde{z} -component of the internuclear vector is $r_{\tilde{z}} = \sqrt{1/3}$, which is straightforward to see if Eq. [34] is set to zero and using $r_{\tilde{x}}^2 + r_{\tilde{y}}^2 = 1 - r_{\tilde{z}}^2$. This corresponds to an angle of $\vartheta = \arccos \sqrt{1/3} = 54.74^\circ$ (the *magic angle*) between the internuclear vector and the \tilde{z} -axis. For the case shown in Figure 6(B) with $A_{\tilde{x}} = -2/15$, $A_{\tilde{y}} = -1/30$, and $A_{\tilde{z}} = 1/6$, the polar angle ϑ , when the scaling factor is zero, depends also on the azimuthal angle φ between the \tilde{x} -axis and the projection of \bar{r} on the \tilde{x}/\tilde{y} plane. For example, in the \tilde{x}/\tilde{z} plane, the scaling factor is zero if $r_{\tilde{z}} = 2/3$ [corresponding to $\vartheta = \arccos(2/3) = 48.19^\circ$], and in the \tilde{y}/\tilde{z} plane, the scaling factor is zero if $r_{\tilde{z}} = \sqrt{1/6}$ ($\vartheta = \arccos \sqrt{1/6} = 65.91^\circ$). In the isotropic case shown in Figure 6(C), the scaling factor $(\overline{\cos^2 \theta} - 1/3)$ is zero for all orientations of the internuclear vector \bar{R} .

APPENDIX

In the Appendix, the key equations (Eqs. [24] and [35]) for the calculation of the residual dipolar coupling constant \bar{D} are reexpressed in various more or less complicated forms found in literature. If the unit vector \bar{r} is defined in terms of the polar coordinates ϑ and φ in the principal axis system of the alignment tensor \mathbf{A} , then

$$\bar{r} = \begin{pmatrix} r_{\tilde{x}} \\ r_{\tilde{y}} \\ r_{\tilde{z}} \end{pmatrix} = \begin{pmatrix} \sin \vartheta \cos \varphi \\ \sin \vartheta \sin \varphi \\ \cos \vartheta \end{pmatrix} \quad [36]$$

and hence (according to Eq. [34]):

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = A_{\tilde{x}} \sin^2 \vartheta \cos^2 \varphi + A_{\tilde{y}} \sin^2 \vartheta \sin^2 \varphi + A_{\tilde{z}} \cos^2 \vartheta. \quad [37]$$

This can be simplified by noting that $\cos^2 \varphi = (1 + \cos 2\varphi)/2$ and $\sin^2 \varphi = (1 - \cos 2\varphi)/2$:

$$\begin{aligned} \left(\overline{\cos^2 \theta} - \frac{1}{3} \right) &= \frac{A_{\tilde{x}}}{2} \sin^2 \vartheta + \frac{A_{\tilde{x}}}{2} \sin^2 \vartheta \cos 2\varphi \\ &+ \frac{A_{\tilde{y}}}{2} \sin^2 \vartheta - \frac{A_{\tilde{y}}}{2} \sin^2 \vartheta \cos 2\varphi \\ &+ A_{\tilde{z}} \cos^2 \vartheta = \end{aligned}$$

$$\frac{A_{\bar{x}} + A_{\bar{y}}}{2} \sin^2 \vartheta + \frac{A_{\bar{x}} - A_{\bar{y}}}{2} \sin^2 \vartheta \cos 2\varphi + A_{\bar{z}} \cos^2 \vartheta. \quad [38]$$

Since \mathbf{A} is a traceless matrix, $A_{\bar{x}} + A_{\bar{y}} = -A_{\bar{z}}$, and we can rewrite Eq. [38] as

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = A_{\bar{z}} \left(\cos^2 \vartheta - \frac{\sin^2 \vartheta}{2} \right) + \frac{A_{\bar{x}} - A_{\bar{y}}}{2} \sin^2 \vartheta \cos 2\varphi. \quad [39]$$

The prefactor of $A_{\bar{z}}$ can be further simplified by using the relation $\sin^2 \vartheta = 1 - \cos^2 \vartheta$:

$$\begin{aligned} \cos^2 \vartheta - \frac{\sin^2 \vartheta}{2} &= \cos^2 \vartheta - \frac{(1 - \cos^2 \vartheta)}{2} \\ &= \frac{1}{2} (3 \cos^2 \vartheta - 1). \end{aligned} \quad [40]$$

Thus, we arrive at

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = \frac{A_{\bar{z}}}{2} (3 \cos^2 \vartheta - 1) + \frac{A_{\bar{x}} - A_{\bar{y}}}{2} \sin^2 \vartheta \cos 2\varphi. \quad [41]$$

Equation [41] can alternatively be expressed in terms of the principal values $S_{\bar{x}}$, $S_{\bar{y}}$, and $S_{\bar{z}}$ of the *Saupe matrix* (or *order matrix*) \mathbf{S} , which is simply the alignment matrix \mathbf{A} scaled by a factor of $3/2$, if the optical axis of the liquid crystal is collinear with the direction of the magnetic field (9, 10):

$$\mathbf{S} = 3/2\mathbf{A}. \quad [42]$$

Hence,

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = \frac{1}{3} \{ S_{\bar{z}} (3 \cos^2 \vartheta - 1) + (S_{\bar{x}} - S_{\bar{y}}) \sin^2 \vartheta \cos 2\varphi \}. \quad [43]$$

Often, the *axial component* A_a of the alignment tensor is defined as (5)

$$A_a = \frac{3}{2} A_{\bar{z}} = S_{\bar{z}}, \quad [44]$$

and the *rhombic component* A_r of the alignment tensor is defined as

$$A_r = A_{\bar{x}} - A_{\bar{y}} = \frac{2}{3} (S_{\bar{x}} - S_{\bar{y}}). \quad [45]$$

With these definitions, we can express Eqs. [41] and [43] as

$$\left(\overline{\cos^2 \theta} - \frac{1}{3} \right) = \frac{1}{3} \left\{ A_a (3 \cos^2 \vartheta - 1) + \frac{3}{2} A_r \sin^2 \vartheta \cos 2\varphi \right\}, \quad [46]$$

which in turn is often written as

$$\begin{aligned} \left(\overline{\cos^2 \theta} - \frac{1}{3} \right) &= \frac{A_a}{3} \left\{ (3 \cos^2 \vartheta - 1) + \frac{3}{2} R \sin^2 \vartheta \cos 2\varphi \right\} \\ &= \frac{A_a}{3} \{ (3 \cos^2 \vartheta - 1) + \eta \sin^2 \vartheta \cos 2\varphi \}, \end{aligned} \quad [47]$$

where

$$R = \frac{A_r}{A_a} \quad [48]$$

is called the *rhombicity* of the alignment tensor and

$$\eta = \frac{A_{\bar{x}} - A_{\bar{y}}}{A_{\bar{z}}} = \frac{S_{\bar{x}} - S_{\bar{y}}}{S_{\bar{z}}} = \frac{3}{2} R \quad [49]$$

is called the *asymmetry parameter*, which describes the deviation from axially symmetric ordering (6).

So far, we have assumed a rigid molecule that tumbles in solution. In the presence of internal motions the derivation of residual dipolar couplings becomes more complicated (6, 18, 19). Provided the alignment process is not affected by intramolecular motion, the analysis is relatively straightforward. If the internal motion of the internuclear vector \vec{r} is axially symmetric with respect to the average orientation \vec{r}_{av} , the dipolar coupling expected for this average orientation is scaled by a factor λ , which is identical to a generalized order parameter S ($0 \leq S \leq 1$) (18). The latter corresponds mathematically to the spin relaxation order parameter (19, 20), but exhibits a sensitivity to motions extending to the millisecond time scale (6, 18). This leads to the following equation of the residual dipolar coupling constant:

$$\bar{D} = S \frac{\kappa A_a}{3 R^3} \{ (3 \cos^2 \vartheta - 1) + \eta \sin^2 \vartheta \cos 2\varphi \}. \quad [50]$$

This expression is often rewritten using the *maximum dipolar coupling* $D_{\max} = (2/3)\kappa/R^3$ (cf. Eq. [7]) or the so called *magnitude of the residual dipolar coupling tensor* $D_a = D_{\max}A_a/2$ (7):

$$\begin{aligned} \bar{D} &= SD_a \{ (3 \cos^2 \vartheta - 1) + \eta \sin^2 \vartheta \cos 2\varphi \} \\ &= S \frac{D_{\max}}{2} A_a \{ (3 \cos^2 \vartheta - 1) \\ &\quad + \eta \sin^2 \vartheta \cos 2\varphi \} \\ &= SD_{\max} A_a \left\{ P_2(\cos \vartheta) + \frac{\eta}{2} \sin^2 \vartheta \cos 2\varphi \right\}, \end{aligned} \quad [51]$$

where $P_2(x) = (3 \cos^2 x - 1)/2$ is the second-order Legendre polynomial.

Finally, we use the results derived in this manuscript to introduce the concepts of the *generalized degree of order* (GDO) of a given alignment tensor \mathbf{A} (22) and the *generalized angle* between two different alignment tensors $\mathbf{A}^{(1)}$ and $\mathbf{A}^{(2)}$ (23).

In complete analogy to the scalar product between two real vectors, the scalar product between two real matrices (e.g., two alignment matrices $\mathbf{A}^{(1)}$ and $\mathbf{A}^{(2)}$) is defined as

$$\langle \mathbf{A}^{(1)} | \mathbf{A}^{(2)} \rangle = \sum_{i,j} A_{ij}^{(1)} A_{ij}^{(2)} \quad [52]$$

and the norm $|\mathbf{A}|$ of the real matrix \mathbf{A} is given by

$$|\mathbf{A}| = \sqrt{\langle \mathbf{A} | \mathbf{A} \rangle} = \sqrt{\sum_{i,j} A_{ij}^2}. \quad [53]$$

The maximum order is found for the static case, where the probability tensor \mathbf{P}_{\max} is given by Eq. [26] in the principal axis system. The corresponding maximum alignment tensor $\mathbf{A}_{\max} = \mathbf{P}_{\max} - 1/3 \mathbf{1}$ has the form

$$\mathbf{A}_{\max} = \begin{pmatrix} -1/3 & 0 & 0 \\ 0 & -1/3 & 0 \\ 0 & 0 & 2/3 \end{pmatrix}. \quad [54]$$

The norm of \mathbf{A}_{\max} is given by

$$|\mathbf{A}_{\max}| = \sqrt{\frac{1}{9} + \frac{1}{9} + \frac{4}{9}} = \sqrt{\frac{2}{3}}. \quad [55]$$

The GDO of a given order matrix \mathbf{A} can be defined as

$$\text{GDO} = \frac{|\mathbf{A}|}{|\mathbf{A}_{\max}|} = \sqrt{\frac{3}{2}} |\mathbf{A}|. \quad [56]$$

In terms of the Saupe matrix $\mathbf{S} = 3/2\mathbf{A}$ (cf. Eq. [42]), this can be written as (6, 22)

$$\text{GDO} = \sqrt{\frac{2}{3}} |\mathbf{S}|. \quad [57]$$

In literature, the symbol ϑ is often used for the GDO, but we do not use the symbol here in order to avoid confusion with the polar angle ϑ defined in Eq. [36].

The GDO is independent of the molecular-fixed frame, in which the alignment tensor \mathbf{A} is expressed. In the principal axis system only the diagonal elements of \mathbf{A} are nonzero and Eq. [56] simplifies to

$$\text{GDO} = \sqrt{\frac{3}{2}} \sqrt{A_x^2 + A_y^2 + A_z^2}. \quad [58]$$

For axially symmetric alignment tensors ($A_x = A_y = -A_z/2$) this simplifies further to (22):

$$\begin{aligned} \text{GDO} &= \sqrt{\frac{3}{2}} \left(\frac{1}{4} A_z^2 + \frac{1}{4} A_z^2 + A_z^2 \right) = \frac{3}{2} \sqrt{A_z^2} \\ &= \frac{3}{2} |A_z| = |S_z|. \end{aligned} \quad [59]$$

With the help of the scalar product, we can also define the generalized angle β between two alignment tensors $\mathbf{A}^{(1)}$ and $\mathbf{A}^{(2)}$, which correspond, e.g., to two different alignment media.

If the matrix representations of $\mathbf{A}^{(1)}$ and $\mathbf{A}^{(2)}$ are given in a common molecular frame of reference, the cosine of the generalized angle β between these alignment tensors can be defined as the normalized scalar product between them (23):

$$\cos \beta = \frac{\langle \mathbf{A}^{(1)} | \mathbf{A}^{(2)} \rangle}{|\mathbf{A}^{(1)}| |\mathbf{A}^{(2)}|}. \quad [60]$$

REFERENCES

1. Bastiaan EW, Maclean C, Van Zijl PCM, Bothner-By AA. 1987. High-resolution NMR of liquids and gases:

- Effects of magnetic-field-induced molecular alignment. *Annu Rep NMR Spectrosc* 19:35–77.
2. Tolman JR, Flanagan J, Kennedy MA, Prestegard JH. 1995. Nuclear magnetic dipole interactions in field-oriented proteins: Information for structure determination in solution. *Proc Natl Acad Sci USA* 92:9279–9283.
 3. Bothner-By AA. 1996. Magnetic field induced alignment of molecules. In: *Encyclopedia of Nuclear Magnetic Resonance*. Grant DM and Harris RK, editors. London: Wiley, p 2932–2938.
 4. Emsley JW. 1996. Liquid crystals: General considerations. In: *Encyclopedia of Nuclear Magnetic Resonance*. Grant DM and Harris RK, editors. London: Wiley, pp 2788–2799.
 5. Tjandra N, Bax A. 1997. Direct measurement of distances and angles in biomolecules by NMR in a dilute liquid crystalline medium. *Science* 278:1111–1114.
 6. Prestegard JH, Al-Hashimi HM, Tolman JR. 2000. NMR structures of biomolecules using field oriented media and residual dipolar couplings. *Quart Rev Biophys* 33:371–424.
 7. Bax A, Kontaxis G, Tjandra N. 2001. Dipolar couplings in macromolecular structure determination. *Methods Enzymol* 339:127–173.
 8. Brunner E. 2001. The use of residual dipolar couplings in protein NMR. *Concepts Magn Reson* 13:238–259.
 9. Saupe A, Englert G. 1963. High-resolution nuclear magnetic resonance spectra of oriented molecules. *Phys Rev Lett* 11:462–464.
 10. Englert E, Saupe A. 1964. Kernresonanzen in kristallinen Flüssigkeiten und in kristallinflüssigen Lösungen. Teil I. *Zeitschrift Naturforschung* 19A:161–171.
 11. Hansen MR, Mueller L, Pardi A. 1998. Tunable alignment of macromolecules by filamentous phage yields dipolar coupling interactions. *Nat Struct Biol* 5:1065–1074.
 12. Tycko R, Blanco FJ, Ishii Y. 2000. Alignment of biopolymers in strained gels: A new way to create detectable dipole-dipole couplings in high-resolution biomolecular NMR. *J Am Chem Soc* 122:9340–9341.
 13. Sass HJ, Musco G, Stahl SJ, Wingfield PT, Grzesiek S. 2000. Solution NMR of proteins within polyacrylamide gels: Diffusional properties and residual alignment by mechanical stress or embedding of oriented purple membranes. *J Biomol NMR* 18:303–309.
 14. Ernst RR, Bodenhausen G, Wokaun A. 1987. *Principles of Nuclear Magnetic Resonance in One and Two Dimensions*. New York: Oxford University Press.
 15. Snyder LC. 1965. Analysis of molecular magnetic resonance spectra of molecules in liquid-crystal solvents. *J Chem Phys* 43:4041–4050.
 16. Losonczi JA, Andrec M, Fischer MWF, Prestegard JH. 1999. Order matrix analysis of residual dipolar couplings using singular value decomposition. *J Magn Reson* 138:334–342.
 17. Zweckstetter M, Bax A. 2000. Prediction of sterically induced alignment in a dilute liquid crystalline phase: Aid to protein structure determination by NMR. *J Am Chem Soc* 122:3791–3792.
 18. Tolman JR, Flanagan JM, Kennedy MA, Prestegard JH. 1997. NMR evidence for slow collective motions in cyanometmyoglobin. *Nature Struct Biol* 4:292–297.
 19. Lipari G, Szabo A. 1982. Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. 1. Theory and range of validity. *J Am Chem Soc* 104:4546–4559.
 20. Lipari G, Szabo A. 1982. Model-free approach to the interpretation of nuclear magnetic resonance relaxation in macromolecules. 2. Analysis of experimental results. *J Am Chem Soc* 104:4559–4570.
 21. Meiler J, Prompers JJ, Peti W, Griesinger C, Brüschweiler R. 2001. Model-free approach to the dynamic interpretation of residual dipolar couplings in globular proteins. *J Am Chem Soc* 123:6098–6107.
 22. Tolman JR, Al-Hashimi HM, Kay LE, Prestegard JH. 2001. Structural and dynamic analysis of residual dipolar coupling data for proteins. *J Am Chem Soc* 123:1416–1424.
 23. Sass J, Cordier F, Hoffmann A, Rogowski M, Cousin A, Omichinski JG, Löwen H, Grzesiek S. 1999. Purple membrane induced alignment of biological macromolecules in the magnetic field. *J Am Chem Soc* 121:2047–2055.

BIOGRAPHIES



Frank Kramer received a diploma in chemistry from the Johann Wolfgang Goethe University in Frankfurt, Germany, in 1999. His doctoral research in the group of Prof. Dr. Steffen J. Glaser at the Technical University Munich dealt with residual dipolar couplings in high-resolution NMR spectroscopy and involved the theoretical analysis, computer-assisted development and experimental application of multipulse-experiments. For his work on residual dipolar couplings he received the Ernst award 2003 of the German Chemical Society (GDCh).



Mandar V. Deshmukh is currently a Ph.D. student in the group of Prof. Dr. Horst Kessler. He was born in Nanded (India) in 1975. In 1997, he received M. Sc. in Chemistry from Dr. B. A. M. University, Aurangabad (India). He later worked as a research assistant at National Chemical Laboratory, Pune (India) where he was introduced to high level Nuclear Magnetic Resonance studies and applications oriented to Polymers. In Oct. 2000, Mr. Deshmukh joined Prof. Dr. Horst Kessler as a Ph.D. student at Technische Universität München. His core topic of Ph.D. is biomolecular NMR spectroscopy. It involves theory and applications of residual dipolar couplings, relaxation, dynamics and ligand binding studies of biological macromolecules.



Horst Kessler was born in Suhl (Thuringia) Germany in 1940. He studied chemistry in Leipzig and Tübingen, where he received his Ph.D. degree with Eugen Müller in 1966 and his habilitation in 1969. He was appointed full professor for organic chemistry at the J. W. von Goethe Universität in Frankfurt in 1971. In 1989, he moved to the Technische Universität München. Prof. Kessler is the

recipient of the Otto Bayer award (1986), the Max Bergmann medal for peptide chemistry (1988), the Emil Fischer medal (1997), the Max-Planck-Forschungspreis (2001), Vincent du Vigneaud Award (2002) of the American Peptide Society and the Philip-Morris Award (2003). Since 1996, he has been a member of the “Bayerische Akademie der Wissenschaft” and of the “Deutsche Akademie der Naturforscher Leopoldina”. Guest professorships led him to Halifax, Tokyo, Madison, Haifa, Austin, and Jerusalem. His current interests are in the area of the development and application of new NMR techniques to peptides, proteins and nucleic acids as well as their complexes. Another field of interest is bioorganic and medicinal chemistry, with specific focus on the study of biological recognition phenomena and on conformationally oriented design of

biologically active molecules, such as peptides, peptidomimetics and carbohydrates.



Steffen J. Glaser was born in Gochsheim (Baden) Germany in 1958. He studied physics in Heidelberg and finished his Ph.D. thesis in the group of Hans-Robert Kalbitzer at the Max Planck Institut für Medizinische Forschung in 1987. For three years he worked as a postdoctoral fellow in the group of Prof. Gary Drobny at the University of Washington, Seattle. In 1990 Steffen Glaser

joined the group of Christian Griesinger at the Universität Frankfurt, where he received his habilitation in 1994. He continued to work as a group leader and Heisenberg fellow in Frankfurt until 1999, when he was appointed professor for organic chemistry at the Technische Universität München. General goals of his group are the development of novel theory and experimental techniques in NMR. His current focus of research is the development of multiple-pulse sequences for applications to partially aligned biomolecules and the application of optimal control theory to NMR and quantum information processing. In 2003, he received the Award for Good Teaching of the Bavarian Ministry of Science, Research and Arts.