JOURNAL OF MAGNETIC RESONANCE 87, 357–362 (1990)

Sensitivity Analysis of Magnetic Resonance Spectra from Unoriented Samples

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Received May 23, 1989; revised August 29, 1989

In a recent paper, Hyde *et al.* (*1*) explored the sensitivity of the EPR spectra of square-planar Cu^{2+} complexes to variations of the spin-Hamiltonian parameters by simulation of spectra both at the rigid limit and under a range of rotational correlation times. The purpose of this sensitivity analysis was to establish criteria for the optimum determination of the various parameters by simulation. The paper raised various questions, the central of which regards the conventional strategy of minimizing the sum of squares (or absolute value) of the deviation between the experimental and simulated spectra throughout the entire anisotropic lineshape. This difficulty arose because of the, at first surprising, result that the same region of the spectrum displayed maximum sensitivity to the parameters corresponding both to the parallel and to the perpendicular orientation of the magnetic field with respect to the principal axis.

A somewhat analogous problem to that considered in Ref. (*1*) is the analysis of the sensitivity of STEPR spectra to anisotropic motion. This was addressed previously by determining those regions of the spectrum that displayed optimum discrimination between axial and off-axial motion (*2*). In the present paper the same approach is employed to sensitivity analysis in conventional EPR. A simple analytical axial model is considered, which contains the essential features of anisotropic powder patterns, and this is used to define the spectral regions with optimum discrimination between the different spin-Hamiltonian parameters.

The general spectral intensity distribution for a sample with an orientational distribution, $p(\Omega)$, is

$$I(\delta) = p(\Omega) \cdot d\Omega/d\delta, \qquad [1]$$

where δ is the spectral scan parameter, either magnetic field or RF frequency. For an axially symmetric system; $p(\Omega) \cdot d\Omega = \sin\theta \cdot d\theta$ $(0 \leqslant \theta \leqslant \pi/2)$, assuming the orientational distribution to be isotropic. The angular dependence of the resonance position is assumed to be

$$\delta = (\delta_{\|} - \delta_{\perp})\cos^2\theta + \delta_{\perp}, \qquad [2]$$

where $\delta_{\|}$, $\delta_{\perp}$ are the line positions corresponding to the magnetic field oriented parallel or perpendicular to the principal axis, respectively. This approximation is valid

0022-2364/90 $3.00

for non-Zeeman splittings in high field, assuming the Zeeman anisotropy to be small, and also for Zeeman splittings with small anisotropy in frequency-swept experiments (e.g., ^{31}P NMR chemical-shift anisotropies, ^{2}H NMR quadrupole splittings, spin label EPR). The resulting normalized lineshape, neglecting line broadening, is

$$I(\delta) = \tfrac{1}{2}[(\delta_{\|} - \delta_{\perp})(\delta - \delta_{\perp})]^{-1/2} \qquad [3]$$

which is valid for the range $\delta_{\perp} \leqslant \delta \leqslant \delta_{\|}$. The first derivative display is correspondingly

$$dI/d\delta = -\tfrac{1}{2}I(\delta)\cdot(\delta - \delta_{\perp})^{-1}. \qquad [4]$$

Sensitivity to spin-Hamiltonian parameters. First the sensitivities, $dI/d\delta_i$, of the absorption lineshape to changes in the parameters, δ_i, will be considered:

$$dI/d\delta_{\|} = -\tfrac{1}{2}I(\delta)\cdot(\delta_{\|} - \delta_{\perp})^{-1} \qquad [5]$$

$$dI/d\delta_{\perp} = \tfrac{1}{2}I(\delta)\cdot(\delta_{\|} - \delta_{\perp})^{-1}[1 + (\delta_{\|} - \delta_{\perp})/(\delta - \delta_{\perp})]. \qquad [6]$$

These equations directly reflect the sensitivities of the non-Zeeman splittings (e.g., hyperfine or quadrupole) or of the chemical-shift anisotropy. A treatment of g-value sensitivity in field-swept EPR experiments will be given later.

The results derived from Eqs. [5] and [6] are presented in Fig. 1. From this it is clear that the sensitivity not only to the $\delta_{\perp}$ parameter but also to the $\delta_{\|}$ parameter diverges at $\delta = \delta_{\perp}$, corresponding to the singularity in the lineshape for the perpendicular orientations to the magnetic field. This can be seen to be a general result, valid also for the case of finite linewidths: regions of large discontinuities in the spectrum will tend to dominate the absolute sensitivities to changes in most, if not all, parameters. This was certainly found to be the case in Ref. (*1*) for the perpendicular and overshoot regions in the EPR spectra of Cu^{2+} square-planar complexes. This swamping effect can be attenuated somewhat, if the fractional sensitivity, $(1/I)dI/d\delta_i$, is considered. For $\delta_{\|}$ this function remains constant throughout the spectrum, rather than peaking in the perpendicular region. Clearly, however, the crucial quantity is the degree of discrimination, $R(\delta) = -(dI/d\delta_{\|})/(dI/d\delta_{\perp})$, between the sensitivities to the parallel and perpendicular parameters. This is given in Fig. 1B and is analogous to the axial/off-axial discrimination ratio introduced previously for the analysis of anisotropic rotation in STEPR spectra (*2*). Figure 1B demonstrates a very high degree of discrimination (infinite in this idealized case) in the sensitivity to the $\delta_{\perp}$ parameter in the perpendicular region. The highest degree of discrimination for $\delta_{\|}$ is in the parallel region, and therefore this latter region should be used for determining $\delta_{\|}$, despite the fact that the absolute sensitivity to this parameter is greatest in the perpendicular region.

Sensitivity to order parameter. As an example of sensitivity to a dynamic parameter governing the spectral lineshape, the time-average angular order parameter will be considered. In the case of motional narrowing of limited amplitude, the spectral extrema, δ_i, are related to the molecular order parameter, S, by

$$\delta_{\|} - \delta_{\perp} = \Delta\delta \cdot S \qquad [7]$$

$$\delta_{\perp} = \delta_0 - (1/3)\Delta\delta \cdot S, \qquad [8]$$

where $\Delta\delta$ is the rigid limit value of $\delta_{\|} - \delta_{\perp}$, and $\delta_0 = (\delta_{\|} + 2\delta_{\perp})/3$. Hence, from Eq. [3],

$$I(\delta) = \tfrac{1}{2}[\Delta\delta \cdot S(\delta - \delta_0 + \Delta\delta \cdot S/3)]^{-1/2} \quad [9]$$

and

$$dI/dS = -\tfrac{1}{2}I(\delta)(\delta - \delta_0 + 2\Delta\delta \cdot S/3)/[S(\delta - \delta_0 + \Delta\delta \cdot S/3)]. \quad [10]$$

These equations are valid for the range $-\Delta\delta \cdot S/3 \leqslant (\delta - \delta_0) \leqslant +2\Delta\delta \cdot S/3$. The sensitivity diverges for $S = 0$, as expected, and also diverges at $\delta = \delta_{\perp}$ (see Fig. 2) as found for the other parameters. The implication here is clear: the spin-Hamiltonian parameters must be determined independently with a high degree of accuracy, if the sensitivity in the perpendicular region of the spectrum is to be used to yield best accuracy in determining the dynamic parameters.

Equation [10] may also be used to determine the sensitivity to the conjugate spin-Hamiltonian parameter set, $\Delta\delta$ and δ_0, and the corresponding dependence on S:

$$dI/d\Delta\delta = -\tfrac{1}{2}I(\delta)(\delta - \delta_0 + 2\Delta\delta \cdot S/3)/[\Delta\delta(\delta - \delta_0 + \Delta\delta \cdot S/3)] \quad [11]$$

$$dI/d\delta_0 = \tfrac{1}{2}I(\delta)(\delta - \delta_0 + \Delta\delta \cdot S/3)^{-1}. \quad [12]$$

Again both sensitivities diverge for $S = 0$ and at $\delta = \delta_{\perp}$ (see Fig. 2). The discrimination ratio, given by $R'(\delta) = -(dI/d\Delta\delta)/(dI/d\delta_0)$, is best for $\Delta\delta$ at $\delta = \delta_{\|}$, and best for δ_0 at $\delta = \delta_{\perp}$ (see Fig. 2). For $S = 0$, the ratio of the discrimination between the parameter sensitivities at the extrema is constant: $R'(\delta_{\|})/R'(\delta_{\perp}) = 4$. However, for $S = 0$, R' is zero for all values of δ and the spectrum is sensitive only to δ_0, as is expected.

Sensitivity to g values. In EPR, the angular dependence of the g value for an axial system is given by

$$g = (g_{\|}^2 \cos^2\theta + g_{\perp}^2 \sin^2\theta)^{1/2}. \quad [13]$$

In a field-swept experiment, the resonance position is then given by

$$\delta = [(\delta_{\|}^{-2} - \delta_{\perp}^{-2})\cos^2\theta + \delta_{\perp}^{-2}]^{-1/2}, \quad [14]$$

where $\delta_{\|}$, $\delta_{\perp}$ are the resonance field positions corresponding to the magnetic field oriented parallel or perpendicular to the principal axis, respectively. Therefore the lineshape for an unoriented sample is, from Eq. [1],

$$I(\delta) = [(\delta_{\|}^{-2} - \delta_{\perp}^{-2})(\delta^{-2} - \delta_{\perp}^{-2})]^{-1/2}\delta^{-3}. \quad [15]$$

The corresponding sensitivities are

$$dI/d\delta_{\|} = I(\delta)\delta_{\|}^{-3}(\delta_{\|}^{-2} - \delta_{\perp}^{-2})^{-1} \quad [16]$$

$$dI/d\delta_{\perp} = -I(\delta)\delta_{\perp}^{-3}[(\delta_{\|}^{-2} - \delta_{\perp}^{-2})^{-1} + (\delta^{-2} - \delta_{\perp}^{-2})^{-1}] \quad [17]$$

and the sensitivities to the g values are given by an additional multiplicative factor,

$$dI/dg_i = (dI/d\delta_i)(d\delta_i/dg_i), \quad [18]$$

where $d\delta_i/dg_i = -h\nu/g_i^2\beta$. The results obtained from Eqs. [16] and [17] are not qualitatively different from those obtained previously from Eqs. [5] and [6]. Again the sensitivity to $\delta_{\|}$ as well as to $\delta_{\perp}$ diverges at $\delta = \delta_{\perp}$, and $dI/d\delta_{\|}$ has the same field

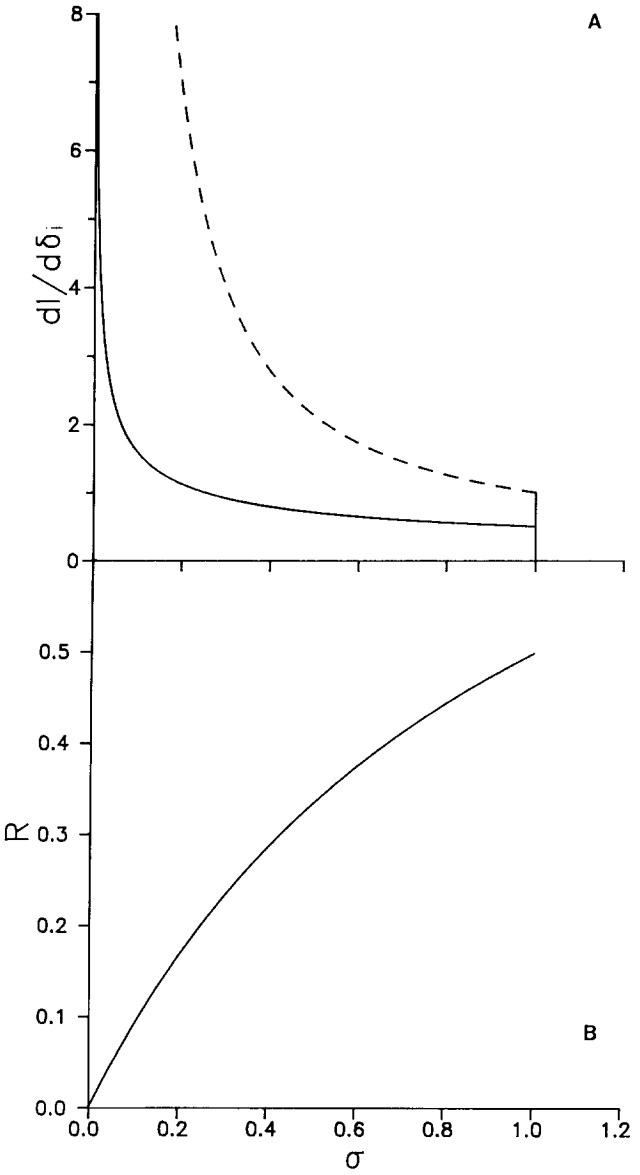

FIG. 1. Parameter sensitivity, $dI(\delta)/d\delta_i$, as a function of spectral position for an axial powder pattern lineshape in absorption. The dimensionless scan parameter is $\sigma = (\delta - \delta_\perp)/(\delta_\parallel - \delta_\perp)$; i.e., $\sigma = 0$ for $\delta = \delta_\perp$ and $\sigma = 1$ for $\delta = \delta_\parallel$. (A) $-dI(\delta)/d\delta_\parallel$ (full line), and $dI(\delta)/d\delta_\perp$ (dashed line), where the ordinate has units of $\frac{1}{2}(\delta_\parallel - \delta_\perp)^{-2}$. The intensity distribution in absorption, $I(\delta)$, is identical to $dI(\delta)/d\delta_\parallel$, except that the ordinate units are $(\delta_\parallel - \delta_\perp)^{-1}$. (B) Discrimination ratio, $R = -(dI/d\delta_\parallel)/(dI/d\delta_\perp)$.

dependence as the absorption lineshape. The discrimination ratio, $R = (dI/dg_\parallel)/(dI/dg_\perp)$, is zero at $\delta = \delta_\perp$ and has its greatest value at $\delta = \delta_\parallel$ (cf. Fig. 1B). These general conclusions are also not materially altered if the anisotropy of the transition probability is taken into account via an additional factor, $\delta^2(\delta^{-2} + \delta_\parallel^{-2})$, in Eq. [15].

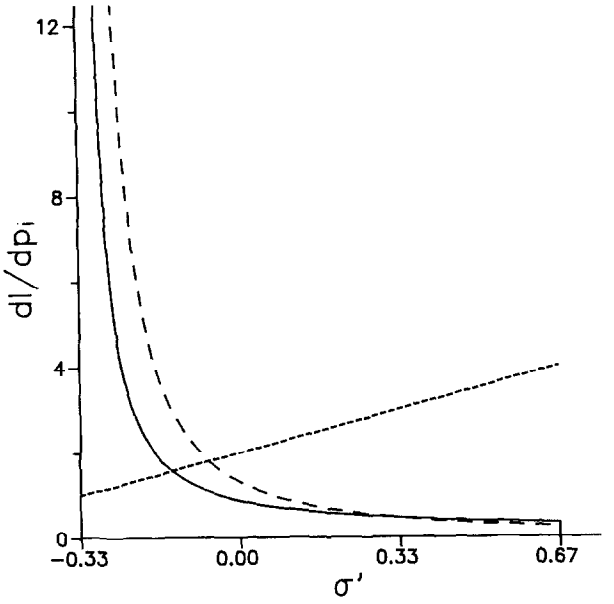

FIG. 2. Sensitivity to order parameter and dependence of spin-Hamiltonian parameter sensitivity on order parameter for an axial powder pattern in absorption. The dimensionless scan parameter is $\sigma' = (\delta - \delta_0)/(S\cdot\delta)$; i.e., $\sigma' = -1/3$ for $\delta = \delta_\perp$ and $\sigma' = 2/3$ for $\delta = \delta_\parallel$. Full line: $dI(\delta)/dS$ in units of $\Delta\delta^{-1}S^{-2}$, and $-dI(\delta)/d\Delta\delta$ in units of $\Delta\delta^{-2}S^{-1}$. Long dashed line: $dI(\delta)/d\delta_0$ in units of $\Delta\delta^{-2}S^{-2}$. Short dashed line: discrimination ratio, $R' = -(dI/d\Delta\delta)/(dI/d\delta_0)$, in units of $(1/3)S$.

Derivative displays. From Eq. [4], the sensitivities in the first derivative display are given by

$$d^2I/d\delta d\delta_\parallel = -\tfrac{1}{2}(dI/d\delta_\parallel)(\delta - \delta_\perp)^{-1} \qquad [19]$$

$$d^2I/d\delta d\delta_\perp = -\tfrac{1}{2}(dI/d\delta_\perp)(\delta - \delta_\perp)^{-1} - \tfrac{1}{2}I(\delta)\cdot(\delta - \delta_\perp)^{-2}. \qquad [20]$$

Clearly the sensitivities in the derivative display vary differently throughout the spectrum from those in absorption. They diverge even more steeply in the perpendicular region. This will be a general result: taking the derivative will bias the sensitivities even further in the direction of those regions of the spectrum which display the largest discontinuities. The sensitivity to $\delta_\perp$ is even greater, relative to that to $\delta_\parallel$, than in the absorption display. Correspondingly, the discrimination ratio, $(d^2I/d\delta d\delta_\parallel)/(d^2I/d\delta d\delta_\perp)$, is reduced relative to that in absorption, by a factor $(1 + \sigma)/(3 + \sigma)$, using the nomenclature of Fig. 1.

In summary, the results of the analysis of a simple axial lineshape given here suggest the following generalizations. The parameter sensitivity in magnetic resonance spectra from unoriented samples exhibiting anisotropy is dominated by those regions of the spectrum which display the largest intensity. This effect is accentuated in derivative displays by the accompanying discontinuities or large gradients in the spectral lineshape. The sensitivity is greatest for those parameters which determine the position of the major spectral peaks or discontinuities. The commonly employed practice of minimizing the sum of squares (or absolute value) of the deviations between exper-

imental and simulated spectra will therefore determine these parameters with high accuracy, but give a poor level of discrimination for those parameters which determine the line positions in regions of the spectrum with lower intensity. This situation will not be improved by considering either the autocorrelation [proportional to $I(\delta)\cdot(dI/d\delta)$] or the cross-correlation [proportional to $I(\delta)\cdot(dI/d\delta_i)$] integrals. Other strategies are therefore indicated. Consideration of the fractional deviations [proportional to $(1/I)(dI/d\delta_i)$] will improve things somewhat, but this will demand high S/N ratio in the low intensity regions and some cut off intensity must be defined to prevent numerical instabilities. Alternatively, individual regions of the spectrum could be considered separately, as proposed in Ref. (*1*), which again points to the necessity of collecting data with high S/N ratio in all regions of the spectrum. A more general approach is to adopt some numerical optimization procedure and first to scale the fitting parameters so as to endow them with comparable sensitivities, i.e., such that a fixed change in any of the variables results in similar changes in the objective function to be minimized (*3*).

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