JOURNAL

OF THE AMERICAN CHEMICAL SOCIETY

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VOLUME 97, NUMBER 14 JULY 9, 1975

The Density Matrix Theory of Nuclear Magnetic Double Resonance Line Shapes in Chemically Exchanging Systems

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Abstract: A general density matrix formulation for describing NMR line shapes of exchanging systems under conditions of double resonance (one weak, ω_2, and one strong, ω_1, field) is presented. It is shown that the double resonance spectrum for the example under consideration is about an order of magnitude more sensitive to slow exchange rates than the equivalent low power single resonance spectrum. Examples of effects in double resonance spectra such as line splitting, line distortion, and varying peak intensities are illustrated. An additional weak "absorption" at the frequency $2\omega_1 - \omega_2$ is shown to exist.

NMR line shapes for chemically reorganizing systems[1-5] have been utilized to obtain rate data and activation parameters for a variety of intramolecular rearrangements such as rotation, pseudorotation, conformational interconversion, as well as a wide collection of chemical exchange process.[2-5] Note that these kinetic parameters extricated from NMR data apply to systems at equilibrium.

So far NMR line-shape analysis has been widely applied only for conditions of cw low rf power.[6-9] The theory has been generalized, using the Permutation of Indices Method (PI) to cover all typical exchange steps as well as combinations of these.[10] Recently this theory has been extended to include conditions of high rf field (saturation) employing a linearization procedure called Selective Neglect of Bilinear terms (SNOB).[11]

Now in this paper, we turn our attention to nuclear magnetic double resonance (NMDR) line shapes of chemically exchanging systems.[12-14] The same SNOB procedure originally developed to calculate the high rf response[11] will also be utilized in the course of the double resonance calculations.

Multiple resonance has been the subject of intensive investigation. The techniques of NMDR have been used to unravel and simplify complicated spectra by means of Overhauser effects, by the introduction of extra fine structure into a spectrum as well as completely decoupling one set of nuclei from another.[14-20] With a few exceptions,[12-14] most existing treatments of double resonance handle only line positions.

It will be shown that double resonance *line-shape* theory permits a clearer qualitative understanding of the double resonance spectrum even without exchange. For instance it is easier to understand, as shown below, how, in a two spin system, the extra fine structure which appears because the large rf field causes a breakdown of the allowed $\Delta m = \pm 1$ selection rules now permits $\Delta m = 0, \pm 2$ transitions. Also we shall predict the existence of extra resonance peaks from a response to a mixed frequency, the so-called pseudoabsorption.

The exact shape of the absorption carries in it information on relaxations including exchange phenomena. In principle one expects that selective decoupling should make the NMR line shape more sensitive to the exchange rate than in single resonance NMR spectra. Two papers dealing with specific examples of these effects have appeared.[12,14]

In this paper, we describe in section I the general density matrix theory for NMDR line shapes of any exchanging system including those where several different exchange processes take place at the same time. The theory allows for individual nuclear relaxation times employing the relaxation operator described by us before.[10] This theory is applied to a model exchanging system. The density matrix equations are derived, and an expression is obtained for the absorption. Section II contains an interpretation of double resonance spectra and section III describes some line shapes. Appendix I consists of a glossary of symbols to ease the reader's progress through this article.

I. Density Matrix Equations for an Exchange System Under Conditions of Double Resonance

The appropriate density matrix equation for a system undergoing chemical exchange is

$$\rho = i[\rho, \mathcal{H}] + R\rho + E\rho \qquad (1)$$

For double resonance in the laboratory frame, the Hamiltonian is given by

$$\mathcal{H} = \sum_i \omega_{0i} I_i^z + \sum_{i>j} J_{ij} I_i \cdot I_j + \sum_i \varphi_1 [I_i^x \cos \omega_1 t + I_i^y \sin \omega_1 t] + \sum_i \varphi_2 [I_i^x \cos \omega_2 t + I_i^y \sin \omega_2 t] \quad (2)$$

where ω_0, ω_1 (ω_2), and φ_1 (φ_2) stand for chemical shift, frequency, and strength of the irradiating fields, respectively and *i,j* . . . sums over the spins. The operator for intermolecular relaxation (R) is given as[10]

$$R\rho = \sum_i \left\{ \frac{1}{T_{1i}} [I_i^x, [I_i^x, \rho - \rho_{eq}]] + \frac{1}{T_{1i}} [I_i^y, [I_i^y, \rho - \rho_{eq}]] + \frac{1}{T_{2i}} [I_i^z, [I_i^z, \rho - \rho_{eq}]] \right. \quad (3)$$

where eq stands for equilibrium and the reorganization term $E\rho$ is

$$E^{sp}\rho = \frac{\rho^{sp}(\text{after exchange}) - \rho^{sp}}{\tau_{sp}} \quad (4)$$

where sp stands for species. As described by us previously, the exact form which $E\rho$ takes is determined by the mechanism of the reorganization process and is different for each typical exchange step.[10] Space does not allow a repetition of all these possibilities. Instead, in this section we treat one model example, that of an AB molecule exchanging fragment B with the outside world (B′)

$$\text{AB} + \text{B}' \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{AB}' + \text{B} \quad (5)$$

where A, B, and B′ each contain one proton, and fragments B and B′ are chemically identical. As discussed in ref 10, the product representation is defined as

AB B′ species (6)

ab c wavefunction (7)

Use of the Permutation of Indices method yields ρ(after exchange), called ρ_{ae} as

$$\langle ab | \rho^{AB}{}_{ae} | a'b' \rangle = \sum_c \rho^{AB}{}_{ac,a'c} \rho^{B'}{}_{b,b'} \quad (8)$$

and

$$\langle c | \rho^{B'}{}_{ae} | c' \rangle = \sum_a \rho^{AB}{}_{ac,ac'} \quad (9)$$

recalling from above the chemical identity of AB to AB′ and of B to B′.

The decoupling signal φ_i is taken to be strong, while that of the observing frequency φ_2 is weak. To treat φ_1 to all orders in φ_1, we go into a coordinate system rotating at frequency ω_1. The density matrix $\bar{\rho}$ in the rotating system is obtained as

$$\bar{\rho}^{AB} = e^{i\omega_1 t I_{AB}{}^z} \rho e^{-i\omega_1 t I_{AB}{}^z} \quad (10)$$

where

$$I_{AB}{}^z = \sum_{A,B} I_A{}^z + I_B{}^z \quad (11)$$

The Hamiltonian in the rotating coordinate system is given by

$$\bar{\mathcal{H}} = \sum_i (\omega_i - \omega_1) I_i^z + \sum_{i,j} J_{i,j} I_i \cdot I_j + \frac{1}{2}\varphi_1 \sum_i (I^+{}_i + I^-{}_i) + \frac{\varphi_2}{2} \sum_i (I^+{}_i e^{-i(\omega_2-\omega_1)t} + I^-{}_i e^{+i(\omega_2-\omega_1)t}) = \mathcal{H}_0 + \mathcal{H}_{RF1} + \mathcal{H}_{RF2} \quad (12)$$

and the density matrix equation for one species is given by

$$\dot{\bar{\rho}} = i[\bar{\rho}, \mathcal{H}_0] - \frac{i\varphi_1}{2} \left[\sum_i (I^+{}_i + I^-{}_i), \bar{\rho} \right] - \frac{i\varphi_2}{2} \times \left[\sum_i I^+{}_i e^{-i(\omega_2-\omega_1)t} + I^-{}_i e^{+i(\omega_2-\omega_1)}, \bar{\rho} \right] + R\rho + E\rho \quad (13)$$

The density matrix equations for the exchanging system defined in (5) are

$$\dot{\bar{\rho}}^{AB} = i[\bar{\rho}^{AB}, \mathcal{H}_0{}^{AB}] - \frac{i\varphi_1}{2} [I^+{}_{AB} + I^-{}_{AB}, \bar{\rho}_{AB}] - \frac{i\varphi_2}{2} \times [I^+{}_{AB} e^{-i(\omega_2-\omega_1)t} + I^-{}_{AB} e^{i(\omega_2-\omega_1)t}, \bar{\rho}^{AB}] + R\bar{\rho}^{AB} + E\bar{\rho}^{AB} \quad (14)$$

$$\dot{\bar{\rho}}^{B'} = i[\bar{\rho}^{B'}, \mathcal{H}_0{}^{B'}] - \frac{i\varphi_1}{2} [I^+{}_{B'} + I^-{}_{B'}, \bar{\rho}^{B'}] - \frac{i\omega_2}{2} \times [I^+{}_{B'} e^{-i(\omega_2-\omega_1)t} + I^-{}_{B'} e^{i(\omega_2-\omega_1)t}, \bar{\rho}^{B'}] + R\bar{\rho}^{B'} + E\bar{\rho}^{B'} \quad (15)$$

Since we want only the low power response to the rf field (φ_2), we solve (14) and (15) by writing

$$\bar{\rho}^{AB} = \rho'^{AB} + \rho^{+AB} e^{i(\omega_2-\omega_1)t} + \rho^{-AB} e^{-i(\omega_2-\omega_1)t} \quad (16)$$

$$\bar{\rho}^{B'} = \rho'^{B} + \rho^{+B'} e^{i(\omega_2-\omega_1)t} + \bar{\rho}^{B'} e^{-i(\omega_2-\omega_1)t} \quad (17)$$

where ρ' is the solution of (1) with $\varphi_2 = 0$, and the $\rho^{\pm}$ are linear in φ_2. We also note that, as $\bar{\rho}$ has to be Hermitian, it follows that

$$(\rho^+)^\dagger + \rho^- \quad (18)$$

Thus we only need to solve for ρ^{+AB} and $\rho^{+B'}$ or for ρ^{-AB} and $\rho^{-B'}$.

What we will eventually want to evaluate is the magnetization in the laboratory system. The x component of this magnetization is given by

$$M_x = (\text{AB})\text{Tr}\rho^{AB} I_{AB}{}^x + (\text{B}')\text{Tr}\rho^{B'} I_{B'}{}^x \quad (19)$$

where (AB) means concentration of AB. Substituting for ρ from (10) into (19) and using the trace identity

$$\text{Tr ABC} \equiv \text{Tr BCA} \quad (20)$$

one obtains

$$M_x = (\text{AB})\text{Tr}\bar{\rho}^{AB} e^{i\omega_1 I_{AB}{}^z t} I_{AB}{}^x e^{-i\omega_1 I_{AB}{}^z t} + (\text{B}')\text{Tr}\bar{\rho}^{B}\, e^{i\omega_1 I_B{}^z t} I_{B'}{}^x e^{-i\omega_1 I_{B'}{}^z t} \quad (21)$$

Next, substitute for $\bar{\rho}$ in (21) using (16) and (17) and recall that

$$e^{i\omega_1 I^z t} I^{\pm} e^{-i\omega_1 I^z t} = I^{\pm} e^{\pm i\omega_1 t} \quad (22)$$

This procedure yields the following expression for M_x:

$$M_x = \tfrac{1}{2}(\text{AB})\text{Tr}\rho'^{AB}(I^+{}_{AB} e^{i\omega_1 t} + I^-{}_{AB} e^{-i\omega_1 t}) + \tfrac{1}{2}(\text{B}')\text{Tr}\rho'^{B'}(I^+{}_{B'} e^{i\omega_1 t} + I^-{}_{B'} e^{-i\omega_1 t}) +$$

$$\tfrac{1}{2}(\text{AB})\text{Tr}\{\rho^{+AB} e^{i(\omega_2-2\omega_1)t} I^-{}_{AB} + \rho^{-AB} e^{-i(\omega_2-2\omega_1)t} I^+{}_{AB}\} + \tfrac{1}{2}(\text{B}')\text{Tr}\{\rho^{+B'} e^{i(\omega_2-2\omega_1)t} I^-{}_{B'} + \rho^{-B'} e^{-i(\omega_2-2\omega_1)} I^+{}_{B'}\} +$$

$$\tfrac{1}{2}(\text{AB})\text{Tr}\{\rho^{+AB} e^{i\omega_2 t} I^+{}_{AB} + \rho^{-AB} e^{-i\omega_2 t} I^-{}_{AB}\} + \tfrac{1}{2}(\text{B}')\text{Tr}\{\rho^{+B'} e^{i\omega_2 t} I^+{}_{B'} + \rho^{-B'} e^{-i\omega_2 t} I^-{}_{B'}\} \quad (23)$$

The absorption, Ab, at frequency ω_2 is given as the x component of magnetization out of phase with the rf field in the x direction; that is, we collect the terms in (23) proportional to $\sin \omega_2 t$ noting that

$$e^{+i\omega_2 t} = \cos \omega_2 t + i \sin \omega_2 t$$

$$e^{-i\omega_2 t} = \cos \omega_2 t - i \sin \omega_2 t$$

to give

$$\mathrm{Ab}(\omega_2) = \frac{(\mathrm{AB})}{2}\{i\mathrm{Tr}\rho^{+\mathrm{AB}}I^{+}{}_{\mathrm{AB}} - i\mathrm{Tr}\rho^{-\mathrm{AB}}I^{-}{}_{\mathrm{AB}}\} + \frac{(\mathrm{B}')}{2}\{i\mathrm{Tr}\rho^{+\mathrm{B}'}I^{+}{}_{\mathrm{B}'} - i\mathrm{Tr}\rho^{-\mathrm{B}'}I^{-}{}_{\mathrm{B}'}\} \quad (24)$$

To illustrate the use of (24), we now apply it to the calculation of the absorption at $\not{\varphi}_2$ for the exchanging system (5). In the spin product basis representation, the states are

$$\begin{array}{ll} \text{AB states} & \text{B states} \\ \psi_1 = \alpha_{\mathrm{A}}\alpha_{\mathrm{B}} & \psi_5 = \alpha_{\mathrm{B}'} \\ \psi_2 = \alpha\beta & \psi_6 = \beta \\ \psi_3 = \beta\alpha & \\ \psi_4 = \beta\beta & \end{array} \quad (25)$$

Employing the relationships

$$\mathrm{Tr}\rho I^{\pm} = \sum_{i,j}\rho^{\pm}{}_{ij}I^{\pm}{}_{j,i} \quad (26)$$

$$\rho^{\mp}{}_{j,i} = \rho^{\pm}{}_{i,j}{}^{*} \quad (27)$$

$$\rho^{+}{}_{i,j} = a_{i,j} + ib_{i,j} \quad (28)$$

then the nonzero terms in the absorption are

$$\mathrm{Ab}(\omega_2) = \frac{(\mathrm{concn})}{2}\left\{\sum_{i>j} i\rho^{+}{}_{i,j}I^{+}{}_{j,i} - \sum_{i>j} i\rho^{-}{}_{j,i}I^{-}{}_{i,j}\right\} \quad (29)$$

so using (27) and (28), we find that

$$\begin{aligned}\mathrm{Ab}(\omega_2) &= (\mathrm{concn})\sum_{i>j} -b_{ij} \\ &= (\mathrm{concn})\sum_{i>j} -Im\rho^{+}{}_{i,j}\end{aligned} \quad (30)$$

Applying (30) to exchange system (5), we obtain

$$\mathrm{Ab}(\omega_2) = -(\mathrm{AB})Im[\rho^{+\mathrm{AB}}{}_{2,1} + \rho^{+\mathrm{AB}}{}_{3,1} + \rho^{+\mathrm{AB}}{}_{4,2} + \rho^{+\mathrm{AB}}{}_{4,3}] - (\mathrm{B}')Im\rho^{+\mathrm{B}'}{}_{6,5} \quad (31)$$

Notice that, in the $\rho^{+}{}_{i,j}$ summed in (31), $m(i) - m(j) = -1$ always.

Density Matrix Equations for ρ^+, ρ^-, and ρ'

To find the density matrix equations for ρ' and $\rho^{\pm}$, substitute for $\bar{\rho}$ from (16) and (17) into (14) and (15) and collect all terms with the same time dependence into separate equations.

$$0 = i[\rho'^{\mathrm{AB}}, \mathcal{H}_0{}^{\mathrm{AB}}] - \frac{i\not{\varphi}_1}{2}[I^{+}{}_{\mathrm{AB}} + I^{-}{}_{\mathrm{AB}}, \rho'^{\mathrm{AB}}] + R(\rho'^{\mathrm{AB}} - \rho_0{}^{\mathrm{AB}}) + E\rho'^{\mathrm{AB}} \quad (32)$$

$$0 = i[\rho'^{\mathrm{B}'}, \mathcal{H}_0{}^{\mathrm{B}'}] - i\not{\varphi}_1[I^{+}{}_{\mathrm{B}'} + I^{-}{}_{\mathrm{B}'}, \rho'^{\mathrm{B}'}] + R(\rho'^{\mathrm{B}'} - \rho_0{}^{\mathrm{B}'}) + E\rho'^{\mathrm{B}'} \quad (33)$$

$$i(\omega_2 - \omega_1)\rho^{+\mathrm{AB}} = i[\rho^{+\mathrm{AB}}, \mathcal{H}_0{}^{\mathrm{AB}}] - \frac{i\not{\varphi}_1}{2}[I^{+}{}_{\mathrm{AB}} + I^{-}{}_{\mathrm{AB}}, \rho^{+\mathrm{AB}}] - \frac{i\not{\varphi}_2}{2}[I^{-}{}_{\mathrm{AB}}, \rho'_{\mathrm{AB}}] + R\rho^{+\mathrm{AB}} + E\rho^{+\mathrm{AB}} \quad (34)$$

$$i(\omega_2 - \omega_1)\rho^{+\mathrm{B}'} = i[\rho^{+\mathrm{B}'}, \mathcal{H}_0{}^{\mathrm{B}'}] - \frac{i\not{\varphi}_1}{2}[I^{+}{}_{\mathrm{B}'} + I^{-}{}_{\mathrm{B}'}, \rho^{+\mathrm{B}'}] - \frac{i\not{\varphi}_2}{2}[I^{-}{}_{\mathrm{B}'}, \rho'^{\mathrm{B}'}] + R\rho^{+}{}_{\mathrm{B}'} + E\rho^{+}{}_{\mathrm{B}'} \quad (35)$$

$$-i(\omega_2 - \omega_1)\rho^{-\mathrm{AB}} = i[\rho^{-}, \mathcal{H}_0{}^{\mathrm{AB}}] - \frac{i\not{\varphi}_1}{2}[I^{+}{}_{\mathrm{AB}} + I^{-}{}_{\mathrm{AB}}, \rho^{-\mathrm{AB}}] - \frac{i\not{\varphi}_2}{2}[I^{+}{}_{\mathrm{AB}}, \rho'] + R\rho^{-\mathrm{AB}} + E\rho^{-\mathrm{AB}} \quad (36)$$

The equation for $\rho^{-\mathrm{B}'}$ is written equivalently to (36). Actually as discussed above, we shall not need ρ^- since the absorption can be written entirely with ρ^+ terms. Note that the relaxation terms in (34) to (36) are in just ρ^+ or ρ^- not $\rho^+ - \rho_{\mathrm{eq}}$. Finally as written in (8), $E\rho^{\mathrm{AB}}$ is bilinear. It would appear to be a function of $\rho^+\rho'$. This is not the case as will shortly be demonstrated.

Solutions of the Equations for an Exchanging System, Double Resonance

The solutions of the set of equations for ρ', (32, 33), the CW high power spectrum, have been described by us before.[11] This procedure involves writing the coupled equations for *all* the density matrix elements, including those involving $\Delta m = 0 \pm 2$. The equations are linearized by means of dropping certain contributions to the $E\rho$ term, the Selective Neglect of Bilinear Terms (SNOB) approximation. SNOB linearization is accomplished in the following way. The diagonal elements of ρ' in the product representation are written as shown in (37), where N is the number of

$$\langle nm|\rho'_{\mathrm{sp}}|nm\rangle = \frac{1}{N_{\mathrm{sp}}} + \langle nm|\Delta\rho'_{\mathrm{sp}}|nm\rangle \quad (37)$$

states, and sp stands for species. The first term in (37) is the infinite temperature probability of the diagonal matrix element. In linearizing $E\rho$, all terms which are products of off-diagonal matrix elements (eq 38) or a product of an off-diagonal matrix element and the diagonal element $\Delta\bar{\rho}'^{\mathrm{AB}}{}_{i,i}$ are dropped (eq 39). Investigation shows that the terms

$$\rho'^{\mathrm{AB}}{}_{i,j}\rho'^{\mathrm{B}'}{}_{k,1} \sim 0 \quad \begin{matrix} i \neq j \\ k \neq 1 \end{matrix} \quad (38)$$

$$\rho'^{\mathrm{B}'}{}_{i,j}\left(\frac{1}{N_{\mathrm{AB}}} + \Delta\rho^{\mathrm{AB}}{}_{k,k}\right) \sim \rho'^{\mathrm{B}}{}_{i,j}/N_{\mathrm{AB}} \quad (39)$$

which are kept are a factor of 10^5 to 10^6 larger than those discarded.

In similar fashion to the above SNOB approximation for ρ', we can linearize the second-order terms in eq 34 and 35 which appear in $E\rho^+$. The maximum value which ρ^+ elements take, both diagonal and off-diagonal is ca. 10^{-6}. Then the following approximations are valid.

$$\begin{aligned}&\rho'^{\mathrm{AB}}{}_{i,i}\rho^{\pm\mathrm{B}'}{}_{k,l} \sim \rho^{\pm\mathrm{B}'}{}_{k,l}/N_{\mathrm{AB}} \quad k \neq l \\ &\rho'^{\mathrm{AB}}{}_{i,j}\rho^{\pm\mathrm{B}'}{}_{k,l} \sim 0\end{aligned} \quad (40)$$

With this linearization in mind, consider the equation for $\rho^{+\mathrm{AB}}{}_{1,2}$. As stated before, we require the ρ^+ elements to solve for the absorption. Also for brevity we can leave off the species label from the density matrix elements since the states already indicate which molecule is referred to, (1–4 for AB and 5,6 for B′). We obtain the equation for $\rho^{+}{}_{1,2}$ by taking the $\langle 1\|2\rangle$ matrix element of eq 34. The result is

$$0 = i\left\{[E_2 - E_1 - (\omega_2 - \omega_1)]\rho^{+}{}_{1,2} + \frac{J_{\mathrm{AB}}}{2}\rho^{+}{}_{1,3} + \frac{\not{\varphi}_1}{2}(\rho^{+}{}_{1,1} - \rho^{+}{}_{2,2} - \rho^{+}{}_{3,2} + \rho^{+}{}_{1,4}) + \frac{\not{\varphi}_2}{2}\rho'{}_{1,4}\right\} + \frac{1}{\tau_{\mathrm{AB}}}[(\rho'{}_{1,1} + \rho'{}_{2,2})\rho^{+}{}_{5,6} + (\rho^{+}{}_{1,1} + \rho^{+}{}_{2,2})\rho'{}_{5,6} - \rho^{+}{}_{1,2}] - \left[\frac{1}{T_{1\mathrm{A}}} + \frac{1}{T_{1\mathrm{B}}} + \frac{1}{T_{2\mathrm{B}}}\right]\rho^{+}{}_{1,2} + \frac{1}{T_{1\mathrm{A}}}\rho^{+}{}_{3,4} \quad (41)$$

where E_i is the diagonal element $\mathcal{H}_{0i,i}$. Using the linearization scheme described above reduces the term in $1/\tau_{\mathrm{AB}}$ to eq 42, which is independent of the state of

$$\tfrac{1}{2}\rho^{+}{}_{5,6} - \rho^{+}{}_{1,2} \tag{42}$$

ρ'. This will be true for all 20 density matrix equations describing the ρ^{+AB} and $\rho^{+B'}$ elements. Without further comment, we will now list in this order the equations for $\rho^{+}{}_{2,1}$, $\rho^{+}{}_{2,3}$, $\rho^{+}{}_{3,2}$, $\rho^{+}{}_{1,4}$, and $\rho^{+}{}_{4,1}$. As seen in eq 31, $\rho^{+}{}_{2,1}$ contributes directly to the absorption, the $\rho^{+}{}_{2,3}$ and $\rho^{+}{}_{3,2}$ are $\Delta m = 0$ transitions, and $\rho^{+}{}_{1,4}$, $\rho^{+}{}_{4,1}$ are $\Delta m = \pm 2$ transitions.

$$\begin{aligned}0 = i\Big\{&[E_1 - E_2 - (\omega_2 - \omega_1)]\rho^{+}{}_{2,1} - \frac{J_{AB}}{2}\rho_{3,1}\\ &+ \frac{\not{\mathcal{H}}_1}{2}[-\rho^{+}{}_{1,1} + \rho^{+}{}_{2,2} + \rho^{+}{}_{2,3} - \rho^{+}{}_{4,1}]\\ &+ \frac{\not{\mathcal{H}}_2}{2}[-\rho'{}_{1,1} + \rho'{}_{2,2} + \rho'{}_{2,3}]\Big\}\\ &+ \frac{1}{\tau_{AB}}[\tfrac{1}{2}\rho^{+}{}_{6,5} - \rho^{+}{}_{2,1}]\\ &- \left[\frac{1}{T_{1A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]\rho^{+}{}_{2,1} + \rho^{+}{}_{4,3}\left[\frac{1}{T_{1A}}\right]\end{aligned} \tag{43}$$

$$\begin{aligned}0 = i\Big\{&[E_3 - E_2 - (\omega_2 - \omega_1)]\rho^{+}{}_{2,3}\\ &+ \frac{\not{\mathcal{H}}_1}{2}[\rho^{+}{}_{2,1} - \rho^{+}{}_{1,3} + \rho^{+}{}_{2,4} - \rho^{+}{}_{4,3}]\\ &+ \frac{J_{AB}}{2}[\rho^{+}{}_{2,2} - \rho^{+}{}_{3,3}] + \frac{\not{\mathcal{H}}_2}{2}[\rho'{}_{2,4} - \rho'{}_{1,3}]\Big\}\\ &- \frac{1}{\tau_{AB}}\rho^{+}{}_{2,3}\\ &- \left[\frac{1}{T_{2B}} + \frac{1}{T_{1B}} + \frac{1}{T_{2A}} + \frac{1}{T_{1A}}\right]\rho^{+}{}_{2,3}\end{aligned} \tag{44}$$

$$\begin{aligned}0 = i\Big\{&[E_2 - E_3 - (\omega_2 - \omega_1)]\rho^{+}{}_{3,2}\\ &+ \frac{\not{\mathcal{H}}_1}{2}[-\rho^{+}{}_{1,2} + \rho^{+}{}_{3,1} - \rho^{+}{}_{4,2} + \rho^{+}{}_{3,4}]\\ &+ \frac{J_{AB}}{2}[-\rho^{+}{}_{2,2} + \rho^{+}{}_{3,3}] + \frac{\not{\mathcal{H}}_2}{2}[\rho'{}_{3,4} - \rho'{}_{1,2}]\Big\}\\ &- \frac{1}{\tau_{AB}}\rho^{+}{}_{3,2} - \left[\frac{1}{T_{1A}} + \frac{1}{T_{2A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]\rho^{+}{}_{3,2}\end{aligned} \tag{45}$$

$$\begin{aligned}0 = i\Big\{&[E_4 - E_1 - (\omega_2 - \omega_1)]\rho^{+}{}_{1,4}\\ &+ \frac{\not{\mathcal{H}}_1}{2}[\rho^{+}{}_{1,2} + \rho^{+}{}_{1,3} - \rho^{+}{}_{2,4} - \rho^{+}{}_{3,4}] - \frac{1}{\tau_{AB}}\rho^{+}{}_{1,4}\\ &- \left[\frac{1}{T_{1A}} + \frac{1}{T_{2A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]\rho^{+}{}_{1,4}\Big\}\end{aligned} \tag{46}$$

$$\begin{aligned}0 = i\Big\{&[E_1 - E_4 - (\omega_2 - \omega_1)]\rho^{+}{}_{4,1}\\ &+ \frac{\not{\mathcal{H}}_1}{2}[-\rho^{+}{}_{2,1} - \rho^{+}{}_{3,1} + \rho^{+}{}_{4,2} + \rho^{+}{}_{4,3}]\\ &+ \frac{\not{\mathcal{H}}_2}{2}[\rho'{}_{4,2} - \rho'{}_{4,3} + \rho'{}_{2,1} + \rho'{}_{3,1}]\Big\}\\ &- \frac{1}{\tau_{AB}}\rho^{+}{}_{4,1}\\ &- \left[\frac{1}{T_{1A}} + \frac{1}{T_{2A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]\rho^{+}{}_{4,1}\end{aligned} \tag{47}$$

In a typical double resonance experiment, a system is strongly irradiated at ω_1 and scanned by the weak rf field ω_2. First the coupled density matrix equations (32, 33) are solved for all the ρ' density matrix elements at frequency ω_1. Then these elements are substituted into the linearized set of coupled equations for ρ^{+} (eq 43-47) and solved with standard matrix inversion techniques. The absorption at ω_2 is obtained as shown in eq 30.

The derivation given above together with the different approximations used is completely general for double resonance NMR line shapes of any exchanging system or set of coupled exchanging systems as long as ω_1 is strong and ω_2 weak.

Table I. NMR Parameters AB + B′ ⇄ AB′ + B

Relative shifts, Hz (J_{AB} = 1 Hz)		All T_1 and T_2 values = 2.0 sec
A (of AB)	+5	[AB] = 2[B′]
B (of AB)	0	$\tau_{AB} = 2\tau_{B'}$
B′ (free)	−5	

II. Density Matrix Interpretation of Effects in Double Resonance

There are three observed effects by which NMDR spectra differ from single resonance spectra: (a) there are changes in peak amplitude ratios; (b) additional splitting is sometimes observed; and (c) there may be changes in line shape because of exchange phenomena not seen in single resonance CW NMR.

The changes in amplitude are best discussed by comparing eq 43 with the $\dot{\rho}_{2,1}$ element describing the low power CW spectrum. This spectrum would result by letting $\not{\mathcal{H}}_1 \to 0$ (eq 48). The principal difference thus seen between eq 43

$$\begin{aligned}0 = i\Big\{&[E_1 - E_2 - (\omega_2 - \omega_1)]\rho^{+}{}_{2,1} - \frac{J_{AB}}{2}\rho_{3,1} +\\ &\frac{\not{\mathcal{H}}_2}{2}[-\rho^{eq}{}_{1,1} + \rho^{eq}{}_{2,2}]\Big\} + \frac{1}{\tau_{AB}}[\tfrac{1}{2}\rho^{+}{}_{6,5} - \rho^{+}{}_{2,1}] -\\ &\left[\frac{1}{T_{1A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]\rho^{+}{}_{2,1} + \frac{1}{T_{1A}}\rho^{+}{}_{4,3}\end{aligned} \tag{48}$$

and 48 lies in the coupling to the rf field which is

$$\frac{\not{\mathcal{H}}_2}{2}[-\rho^{eq}{}_{1,1} + \rho^{eq}{}_{2,2}] \tag{49}$$

for the low power single frequency response and

$$\frac{\not{\mathcal{H}}_2}{2}[-\rho'{}_{1,1} + \rho'{}_{2,2} + \rho'{}_{2,3}] \tag{50}$$

for the double resonance absorption. The other difference between eq 42 and 48 lies in the additional term

$$\frac{\not{\mathcal{H}}_1}{2}[\rho^{+}{}_{1,1} + \rho^{+}{}_{2,2} + \rho^{+}{}_{2,3} - \rho^{+}{}_{4,1}] \tag{51}$$

This contribution (eq 51) appears because we have chosen the product representation rather than one which diagonalizes $\mathcal{H}_{AB} + \not{\mathcal{H}}_1 I^x$. The principal effect of the excluded terms is one of splitting the first-order absorption peaks in the limit of very large $\not{\mathcal{H}}_1$.[20] Temporarily ignoring the peak splittings, we conclude that the Overhauser like change in amplitude of the first-order double resonance peaks relative to the equivalent low power single resonance peaks is given by the ratio of the amplitude terms of eq 43 to 48.

Now we return to the extra line splitting phenomena in double resonance spectra which in most cases will appear only as a line-shape distortion. To obtain a qualitative feeling for the effect assume no exchange ($\tau \sim \infty$) and $J_{AB}/(\omega_{0A} - \omega_{0B}) \ll 1$. The energy levels for $\mathcal{H}_0{}^{AB}$ which we have called E_i) and allowed $\Delta m = \pm 1$ transitions are shown to first order in Scheme I and eq 52. NMR parameters used

$$\begin{aligned}E_1 &= \tfrac{1}{2}(\omega_{0A} - \omega_1 + \omega_{0B} - \omega_1) + \frac{J_{AB}}{4}\\ E_2 &= \tfrac{1}{2}(\omega_{0A} - \omega_1 - \omega_{0B} + \omega_1) - \frac{J_{AB}}{4}\\ E_3 &= \tfrac{1}{2}(-\omega_{0A} + \omega_1 + \omega_{0B} - \omega_1) - \frac{J_{AB}}{4}\\ E_4 &= \tfrac{1}{2}(-\omega_{0A} + \omega_1 - \omega_{0B} + \omega_1) + \frac{J_{AB}}{4}\end{aligned} \tag{52}$$

below are listed in Table I. The resonance condition for $\rho^{+}{}_{2,1}$ is met at its maximum values. As seen from eq 43, this

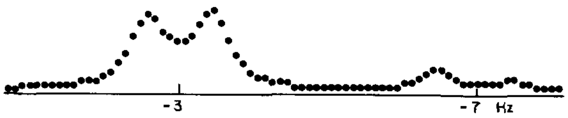
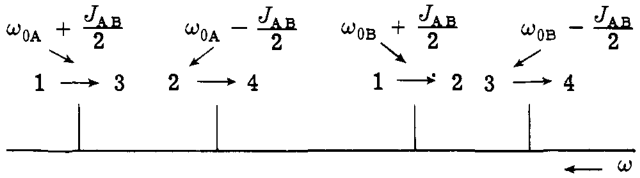


Figure 1. NMDR line shape, B resonance of AB system, $J_{AB} = 4$ Hz, $\delta_{A,B} = 10$ Hz, $T_1 = T_2 = 2$ sec, when A peak at +7 Hz is irradiated at $\not{\nu}_1 = 0.5$ Hz. Center of AB system defined as 0 Hz.

Scheme I

M	ψ
1	1 $\alpha\alpha$
0	2 $\alpha\beta$
0	3 $\beta\alpha$
−1	4 $\beta\beta$



condition is approximately realized when the denominator on the rhs of (53) approaches zero

$$\rho^+_{\underset{\max}{2,1}} \propto \frac{1}{i[E_1 - E_2 - (\omega_2 - \omega_1)] - \left[\frac{1}{T_{1A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]} \tag{53}$$

that is

$$E_1 - E_2 - (\omega_2 - \omega_1) \sim 0 \tag{54}$$

After substituting for the E's from (52), we find that

$$\omega_2 = \omega_{0B} + \frac{J_{AB}}{2}$$

which is just the location of the usual first order peak derived from the 1,2 transition. The same considerations apply to the other transitions.

Consider next with the same provisos as above the resonance condition for $\rho^+_{2,3}$ ($\Delta m = 0$). We now find that

$$E_3 - E_2 - (\omega_2 - \omega_1) \sim 0 \tag{55}$$

and substituting from (52)

$$\omega_2 = \omega_1 - \omega_{0A} + \omega_{0B} \tag{56}$$

The amplitude for the $\rho'_{2,3}$ transition will be large when $\rho'_{2,4}$ or $\rho'_{1,3}$ have their maximum values, that is when

$$\omega_1 = \omega_{0A} \pm \frac{J_{AB}}{2} \tag{57}$$

as seen from Scheme I. Substituting in (56) for ω_1 using (57) we find

$$\omega_2 = \omega_{0B} \pm \frac{J_{AB}}{2} \tag{58}$$

Thus on irradiating strongly (ω_1) near the 1-3 or 2-4 transition for the A proton, there will be a peak in the ω_2 spectrum near the 1-2 or 3-4 positions, respectively, for B. The resonance condition on $\rho^+_{3,2}$ is just the opposite to that of $\rho^+_{2,3}$. The application of ω_1 to the 1-2 or 3-4 transitions induces ω_2 transitions near the 1-3 or 2-4 peaks. We use "near" advisedly, for the terms appearing in eq 45 shift the $\Delta m = 0$ peak $\omega_2 = \omega_{0B} + (J_{AB}/2)$ from the usual first-order peak arising from $\rho^+_{2,1}$. Depending on the size of $\not{\omega}_1$, these two peaks can be seen separately or combined. Examples are discussed in section III.

We now consider the $\Delta m = 2$ transitions determined by the amplitude of $\rho^+_{1,4}$ and $\rho^+_{4,1}$. $\rho^+_{1,4}$ can be thrown out for, as shown in eq 46, it does not couple to any ρ' terms. On the other hand, $\rho^+_{4,1}$ couples to all four resonant peaks. Thus the resonant condition, see (47), corresponds to

$$\rho^+_{\underset{\max}{4,1}} = \frac{-\omega_2[\rho'_{4,2} + \rho'_{4,3} - \rho'_{2,1} - \rho'_{3,1}]}{2i[E_1 - E_4 - \omega_2 + \omega_1] - \left[\frac{1}{T_{1A}} + \frac{1}{T_{2A}} + \frac{1}{T_{1B}} + \frac{1}{T_{2B}}\right]} \tag{59}$$

and

$$\omega_2 = \omega_{0A} + \omega_{0B} - \omega_1 \tag{60}$$

The ω_2 response is maximized under the following sets of conditions

$$\begin{aligned} &\omega_1 = \omega_{0B} - (J_{AB}/2) \text{ and } \omega_2 = \omega_{0A} + (J_{AB}/2) \\ &\omega_1 = \omega_{0B} + (J_{AB}/2) \text{ and } \omega_2 = \omega_{0A} - (J_{AB}/2) \\ &\omega_1 = \omega_{0A} - (J_{AB}/2) \text{ and } \omega_2 = \omega_{0B} + (J_{AB}/2) \\ &\omega_1 = \omega_{0A} + (J_{AB}/2) \text{ and } \omega_2 = \omega_{0B} - (J_{AB}/2) \end{aligned} \tag{61}$$

Again note that the ω_2 condition is only approximate and is shifted slightly by $\not{\omega}_1$.

Finally we wish to show that, if instead of the absorption at ω_2 we consider the component of M_x which has the time dependence sin $(2\omega_1 - \omega_2)t$, we find from eq 23 that the amplitude of this time dependence is as given in eq 62. Notice how, in the $2\omega_1 - \omega_2$ response, the $\rho^+_{i,j}$ terms all have $m(i) - m(j) = +1$. From eq 41, we see the $\rho^+_{1,2}$ is coupled to $\rho'_{1,4}$ which only becomes large when

$$\text{Ab}(2\omega_1 - \omega_2) = (\text{AB})Im[\rho^+_{1,2} + \rho^+_{1,3} + \rho^+_{2,4} + \rho^+_{3,4}] + (\text{B})Im[\rho^+_{5,6}] \tag{62}$$

$$\omega_1 = (\omega_{0A} + \omega_{0B})/2 \tag{63}$$

the so-called double-quantum resonance. The resonance condition for $\rho^+_{1,2}$ from eq 41 is

$$\omega_2 = -[\omega_{0B} + (J_{AB}/2)] + 2\omega_1 \tag{64}$$

and on substituting from (63)

$$\omega_2 = \omega_{0A} - (J_{AB}/2) \tag{65}$$

In a similar manner, we obtain a resonance at each of the first-order peak positions for the other elements of ρ^+, $\rho^+_{1,3}$, $\rho^+_{2,4}$, and $\rho^+_{3,4}$. Thus for ω_1 at the center of the AB quartet, there is a difference frequency absorption.

III. Double Resonance Line Shapes

Double resonance line shapes are displayed in Figures 1-7. The NMR parameters used in these calculations are listed in Table I. We now discuss for each case the results for the slow exchange limit and then consider effects due to exchange.

As explained above, irradiation of the 1-2 transition (0.5 Hz) should produce one extra peak in the neighborhood of the 1-3 transition (due to $\Delta M = 0$) and another near the 2-4 (A resonance) due to $\Delta M = \pm 2$. Actually this effect can be seen very clearly for an AB system with $J_{AB} = 4$ Hz and $\delta_{A,B} = 10$ Hz. When the A peak at +7 Hz is irradiated at $\not{\nu}_1 = 0.8$ Hz, there is a distinct doubling of the B resonances, shown in Figure 1. However in general one often

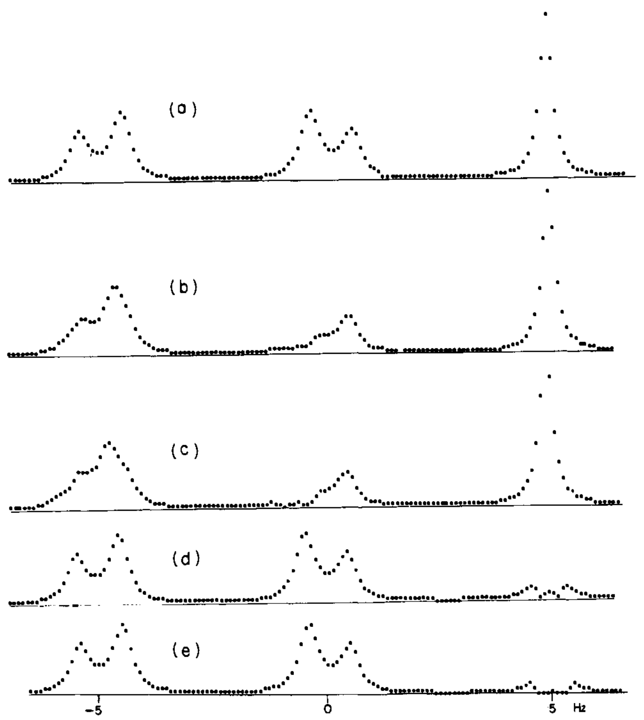


Figure 2. NMR line shapes, system 5, slow exchange limit, τ = 6000 sec: (a) double resonance, ν_1 = +0.5 Hz, $\mathcal{H}_1$ = 10^{-5} Hz; (b) double resonance, ν_1 = +0.5 Hz, $\mathcal{H}$ = 0.3 Hz; (c) double resonance, as in b with $\mathcal{H}_1$ = 0.4 Hz; (d) double resonance, ν_1 = −5 Hz (B′), $\mathcal{H}_1$ = 0.3 Hz; (e) double resonance, as in d with $\mathcal{H}_1$ = 0.4 Hz.

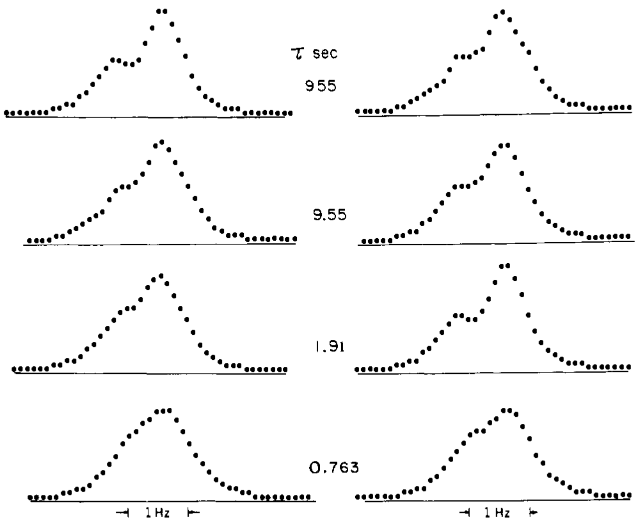


Figure 3. Double resonance line shapes, system 5, A absorption, ν_1 = +0.5 Hz (B). Left, $\mathcal{H}_1$ = 0.4 Hz. Right, $\mathcal{H}_1$ = 0.3 Hz. τ values are labeled on diagram.

observes line distortions and broadening effects as demonstrated for our exchanging system (5) in Figures 2 b,c and 3 a–c, which show the A resonance when the 1 → 2 transition of B (+0.5 Hz) is irradiated at different rf fields. At slow exchange, there is a definite broadening at +4.5 Hz and flattening at +5.5 Hz compared with the low rf spectrum. At faster rates of exchange, these four resonances in the +5 Hz region should coalesce progressively to one line. In fact by τ = 0.76 sec such signal averaging gives a narrower line in the $\mathcal{H}_1$ = 0.4 Hz spectrum than in the low power response (Figure 3). In this calculation, the effects of exchange on the B′ resonance in both single and double (ν_1 = +0.5 Hz) resonance spectra are about the same and thus not displayed.

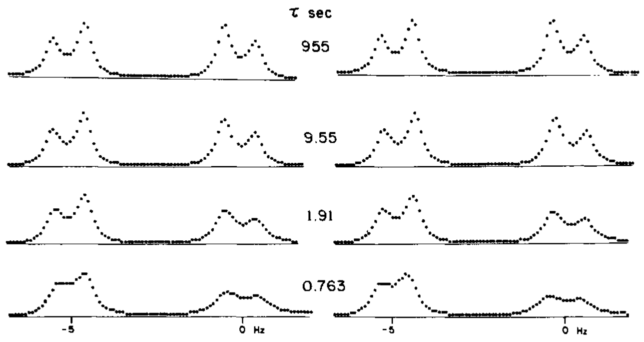


Figure 4. Double resonance AB line shapes, system 5, ν_1 = −5 Hz (B′). Left, $\mathcal{H}_1$ = 0.3 Hz. Right, $\mathcal{H}_1$ = 0.4 Hz. τ values indicated.

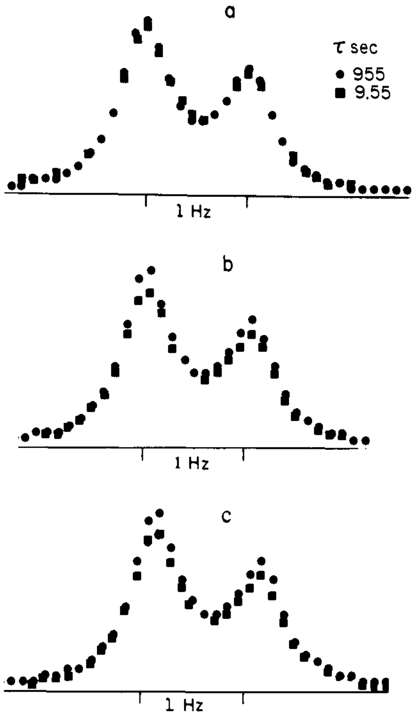


Figure 5. Comparison of double resonance line shapes for B of AB at different τ values when B′ is irradiated, ν_1 = −5 Hz: (a) limiting low rf, $\mathcal{H}_1$ = 10^{-5} Hz; (b) $\mathcal{H}_1$ = 0.3 Hz; (c) $\mathcal{H}_1$ = 0.4 Hz. (●) τ = 955 sec; (■) τ = 9.55 sec.

Next, consider what happens to the double resonance line shapes when B′ is irradiated at different rf fields (Figures 2 d,e and 4). The radiation burns a hole (with a small blip at the center) in the B′ peak, with considerable saturation in the wings (Figures 2 d,e). At slow exchange, the B resonance is independent of the $\mathcal{H}_1$ rf field. However beginning with τ < 10 sec transfer of saturation by exchange causes substantial changes in the B resonance as a function of the exchange rate, particularly in the slow exchange region. Actually a comparison of single with double resonance line shapes (Figure 5) shows that of the two the double resonance B line shape is by far the more sensitive to changes in exchange rate. Even comparing B line shapes for τ = 9.6 sec with τ = 960 sec, the single resonance absorptions are nearly identical, whereas those for $\mathcal{H}_1$ = 0.40 Hz show a 10% difference in intensity. Experimentally the ratio of the A to B maxima obtained under double resonance conditions (B′ irradiated) should be a sensitive parameter for measuring slow exchange rates. This result is the CW equivalent to the time dependent saturation recovery technique due to Hoffmann and Forsén.[21]

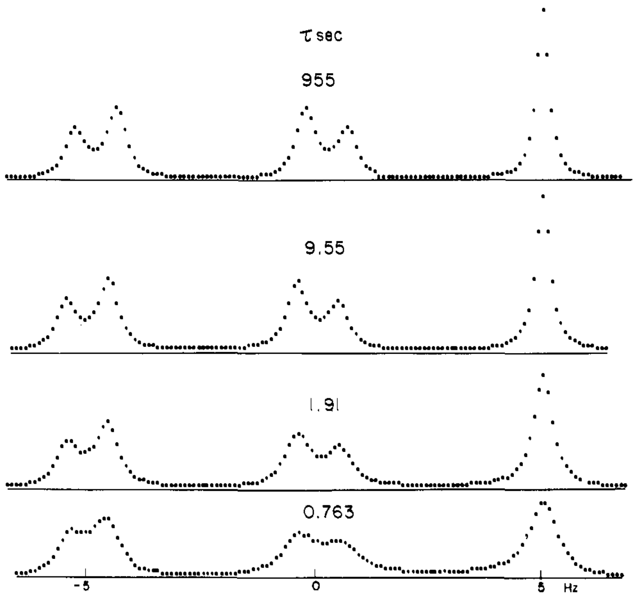


Figure 6. Single resonance, low rf line shapes, system 5, at different τ's.

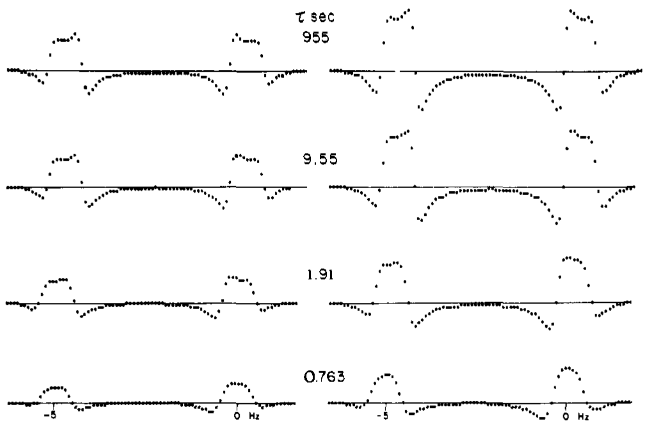


Figure 7. Pseudoabsorption for system 5 at different τ values, ν_1 = +2.5 Hz. Left, $\not{\nu}_1$ = 0.3 Hz. Right, $\not{\nu}_1$ = 0.4 Hz.

Figure 6 shows NMR line shapes for exchanging system (5) at low rf single resonance. These curves are shown for purposes of comparison to the double resonance line shapes (Figures 2–5).

Finally the pseudoabsorption, the response at $2\omega_1 - \omega_2$, is illustrated in Figure 7 for $\not{\nu}_1$ = 0.4 Hz, ν_1 = +2.5 Hz, the center of the AB quartet. Here, since the magnitude of the $\rho^{+}{}_{1,2}$, $\rho^{+}{}_{1,3}$, $\rho^{+}{}_{2,4}$, and $\rho^{+}{}_{3,4}$ terms is determined by $\rho'_{1,4}$ (see eq 41), the pseudoabsorption is down roughly by the ratio of the double quantum transition $\rho'_{1,4}$ compared with a typical 1,4 resonance. Notice here that increasing the exchange rate substantially lowers the absorption intensity.

Conclusion

What we have shown in this paper is that NMDR line shapes for exchanging systems are in some cases more sensitive to the rate in the slow exchange region than under single resonance conditions. This should have the effect of expanding the range of rate constants which can be extracted from NMR line shapes by a factor of 10^2.

Experiments to determine exchange rates with double resonance techniques will be most useful when the transition irradiated is coupled to that (those) observed by means of an exchange process. Needless to say, all this supposes that modern NMR equipment has the capability to produce precisely defined and controlled ω_1 and ω_1 irradiation.

Finally, in this paper, we have used a relaxation operator appropriate for intermolecular relaxation. Effects arising from intradipole relaxation (Overhauser effect) are not considered here but will be so in later work.

Acknowledgment. This research was supported by the National Science Foundation Grant No. GP 36633-X1, by the Office of Naval Research N. 014-67-A-0232-0023, and by the National Institutes of Health Grant No. R01 CA 11820-03.

Appendix I. Glossary of Symbols

Ab	absorption
AB,B′	chemical species
ab,*c*	product representation wavefunctions
E	exchange operator
$\mathcal{H}$	Hamiltonian laboratory frame
$\overline{\mathcal{H}}$	Hamiltonian rotating frame
i,*j*	labels of spins
R	relaxation operator
T_{1_i}, T_{2_i}	relaxation times nucleus *i*
ρ	density matrix laboratory frame
$\bar{\rho}$	density matrix rotating frame, two rf fields
ρ'	density matrix, rotating frame, one rf field; all values
$\rho^{\pm}$	perturbation term in $\bar{\rho}$ due to second rf field
τ_{sp}	preexchange lifetime of species
ω_{0_i}	frequency, chemical shift
ω_1,ω_2	rf frequencies, rad/sec
φ_1,φ_2	rf power, rad/sec
ν_1,ν_1	rf frequencies, Hz
$\not{\nu}_1$,$\not{\nu}_2$	rf power, Hz

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