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Transient Decay of Longitudinal Magnetization in Heterogeneous Spin Systems under Selective Saturation. IV. Reformulation of the Spin-Bath-Model Equations by the Redfield–Provotorov Theory*

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Alternative formulations to the conventional Bloch equations for the RF saturation of the solid component in heterogeneous spin systems according to a spin-bath model are derived using the concept of spin temperature as suggested by Redfield and Provotorov. These formulations and the resulting equations derived by the projection-operator technique provide an analytical and explicit solution to the general problem of solid saturation under continuous RF irradiation. Using the Provotorov theory, a set of generalized (non-Markovian) equations of motions is derived. The solutions to these generalized equations approach those of the conventional Bloch formulation at one extreme when the applied RF is weak and the Redfield formulation at another when the applied RF is strong. In short, this development provides a simple alternative which removes the restriction of the lineshape function used to represent the solid component; the latter is well known to be non-Lorentzian, contrary to the tacit assumption made in the conventional Bloch formulation. Experimental verification of the generalized theory is provided by transient and steady-state longitudinal magnetization data acquired from cross-linked bovine serum albumin under selective saturation by continuous off-resonance RF irradiation.

In previous developments (*1–3*) concerning the general solutions for the coupled equations which describe the response of a heterogeneous spin system subjected to selective RF saturation, the equations of motion have been based on a set of coupled Bloch equations formulated assuming a binary spin-bath model (*4–7*). This model was invoked (*4*, *5*) to provide a simple framework for the description of the nuclear spins in a heterogeneous system consisting of two thermodynamic reservoirs. The spins in one reservoir, labeled A, are water protons which are mobile with a typical spectral linewidth of tens of hertz while the spins in the other reservoir, labeled B, are macromolecular protons which are immobile with a typical linewidth on the order of tens to a hundred kilohertz. Because of the vast difference in linewidths of these two spin species, it is possible to saturate the B spins selectively, while leaving the A spins virtually unaffected, by applying a narrowband RF irradiation at a frequency far from the water resonance. To study the transient response of such a heterogeneous system, one simply saturates the B spins selectively using off-resonance RF irradiation while monitoring the time development of the longitudinal magnetization of the A spins.

In our last article (*3*) in this series, we proposed and demonstrated the use of projection-operator techniques (*8*, *9*) to obtain a simplified equation of motion and analytical solutions to the general problem formulated by the Bloch equations. In this article, the problem of the validity of the Bloch equations when applied to saturation of the solid component in such spin systems is addressed. This problem arises from our previous attempts (*1*) to interpret the relaxation-rate data of heat-denatured albumin in terms of the conventional Bloch equations. In these attempts, it was found that the experimental data showed a systematic discrepancy with respect to the theoretical curve at mid-frequency range. This mid-frequency discrepancy raises the question about the validity of the Bloch equations. It is well known that the Bloch equations cannot fully account for the experimentally observed nuclear relaxation in solids under RF saturation (*10–12*). For this reason, it is intriguing to explore alternative formulations of the relaxation equations based on the concept of spin temperature according to the Redfield (*10*) and Provotorov (*11*) theories.

In the following sections, we start by giving a heuristic and semiempirical derivation of the appropriate equations governing the solid spins (the spins of the B reservoir) according to the concept of spin temperature. We then solve, once again utilizing projection-operator techniques, the equations of motion for the binary spin-bath model in a similar manner to the Bloch formulation except that the solid-spin component is now described according to the Redfield and Provotorov formulations, respectively. We subsequently show that the solution of the Provotorov formulation can be written in a generalized form which ap-

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proaches the Bloch formulation in one limiting case and the Redfield formulation in another. These results differ from the solutions of the Bloch equations in an important way; the prescription of the lineshape function for the solid spins is now completely general rather than strictly Lorentzian. To verify this generalized formulation of the spin-bath model, we first attempted to reinterpret the transient and steady-state longitudinal magnetization data of heat-denatured hen egg white albumin presented in I (*1*), using a multiple-parameter fitting program. This attempt failed since neither Lorentzian nor Gaussian lineshape (nor their convolutions) functions yielded good fits for this biophysically "complex" (as far as the NMR lineshape function is concerned) system. For this reason, we choose a simpler system, consisting of cross-linked bovine serum albumin (XL-BSA), in which both transient and steady-state magnetization and relaxation-rate data are acquired using techniques similar to those described in Ref. (*1*).

THE REDFIELD–PROVOTOROV FORMULATION FOR COUPLED BINARY SPIN BATHS

Redfield (*10*) and later Provotorov (*11*) introduced the concept of spin temperature in the rotating frame to explain saturation phenomena in solids for which the conventional Bloch equations failed. Since their theories are well known and were thoroughly reviewed by Goldman (*12*), only the essential parts pertinent to the present development are presented here. The coupled spin bath with RF saturation of the immobile spins in the Redfield–Provotorov picture is best illustrated by the schematic diagrams shown in Fig. 1. We focus our attention here on the solid or B spins (Fig. 1b). We first remove the spin–lattice effects by assuming T_{1B} is infinitely long. In the rotating frame, the spin Hamiltonian of the B spins is the sum of two terms,

$$\mathcal{H} = \mathcal{H}_Z + \mathcal{H}_D^0, \qquad [1]$$

where $\mathcal{H}_Z$ is the Zeeman interaction, $\mathcal{H}_Z = -\gamma \mathbf{I} \cdot \mathbf{H}_e$; $\mathbf{H}_e = (H_0 - \omega_0/\gamma)\mathbf{k} + H_1\mathbf{i}$ with $\mathbf{i}$ and $\mathbf{k}$ being the unit vectors along the x and z axes, respectively. $\mathcal{H}_D^0$ is the properly truncated dipolar Hamiltonian, i.e., the secular parts of $\mathcal{H}_D$ that commute with I_z. In the absence of the RF field, $\mathcal{H}_Z$ and $\mathcal{H}_D^0$ themselves commute and are separately constants of motion. In other words, the Zeeman and dipolar reservoirs are thermally insulated. If we assume they are initially at equilibrium with the thermal lattice, then their spin temperatures in the laboratory frame are all equal, $\theta_Z^L = \theta_D^L = \theta^L$, θ^L being the lattice temperature.

In the rotating frame, however, since the z component of the effective field is much smaller than H_0, $\theta_Z' \ll \theta_Z^L$ according to Curie's law, while $\theta_D' = \theta_D^L$ since $\mathcal{H}_D^0$ is invariant under rotation around the z axis. Here the primes denote variables in the rotating frame. The Zeeman reservoir is therefore much cooler than the dipolar one in the rotating frame. Upon turning on the RF field, $[\mathcal{H}_Z, \mathcal{H}_D^0] \neq 0$ and the Zeeman and dipolar systems exchange energy. Since $\theta_Z' \ll \theta_D'$, energy flows from the dipolar to the Zeeman reservoir. When the RF field is large, this redistribution of energy occurs rapidly with the formation of a quasiequilibrium state describable by a temperature θ^* (i.e., the density matrix is diagonal and its elements follow a Boltzman distribution) common to both of these two reservoirs.

The characteristic rate $1/\tau^*$ for the establishment of such a quasiequilibrium state was found (*11*) to be dependent on the offset frequency $\delta\omega$, the dipolar linewidth Δ_D, and the transition probability W,

$$\frac{1}{\tau^*} = W\left\{1 + \left(\frac{\delta\omega}{\Delta_D}\right)^2\right\}; \quad W = \pi\omega_1^2 g(\delta\omega), \qquad [2]$$

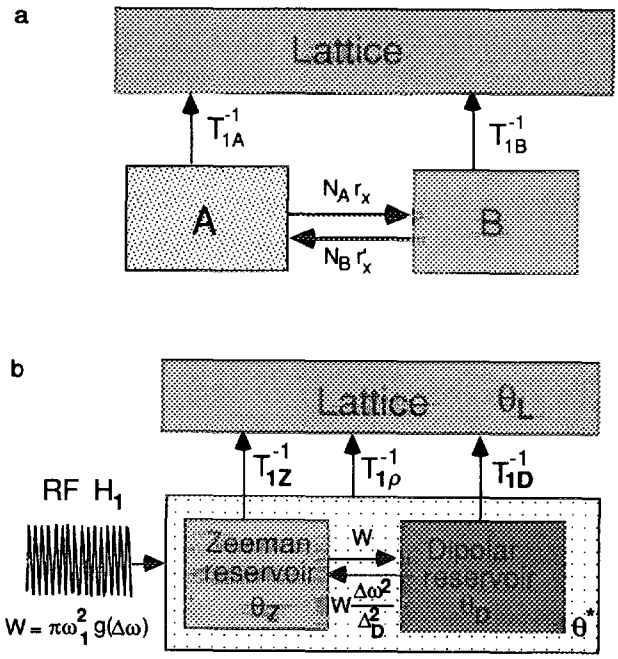

FIG. 1. (a) Schematic of the binary coupled spin-bath model by Edzes and Samulski (*4*, *5*). T_{1A}^{-1} and T_{1B}^{-1} are the intrinsic longitudinal relaxation rates of the mobile (A) and the immobile (B) spins, respectively. $N_A r_x$ and $N_B r_x'$ are the forward and backward rates of magnetization transfer, respectively, from the A- to B-spin reservoirs, where N_A and N_B are the number of nuclei in the A and B reservoirs and r_x and r_x' are the corresponding specific cross-relaxation rates. Since, according to the principle of microscopic reversibility (or detailed balance), $N_A r_x = N_B r_x'$, $r_x' = r_x/f$, where $f = N_B/N_A$. Note here that N_A and N_B refer to the nuclei in the reservoirs only, which do not necessary include all nuclei in the liquid and solid phases. (b) Schematic diagram of the solid-spin reservoir under RF saturation. The vertical arrows indicate energy transitions by spin–lattice relaxation processes while the horizontal arrows indicate energy flows as dictated by the Provotorov equations. When the RF amplitude is sufficiently high that the RF-induced transition rate $1/\tau^*$ between the Zeeman and dipolar reservoirs is much larger than the Zeeman relaxation rate, T_{1Z}^{-1}, the Z and D reservoirs can be fused into a metastable or quasiequilibrium state characterized by the spin temperature θ^* and with a thermal relaxation rate of $T_{1\rho}^{-1}$.

with $g(\delta\omega)$ being the lineshape function. In this state of quasiequilibrium, the magnetization aligns with the effective field $\mathbf{H}_e$, a condition commonly referred to as a spin-lock (*10*). The rate constant $1/\tau^*$ describes the rate at which the RF induces transitions between the dipolar and the Zeeman reservoirs. We note from [2] that $1/\tau^* \geqslant W \sim \omega_1^2 T_{2B}$, W being the transition probability and $\pi g(0) \sim T_{2B}$. Thus, if $\omega_1 \gg 1/\sqrt{T_{2B}T_{1Z}}$, one can assume $1/\tau^* \gg 1/T_{1Z}, T_{1Z}$ where is the Zeeman relaxation time.

So far, we have excluded our main concern here: the effects of the thermal lattice and the cross-relaxation effect with the A spins. To include these effects within the Redfield–Provotorov picture as described above, one abandons the Bloch equation description of the B spins and replaces it with a set of equations that describe the rate of change of spin energy or the inverse spin temperature $1/\theta^*$, which includes effects of interaction with thermal lattice and cross relaxation with the A spins. The problem that remains is to find a method for including the two effects mentioned above. The relaxation problem in the presence of an RF field has been solved (*10–12*). To illustrate these solutions, we divide the problem into two regimes according to the strength of the saturation RF field. Here the RF field strength is considered high if $\omega_1 > 1/\sqrt{T_{2B}T_{1Z}}$ and low otherwise.

High-RF-Field Regime—The Redfield Formulation

When ω_1 is large, as mentioned in the previous paragraphs, one can assume that the energy redistribution among the B spins occurs so rapidly that the spin states are effectively in quasiequilibrium at all times. Therefore, the spin–lattice interaction can be described by a phenomenological equation for the expectation value of a Hamiltonian characterizing the quasiequilibrium $\mathcal{H}^*$, $\langle \mathcal{H}^* \rangle$, or equivalently the inverse spin temperature $1/\theta^*$,

$$\left(\frac{d}{dt}\right)_{SL}\left(\frac{1}{\theta^*}\right) = \frac{1}{T_{1\rho}}\left\{\left(\frac{1}{\theta^*}\right)_{eq} - \left(\frac{1}{\theta^*}\right)\right\}, \qquad [3]$$

where $T_{1\rho}$ is well-known spin–lattice relaxation time in the rotating frame. Since from Curie's law, $M \propto \mathbf{H}_e/\theta^*$, M being the magnitude of the magnetization along $\mathbf{H}_e$, one can write an equation analogous to [3] for M_B of the B spins,

$$\left(\frac{d}{dt}\right)_{SL} M_B = \frac{1}{T_{1\rho}}\{M_{eq}^B - M_B\}, \qquad [4]$$

where $T_{1\rho}$ is functionally dependent upon T_1, ω_1, $\delta\omega$, and the dipolar linewidth Δ_D. This dependence assumes a particularly simple form if one assumes that nuclear relaxation is caused by random uncorrelated fields with short correlation time $\tau_c \ll 1/\omega_0$,

$$\frac{1}{T_{1\rho}} = \frac{1}{T_1}\frac{\delta\omega^2 + \omega_1^2 + 2\Delta_D^2}{\delta\omega^2 + \omega_1^2 + \Delta_D^2}. \qquad [5]$$

If the short-correlation-time condition is not satisfied, [5] must be modified to

$$\frac{1}{T_{1\rho}} = \frac{1}{T_1}\frac{\delta\omega^2 + c_u\omega_1^2 + c_D\Delta_D^2}{\delta\omega^2 + \omega_1^2 + \Delta_D^2}, \qquad [6]$$

where c_u is the ratio of the component relaxation rate of u (along H_1 toward 0) to that of the Zeeman term along the z axis, or $1/T_{1Z}$, and c_D is the ratio of the dipolar relaxation rate (toward $\langle \mathcal{H}_D^0 \rangle_{eq}$) to $1/T_{1Z}$; i.e.,

$$c_u \equiv \frac{T_{1u}^{-1}}{T_{1Z}^{-1}} = \frac{T_{1Z}}{T_{1u}} \quad \text{and} \quad c_D \equiv \frac{T_{1D}^{-1}}{T_{1Z}^{-1}} = \frac{T_{1Z}}{T_{1D}}. \qquad [7]$$

Since the heat capacity of the dipolar reservoir is much larger than that of the RF field, $\Delta_D \gg \omega_1$, the terms associated with ω_1 in [5] and [6] can be ignored.

Low-RF Regime—The Provotorov Formulation

When ω_1 is not sufficiently large for the transitions induced by W to be comparable to those induced by the spin–lattice coupling, or $W \sim 1/T_1$, the Provotorov theory (*11*, *12*) must be invoked to evaluate the time evolution of the spin system. Under this condition, one can no longer assume that the Zeeman and dipolar reservoirs have a common spin temperature. We therefore let θ_Z and θ_D, respectively, be the temperatures of these two reservoirs (see Fig. 1b and the figure legend). The differential equations which govern the time evolution of the corresponding inverse temperatures can be written (*9*, *10*) as

$$\left(\frac{d}{dt}\right)\left(\frac{1}{\theta_Z} - \frac{1}{\theta_Z^L}\right) = -\left[W + \frac{1}{T_1}\right]\left(\frac{1}{\theta_Z} - \frac{1}{\theta_Z^L}\right) + W\left(\frac{1}{\theta_D} - \frac{1}{\theta_D^L}\right) - W\left(\frac{1}{\theta_Z^L} - \frac{1}{\theta_D^L}\right) \qquad [8a]$$

$$\left(\frac{d}{dt}\right)\left(\frac{1}{\theta_D} - \frac{1}{\theta_D^L}\right) = -\left[W\frac{\delta\omega^2}{\Delta_D^2} + \frac{1}{T_{1D}}\right]\left(\frac{1}{\theta_D} - \frac{1}{\theta_D^L}\right) + W\frac{\delta\omega^2}{\Delta_D^2}\left(\frac{1}{\theta_Z} - \frac{1}{\theta_Z^L}\right) + W\frac{\delta\omega^2}{\Delta_D^2}\left(\frac{1}{\theta_Z^L} - \frac{1}{\theta_D^L}\right). \qquad [8b]$$

Since $\theta_Z^L \ll \theta_D^L = \theta^L$, one can ignore $1/\theta_D^L$ in the last term in [8a] and [8b].

To introduce the cross-relaxation effect between the A and B spins on the coupled spin system, we provide the details for the Provotorov formula in Eq. [8] here. In the next section, a generalized solution to the apparent relaxation for all three different formulations mentioned above is given. Cross

relaxation occurs between the longitudinal magnetization of the A and B spins. The contribution to the relaxation of the B spins from the A spins is the same term, $r_X(M_A^Z - M_A^{Z^0})$, where r_X is the specific rate of magnetization transfer from the A spins to the B spins (for the symbol definitions of the spin-bath parameter, see Fig. 1a and the figure legend), as used in the coupled Bloch equations. On the other hand, for the B-spin contribution to the A-spin relaxation, although the components that are involved in energy exchange are no longer purely longitudinal, one may introduce the cross-relaxation term through the Zeeman reservoir in Eq. [8a]. Furthermore, since Eqs. [8a] and [8b] are written for the inverse spin temperatures, they equally apply to the expectation value of any traceless operator A, such as I_x, I_z, or $\mathscr{H}_D^0$, since $\langle A \rangle \propto \mathrm{Tr}\{[1 - \mathscr{H}/k\theta]A\} \propto 1/\theta$. The B-to-A cross-relaxation term is therefore $(r_X/f)(M_B^z - Z_B^{ZL})$. Note that the difference between the Provotorov and the Bloch formalisms is not at all how the cross-relaxation terms are introduced, but rather the way these two formulations treat the magnetization in the presence of RF irradiation. In the Bloch equations, the magnetization is driven by a torque due to an effective field. In the Redfield and Provotorov formulations, on the other hand, the motions of the "magnetization components" polarized along the Zeeman and dipolar interactions, respectively, are described by spin thermodynamics. A dipolar "magnetization," for example, can be defined by the Curie's Law as CH_D/θ_D, where C is the heat capacity, H_D and θ_D being the local field and temperature, respectively, of the truncated dipolar Hamiltonian. With this understanding, the equations of motion that govern the energy exchange between these two reservoirs and the thermal lattice can thus be written as

$$\frac{dM_B^z}{dt} = \left[W + \frac{1}{T_{1B}} + \frac{r_X}{f}\right](M_B^{ZL} - M_B^z) - W_\gamma \frac{\delta\omega}{\Delta_D^2}\{\langle \mathscr{H}_D^0 \rangle_B^L - \langle \mathscr{H}_D^0 \rangle\} - r_X(M_A^{ZL} - M_{AZ}) - WM_B^{ZL} \quad [9a]$$

$$\frac{d}{dt}\langle \mathscr{H}_D^0 \rangle = -\left[W\frac{\delta\omega^2}{\Delta_D^2} + \frac{1}{T_{1D}}\right]\{\langle \mathscr{H}_D^0 \rangle^L - \langle \mathscr{H}_D^0 \rangle\} + W\left(\frac{\delta\omega}{\gamma}\right)(M_B^{ZL} - M_B^z) + W\frac{\delta\omega}{\gamma}M_B^{ZL} \quad [9b]$$

$$\frac{dM_A^Z}{dt} = \omega_1 M_A^Y + (r_A + r_X)(M_A^{ZL} - M_A^z) - \frac{r_X}{f}(M_B^{ZL} - M_B^z), \quad [9c]$$

with the superscripts Z denoting Zeeman (which in our cases is synonymous with the Z direction) and L the lattice.

SOLUTION OF THE COUPLED EQUATIONS USING REDFIELD–PROVOTOROV FORMULATION OF THE B SPINS

With the cross-relaxation terms between the two spin baths modified according to Eq. [9] above, we can rewrite the equations of motion of the heterogeneous spin system in the cardinal form (*3*),

$$\frac{d\mathbf{X}}{d\tau} + \mathbf{R}\mathbf{X} = \mathbf{Y}, \quad [10]$$

where all parameters and variables are defined as nondimensional quantities; with $\tau = \omega_1 t$; and with the vectors $\mathbf{X}$, $\mathbf{Y}$ and the matrix $\mathbf{R}$ defined respectively by

$$\mathbf{X} = \mathrm{col}\{w'_{BZ}, w'_{BD}, u_A, v_A, w_A\} \quad [11]$$

$$\mathbf{Y} = \mathrm{col}\left\{\frac{1}{2}\alpha_W, -\frac{\alpha_W}{2F}\left(\frac{\delta}{\beta_B}\right)^2, 0, -1, 0\right\} = \frac{1}{2}\alpha_W \mathbf{e}_1 - \frac{\alpha_W}{2F}\left(\frac{\delta}{\beta_B}\right)^2 \mathbf{e}_2 - \mathbf{e}_4 \quad [12]$$

$$\mathbf{R} = \begin{bmatrix} \alpha_W + \alpha_B + \dfrac{\alpha_X}{f} & -\alpha_W F & 0 & 0 & -\dfrac{\alpha_X}{f} \\ \dfrac{\alpha_W}{F}\left(\dfrac{\delta}{\beta_B}\right)^2 & -\left[\alpha_W\left(\dfrac{\delta}{\beta_B}\right)^2 + c_D\alpha_B\right] & 0 & 0 & 0 \\ 0 & 0 & \beta_A & \delta & 0 \\ 0 & 0 & -\delta & \beta_A & -2 \\ -\alpha_X & 0 & 0 & \dfrac{1}{2} & \alpha_A + \alpha_X \end{bmatrix}, \quad [13]$$

where

$\alpha_s = 1/(\omega_1 T_{1s}) = r_{1s}/\omega_1$, $\beta_s = 1/(\omega_1 T_{2s})$;

s = A, B, $\alpha_X = r_X/\omega_1$,

$\alpha_W = \dfrac{W}{\omega_1} = \pi g^B(\delta)$;

$g^B(\delta)$, normalized B-spin lineshape function,

$$F = \frac{\theta_Z^L}{\theta_D^L} = \frac{\omega - \omega_0}{\omega_0}, \qquad [14]$$

$$w'_{BZ} = \frac{M_B^{ZL} - M_B^{\bar{z}}}{2M_B^{ZL}}, \quad w'_{BD} = \frac{\langle \mathscr{H}_D^0 \rangle_B^L - \langle \mathscr{H}_D^0 \rangle}{2\langle \mathscr{H}_D^0 \rangle_B^L}, \qquad [15]$$

and $\mathbf{e}_i = \text{col}\{\delta_{ij}\}$.

By using the same procedure as that illustrated in (*3*) applied to Bloch formulation, one can show that, under the Provotorov formulation, the "secular" part of the spin system will satisfy an asymptotic equation,

$$\frac{dw_A}{d\tau} + \alpha_{app}^P (w_A - w_A^{ss}) = 0, \qquad [16]$$

in which the apparent relaxation rate of the observed A spins is given by

$$\alpha_{app}^P = (\alpha_A + \alpha_X) - \frac{\alpha_X^2}{f}\left[\left(\alpha_B + \frac{\alpha_X}{f}\right) + \frac{\alpha_W c_D \alpha_B \beta_B^2}{\alpha_W \delta^2 + c_D \alpha_B \beta_B^2}\right]^{-1} + \pi g_L^A(\delta), \qquad [17a]$$

where the subscript L in $g_L(\delta)$ indicates a Lorentzian lineshape:

$$g_L(\delta) = \frac{\beta}{\pi}\frac{1}{\delta^2 + \beta^2}. \qquad [17b]$$

The steady-state magnetization w_A^{ss} is then given by

$$w_A^{ss} = \frac{1}{\alpha_{app}^P}\left\{\frac{1}{2}a'\alpha_W - b'\frac{\alpha_W}{2F}\left(\frac{\delta}{\beta_B}\right)^2 - d'\right\}, \qquad [18a]$$

where

$$a' = \frac{\alpha_X\{\alpha_W(\delta/\beta_B)^2 + c_D\alpha_B\}}{(\alpha_B + \alpha_X/f)[\alpha_W(\delta/\beta_B)^2 + c_D\alpha_B] + \alpha_w c_D \alpha_B}, \qquad [18b]$$

$$b' = -\frac{\alpha_X \alpha_W F}{(\alpha_B + \alpha_X/f)[\alpha_W(\delta/\beta_B)^2 + c_D\alpha_B] + \alpha_W c_D \alpha_B}, \qquad [18c]$$

$$d' = \frac{-\beta_A/2}{\delta^2 + \beta_A^2}. \qquad [18d]$$

Substituting [18b]–[18d] into [18a], one has

$$w_A^{ss} = \frac{1}{2\alpha_{app}^P}\left\{\frac{\alpha_X\{2\alpha_W^2(\delta/\beta_B)^2 + c_D\alpha_B\alpha_W\}}{(\alpha_B + \alpha_X/f)[\alpha_W(\delta/\beta_B)^2 + c_D\alpha_B] + c_D\alpha_B\alpha_W} + \pi g_L^A(\delta)\right\}. \qquad [19]$$

Note that the first and the third terms in [17a] are the same as those in the equivalent expression derived in (*3*) starting from the conventional Bloch equations. The difference occurs, as expected, in the second term, which represents the correction of the cross-relaxation contribution between the A and B spins without the simplifying assumption of constant saturation of the A spins.

The form of α_{app}^R, the apparent relaxation rate for the Redfield formulation, can be obtained in a similar fashion. In fact, it can be shown that α_{app} for all three of these formulations can be written in a simple unified manner as

$$\alpha_{app}^{\Xi} = \alpha_A + \alpha_X - \frac{\alpha_X^2/f}{(\alpha_B + \alpha_X/f) + \zeta^{\Xi}} + \pi g_L^A(\delta);$$

Ξ = B, P, R, [20a]

$$\zeta^B = \pi g_L^B(\delta), \quad \zeta^P = \frac{\pi g^B(\delta) c_D \alpha_B \beta_B^2}{\pi g^B(\delta)\delta^2 + c_D\alpha_B\beta_B^2}, \quad \zeta^R = \frac{(c_D - 1)\alpha_B\beta_B^2}{(\delta^2 + \beta_B^2)}, \qquad [20b]$$

where the labels B, P, and R represent, respectively, the Bloch, Provotorov, and Redfield formulations, and ζ^{Ξ} can be considered a generalized nondimensional lineshape function for the B spins. Note, for instance, that $\zeta^P = \alpha_W = \pi g_L^B(\delta) = \zeta^B$ when the B-spin lineshape is Lorentzian and δ small or

$$c_D \gg \frac{\alpha_W}{\alpha_B}\left(\frac{\delta}{\beta_B}\right)^2 = \frac{1}{\alpha_B\beta_B}\frac{1}{1 + (\beta_B/\delta)^2}$$

$$\text{or} \quad c_D \gg \frac{1}{\alpha_B\beta_B} = \omega_1^2 T_{1B} T_{2B}. \qquad [21]$$

In other words, the Provotorov solution approaches that of the Bloch equations in the limiting case for which $g^B(\delta)$ is Lorentzian and δ or ω_1 is small. Conversely, when the H_1 field is large, $\alpha_W > c_D\alpha_B$, and when δ is large, the Provotorov solution approaches the Redfield limit. These consequences are exactly what one would expect on physical grounds. For when H_1 is small, so is W, and when c_D is large, $T_{1Z} \gg T_{1D}$,

the dipolar reservoir can be considered as part of the lattice. Therefore, the condition of Eq. [20] guarantees the applicability of perturbation theory from which the Bloch equations result. On the other hand, under conditions opposite to Eq. [21], the Zeeman and the dipolar reservoirs quickly reach a state of quasiequilibrium corresponding to the Redfield picture described earlier.

COMPARISON OF CALCULATIONS TO EXPERIMENTAL DATA OF THE SPIN-BATH MODEL

Cross-linked bovine serum albumin was prepared by adding 200 μl of 20% glutaraldehyde (Sigma Chemical Co., St. Louis, Missouri) to a 20 ml solution of 20% (w/w) BSA (Sigma Chemical Co., No. A-8022). Data consisting of dispersive relaxation-rate and steady-state longitudinal magnetization under "broadband saturation" (*13*) were obtained using a similar experimental procedure to that described in I (*1*). The generalized spin-bath model described above was fitted to the data. In this procedure, the experimentally determined parameter T_{2A} (23.7 ms) was fixed. In addition, the relaxation rate $1/T_{1B}$ could not be varied independently since its value, along with the other variables, is constrained by the measured $1/T_{1A}^{NS} = 0.83\ s^{-1}$. For the Provotorov formulation, we also need the parameter c_D, the ratio of spin-lattice relaxation rates of the dipolar to Zeeman reservoirs for the solid spins ($c_D \equiv T_{1Z}/T_{1D}$). As discussed by Goldman (*12*), for nuclear relaxation in solids caused by correlated randomly fluctuating fields, $c_D = 3$. For uncorrelated fields, however, c_D is instead given by

$$c_D = 2 + \tfrac{1}{3}\omega_0^2\tau_c^2. \qquad [22]$$

Thus, for correlation times satisfying the extreme narrowing condition $\omega_0\tau_c \ll 1$, $c_D = 2$. But when $\omega_0\tau_c > 1$, c_D can be very large. For the types of heterogeneous systems that are of biological interest, the latter condition is most likely satisfied. This conjecture is partly substantiated by our experience in fitting Eqs. [17] and [19] to the experimental data for the heat-denatured albumin and the XL-BSA. We found that large values of c_D (e.g., >2500) give consistently better fits to the data than any smaller values. As noted earlier, a large c_D tends to lend support to the Bloch formulation for these systems, provided that the solid-spin lineshape is Lorentzian. However, for heat-denatured albumin and for XL-BSA, we found that in fitting the experimental data, the assumption of a Lorentzian lineshape for the solid spins is not supported in either case. For the XL-BSA data, as shown below, a Gaussian lineshape provides a much better fit to the experimental data than a Lorentzian shape.

Theoretical fits to the experimental data were performed with a multiparameter nonlinear fitting program contained in an interactive software package called MATLAB (South Natick, Massachusetts). These were performed using a Macintosh computer. The experimental data, as we reported previously in I (*1*), consisted of a set of apparent T_1 values as well as steady-state M_z data acquired at different amplitudes

FIGS. 2 and 3. The figures show the resulting plots of the fits of a binary spin-bath model using Provotorov formulation of the solid spins to the experimental data of cross-linked bovine serum albumin at different saturation RF amplitudes. The consistent sets of the model parameters obtained with two different B-spin lineshape functions are shown in the following table:

Lineshape	f	T_{1A}^{-1} (s^{-1})	T_{1B}^{-1} (s^{-1})	r_{1X} (s^{-1})	T_{2B} (μs)	T_{1Z}/T_{1D}
Lorentzian	0.086	0.752	1.80	3.47	35.8	3500
Gaussian	0.075	0.832	0.85	3.47	11.6[b]	2750

[a] T_{1B}^{-1} is obtained by implication (rather than by independent fit) from its relationship with the measured apparent T_{1NS}^{-1} and the other parameters such as f, T_{1A}^{-1}, and r_{1X}.

[b] The time constant T_2 for a Gaussian lineshape is defined here as the inverse of the half-width at half-maximum, $1/\delta$, where $\delta = 1.18\sqrt{M_2}$, with M_2 the second moment of the normalized Gaussian curve.

Figure Symbols

RF amplitude (rad/s)	Model calculation	Experimental data
832.5	...	#
1665.0	---	○
2497.6	- - -	◩
3330.0	—	▲

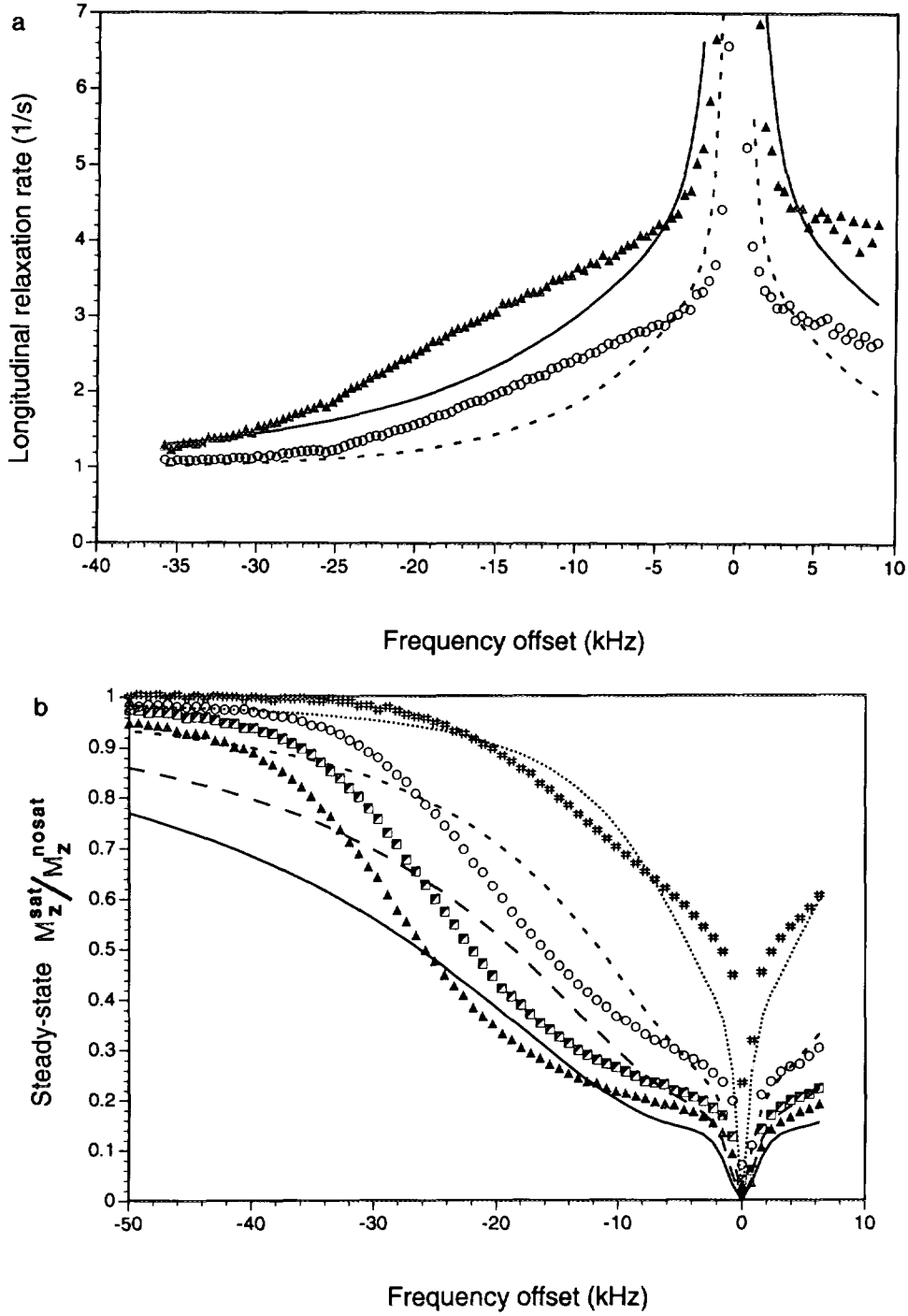

FIG. 2. (a) Apparent T_1^{-1} vs $\Delta\omega$ and (b) steady-state M_z vs $\Delta\omega$ assuming a Lorentzian lineshape for solid spins.

and frequency offsets of the saturation RF. While the key subroutine used in the fitting program is basically an unrestricted (downhill simplex) minimization procedure for a single data line, the MATLAB software provides a convenient environment for combining various data inputs with adjustable weights in their contribution to the sum-square deviation. This feature allows us not only to fit a combined set of dispersive relaxation-rate or M_z^{sat} data at various RF amplitudes, but also to fit simultaneously both the $1/T_1$ and the M_z^{sat} data sets, weighted individually according to some subjective criteria. We believe that for a parameter set obtained by such a fit to be credible, it must satisfy multiple

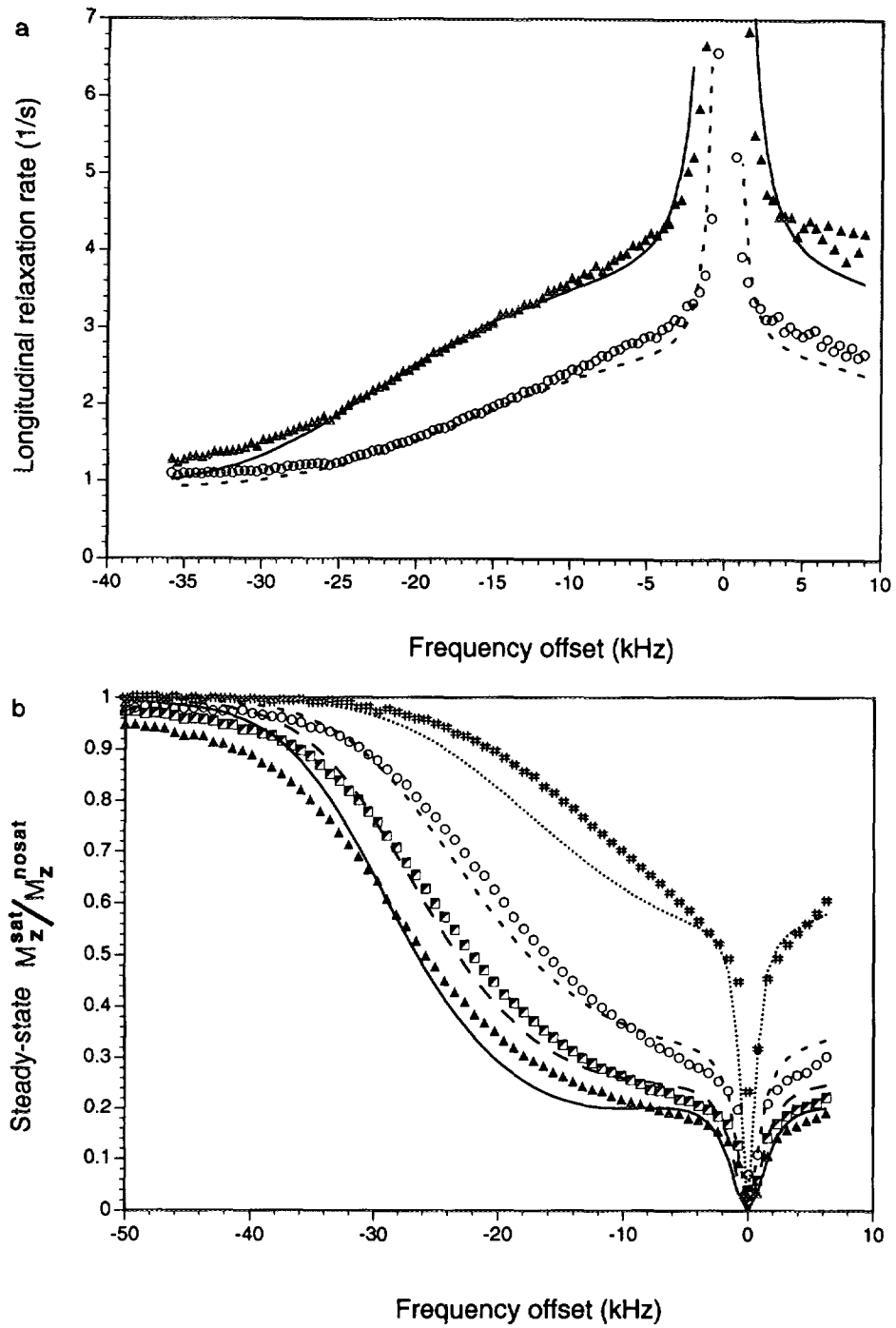

FIG. 3. (a) Apparent T_1^{-1} vs $\Delta\omega$, and (b) steady-state M_z vs $\Delta\omega$ assuming a Gaussian lineshape for solid spins.

data lines, rather than one or two. Ideally all data points should be fitted with equal weights, if they are equally accurate.

In the results presented herein, the fits were all performed with a combination of two rate data lines ($1/T_1$ vs frequency offset) and four steady-state M_z^{sat} data lines corresponding to two and four, respectively, distinct RF amplitudes. Assuming a Gaussian lineshape, one can obtain good fits to each of the rate and M_z^{sat} data independently, as one may expect. But the parameter sets obtained by these fits are not consistent. A consistent fit of the these two data sets can be obtained by the minimization of the weighted sum-square deviations of these two individual fits. By adjusting the weighting factors, one can arbitrarily bias the weight toward

either of the two sets. In our case, we assume both data sets are equal in accuracy and thus should be "equally weighted" in the fitting process. Figure 2 and 3 show the results of such fits to the experimental data using the Provotorov formulation with a Lorentzian and Gaussian lineshape, respectively, for the solid spins. It is clear from these results that, at least for XL-BSA, the solid lineshape function is better represented as a Gaussian than a Lorentzian.

DISCUSSION

Transient decay experiment were first performed by Forsén and Hoffman (*14*, *15*) to obtain dynamic information for a simple chemical system with resolvable peaks undergoing chemical exchange. Since the system of concern here is more complex, it is no longer possible to extract an isolated dynamic parameter, such as the rate of magnetization transfer, by performing one or two simple experiments as was done by Forsén and Hoffman. For a complex heterogeneous system, our only alternative, as we have illustrated by our present and previous (*1*) work, is to perform an entire series of experiments enabling determination of the multiple-parameter set required by the theoretical model.

From the data and analysis just presented, it is doubtful that in the general case one can always achieve this goal. There are two possible situations in which the procedures outlined above would not be expected to work. In one case, the lineshape function of the immobile spins does not conform to any well-known analytical function and as a result confounds any attempt to fit the data. The second is possibly even less optimistic. It is possible that at least in some cases, the binary model is too simplistic. In the first case, one must determine the solid lineshape function experimentally by recording the free induction decay of the solid protons after exhaustive substitution of the freely exchangeable protons with deuterium (there are other fine points to this technique, e.g., the correction for residue signal due to nonexchangeable mobile protons such as imides and the experimental setup for recording fast transients). In the second case, it is theoretically straightforward to extend the theory, again using projection operators, to accommodate the situation which allows more than two components in the system. The real problem arises when one tries to experimentally verify the more complex models. As the number of components increase, so do the number of parameters characterizing these components. The resulting multiparameter fits are subject to much greater ambiguity, resulting in less confidence in the fitting process.

We conclude with the following remarks: First, in comparison to our previous effort (*1*), we have significantly extended the validity of the calculations, both by increasing the range of applicable frequency offsets and by increasing the capacity to encompass various B-spin lineshape functions. We have also demonstrated that, at least for XL-BSA, the model-predicted transient and steady-state responses agree well with experimental data under the assumption of a Gaussian lineshape for the solid spins. We shall leave the pursuit of finding the correct lineshape for more complex system such as tissue-like substance to a future effort.

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