On the Treatment of the Transient Response of a Heterogeneous Spin System to Selective RF Saturation

For the past few years since the discovery of magnetization transfer contrast (MTC) (1–3), it has been common practice to use the model by Forsen and Hoffman (4, 5) to interpret their experimental results (1, 2, 6) in tissues or tissue-like materials. Before we can accept this model for such a purpose, it is important to question its validity. Forsen and Hoffman's model (FHM) was originally conceived for saturation transfer of chemical systems with protons in two different environments undergoing chemical exchange. It is therefore valid in their case to assume that the protons pertaining to one of these spectral lines can be completely saturated by frequency-selective RF irradiation. One of the consequences of this assumption is that the apparent longitudinal relaxation rate for a binary system under this kind of RF irradiation is given by

$$T_{1sat}^{-1} = T_{1A}^{-1} + k \qquad [1]$$

where T_{1A}^{-1} is the intrinsic longitudinal relaxation rate of the unsaturated component and k is the rate of magnetization transfer. Another consequence, which is a corollary of [1], is that k is given as

$$k = \frac{1}{T_{1sat}}\left(1 - \frac{M_{AS}}{M_{AO}}\right) \qquad [2]$$

where M_{AS} and M_{AO} are the steady-state and equilibrium longitudinal magnetizations of the A spins, respectively.

For tissue or tissue-like substance in which at least one of its components is solid-like (having a broad-line spectrum), the FHM is in general not valid. As a result, neither are the relations [1] and [2]. This can be easily demonstrated by the following argument. Let us first suppose the FHM is valid, then according to [1] and [2], since both k and T_{1A} are fundamental constants which depend on the tissue properties only, the apparent relaxation rate T_{1sat}^{-1} and the steady-state magnetization M_{AS} should also be constant, independent of the applied saturation RF parameters. But this contradicts experimental observations which showed that both the observed M_{AS}/M_{AO} (1, 2, 7–10) and T_{1sat}^{-1} (9, 10) depend strongly on the frequency-offset as well as on the amplitude of the saturating RF field.

If the FHM is not the correct model, what should one use to interpret the experimental results? The correct model is likely to be complicated and has, to the best of the author's knowledge, not yet been reported. What we do know is a very simple binary spin-bath model (BSBM) first proposed by Edzes and Samulski (11, 12). While this model undoubtedly over-simplifies the real picture, it nevertheless serves the much needed function in providing a framework from which equations of motion of the spin system can be written, either in the form of a set of modified Bloch equations (7–9, 11–12) or a set of hybrid equations (10) in which the solid component is described by the Redfield-Provotorov theory (13, 14) based on spin temperature. Once the model equations are written, they can be solved (10, 15) and experimentally verified (10).

One question remains for those who had used [2] in interpreting their previous experimental results but would be interested to know how much a difference it would make if the BSBM were invoked. The question is "Under what condition, if any, can k, evaluated according to [2], approaches the value of the rate of magnetization transfer obtained according to BSBM?" To answer this question, we evaluate k defined as [2] in terms of the BSBM parameters and compare it to the parameter rX, the cross-relaxation rate in the solution of the BSBM (Bloch Equations formalism) obtained in ref 15. It can be shown that

$$k = r_x\left\{\frac{1}{1 + \xi(\omega_1,\delta\omega)}\right\} + \epsilon(\omega_1,\delta\omega) \qquad [3]$$

where

$$\xi(\omega_1,\delta\omega) = \frac{1}{\omega_1^2}\left(\frac{1}{T_{1B}} + \frac{r_x}{f}\right)\left(\delta\omega^2 T_{2B} + \frac{1}{T_{2B}}\right);$$

$$\epsilon(\omega_1,\delta\omega) = \frac{\omega_1^2 T_{2A}}{1 + (T_{2A}\,\delta\omega)^2} \qquad [4]$$

and T_1^{-1} and T_2^{-1}; = A,B, are the longitudinal and transverse relaxation rates, respectively of the A or B spins (The A spins by convention are the mobile water protons and the B spins are the immobile protons from the macromolecules), f is the molar ratio of the B spins over the A spins in their respective reservoirs and, finally, ω_1 and $\delta\omega$ are the amplitude and resonance offset frequency, respectively, of the saturating RF field.

According to [3], the conditions that k is a good estimate of r_X are simply:

$$\xi \ll 1 \text{ and } \epsilon \ll r_x. \qquad [5]$$

The choice of frequency offset is normally based on the criterion: $T_{2B}^{-1} > \delta\omega \gg T_{2A}^{-1}$. Thus for the saturating RF to satisfy this criterion, the conditions in [5] reduce to the requirement that the RF amplitude ω_1 has to satisfy

$$\left(\delta\omega^2 T_{2B} + \frac{1}{T_{2B}}\right)\left(\frac{1}{T_{1B}} + \frac{r_x}{f}\right) \ll \omega_1^2 \ll r_x T_{2A}\delta\omega^2 \qquad [6]$$

In physical terms, the inequality on the left side of [6] states that the RF amplitude has to be sufficiently strong and resonance offset sufficiently small to satisfy the

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(somewhat modified) classical saturation condition of the immobile spins while the right inequality specifies the opposite condition that the RF amplitude has to be sufficiently weak and resonance offset sufficiently large to avoid direct saturation of the mobile spins. Unfortunately, for most tissues, it is not easy, if not impossible, to find RF parameters to satisfy condition [6].

One additional note on a related subject concerning the experimental determination of T_{1sat}^{-1} is worth mentioning. The common practice of this determination, to follow Hsieh and Balaban (16), is to apply off-resonance saturation before and throughout all the idling periods of an inversion recovery sequence. However, as we have shown both theoretically and experimentally (9) T_{1sat}^{-1} is a quantity independent of the initial condition of the spin system. As a consequence, the pre-saturation used in the "conventional" technique is not only superfluous but also detrimental to the measurement since it reduces the dynamic range of the relaxation curve and, as a result, also the accuracy of the measurement.

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