Is a two-pool MT model valid in tissues with multicomponent T2?

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INTRODUCTION: A variety of models have been applied to the interpretation of magnetization transfer (MT) effects in tissues. Of these, the most widely used is the Two Pool Model of MT exchange, where tissue protons are divided into two groups: a liquid pool composed of mobile protons bound to water molecules and a semisolid pool made up of restricted protons that exist within macromolecules. Quantitative MT experiments can be performed to determine all the parameters that characterize the Two Pool Model, including:

- T_{1A}, T_{2A}, T_{1A}, and T_{2B}, the longitudinal and transverse relaxation times of the liquid (A) and semisolid (B) pools,
- R, the rate of magnetization transfer between the two pools, and
- M_0^B, the macromolecular proton fraction.s

A known shortcoming of the Two Pool Model is its failure to account for the multiple liquid T_2 components that occur in biological tissues. As a result, the physical interpretation of T_{2A} estimates derived from fits to MT data (T_{2A}^{MT}) remains uncertain. Several investigators have reported that T_{2A}^{MT} often disagrees with liquid pool T_2 measurements obtained from spin echo experiments (T_{2A}^{OBS}) [1,2]. By comparing MT and T_2 decay data in samples of agar, mouse spinal cord, and bovine optic nerve, this study presents new insight into the physical nature of T_{2A}^{MT} estimates.

HYPOTHESIS: On the time scale of typical MT experiments, which measure longitudinal magnetization following several seconds of off-resonance irradiation, complete mixing occurs between the various liquid T_2 components. In this context, the T_2 components can be viewed to merge, forming a single pool with a T_2 relaxation time given by the reciprocal of the mean transverse relaxation rate. Expressed mathematically,

$$T_{2A}^{MT} = \left[\sum_{1}^{n} \frac{a_n}{T_2^n}\right]^{-1} = \left(R_2^{AV}\right)^{-1}, \quad [1]$$

for a tissue with n liquid T_2 components with amplitudes a_n and relaxation times T_2^n. Note that equation 1 is not equivalent to the more commonly used mean T_2 relaxation time (T_2^{AV}). In multi-compartmental systems, it is both more intuitive and physically relevant to express T_2 relaxation in terms of rates.

METHODS:

MR Measurements: T_2 and MT data were collected for samples of bovine optic nerve, mouse spinal cord, and 0.5% agar (doped with $MnCl_2$). All NMR measurements were performed on a 20 cm. horizontal bore superconducting magnet (Nalorac, Martinez, CA), operating at 1.5 T, equipped with a spectroscopy console (SMIS, Surrey, England).

- MT data were acquired using a continuous wave (CW) saturation pulse followed by a $\pi/2$ pulse to measure the remaining z magnetization. The pulse sequence was performed for 7 saturation pulse amplitudes ($\omega_1/2\pi$) ranging from 0.085 to 5.34 kHz and 27 off-resonance frequencies (Δ) logarithmically distributed from 0.014 to 213 kHz. The effect of any residual transverse magnetization following the off-resonance irradiation was removed by phase cycling of the $\pi/2$ pulse.
- T_2 relaxation data were acquired using a CPMG sequence with TE/TR =1/8000 msec, 3000 even echoes sampled, and 8 averages.
- For completeness, T_1 relaxation time data were also obtained using an inversion recovery (IR) sequence with 15 TI values logarithmically spaced from 1 to 32000 msec, 10 sec between each acquisition and the next inversion pulse, and 4 averages.

Data Analysis:

- All T_2 decay data were fitted to a multi-component T_2 model in which the relaxation of each component had a Gaussian distribution on a logarithmic time scale.
- MT data were fitted to a Two Pool Model to obtain estimates of all parameters [3]. To ensure that a unique set of model parameters was obtained, the T_1 measurement derived from the IR sequence was also entered into the fitting procedure.

RESULTS & DISCUSSION:

Table 1 shows a comparison of T_{2A}^{OBS} (estimated from a mono-exponential fit to T_2 decay data), T_{2A}^{MT} (derived from a Two Pool Model fit to MT data), and $(R_2^{AV})^{-1}$ (calculated from T_2 spectrum – Figure 1). In the spinal cord and optic nerve samples, T_{2A}^{MT} is significantly shorter than T_{2A}^{OBS}. In agar, however, $T_{2A}^{OBS}=T_{2A}^{MT}=(R_2^{AV})^{-1}$. This is to be expected, as agar has only a single T_2 component and is thus fully characterized by a Two Pool representation.

For all samples, agreement between T_{2A}^{MT} and $(R_2^{AV})^{-1}$ is excellent considering the complete independence of the two experiments. This suggests that, as hypothesized, multiple liquid T_2 components are indistinguishable on the time scale of typical (steady state) MT measurements. As such, relaxation properties of the water pool determined from MT data reflect a weighted average of all the individual water components. This further implies that for MT measurements obtained in the steady state, models with only a single liquid pool are completely valid.

A final point worth noting is that the disagreement between T_{2A}^{OBS} and T_{2A}^{MT} in biological tissues is not surprising. In these multi-compartmental systems, T_{2A}^{OBS} is obtained from a mono-exponential fit to multi-exponential data, and thus lacks physical meaning. The results presented demonstrate that, unlike T_{2A}^{OBS}, T_{2A}^{MT} has a specific physical interpretation.

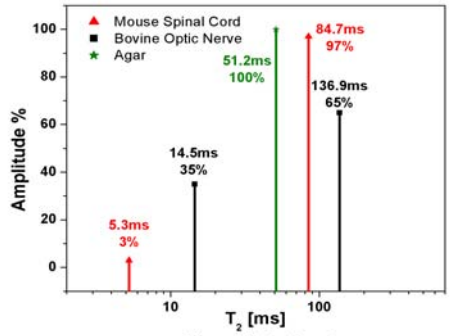

Figure 1: T_2 Spectra

Table 1: Comparison of T_{2A}^{OBS}, T_{2A}^{MT}, and $(R_2^{AV})^{-1}$

Sample	T_{2A}^{OBS} (ms)	T_{2A}^{MT} (ms)	$(R_2^{AV})^{-1}$ (ms)
Mouse Spinal Cord	86 ± 5	54.9 ± 9	$\left\{0.03\frac{1}{5.3ms}+0.97\frac{1}{84.7ms}\right\}^{-1}$ = 58.5
Bovine Optic Nerve	117 ± 6	41.5 ± 6	$\left\{0.35\frac{1}{14.5ms}+0.65\frac{1}{137ms}\right\}^{-1}$ = 34.6
Agar ($MnCl_2$ doped)	51.2 ± 3	53.7 ± 4	$\left\{\frac{1}{51.2ms}\right\}^{-1}$ = 51.2

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