Describing Magnetization Transfer Parameters in White Matter Using a Four-Pool Model

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Introduction: Recently, the NMR behaviour of bovine white matter was characterized using a four-pool model [1]. Other investigators [2], [3] have used a two-pool model to characterize magnetization transfer (MT) in white matter. By comparing the two-pool model with the four-pool model, one can derive two-pool MT parameters from the four-pool model.

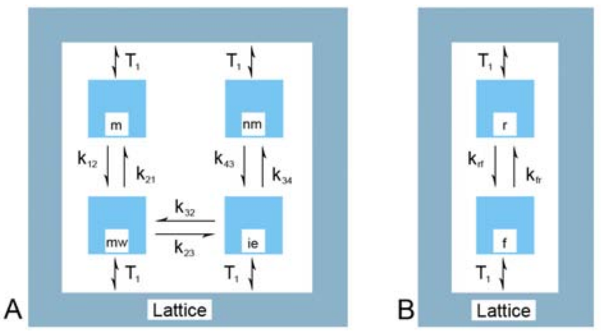

Fig. 1: *Schematics of white matter models. The four-pool model is shown in A; the two-pool model in B.*

Methods: Schematic representations of the four- and two-pool models are shown in Fig. 1. The restricted proton pools are on top represented by m, nm, and r standing for myelin, non-myelin, and restricted, respectively. The mobile proton pools are on the bottom represented by mw, ie, and f standing for myelin water, intra/extracellular water, and free water.

The Bloch equations of the four-pool model are shown in Eqs. 1 [1], while the two-pool model Bloch equations [2] can be written as shown in Eqs. 2. In these equations the *M*s and $M(\infty)$s denote the time dependent and equilibrium magnetizations of the two proton pools, *k*s denote the rate constants between the pools with directionality as indicated in Fig. 1, and T_1s are the longitudinal relaxation times of the compartments. From Fig. 1 and Eqs. 1 and 2 one can derive $M_f(\infty)=M_{mw}(\infty)+M_{ie}(\infty)$, $M_r(\infty)=M_m(\infty)+M_{nm}(\infty)$, $k_{fr}=(k_{21}M_{mw}+k_{34}M_{ie})/(M_{mw}+M_{ie})$, and $k_{rf}=(k_{12}M_m+k_{43}M_{nm})/(M_m+M_{nm})$. Defining Henkelman *et al.*'s $R_A=1/T_1^f=\text{MWF}/T_1^{mw}+(1-\text{MWF})/T_1^{ie}$, where MWF stands for the myelin water fraction, one of Henkelman *et al.*'s parameters can be derived as $RM_0^B/R_A=k_{fr}/R_A$. Henkelman *et al.*'s $R=[M_f(\infty)+M_r(\infty)]/T_{cr}^{fr}M_r(\infty)$, where $T_{cr}^{fr}=k_{fr}^{-1}+k_{rf}^{-1}$ [1]. In the work of Sled & Pike [3] the fraction of protons that reside in the non-aqueous pool can be defined as $F=[1-M_f(\infty)]/M_f(\infty)$.

$$\frac{d}{dt}M_m=-k_{12}M_m-\frac{M_m-M_m(\infty)}{T_1^m}+k_{21}M_{mw};\quad \frac{d}{dt}M_{mw}=-k_{21}M_{mw}-\frac{M_{mw}-M_{mw}(\infty)}{T_1^{mw}}-k_{23}M_{mw}+k_{12}M_m+k_{32}M_{ie}$$
$$\frac{d}{dt}M_{ie}=-k_{32}M_{ie}-\frac{M_{ie}-M_{ie}(\infty)}{T_1^{ie}}-k_{34}M_{ie}+k_{23}M_{mw}+k_{43}M_{nm};\quad \frac{d}{dt}M_{nm}=-k_{43}M_{nm}-\frac{M_{nm}-M_{nm}(\infty)}{T_1^{nm}}+k_{34}M_{ie} \tag{1}$$

$$\frac{d}{dt}M_f=-k_{fr}M_f-\frac{M_f-M_f(\infty)}{T_1^f}+k_{rf}M_r;\quad \frac{d}{dt}M_r=-k_{rf}M_r-\frac{M_r-M_r(\infty)}{T_1^r}+k_{fr}M_f \tag{2}$$

Results: In Table 1, two-pool MT parameters derived from the four pool model [1] are compared with the results of Morrison & Henkelman's bovine MT study carried out at 20-22 ºC [4] and with Sled & Pike's human *in vivo* white matter MT results [3]. The fundamental rate constant, *R*, and a dimensionless parameter, k_f/R_A, agree within stated error using the two models of white matter. The *k* values agree within stated error, while the *F* parameter does not.

Table 1: *Comparing four-pool model derived values with reported MT results.*

	R (s^{-1})	k_{fr}/R_A	k_{fr} (s^{-1})	k_{rf} (s^{-1})	F
Values from four pools	15.8±9.3 [a]	2.8±1.6 [a]	7.3±3.9 [b]	24.1±7.0 [b]	0.230±0.029 [b]
Values from two pools	21±3 [c]	2.0±0.1 [c]	4.6±1.3, 4.3±1.0 [d]	30±13, 27±10 [d]	0.152±0.023, 0.161±0.025 [d]

[a]Bovine white matter at 24 ºC [1]. [b]Bovine white matter at 37 ºC [1]. Both [a] and [b] where calculated from four-pool model results. [c]Bovine white matter at 20-22 ºC [4]. [d]Human white matter *in vivo* [3].

Discussion: The bovine white matter results agree within stated error, and two of the three parameters agree within stated error when comparing bovine white matter *in vitro* at 37 ºC with human *in vivo* white matter.

Conclusion: After examining the similarities between the two models of white matter we have shown that it is possible to derive MT parameters using four-pool model results. The four-pool model is more suitable for white matter because the two-pool model ignores the known existence of two water reservoirs in white matter. The parameter *F* characterizes all non-aqueous protons and its use as a myelin-specific marker is not appropriate. We believe that future work on modeling MT results should involve at least four pools [5].

1. Bjarnason *et al*. MRM 54:1072-81 (2005)
2. Henkelman *et al*. MRM 29:759-66 (1993)
3. Sled & Pike. MRM 46:923-31 (2001)
4. Morrison & Henkelman. MRM 33:475-82 (1995)
5. Stanisz *et al*. MRM 42:1128-36 (1999)

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