Supplementary material S1: the two-pool MT model

The two-pool magnetisation transfer (MT) model is used in this paper in both simulations and in vivo analyses. The model describes the evolution of the magnetisation of two exchanging ^{1}H pools, i.e. free protons in bulk water and protons bound to macromolecules (Henkelman et al., 1993), in presence of off-resonance irradiation $b_{1,\mathrm{off}}(t)$ with carrier frequency $f_0 + \Delta f_c$ (with Δf_c being the offset with respect to water resonance frequency f_0), assumed to be played out at times $0 \leq t \leq t_{\mathrm{off}}$. On-resonance excitation is then assumed to be played out at $t > t_{\mathrm{off}}$, after a generic delay t_{delay}.

Let us indicate with $\mathbf{m}^{\mathrm{F}}(t) \stackrel{\mathrm{def}}{=} \begin{bmatrix} m_x^{\mathrm{F}}(t) & m_y^{\mathrm{F}}(t) & m_z^{\mathrm{F}}(t) \end{bmatrix}^{\mathrm{T}}$ and $\mathbf{m}^{\mathrm{B}}(t) \stackrel{\mathrm{def}}{=} \begin{bmatrix} m_x^{\mathrm{B}}(t) & m_y^{\mathrm{B}}(t) & m_z^{\mathrm{B}}(t) \end{bmatrix}^{\mathrm{T}}$ the free and bound proton magnetisations during the off-resonance irradiation, and with $\mathrm{T}_1^{\mathrm{F}}$ and $\mathrm{T}_1^{\mathrm{B}}$ and with $\mathrm{T}_2^{\mathrm{F}}$ and $\mathrm{T}_2^{\mathrm{B}}$ their respective longitudinal and transverse relaxation times (Portnoy and Stanisz, 2007). Let us also indicate with k the exchange rate between free to bound protons, with BPF the bound pool fraction (fraction of protons belonging to the bound pool) and with γ the proton gyromagnetic ratio ($\frac{\gamma}{2\pi} \cong 42.577 \frac{\mathrm{MHz}}{\mathrm{T}}$).

The MT-weighting factor w in Eq. 5 (main manuscript) is defined as the value of the free pool longitudinal magnetisation at the end of off-resonance irradiation, i.e.:

$$w = m_z^{\mathrm{F}}(t = t_{\mathrm{off}}). \qquad (S1.1)$$

The value of w in Eq. S1.1 is obtained directly by numerical integration of the two-pool Bloch equations, which are written as:

$$\frac{d}{dt}\begin{bmatrix} m_x^{\mathrm{F}} \\ m_y^{\mathrm{F}} \\ m_z^{\mathrm{F}} \\ m_z^{\mathrm{B}} \end{bmatrix}(t) = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{1}{\mathrm{T}_2^{\mathrm{F}}} & 2\pi\,\Delta f_c & 0 & 0 \\ 0 & -2\pi\,\Delta f_c & -\frac{1}{\mathrm{T}_2^{\mathrm{F}}} & \gamma\, b_{1,\mathrm{off}}(t) & 0 \\ \frac{1}{\mathrm{T}_1^{\mathrm{F}}} & 0 & -\gamma\, b_{1,\mathrm{off}}(t) & -\left(\frac{1}{\mathrm{T}_1^{\mathrm{F}}} + k\right) & k\frac{(1-\mathrm{BPF})}{\mathrm{BPF}} \\ \frac{1}{\mathrm{T}_1^{\mathrm{B}}}\frac{\mathrm{BPF}}{(1-\mathrm{BPF})} & 0 & 0 & k & -\left(\frac{1}{\mathrm{T}_1^{\mathrm{B}}} + R_{\mathrm{RF}}^{\mathrm{B}} + k\,\frac{(1-\mathrm{BPF})}{\mathrm{BPF}}\right) \end{bmatrix} \begin{bmatrix} \frac{1}{2} \\ m_x^{\mathrm{F}} \\ m_y^{\mathrm{F}} \\ m_z^{\mathrm{F}} \\ m_z^{\mathrm{B}} \end{bmatrix}(t).$$

$$(S1.2)$$

For the integration of equation S1.2, it is assumed that $\mathbf{m}^{\mathrm{F}}(t=0) \stackrel{\mathrm{def}}{=} [0 \quad 0 \quad (1-\mathrm{BPF})]^{\mathrm{T}}$, $\mathbf{m}^{\mathrm{B}}(t=0) \stackrel{\mathrm{def}}{=} [0 \quad 0 \quad \mathrm{BPF}]^{\mathrm{T}}$, $m_x^{\mathrm{B}}(t=\ t_{\mathrm{off}}) = m_y^{\mathrm{B}}(t=\ t_{\mathrm{off}}) \approx 0$ and that the bound pool off-resonance absorption can be modelled based on a super-Lorentzian line shape. Under this assumption, the absorption term $R_{\mathrm{RF}}^{\mathrm{B}}$ is a function of $(t, \Delta f_c, \mathrm{T}_2^{\mathrm{B}})$ and is modelled as (Portnoy and Stanisz, 2007):

$$R_{\mathrm{RF}}^{\mathrm{B}}(t, \Delta f_c, \mathrm{T}_2^{\mathrm{B}}) = \pi\, \gamma^2 b_{1,\mathrm{off}}^2(t) \int_0^{\frac{\pi}{2}} \sqrt{\frac{2}{\pi}}\, \frac{\sin(\varphi)}{|3\ \cos^2(\varphi) - 1|}\ \mathrm{T}_2^{\mathrm{B}} \exp\left(-2\left(\frac{2\pi\, \Delta f_c\, \mathrm{T}_2^{\mathrm{B}}}{3\ \cos^2(\varphi) - 1}\right)^2\right) d\varphi \quad (S1.3).$$

For the practical integration of Eq. S1.2, it is assumed that $\mathrm{T}_1^{\mathrm{B}} \approx 1\,s$ (Battiston et al., 2018), and that the free pool longitudinal relaxation time (i.e. $\mathrm{T}_1^{\mathrm{F}}$) is linked to the observable T_1 relaxation time as (Portnoy and Stanisz, 2007):

$$\frac{1}{\mathrm{T}_1^{\mathrm{F}}} \approx \frac{1}{\mathrm{T}_1} - \frac{k\left(\frac{1}{\mathrm{T}_1^{\mathrm{B}}} - \frac{1}{\mathrm{T}_1}\right)}{\frac{1}{\mathrm{T}_1^{\mathrm{B}}} - \frac{1}{\mathrm{T}_1} + k\left(\frac{1-\mathrm{BPF}}{\mathrm{BPF}}\right)}\ . \quad (S1.4)$$

References

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