

New ODE Model for diffusion MRI Signal

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Introduction: Water diffusion in biological tissues is not Gaussian and signal attenuation is not monoexponential with b-value[1]. Two approaches to deal with this behavior are bi-exponential model [1,2], often corrected using Karger model [3], and Kurtosis approach [4]. We formulate an ODE model for diffusion MRI signal that is more general than Karger model, valid for many diffusion gradient shapes and gives a good approximation to ADC and Kurtosis. Given DMRI signals before and after cell swelling, we can estimate the amount of cell swelling after numerically solving an ODE system.

New ODE model: We propose a two compartment model for the DMRI signal, with ψ^e and ψ^i , the signals from the extra- and intra- cellular compartments Ω^e , Ω^i (with effective diffusion coefficient D^e , D^i). The intra- and extra-cellular residence times are τ^i and $\tau^e = \tau^i v^e / v^i$, where v^e and v^i are the volume fractions. Given a diffusion gradient with profile $f(t)$, where $f(t)$ is anti-symmetric with respect to $t_d/2$, t_d is diffusion time, and gradient strength $\vec{g} = \vec{q}/\gamma$, new ODE model is the following:

$$\begin{aligned} \frac{\partial \psi^e(\vec{q}, t)}{\partial t} &= -c(t) D^e \|\vec{q}\|^2 \psi^e(\vec{q}, t) - \frac{1}{\tau^e} \psi^e(\vec{q}, t) + \frac{1}{\tau^i} \psi^i(\vec{q}, t) \\ \frac{\partial \psi^i(\vec{q}, t)}{\partial t} &= -c(t) D^i \|\vec{q}\|^2 \psi^i(\vec{q}, t) - \frac{1}{\tau^i} \psi^i(\vec{q}, t) + \frac{1}{\tau^e} \psi^e(\vec{q}, t) \end{aligned} \quad \text{subject to condition} \quad \begin{aligned} \psi^e(\vec{q}, 0) &= v^e \\ \psi^i(\vec{q}, 0) &= v^i \end{aligned}$$

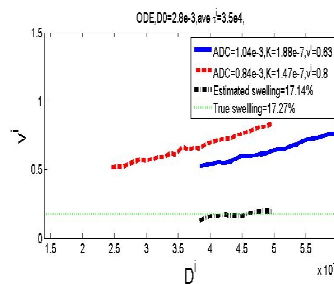
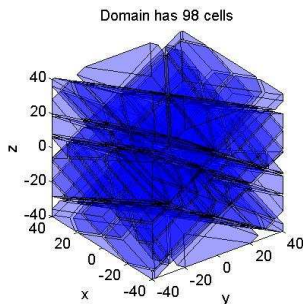
where the time dependent coefficient $c(t) = \frac{\partial}{\partial t} \left(\int_0^t du \left(\int_s^u f(s) ds \right)^2 \right)$. The justification for this choice of $c(t)$ is that in a homogeneous medium the total signal satisfies: $\frac{\partial}{\partial t} \Psi(\vec{q}, t) = c(t) D \|\vec{q}\|^2 \Psi(\vec{q}, t)$.

Measuring cell swelling: From DMRI signal, we obtain ADC (apparent diffusion coefficient) and KUR (Kurtosis) which are defined as the first and second order terms of the Taylor expansion in b-value of the logarithm of signal $\Psi(b) = \Psi^e(b) + \Psi^i(b)$: $\log \Psi(b) = 0 - ADC * b + KUR * b^2 + O(b^3)$.

$$ADC^{ODE} = v^i D^i + v^e D^e \quad KUR_{PGSE}^{ODE} \approx (D^i - D^e)^2 v^i v^e \frac{e^{-k} - (1-k)}{k^2}, k = \frac{\Delta - \delta/3}{\tau^i v^e}$$

From two DMRI signals, corresponding to times before and after cell swelling, we want to estimate the change in the intra-cellular volume fraction Δv^i . From simulations and experimental data [1] we hypothesized that both τ^i and D^i do not change much with volume fraction changes. Matching ADC and Kurtosis, we search through all possible solution space of τ^i and D^i , then find that only a very small range of τ^i and D^i can give physically reasonable solutions of v^i (between 0-1) and D^e (between $0.5 \times 10^{-3} - 2 \times 10^{-3} \mu\text{m}^2/\mu\text{s}$) and that within this range of τ^i and D^i the estimated change in v^i is almost constant. From this, we can compute the change in v^i without knowing the true values of τ^i and D^i .

Results and discussion: Two simulated DMRI signal from PGSE $\delta = 10\text{ms}$, $\Delta = 10\text{ms}$ by numerically solving the two compartment Bloch-Torrey PDE on a sample consisting of 3D convex-shaped cells (**Fig 1a**). The original volume fraction is $v^i = 0.63$. Reducing the size of the extra-cellular space to obtain $v^i = 0.80$, true swelling is $\Delta v^i = 0.17$. We plot family of v^i and D^i matching the simulated ADC and KUR with expressions obtained from ODE model. These v^i and D^i (physically reasonable for v^i and D^e) lie on two curves $C(v^i, D^i)$ of signals before (blue) and after cell swelling (red) in **Fig 1b**. The difference of two curves (black) is an almost constant value of $\Delta v^i = 0.17$ on the entire interval of D^i . In **Table 1** we show the average Δv^i for some permeabilities which is close to the true value of 0.17.



Perm ($\mu\text{m}/\mu\text{s}$)	PGSE		Estimat ed swellin g
	δ (ms)	Δ (ms)	
$\kappa = 5 \times 10^{-6}$	10	20	0.16
$\kappa = 1 \times 10^{-5}$	10	20	0.17
$\kappa = 5 \times 10^{-5}$	10	10	0.14
$\kappa = 1 \times 10^{-4}$	10	10	0.16

Fig 1a. Convex cells: $S/V = 1.9 \mu\text{m}^{-1}$

Fig 1b. Cell swelling $v^i = 0.63$ to 0.8 .

Table 1. Estimated Δv^i close to true 0.17

[1] Niendorf Th et al. MRM (1996) 36:847-857; Clark C, Le Bihan D. MRM (2000) 44:852-859; [2] Nilsson et al. JMR (2010) 206:59—67; [3] Karger et al. Adv Mag Res (1988) 12:1—89; [4] Jensen et al. NMR Biomed (2010) 23:698—710.