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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]. Approaches to deal with this behavior include the bi-exponential model [1,2], the 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 more general diffusion gradient shapes and gives a good approximation to the 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-cellular and intra-cellular compartments Ω^e & Ω^i with effective diffusion coefficients D^e , D^i). The intra-cellular and extra-cellular residence times are τ^i and $\tau^e = \tau^i v^e / v^i$ where v^i and v^e are the volume fractions. Given a diffusion gradient with profile $f(t)$ (where $f(t)$ is anti-symmetric respect to t_d , where t_d is diffusion time) and gradient strength $\vec{g} = \vec{q}/\gamma$ (γ is the gyromagnetic ratio), new ODE model is following:

$$\frac{\partial \Psi^e(\vec{q},t)}{\partial t} = -c(t) D^e \|\vec{q}\|^2 \Psi^e(\vec{q},t) - \frac{1}{\tau^e}\Psi^e(\vec{q},t) + \frac{1}{\tau^i}\Psi^i(\vec{q},t)$$
$$\frac{\partial \Psi^i(\vec{q},t)}{\partial t} = -c(t) D^i \|\vec{q}\|^2 \Psi^i(\vec{q},t) - \frac{1}{\tau^i}\Psi^i(\vec{q},t) + \frac{1}{\tau^e}\Psi^e(\vec{q},t)$$

subject to initial condition $\Psi^e(\vec{q},0) = v^e$, $\Psi^i(\vec{q},0) = v^i$ where $c(t) = \left(\int_0^t f(s)\,ds\right)^2$

The justification of the time dependent coefficient $c(t)$ is that in a homogeneous medium the total signal satisfies:

$$\frac{\partial}{\partial t}\Psi(\vec{q},t) = c(t) D \|\vec{q}\|^2 \Psi(\vec{q},t)$$

. For PGSE : $c(t) = t^2, 0 \le t \le \delta$; $c(t) = \delta^2, \delta \le t \le \Delta$; $c(t) = (t - \Delta - \delta)^2, \Delta \le t \le t_d$

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 $\Psi(b) = \Psi^e(b) + \Psi^i(b)$:

$$\log \Psi(b) = 0 - ADC * b + KUR * b^2 + O(b^3)$$

where $ADC^{ODE} = v^i D^i + v^e D^e$, KUR can be obtained exactly by numerically solving ODE system or using an approximation :

$$KUR^{ODE} \approx (D^i - D^e)^2 v^i v^e \frac{e^{-k} - (1-k)}{k^2}, k := \frac{\Delta - \delta/3}{\tau^i v^e}$$

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 KUR, 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 1x10-3 μm2/μs and 2x10-3μm2/μs) 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 Conclusion

Two simulated DMRI signals are obtained from PGSE sequences $\delta = 10$ms, Δ=10 ms (or 20 ms) (**Fig 1)** by numerically solving the two-compartment Bloch-Torrey PDE on a sample consisting of 3D convex-shaped cells (**Fig 2**). 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 the ODE model. These v^i and D^i (physically reasonable for v^i and D^e) lie on 2 curves $C(v^i, D^i)$ of signals before **(blue)** and after cell swelling **(red)** in **Fig 3**. The difference of 2 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.

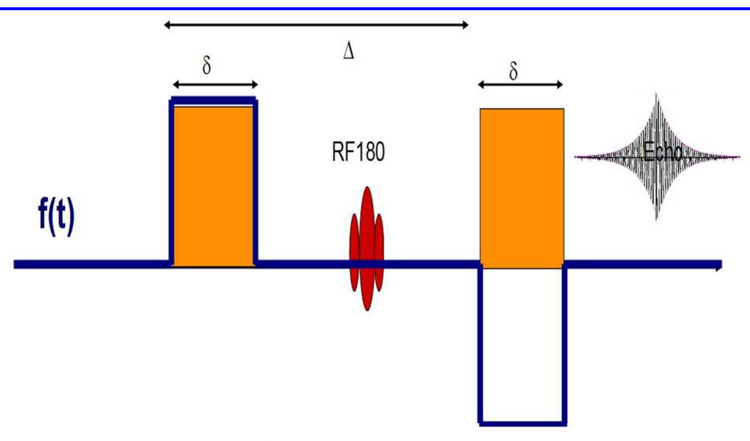

Fig.1 PGSE: $\delta = 10$ms ; Δ=10 ms & 20 ms

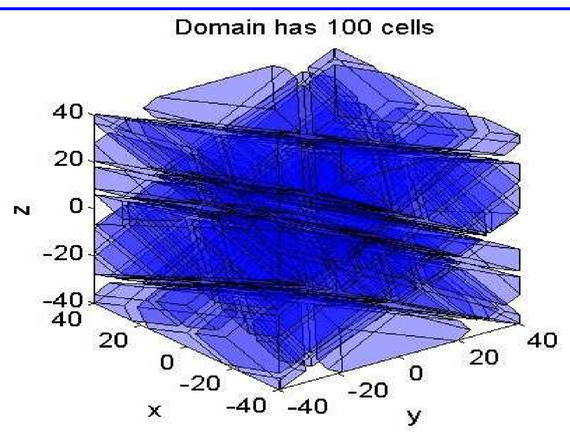

Fig.2 Convex shaped cells S/V= 1.9/μm

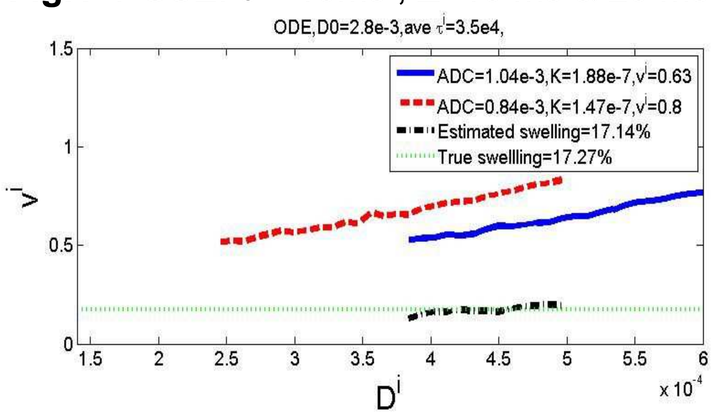

Fig.3 Cell swelling Δv^i = 0.63 to 0.8

Perm (μm/μs)	δ (ms)	Δ (ms)	Estimated Swelling
κ= 5e-6	10	20	0,16
κ= 1e-5	10	20	0,17
κ= 5e-5	10	10	0,14
κ= 1e-4	10	10	0,16

Table.1 Estimated Δv^i close to true 0.17

Refrences

[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.

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