Monte Carlo Study of a Two-Compartment Exchange Model of Diffusion

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Introduction

Chemical exchange models have been frequently applied to quantify measurements of diffusion in living tissues. While the simplicity of such models is attractive, the precise relationship of the model parameters to tissue properties may be difficult to ascertain. Here we investigate numerically a two-compartment exchange (Kärger) model as applied to diffusion in a system of parallel cylinders with permeable walls.

Theory

The Kärger model (KM) [1,2] considers 2 compartments, each containing a fraction p_1 and p_2 of the water molecules. The water residence times for the 2 compartments are τ_1 and τ_2 and the time $\tau_{ex} = \tau_1 p_2 = \tau_2 p_1$ is the water exchange time for the system. The diffusion in each compartment is assumed to be Gaussian with a diffusion coefficient D_1 and D_2. The KM predicts a constant diffusion coefficient D_{KM} and a time-dependent diffusional kurtosis K_{KM} according to [3]:

$$D_{KM} = p_1 D_1 + p_2 D_2, \qquad (1)$$

$$K_{KM} = 3\frac{p_1 p_2 (D_1 - D_2)^2}{D_{KM}^2}\frac{2}{\bar{t}}\left[1 - \frac{1}{\bar{t}}\left(1 - e^{-\bar{t}}\right)\right], \quad \bar{t} \equiv \frac{t}{\tau_{ex}} \qquad (2)$$

The KM is applied here to a tissue model consisting of parallel randomly packed identical cylinders with radius R. The space inside the cylinders is referred to as the intracellular space (ICS) and the space outside as the extracellular space (ECS). The ICS and ECS are characterized by the bare diffusion coefficients D_i and D_e, and residence times τ_i and τ_e.

Due to coarse-graining, the KM becomes valid when the exchange is barrier limited and the diffusion is in the long time limit, where the diffusivities in both the ECS and the ICS are constant with

$$D_{i,\infty}(\theta) = D_i \cos^2\theta \quad \text{and} \quad D_{e,\infty}(\theta) = D_e\left(\cos^2\theta + \frac{1}{\lambda}\sin^2\theta\right), \qquad (3)$$

where θ is the angle with respect to the cylinder axis and λ is the ECS tortuosity for the perpendicular direction. The KM description of the diffusion in a given direction θ corresponds to identifying D_1 and D_2, p_1 and p_2 as respectively $D_{i,\infty}(\theta)$ and $D_{e,\infty}(\theta)$, 1-α and α in eqns (1) and (2) with the exchange time $\tau_{ex} = \tau_e(1-\alpha) = \tau_i\alpha$. Due to the anisotropy of the tissue model, D_{KM} and K_{KM} depend on θ, as shown in Figure 1.

Methods

To evaluate the accuracy of the KM, the diffusion is simulated in a geometry of cylinders, with radius, packing density and bulk diffusivities in the ICS and ECS chosen similar to those observed in the human corpus callosum [4]: $R = 0.63$ μm, $\alpha = 0.5$, $D_i = 0.5$ μm^2/ms and $D_e = 2$ μm^2/ms. The time-dependent $D(t)$ and $K(t)$ in a given direction were simulated in C++ based on the dynamics of 2.0×10^6 random walkers [5]. A range of values between 0.008 μm/ms and 4 μm/ms for the membrane permeability κ were considered such that the corresponding exchange varied between 0.075 ms and 20 ms.

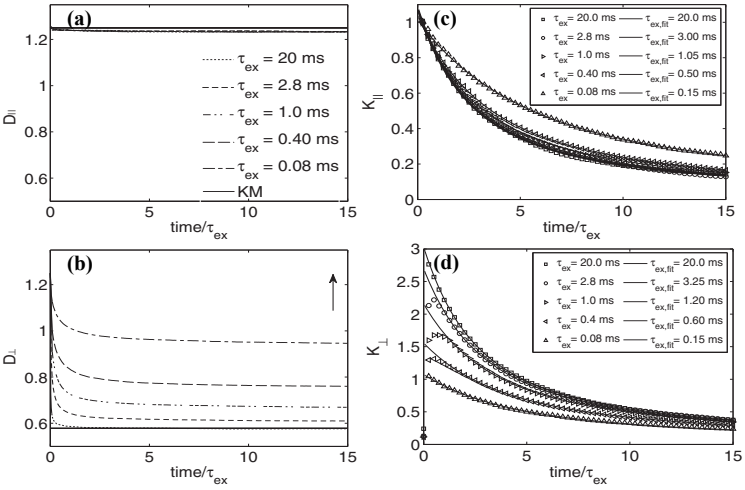

Figure 1: Comparison between the KM and the simulated diffusion for varying exchange times: $D(t)$ in the parallel direction (a) and the perpendicular direction (b), $K(t)$ in the parallel direction (c) and the perpendicular direction (d). The KM approximation given by eqn (2) is fitted through each series of data points in (c) and (d) and the fitted and real values for τ_{ex} are listed.

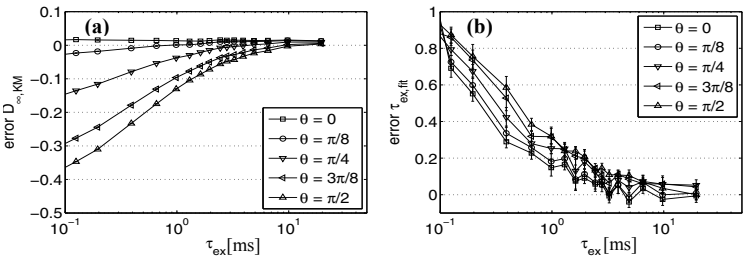

Figure 2: Relative errors made by the KM in the long term diffusivity D_∞ (a) and the fitted exchange time $\tau_{ex,fit}$ (b). The errors increase for decreasing τ_{ex} and increasing angle θ.

Results

Figure 1 shows the comparison between the KM and the numerical results. The diffusion coefficient $D_{||}$ in the parallel direction (Figure 1(a)) is independent of the permeability and agrees with the KM theory, while $D_\perp$ in the perpendicular direction depends strongly on τ_{ex} and agrees with the KM theory for low permeabilities (long τ_{ex}) at long observation times. The relative error in the diffusion coefficient when using the KM is shown in Figure 2(a) for different directions. The diffusional kurtosis $K_{||}$ monotonically decreases with time in the parallel direction (Figure 1(c)), whereas in the perpendicular direction (Figure 1(d)), the kurtosis first peaks before decreasing towards zero. The KM agrees for long τ_{ex} with the simulated kurtosis in the time-interval for which it decreases with time. Figure 1 (d) shows that, although the KM fits all the data curves well, the fitted values for τ_{ex} deviate from the real τ_{ex} for short τ_{ex}. The relative error in τ_{ex} when fitting the data to the KM is shown in Figure 2(b) for different directions.

Discussion

The present study shows that the KM, although highly idealized, can accurately model the diffusion in a two-compartment system for long observation times, providing the compartment diffusivities are time-independent and the permeability is low enough such that the exchange between the compartments is barrier-limited. The time-independent KM diffusivity does not depend on the exchange time, but the time-dependence of the KM kurtosis allows the exchange time to be determined. The simulations show that for more permeable membranes, the KM derived exchange times are overestimated. The simulation results shown here for a geometry of parallel cylinders can be applied to the diffusion in tissues with a strongly aligned fibrous microstructure such as found in brain white matter. Due to the tissue anisotropy, the KM kurtosis along and across the fibers contains complementary information. The initial KM kurtosis in the direction along the fibers reflects the diffusional heterogeneity between the ICS and the ECS, whereas in the perpendicular direction, it is determined by the fiber volume fraction. Hence, the KM could potentially provide important information for assessing white matter pathologies. The results for diffusion in the perpendicular direction can also be extrapolated qualitatively to isotropic tissues and cell suspensions.

References: [1] Kärger, J.. *Adv. Colloid Interfac.*, 23:129-148, 1985; [2] Lee, J.-H. et al. *Magn.Reson. Med.*, 49(3):450--458, 2003; [3] Jensen, J H. et al. *Magn. Reson. Med.*, 53(6):1432--1440, 2005; [4] Assaf et al, *Magn. Reson. Med.,* 52:965-978, 2004; [5] Fieremans, E. et al. *J. Magn. Reson.*, 190:189-199, 2008.

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