# DWI signal from a medium with heterogeneous diffusivity

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**Introduction:** In the context of diffusion in tissues, one can think of the two broad classes of restrictions to molecular motion: (i) *surface restrictions (membranes)*, and (ii) *diffusivity heterogeneity in the bulk of the tissue*. The latter class encompasses variation of diffusion properties on a finite length scale, such as diffusivity contrast between cells, or between the intra- and extracellular space, or between clusters of cells of different types within a voxel. Any tissue generally possesses both classes of restrictions. To assess their relative contributions and importance, it is useful to understand them separately. The case (i) of membrane restrictions has been recently considered [1]. The present work deals with the effect (ii) of the heterogeneous diffusivity using the effective-medium framework [2,3].

**Results:** Consider any medium with a spatially varying diffusivity. An example is the $d$=2-dimensional model medium consisting of randomly-packed disks (white) with diffusion coefficient, $D_2 < D_1$, different from that of the extracellular space (black), $D_1$. According to the effective-medium framework [3], we obtain the DWI signal in terms of the correlation function $\Gamma(\mathbf{r}) = <\delta D(\mathbf{r})\delta D(0)>$ of the varying diffusivity component $\delta D(\mathbf{r}) = D(\mathbf{r}) - \overline{D}$, where $\overline{D} = <D(\mathbf{r})>$ is the voxel-averaged diffusion coefficient. Often times, $\Gamma(\mathbf{r})$ has one well-defined *correlation length* $l_c$ (or a small number of them). In our example, $l_c$ corresponds to both the disk size and the typical separation between them; this length defines the wave vector $k_c = 2\pi/l_c$ at which the Fourier transform $\Gamma(k)$ peaks (see Figures). Using the general formalism [3], we find the Lorentzian-shaped frequency-dependent diffusivity for this case

$$D_v(\omega) = \overline{D}\left[1 - \frac{\alpha^2/d}{1 - i\omega t_c}\right], \quad \alpha = \frac{\langle(\delta D)^2\rangle^{1/2}}{\overline{D}}, \quad t_c = \frac{1}{\overline{D}k_c^2}. \tag{1}$$

Here $\alpha \ll 1$ is an expansion parameter characterizing the width of the local diffusivity distribution. The dispersive diffusivity (1) is measurable via the oscillating gradient technique [4,5]. It leads to the exponentially decaying contribution (non-Markoffian memory) in the velocity autocorrelation function

$$D_v(t) = <v(t)v(0)> = \overline{D}\left[\delta(t) - \left(\alpha^2/t_c d\right)e^{-t/t_c}\right] \quad t > 0, \tag{2}$$

with the correlation time $t_c$. The corresponding *time-dependent* diffusivity $D(t)$ and kurtosis $K(t)$ read

$$D(t) = \overline{D}\left[1 - \frac{\alpha^2}{d}\tau h_{12}(\tau)\right] \approx \overline{D}\begin{cases} 1 - \alpha^2\tau/(2d), & \tau \ll 1, \\ 1 - \alpha^2/d + \dfrac{\alpha^2/d}{\tau}, & \tau \gg 1; \end{cases} \tag{3}$$

$$K(t) = 6\alpha^2\left[h_{12}(\tau) - \frac{4}{d}\tau h_{22}(\tau) + 4\beta_d\tau^2 h_{32}(\tau)\right] \approx \begin{cases} 3\alpha^2, & \tau \ll 1, \\ 6\left(1 - \dfrac{4}{d} + 4\beta_d\right)\alpha^2/\tau, & \tau \gg 1, \end{cases} \tag{4}$$

where $\tau \equiv t/t_c$, $\beta_d = 1, 3/8, 1/5$ in dimensions $d=1,2,3$ correspondingly, $h_{12} = (e^{-\tau} - 1 + \tau)/\tau^2$, and the known functions $h_{22}$ and $h_{32}$, which are defined in [2], are not included here for brevity. The diffusivity and kurtosis agree with their Monte-Carlo simulated values in the model medium fairly well for $\alpha < 0.5$.

**Discussion:** Our model provides the explicit time dependence for the diffusion coefficient, which is indeed empirically known to decrease with time. This can be contrasted with the popular two-compartment exchange model (Kärger) [6] with constant diffusivity. Remarkably, the DWI signal up to $O(q^2)$ has an approximately biexponential form with a somewhat atypical dependence on $q$:

$$S(t,q) \approx w_+ e^{-t/t_c} + w_- e^{-D_\infty q^2 t}, \quad w_+ \approx \frac{\alpha^2}{d}\overline{D}q^2 t_c, \quad w_- \approx 1 - \frac{\alpha^2}{d}\overline{D}q^2 t_c, \tag{5}$$

where $D_\infty \equiv D(\infty) = \overline{D}(1 - \alpha^2/d)$ is the tortuosity asymptote. This form is also qualitatively different from that of the Kärger model. Multiple length scales would yield additive dispersive contributions to Eqs. (1)-(4) with the corresponding correlation times. This way, by measuring the time- or frequency-dependence of DWI signal characteristics, one can quantify diffusivity variance and length scales.



Top to bottom: A portion of model medium; correlator $\Gamma(k)$; $D(t)$ and $K(t)$ from Monte Carlo simulations (blue), from general analytical result with exact $\Gamma(k)$ (solid red) and Eqs.(3,4) (dashed magenta). Deviations in $K(t)$ for short times is simulation artifact.

**References**: [1] D.S. Novikov et al., proc. ISMRM 2009, 450; [2] D.S. Novikov and V.G. Kiselev, JMR 195(2008)33; [3] D.S. Novikov and V.G. Kiselev, submitted to ISMRM 2010; [4] J. Stepisnik, Physica 104B(1981)350; [5] M. Schachter et al. JMR 147 (2000) 232; [6] J. Kärger, Adv. Col. Int. Sci. 23(1985)129.