The effects of cellular polydispersity on constant-time diffusion experiments

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Purpose: To introduce an extension of the Kärger model describing diffusion in a multicomponent system and to analyze its consequences for tissues with cellular polydispersity.

Introduction: Despite its widespread clinical applicabilities, the biophysical mechanisms underlying diffusion weighted contrast remains to be elucidated. In brain stroke, for instance, infarcts can be detected very early using diffusion weighted images due to a decrease in the apparent diffusion constant (ADC)(1). Several theories to explain this have been proposed: a shift of water from the extracellular to the intracellular space, a decrease in intracellular viscosity, shutdown of intracellular water circulation, increased tortuosity of the extracellular space and more(2-5). Progress in this direction is impeded by several confounding experimental results and limitations of the models used to interpret the data. Therefore it is necessary to re-examine and further develop existing models of diffusion in biological tissue. In this study, the diffusion of water in biological tissue is studied using an extension of the Kärger model(6). In the mammillary Kärger model each cell can be described by its own value of the exchange time, the size and the diffusion constant, and protons can diffuse from one cell to another only through the extracellular space. Diffusion in the extracellular space is likewise described by a diffusion constant and an exchange time.

Methods: Computer simulations are used to study a Stejskal-Tanner constant time experiment on the mammillary Kärger model. The set of generalized Kärger equations are solved in a system of 100 spherical cells of average radius R=6 µm and intracellular diffusion constant 0.05 μm^2 millisecond. The actual size of each cell is chosen randomly from a Gaussian distribution of variable width $\sigma=W\cdot R$ with a corresponding influence on the cellular exchange time. The extracellular diffusion constant is set to 1.3 μm^2/ms and the probability to enter a particular cell is proportional to its surface area. The volume fra ctions are chosen to be 0.8/0.2 intracellular/extracellular in the absence of cellular polydispersity, i.e. W=0. The diffusion q-value is varied from 0.1-1.0 μm^{-1} and the calculated signal S(t) fit to a biexponential decay $S(t)=p_1\exp(-q^2tADC_1)+p_2\exp(-q^2tADC_2)$ in order to estimate the effective volume fractions (p_1 and p_2) and diffusion constants (ADC_1 and ADC_2).

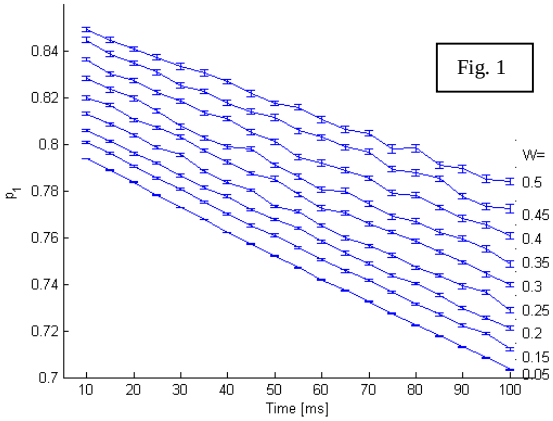
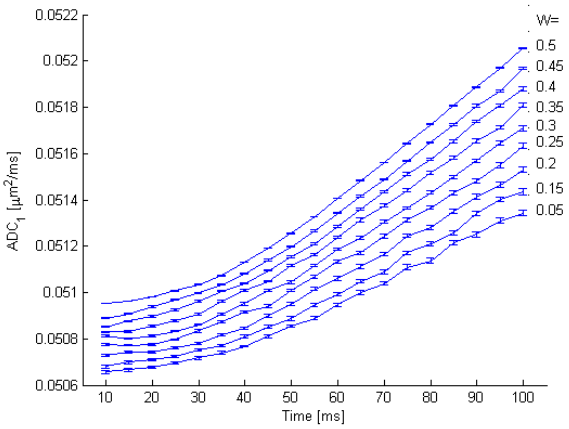


Fig. 1

Results: The effective intracellular volume fraction p_1 is plotted in figure 1 as a function of diffusion time t and for polydispersities W = 0.5, 0.45, 0.4, 0.35, 0.3, 0.25, 0.2, 0.15, 0.05 from top down. The relative volume of the intracellular space is slightly overestimated for all values of the diffusion time, and more so the higher the diffusion time. For the shortest diffusion time however, the W dependence of p_1 is quite close to the true volume fraction (data not shown). The variability of p_1 as a function of W is roughly similar in magnitude to the variability of p_1 as a function of diffusion time. The apparent diffusion constants ADC_1 (intracellular diffusion constant) and ADC_2 (extracellular diffusion constant) are shown in figure 2 as a function of the diffusion time. For ADC_2 the influence of cellular polydispersity is negligible: on the other hand, the diffusion time has a profound impact on the estimate of the extracellular diffusion constant. The intracellular diffusion constant is much less sensitive to the diffusion time, and can be determined within an accuracy of roughly 4% regardless of the value of t and W.



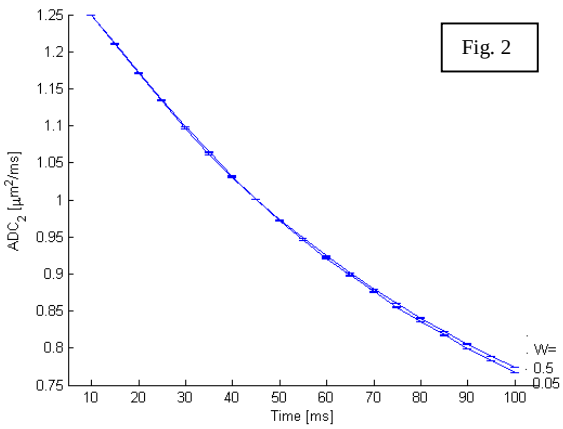


Fig. 2

Conclusions: We introduced and demonstrated the mammillary Kärger model. This model describes multicomponent diffusion in polydisperse cellular tissues, among other things. For the particular implementation shown here, it was demonstrated that cellular polydispersity has a minor influence on the estimated apparent diffusion constants as well as volume fractions. The effect of diffusion time variations as well as differential T1 and T2 relaxation is expected to dominate.

References:

1. Moseley ME, Cohen Y, Mintorovitch J, Chileuitt L, Shimizu H, Kucharczyk J, Wendland MF, Weinstein PR. Early detection of regional cerebral ischemia in cats: comparison of diffusion- and T2-weighted MRI and spectroscopy. Magn Reson Med 14: 330-46, 1990.
2. Latour LL, Svoboda K, Mitra PP, Sotak CH. Time-dependent diffusion of water in a biological model system. Proc Natl Acad Sci U S A 91: 1229-33, 1994.
3. Schwarcz A, Bogner P, Meric P, Correze JL, Berente Z, Pal J, Gallyas F, Doczi T, Gillet B, Beloeil JC. The existence of biexponential signal decay in magnetic resonance diffusion-weighted imaging appears to be independent of compartmentalization. Magn Reson Med 51: 278-85, 2004.
4. Branco G. An alternative explanation of the origin of the signal in diffusion-weighted MRI. Neuroradiology 42: 96-8, 2000.
5. Duong TQ, Ackerman JJ, Ying HS, Neil JJ. Evaluation of extra- and intracellular apparent diffusion in normal and globally ischemic rat brain via 19F NMR. Magn Reson Med 40: 1-13, 1998.
6. Karger J, Pfeifer H, Heink W. Principles and application of self-diffusion measurements by nuclear magnetic resonance. Adv.Magn.Res. 12, 1-88. 1988.