Agreement and disagreement between two models of diffusion MR signal

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Introduction

Several authors (e.g. [1]) have reported a decrease in the measured apparent diffusion coefficient (ADC) in the immediate aftermath of ischemic stroke, which slowly gives way to a region of greatly increased ADC after a period of hours to days. This initial decrease in ADC has lead to the conjecture that inflammation of the affected tissue leads to a reduction in the size of a fast-diffusing extra-cellular compartment in favour of a slower diffusing intracellular compartment, reducing the ADC of the overall sample. In this work we hypothesise that the change in volume is only partially responsible for the changes in ADC, which is also the product of a loss of percolation in the extracellular space. We test this hypothesis using a Monte-Carlo diffusion simulation within a substrate of cylindrical axons that swell artificially.

Methods

We construct an idealised geometric model of white matter, which is the substrate within which we run the diffusion simulation. The substrate is constructed from 200 initially non-intersecting cylinders with circular cross section aligned parallel to the z-axis positioned randomly in the *xy*-plane (see Fig-1). We gradually swell the cylinders over 10 iterations to create a series of substrates. In each iteration, the radius of cylinders is increased by a fixed increment. If two cylinders intersect, the two sections of arc in the cross section are replaced by a chord, with intersections between chords also accounted for (see Fig-2). Cylinders had initial radius 1µm expanding to a maximum of 3µm, although cylinders overlapping by more than a critical threshold angle of arc in any iteration stop expanding in subsequent iterations. This is a crude approximation of the effects of pressure on expanding cells.

The overlap of cylinders eventually divides the space extracellular space into disconnected regions in which the diffusion in restricted, much like in the intra-cellular space. This is known in statistical mechanics literature as the *percolation threshold*, at which point clusters of overlapping cylinders merge a single cluster of cylinders spanning the whole substrate is formed (see Fig-3).

Diffusion is simulated via a population of point-like spins initialized randomly across the substrate. Spin positions are updated throughout the duration of a simulated PGSE sequence, with spin phases updated according to their positions during the application of field gradients. The phase-shift for each spin φ_j and synthetic signals $S(\mathbf{q})$ are calculated using the method of [2]. In a timestep spin positions are updated by picking a step of fixed length set from the diffusivity of water at body temperature. Each step is checked for intersection with the constraining substrate and elastically reflected if it intersects a barrier. We run 10 simulations with different random seeds in each of the 10 substrates with increasing cell radii, with 100000 spins over 1000 timesteps with one diffusion-sensitised direction parallel and two perpendicular to the cylinders at b=1048 s mm^{-2}.

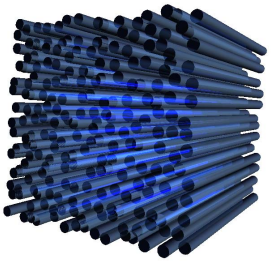

Fig-1:Randomly positioned, non-overlapping cylinders

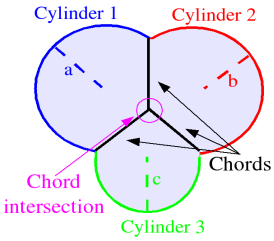

Fig-2: Cylinder intersections in cross-section. Cylinders of different radius deform along chords of intersection

Data from the Monte-Carlo model is compared to the predictions of an analytical model of diffusion in two tissue compartments: an intracellular component from [3], and an extracellular compartment with diffusion modified by a tortuosity factor from [4], with volume fractions from assuming hexagonal packing of cylinders.

Results

Synthetic diffusion-weighted measurements were generated perpendicular to the cylinder axes as well as a synthetic b=0 unweighted measurement. Fig-4 shows the synthetic signal perpendicular to the cylinder axis against volume fraction of intracellular space. The analytical model shows a smooth increase as a function of V_I, whereas the Monte-Carlo model increases more rapidly, before a small drop-off as V_I approaches 1.

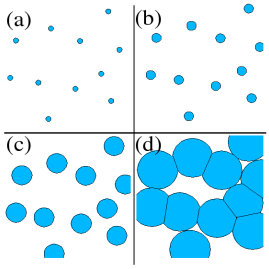

Fig-3: Percolation. (a) Small cylinders, well-separated allow diffusion.(b)-(c) Cylinders swell. (d) Overlapping cylinders prevent diffusion

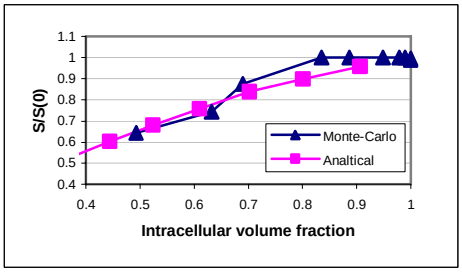

Fig-4: Synthetic diffusion-weighted signals perpendicular to cylinder axes. Insert shows a magnification of the peak area and shows a turnover as extracellular connectivity is lost

Discussion and Conclusions

The steady rise in signal (i.e. reduction in ADC) at lower V_I is an effect of the reduction in extracellular volume fraction due to cylinder inflammation.

We postulate that the difference between the two models is caused by cylinders abutting and overlapping in the Monte-Carlo model and the subsequent loss of connectivity in the extracellular space due to loss of percolation in the extracellular space due to abutting cylinders. This effect is not captured in the analytical model.

The results suggest that loss of percolation is a detectible effect, although including the effect in addition to the increase in intracellular volume fraction does not have a dramatic effect. The effect may be more dramatic with less ordered configurations of cylinders with a distribution of radii. Future work will investigate the effect with more realistic geometric models of white matter.

Acknowledgements

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