A Fractal Model of Diffusion Weighted MRI in Brain Tissue

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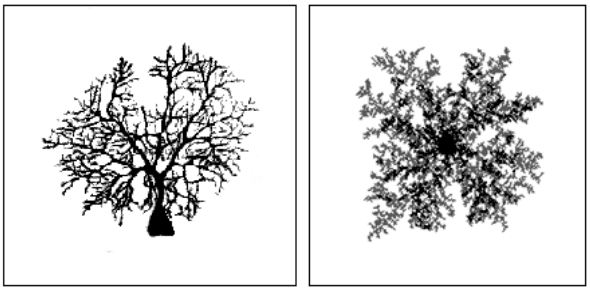
INTRODUCTION: The complexity of biological tissue is due to the morphology of its constituent cells and their organization. This complexity influences the water diffusion in the tissue and hence the Diffusion Weighted (DW) MRI signal, the properties of which are not yet entirely understood. The need to understand the biophysics behind the DW MRI signal renders mathematical models necessary. The aim is to explain the observed non-mono-exponential signal decay along with the changes in the Apparent Diffusion Coefficient (ADC) seen in pathology (ischemia). To this end several effects such as restriction, tortuosity and heterogeneity of diffusion and relaxation properties have been proposed and included in analytical models [1][2]. These models use spheres and ellipsoids as approximations to the cells of the tissue. These are clearly rough approximations, and we believe that our new numerical model comes closer to the actual geometry of grey matter by exploiting the morphological similarity between neurons and computer generated Diffusion Limited Aggregation (DLA) clusters [3] (Fig. 1). This geometry approaches a level of complexity comparable to that of grey matter cells. Quantitatively the fractal dimension of neurons has been determined to 1.68±0.15, overlapping with the value of 1.70±0.10 for typical DLA clusters [4]. This is an interesting result from quantitative cellular morphometry [5]. The resemblance has been ascribed to a similarity of growth mechanisms [6], which is a physiological argument for using a DLA structure as a general neuron model. Considering the similar morphologies of neurons and glial cells DLA structures might serve as a physiologically relevant general grey matter cell model.



a: Mammalian neuron b: A typical DLA cluster

Fig. 1: The neuronal morphology (a) is similar to the DLA archetype (b).

METHODS: Our model uses a pre-generated DLA cluster as geometry. The DLA cluster is generated using a standard method, where 1x1µm particles attach to a soma-sized core (Fig. 1b). A population of diffusing spins are distributed randomly on the cluster. This constitutes our intra-cellular (IC) spin population. Diffusion of an extra-cellular (EC) spin population is also included. This is our grey matter unit cell. On contact with the border of the DLA cluster (the cell membrane) the spins are reflected or allowed to exchange between EC and IC compartments based on a probability of crossing, which determines the permeability of the cell membrane. The outer walls of the EC compartment have reflecting boundaries. Cluster and EC areas are made to coincide with the ¼ ratio commonly accepted for EC/IC spaces. Compartments have equal spin densities, but are given their own properties of diffusion and transverse relaxation. On crossing from one compartment to the other a spin acquires the diffusion coefficient and transverse relaxation of its new environment. The signal from a PGSE NMR sequence is simulated from the model system. The model allows variable values for pulse-width, δ, diffusion time, Δ, and gradient strength, *g*. Our model includes a variable concentration of randomly distributed static sinks, which will eliminate spin transverse magnetization upon contact. This is to model the presence of relaxation sinks such as macromolecules and boundary membranes, which induce transverse relaxation times of the order of µ-secs.

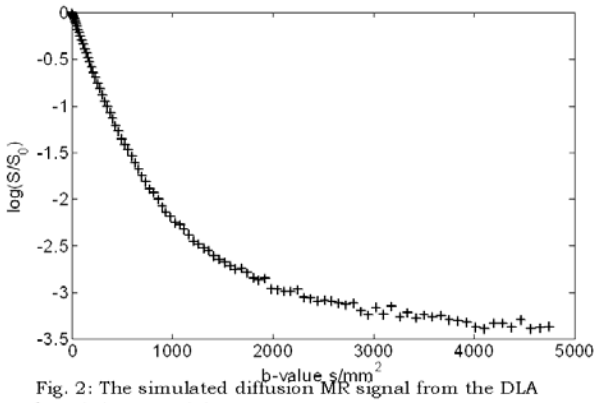


Fig. 2: The simulated diffusion MR signal from the DLA based tissue model.

RESULTS: Our results (using $\delta/\Delta = 2/5$ ms; timestep 10µsec) show a clearly non-mono-exponential signal decay from the system (Fig. 2). In this first simulation each compartment (IC/EC) has the physical diffusion coefficient of water. Therefore the signal behaviour is produced by restriction effects from the fractal geometry of the cluster. No exchange, sink-distribution or relaxation was included in the test run presented here. Each point is averaged over 80 runs. This test does not include averaging over clusters.

DISCUSSION: Our model is based on a physiologically relevant complex geometry directly comparable to that of tissue. We see this as a major improvement over previous model geometries. We believe the inclusion of a random distribution of magnetization sinks is a novel feature in diffusion models. The DW signal behaviour from diffusion in a medium with sinks is interesting because compact walks encounter sinks with lower probability than far-reaching walks. We expect this preference for localized walks to be reflected in the DW signal. Where earlier models have included exchange using a mean-field approach, our new model is closer to the actual mechanism with exchange occurring near membranes only. The effects of transverse relaxation and exchange between compartments in DW MRI are currently not fully understood; our model may help elucidate these effects. Our ongoing research includes all model parameters in a multi-dimensional optimization to fit simulation data to experimental *in vivo* data. This will produce a map of good fits in the parameter space of the model, yielding valuable information of the interplay between biophysically interpretable model parameters. We believe that our model can contribute significantly to the understanding of the biophysics behind DW-MRI signal formation in health and pathology.

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