

The Open-Access Journal for the Basic Principles of Diffusion Theory, Experiment and Application

## A Fractal Based Model of Diffusion MRI in Cortical Grey Matter.

Brian Hansen, Leif Østergaard, Peter Vestergaard-Poulsen

Center of Functionally Integrative Neuroscience (CFIN), University of Aarhus / Aarhus University Hospital, Nørrebrogade 44, Building 30, 8000 Aarhus C, Denmark.

Email: [brianh@phys.au.dk](mailto:brianh@phys.au.dk)

### 1. Introduction

Diffusion Weighted Magnetic Resonance (DWMR) imaging is an important tool in diagnostic neuroimaging [1], but the biophysical basis of the DWMR signal from biological tissue is not entirely understood. Testable, mathematical models relating the DWMR signal to the tissue, therefore, are crucial. This work presents such a theoretical model of water DWMR signals in brain grey matter. The model describes grey matter tissue using computer generated Diffusion Limited Aggregation clusters. Model output is compared to experimental DWMR data from normal human grey matter to determine whether this model reproduces the observed signal with credible values for all model parameters. The model is also used for simulating the effect on the DWMR signal of cellular events known to occur in ischemic stroke. With such models, it is anticipated that sensitivity and specificity of DWMR in tissues can be improved, leading to better understanding of the origins of MR signals in biological tissues, and improved diagnostic capability.

### 2. Methods and Materials

#### 2.1. Modeling

The numerical model presented here can simulate the DWMR signal from diffusing particles in any 2D two-compartment system. Diffusion is implemented as a random walk process on a square lattice. The simulations of the DWMR signal from grey matter take into account tissue geometry, intra- and extra-cellular diffusivity, membrane permeability, diffusion time ( $\Delta$ ), encoding gradient duration ( $\delta$ ) and strength ( $g$ ). All model parameters can be directly interpreted as biophysical properties of the tissue such as diffusion coefficients and membrane permeability allowing comparison to known values. This model uses computer generated Diffusion Limited Aggregation (DLA) clusters to describe grey matter complexity. DLA clusters are relevant in modeling grey matter structure for two reasons. Firstly, the nerve cells of the brain are similar in shape to the DLA archetype. This morphological similarity is illustrated in Fig. 1 and has been

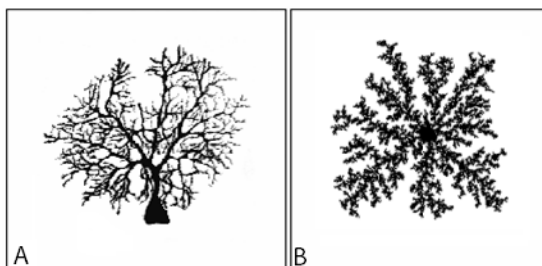


Fig. 1: A) Mammalian neuron. B) Typical DLA cluster. The DLA archetype is similar to the neuronal membrane morphology.

quantified by comparing the fractal dimension of neuron profiles and typical DLA clusters in [2] (and references herein) where the fractal dimension of typical neurons (2D projection) is reported to be  $1.68 \pm 0.15$  coinciding with the value of  $1.70 \pm 0.10$  for typical DLA clusters. Secondly, the DLA growth mechanism has been suggested as a mechanism in neuronal growth [3]. We therefore believe that DLA clusters are biologically relevant and physically realistic geometries in the description of grey matter tissue. In our simple 2D model we define a "grey matter unit cell" using a single DLA cluster to describe the separation between the extra- and intra-cellular spaces (ECS and ICS, respectively). All simulations were averaged 40 times to ensure satisfactory statistics and results were obtained using four different DLA clusters to examine variability between clusters.

### 2.2. Experiments

All experiments were performed on a 1.5 T magnet (GE Medical Systems) with a 40 mT/m gradient system and quadrature head coil. Five healthy male volunteers (age 24-36 yrs) were used. All experiments were approved by the local ethics committee. Data were obtained at 14 different diffusion weightings (b-values) ranging from 0-4500  $\text{mm}^2/\text{s}$ .

### 3. Results

The model reproduces the experimental DWMR signal from normal grey matter using experimentally validated values for membrane permeability, ICS and ECS volume fractions and diffusivities. An example of the agreement between model output and experimental data is given in Fig. 2. Further simulations show that cell swelling in combination with decreased intra-cellular diffusivity (possibly as a result of energy failure in the cell [4]) is a probable cause of the decreased tissue water diffusivity observed in ischemic stroke.

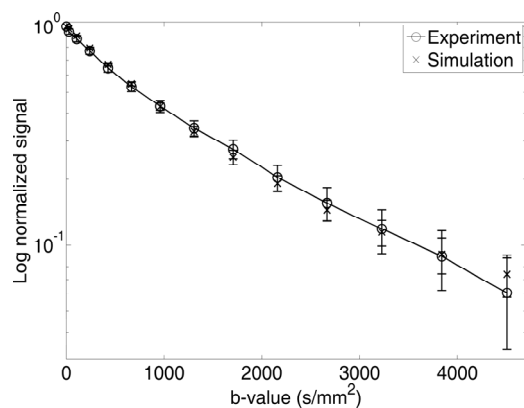


Fig. 2: Experimental data from normal grey matter and result of a DLA cluster based simulation using credible values for all model parameters.

### 4. Conclusion

The model provides insights into underlying causes of DWMR-signal changes in neural tissue of potential importance for diagnostic and therapeutic approaches to ischemia.

### References

- [1] P. Tofts, Quantitative MRI of the brain, WileyBlackwell, 2004.
- [2] S. Havlin *et al.*, Fractals in biology & medicine, Chaos, Solitons & Fractals 6, 1995.
- [3] F. Caserta *et al.*, Determination of fractal dimension of physiologically characterized neurons in two and three dimensions. Journal of Neuroscience Methods 56, 1995.
- [4] J. Sehy *et al.*, Intracellular water ADC decrease following a reduction in cell ATP levels, in: Proceedings of 10th Annual Meeting of ISMRM 2002, p. 1149.