**Brain Tissue Modeled as a Porous Medium with parameters derived from Micro-Iontophoresis Experiments**

Charles Nicholson

Dept. Neuroscience and Physiology, New York University School of Medicine, 435 E 30th St., New York, NY 10016, USA
email for correspondence: charles.nicholson@nyu.edu

The cellular structures of the brain are separated by a narrow fluid-filled extracellular (interstitial) space giving brain tissue properties of a porous medium. The porosity and tortuosity can be measured by releasing tetramethylammonium cations from a micropipette and measuring the time-dependent concentration about 100 µm away using an ion-selective microelectrode (ISM), as shown in Fig. 1 [1].

Fitting the results of experiments to an appropriate solution to the diffusion equation [1, 2] revealed that that the typical **porosity is *φ* ~ 0.2** and the **tortuosity is *τ* ~ 1.6**, where tortuosity = (*D/D\**)0.5, *D* is free diffusivity and *D\** is effective diffusivity. These results were modeled by regarding the brain as an ensemble of cubic cells of side 2*a* with cubic voids (expansions of interstitial space) of side *b* at each corner. Cells were separated by sheets of interstitial space of width 2*w* and the packed cells formed composite voids of width 2*b,* as shown in Fig. 2.



Fig.1. Experimental setup. Diffusion measurements made in agarose (*D*) or brain slice (*D\**). Analysis with custom MATLAB software (Wanda and Walter) [1].

Monte Carlo simulations took place in this ensemble using the MCell program [3]. It was found that, to obtain the experimental *φ* and *τ*, the required geometry was ***a* = 0.742 µm, *b* = 0.379 µm and *w* = 20** nm [4]. The presence of voids was essential to obtain the measured tortuosity and this feature was consistent with freeze-fixed electron microscopy and super-resolution optical imaging [4].



Fig. 2. Model of brain tissue. (*a*) unit cell with cubic corner voids. (*b*) top view of cell (*c*) ensemble of cells spaced 2*w* apart. In practice, 323 or 643 cells used for Monte Carlo simulations [4].

**References**

1. J. Odackal, R. Colbourn, N. J. Odackal, L. Tao, C. Nicholson, and S. Hrabetova. Real-time iontophoresis with tetramethylammonium to quantify volume fraction and tortuosity of brain extracellular space, *JoVE*: e55755 (2017).

2. E. Syková, and C. Nicholson. Diffusion in brain extracellular space, *Physiological Reviews*, 88 (2008) 1277-1340.

3. J.R. Stiles, and T.M. Bartol. 2001. Monte Carlo methods for simulating realistic synaptic microphysiology using MCell. in E. De Schutter, Editor, Computational Neuroscience: Realistic Modeling for Experimentalists*,* CRC Press: London; 2001, p 87 - 127.

4. C. Nicholson, Sheet and void porous media models for brain interstitial space, *Journal Royal Society Interface*, 20 (2023): 20230223.