Diffusion processes in the extracellular space

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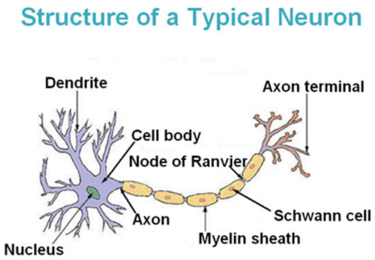
Contents

Brief introduction to the brain

Cells in the brain

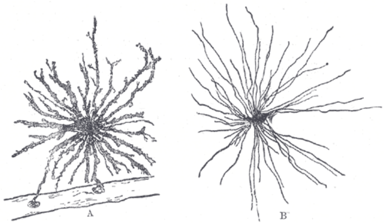
Neurons:

- Signal processing



Neuroglia:

- Janitorial tasks



The extracellular space

- Space surrounding neurons and neuroglia
- Accounting for $\sim 20\%$ of total brain volume
- Important for transport of nutrients, medicines etc.

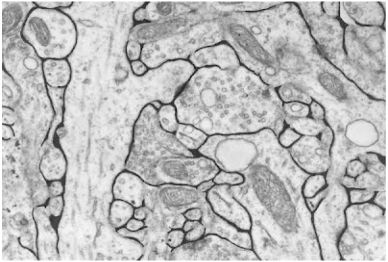


Figure: Extracellular space marked as dark grey.

Basic diffusion

The basic diffusion equation reads

$$\frac{\partial C}{\partial t} = D\nabla^2 C \tag{1}$$

Einstein relations

$$D = \frac{k_B T}{6\pi\eta r} \tag{2}$$

$$\langle r^2 \rangle = 2dDt \tag{3}$$

Diffusion in ECS

Network simulations:

- Verification against experimental results
- Local field potential
- Extracellular conductance

$$\sigma = \frac{cq}{k_B T} D \qquad (4)$$

$$\nabla \cdot (\sigma(\mathbf{r}) \nabla \phi(\mathbf{r}, t)) = -C(\mathbf{r}, t)$$

Modified diffusion equation

A modified version of the basic diffusion equation is needed to account for

- Sources
- Uptake of diffusing molecules
- evt. bulk flow (absent below)

This new equation reads

$$\frac{\partial C}{\partial t} = D^* \nabla^2 C + \frac{s}{\alpha} - k' C \quad (5)$$

$$\lambda = \sqrt{\frac{D}{D^*}} \quad (6)$$

Numerical simulations

This will be addressed in the Molecular Dynamics part.

Optical measurements

- Developed in 1993 by Nicholson and Tao
- Based on thin slices and macromolecules with fluorescent label
- Problems with slice thickness and photobleaching
- Quantum dot IOI

TMA^+ measurements

- Micro-pipette
- Ion sensitive micro-electrodes a known distance away ($\sim 100\mu$m)
- Measures concentration curve at the electrode position
- Time resolution as well as spatial resolution
- Some refinements possible

Radiotracer measurements

- “Oldest trick in the book“ - most intuitive
- Good method, but slightly out dated due to radioactivity
- Results still used as verification
- Offers independent reference and cross-species data

Diffusion Tensor Imaging

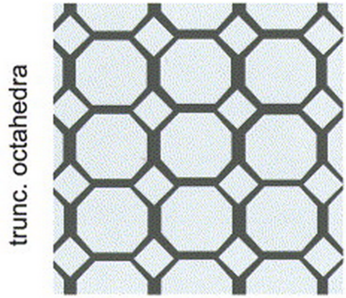
- Non invasive method based on MRI
- Immensely complicated; I have no idea what I'm doing!

Molecular dynamics

- Study of systems of atoms and their time-development
- Most research towards fracture mechanics and flow in tight rocks
- Much of the geometry is similar, but the length scale is a bit to small
- Dissipative fluid dynamics

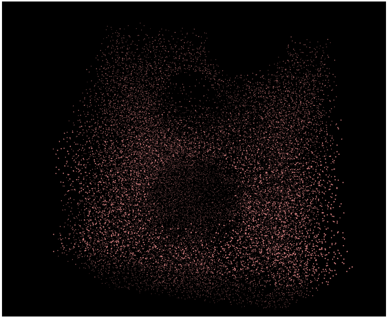
My experiment - motivation

- Results from 2003 article by Hrabětová and Nicholson
- Max value of tortuosity $\lambda \leq 1.225$
- Diffusion modeling on regular geometries



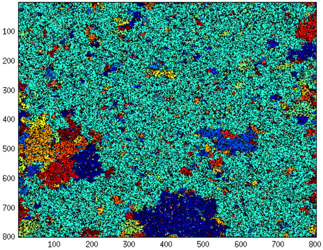
My experiment - results

- Making spheres of stationary atoms
- Measuring self diffusion constant of liquid using Einstein relation
- Comparing to self diffusion constant of bulk fluid
- Found $\lambda \approx 1.41$
- Limitations



Random walks

- Percolation theory
- Random walks and diffusion
- Spanning cluster
- Results from by Hrabětová and Nicholson
- Limitations



Outlook

- Unanswered questions (limitation of tortuosity)
- Other modeling methods
- Multi scale models; the best from both worlds?