Modeling Convection-Enhanced Delivery into Brain Tissue using Information from MRI

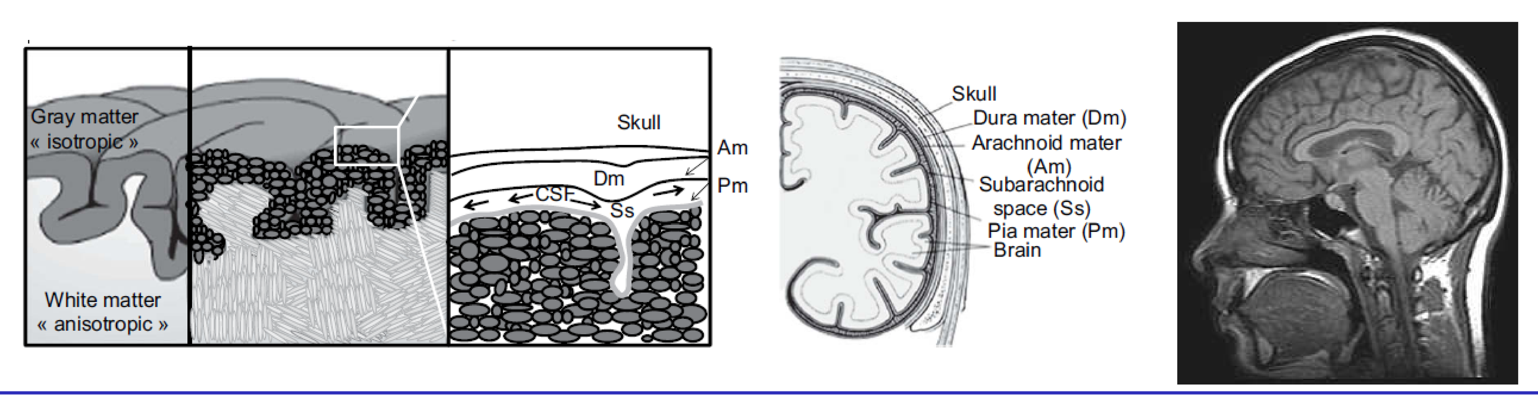
International Research Training Group nupus

K.Støverud, R. Helmig, M. Darcis, K. Erbertseder, S.M. Hassanizadeh
Institute for Hydraulic Engineering
Department for Earth Sciences

Universiteit Utrecht
Universität Stuttgart

Introduction

Brain Tissue



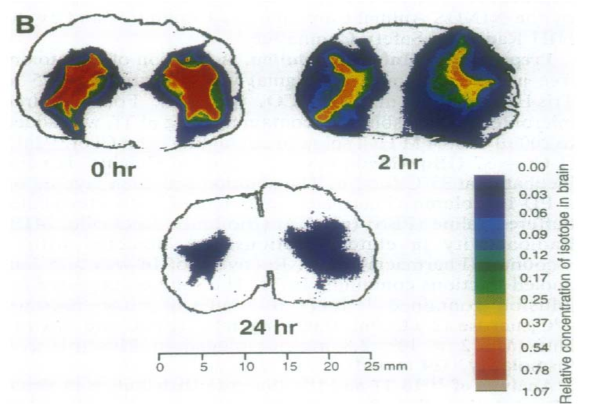
Looking at the brain as a porous medium on different scales. (From Allard et.al., 2009)

Convection-Enhanced Delivery (CED)

Method:
Infusing a therapeutic agent under a positive pressure gradient directly into brain tissue via catheters.

Advantage:
Avoid problems related to the blood-brain barrier and dilution of the drug.

Challenge:
Final distribution dependence on:
- Heterogeneities and anisotropy of the tissue.
- Geometrical boundaries.
- Properties of the catheter and natural occurring flow processes.



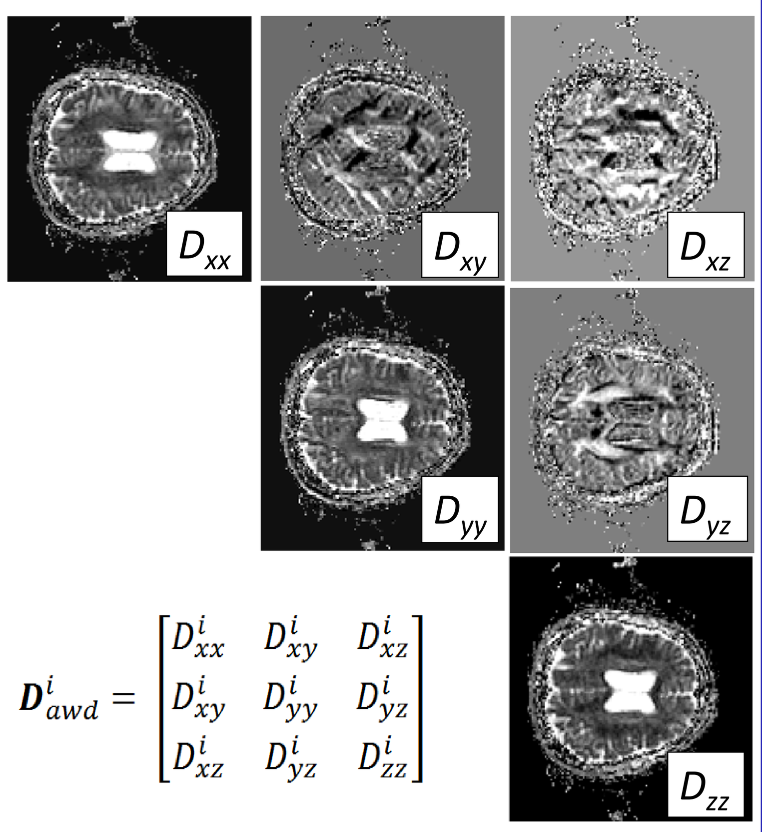
Concentration profiles AFTER 2hr of infusion into white matter of a cat brain. Less spreading in grey matter observed. (Bobo et.al.,1994)

Models

Rigid models:	Poro-Elastic models:
• Realistic geometry	• Spherical geometry
• Patient-specific parameters	• Generalized parameters
• Source term as point source or including catheter.	• Fixed pressure in the infusion point.
• Flow and transport modeled	• Commonly only flow modeled
• Heterogeneous and anisotropic	• Homogeneous and isotropic

Aim of this study:
1) Implement patient-specific parameters and geometry in a poro-elastic model.
2) Compare the result from the poro-elastic model with a rigid model.
3) Investigate effects of anisotropy and heterogeneities on the final concentration distribution..

Parameters from MRI



$$D^i_{awd} = \begin{bmatrix} D^i_{xx} & D^i_{xy} & D^i_{xz} \\ D^i_{xy} & D^i_{yy} & D^i_{yz} \\ D^i_{xz} & D^i_{yz} & D^i_{zz} \end{bmatrix}$$

Cross section of the components of the D_{awd} obtained from a patient at OVGU-Magdeburg. The data set consist of 128x128x65 voxels with a resolution of 2 mm.

Diffusion tensor imaging (DTI)

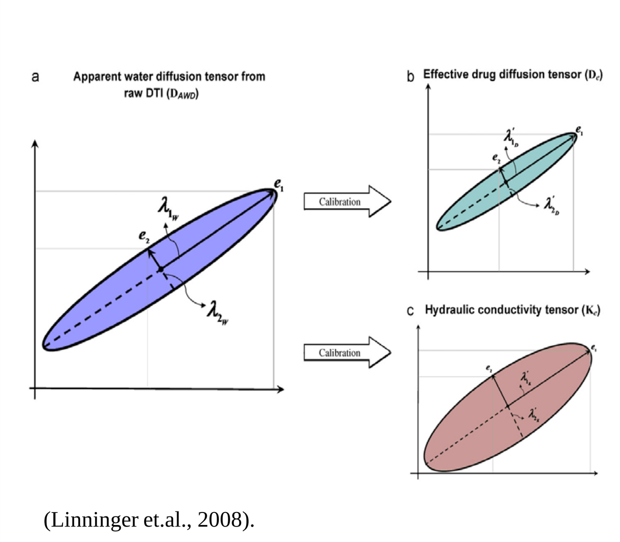
Method:
- MRI technique capable of measuring self-diffusion of water (D_{awd}) in tissue.

Advantage:
- Direction of the white matter fibers can be found from DTI the .
- The permeability tensor (K), diffusion tensor (D^*) and D_{awd} share the same set of eigenvectors.
- Delineating geometrical boundaries possible.

Challenge:
- Literature values of K and D necessary for calibration.
- High resolution images needed.
- Elastic properties and porosity of the tissue still unknown.

Parameters from MRI

Calibration of K and D*



Step 1:

$$D = E\cdot\Lambda\cdot E^T, \Lambda = \begin{bmatrix} \lambda_{1_w} & 0 & 0 \\ 0 & \lambda_{2_w} & 0 \\ 0 & 0 & \lambda_{3_w} \end{bmatrix}$$

$$E = \{\vec{e}_1, \vec{e}_1, \vec{e}_1\}$$

Step 2:

$$\bar{\lambda}_w = \frac{1}{3}\sum_{i=1}^{3}\lambda_{i_w} \quad \lambda'_{i_K} = \bar{K}\cdot\left(\frac{\lambda_{i_w}}{\bar{\lambda}_w}\right)$$

Step 3:

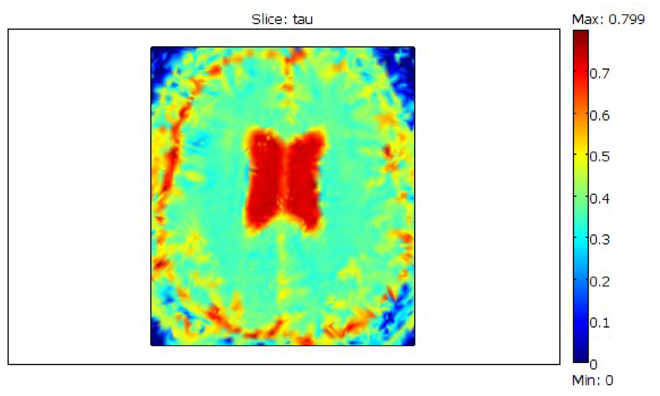
$$K = E\cdot\Lambda'\cdot E^T, \Lambda' = \begin{bmatrix} \lambda'_{1_w} & 0 & 0 \\ 0 & \lambda'_{2_w} & 0 \\ 0 & 0 & \lambda'_{3_w} \end{bmatrix}$$

*Step 1) D_{awd} is voxel wise decomposed into eigen-values and eigenvectors. Step 2) An average K (from literature) is calibrated using the eigenvalues . Step 3) The direction of the **K** is found based on the eigen-vectors. Same method is applicable to **D***.*

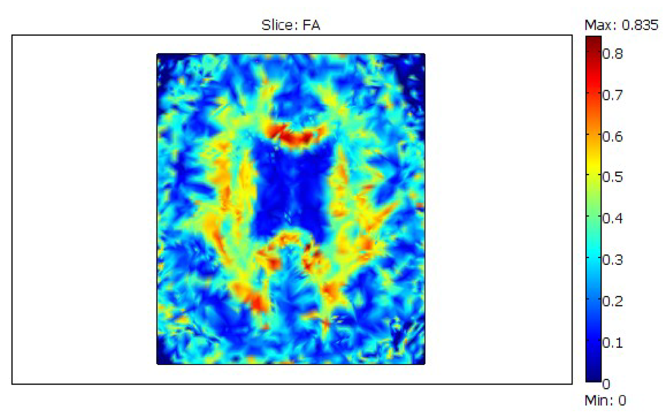
Geometry

From D_{awd} also tortuosity (τ) and fractional anisotropy (FA) are calculated The fluid filled cavities in the brain are obviously not tortuous and τ can be used to delineate geometrical boundaries in the brain. FA represents the fraction of D_{awd} assigned to anisotropic diffusion, and is used to distinguish between grey- and white matter.

$$\frac{1}{\tau} = \sqrt{\frac{D_w}{\frac{1}{3}(D_{xx}+D_{yy}+D_{zz})}}$$



$$FA = \frac{\sqrt{3}}{\sqrt{2}}\cdot\frac{\sqrt{(\lambda_1-\lambda)^2+(\lambda_2-\lambda)^2+(\lambda_3-\lambda)^2)}}{\sqrt{\lambda_1^2+\lambda_2^2+\lambda_3^2}}$$

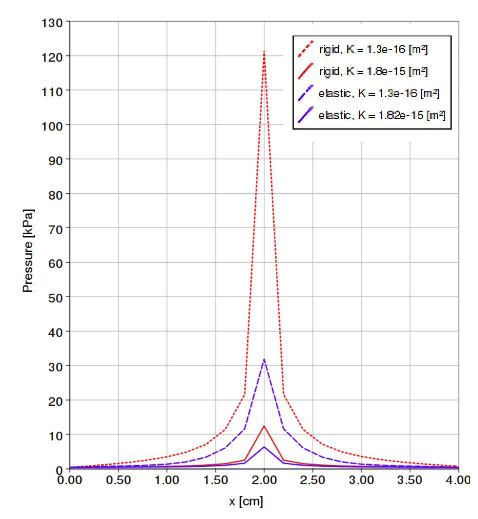


(left) Tortuosity calculated from the mean of D_{awd} and the self-diffusion coefficient of water (D_w). (right) Fractional Anisotropy (FA) found from the eigenvalues of D_{awd}.

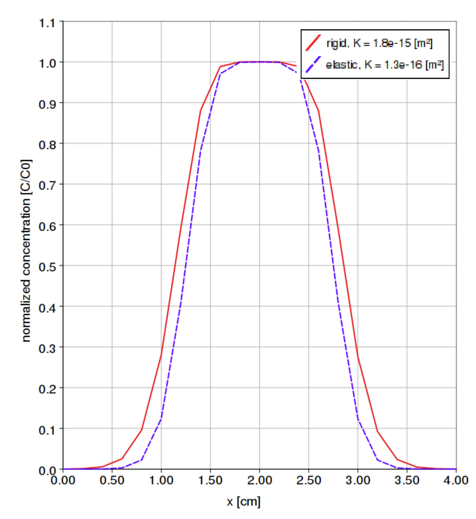
Results

Rigid versus elastic model

Simulations done for a homogenous case for two hours with a source term of 0.3ml/hr. In the elastic model the permeability is dependent on the deformation. The maximum pressures predicted are thus lower than for the rigid case. Nevertheless, the concentration distribution only differs for low permeabilities.



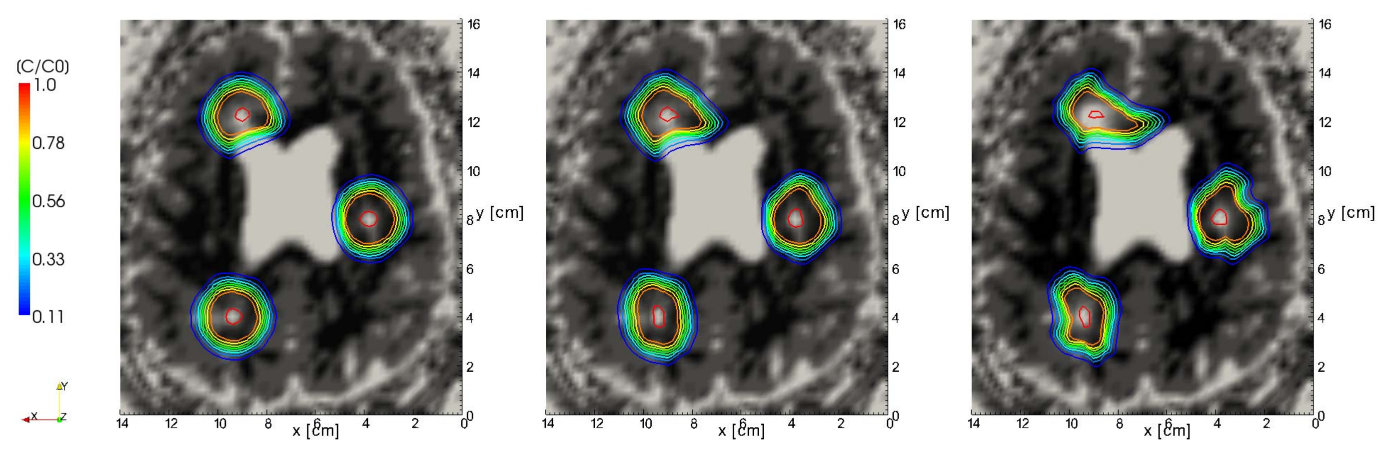
a) pressure



b) concentration

Effects of Heterogeneities and Anisotropy

Concentration distribution after 12 hours of infusion with a source term of 0.3ml/hr. Max pressure elevation: 7300 Pa.



(left) Homogeneous and isotropic. (middle) Hetereogenous and anisotropic. (right) $K_{white\ matter}$ = 10$K_{grey\ matter}$

Outlook

- Simulations on more DTI datasets with higher resolution.
- Include patient-specific porosity and elasticity properties from MRI.
- Compare results from simulations with clinical trials.