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waterscales

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Brain modelling: from magnetic resonance images to finite element simulation

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Research | Open Access | Published: 30 September 2019

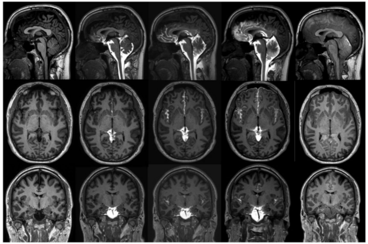
Uncertainty quantification of parenchymal tracer distribution using random diffusion and convective velocity fields

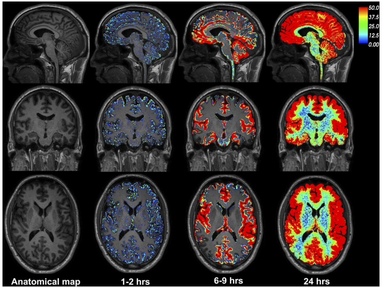
Matteo Croci, Vegard Vinje & Marie E. Rognes

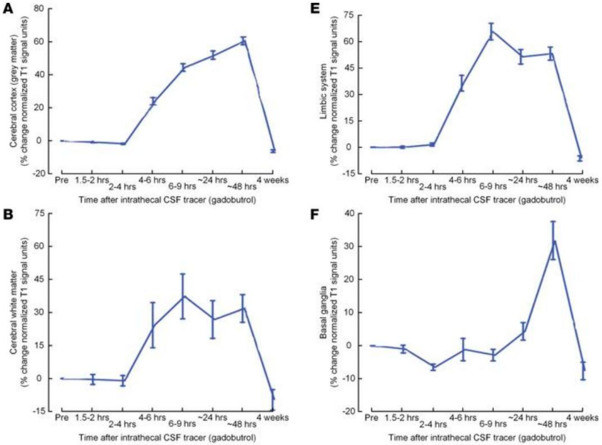
Fluids and Barriers of the CNS **16**, Article number: 32 (2019) | Cite this article

[Croci et al, FBCNS, 2019]

MRI studies indicate that CSF tracer distributes brain-wide in humans

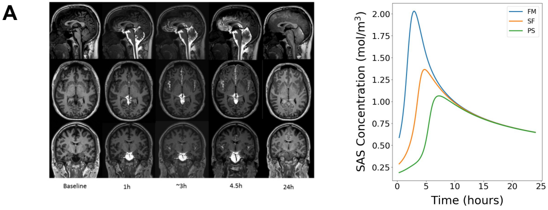


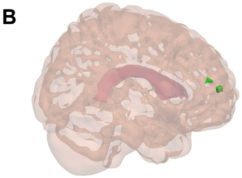




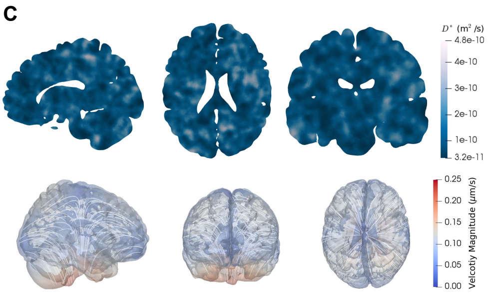
"... unlikely that diffusion alone explains brain-wide distribution."

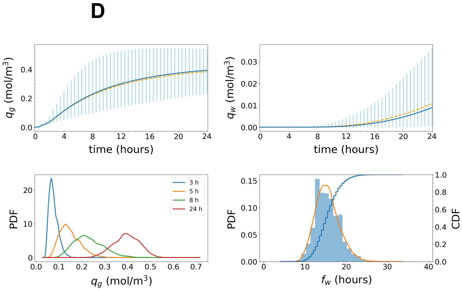
What can uncertainty quantification via convection-diffusion-reaction models with stochastic coefficients tell us about likely tracer distributions?



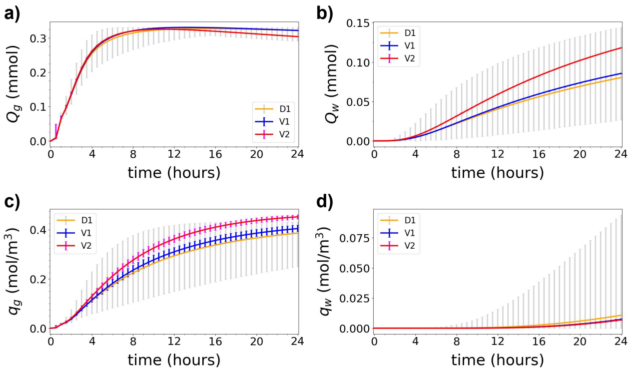


1.8M vertices,
9.7M cells,
3200 samples





A glymphatic velocity field may increase tracer enhancement, but only when adding a large-scale directional structure to the glymphatic circulation



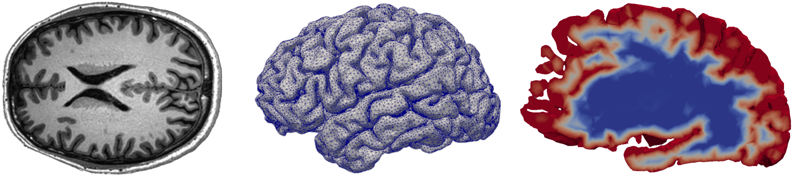
Uncertainty in the diffusion parameters substantially impacted all output quantities.

Diffusion was not sufficient, with high likelihood, to transport tracer deep into the parenchyma.

A glymphatic velocity did not increase transport into any region considered

– unless augmented by a flow field with a large-scale directionality.

Outline of lectures



Lecture 1-2 Quick start: From brain MRI to FEM

- Why simulate the brain's waterscape?
- Where can I find the slides (and book, data, and scripts)?
- Introduction to brain physiology and imaging
- From T1w MRI images to numerical simulation

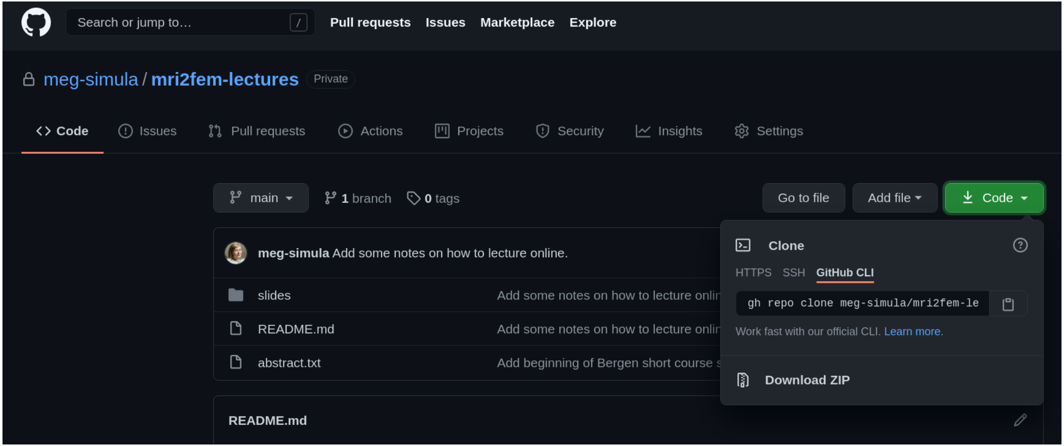
Lecture 3-4 Meshing hemispheres, brains, ventricles, parcellations

Lecture 5-6 Introducing anisotropy and heterogeneities (DTI)


ASUS

Lecture series resources

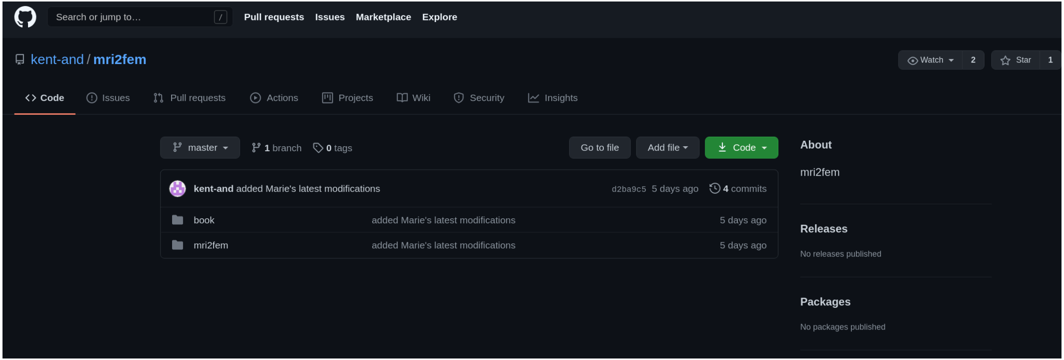
These slides and other lecture material are openly available via GitHub



[https://github.com/meg-simula/mri2fem-lectures]

Mathematical modeling of the human brain – book available on GitHub

by KA Mardal, ME Rognes, TB Thompson and LM Valnes; Simula SpringerBrief on Computing (2021)



[Mardal et al (2021): https://github.com/kent-and/mri2fem]

Resources (data, software) are openly available with our Zenodo community

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Mathematical modeling of the human brain - from magnetic resonance images to finite element simulation

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December 22, 2020 (v0.7) | Software | Open Access

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Software for Mathematical modeling of the human brain - from magnetic resonance images to finite element simulation

Kent-Andre Mardal; Marie E Rognes; Travis B. Thompson; Lars Magnus Valnes;

Software collection for Mathematical modeling of the human brain From magnetic resonance images to finite element simulation by Kent-Andre Mardal, Marie E. Rognes, Travis B. Thompson, and Lars Magnus Valnes Python modules, Bash scripts, and input files organized by chapter but with otherw

Uploaded on December 23, 2020

December 22, 2020 (v1.0) | Dataset | Open Access

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MRI2FEM data set

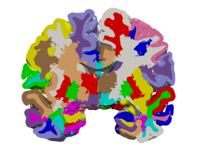
Kent-Andre Mardal; Marie E. Rognes; Travis B. Thompson; Lars Magnus Valnes;

DICOM data and FreeSurfer recon-all generated files for Mathematical modeling of the human brain: from magnetic resonance images to finite element simulation (MRI2FEM)

Uploaded on December 23, 2020

New upload

Community



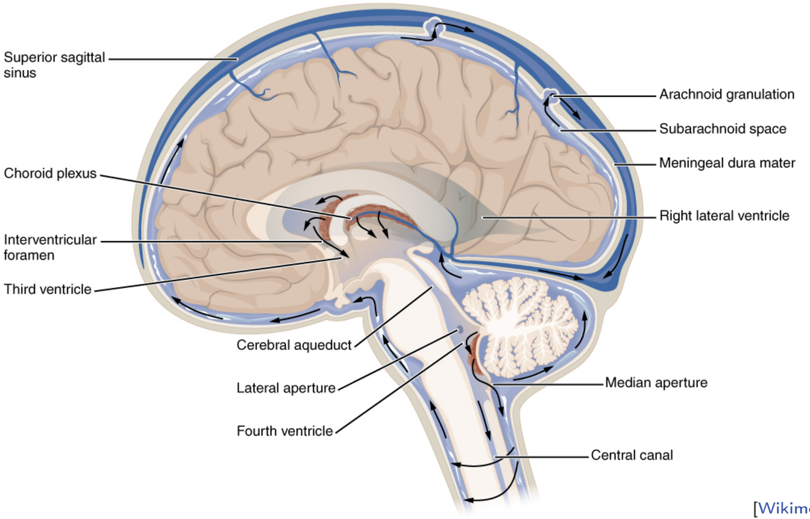
Mathematical modeling of the human brain - from magnetic resonance images to finite element simulation

Data and software associated with "Mathematical modeling of the human brain - from magnetic resonance images to finite element simulation" by Mardal, Rognes, Thompson and Valnes (2021).

[https://zenodo.org/communities/mri2fem/]

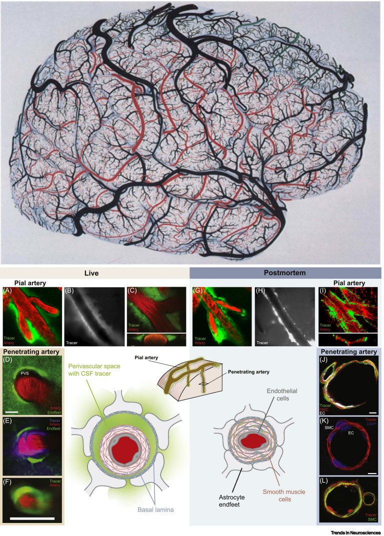
The brain’s waterscape: anatomy

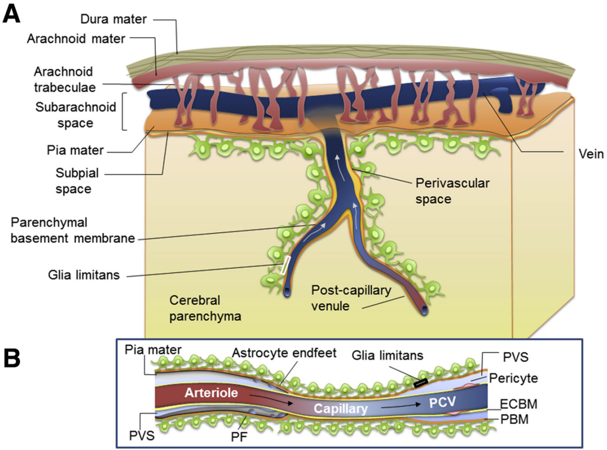
Cerebrospinal fluid (CSF) circulates in spaces surrounding the brain



[Wikimedia Commons]

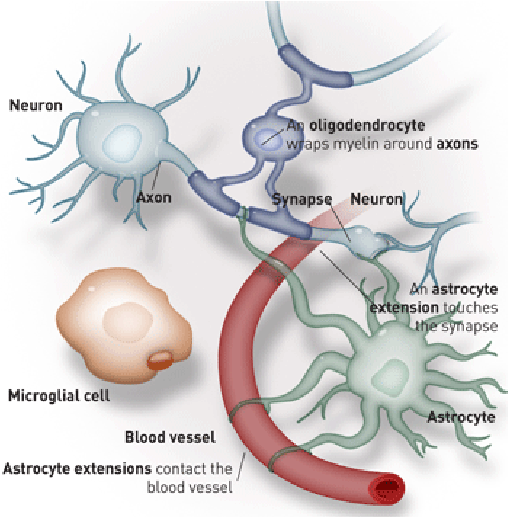
Brain vasculature and paravascular spaces

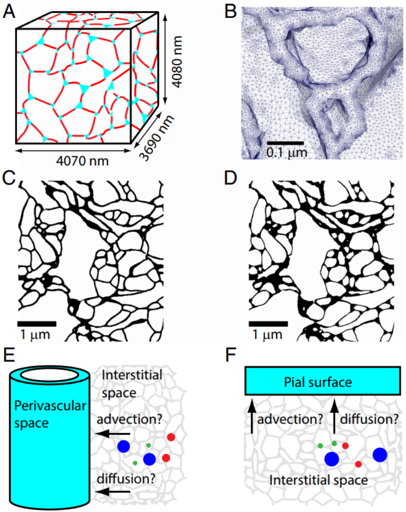




[Uludag et al (2018) (Fig. 2); Mestre, Mori and Nedergaard (2020) (Fig. 2); Kaufman-Francis et al (2018) (Fig. 1)]

Brain anatomy at the cellular level

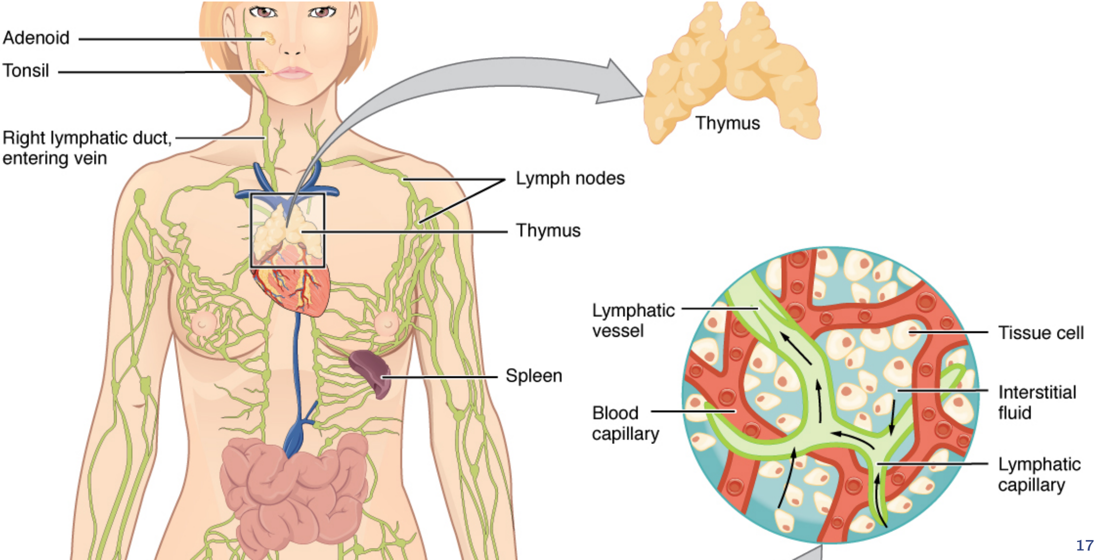




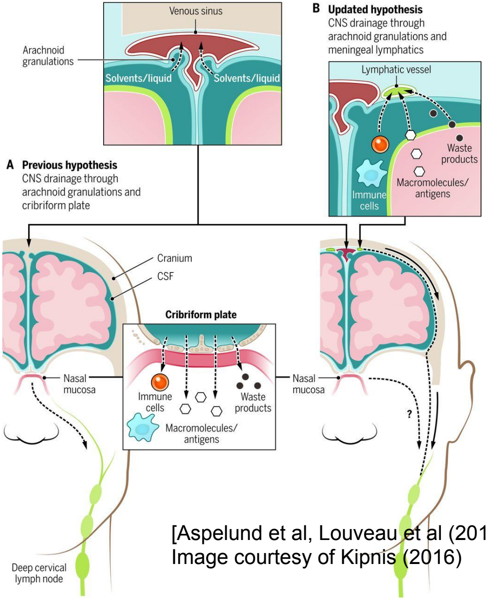
[Stanford Medicine (2009); Holter et al (2017) (Fig 1)]

The brain's waterscape: physiology

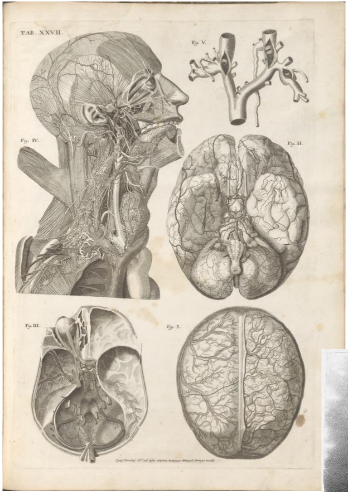
The lymphatic system drains tissue fluid and collects metabolic waste, bacteria and cellular debris



Lymphatic vessels extend into the dura membrane, but not into the brain

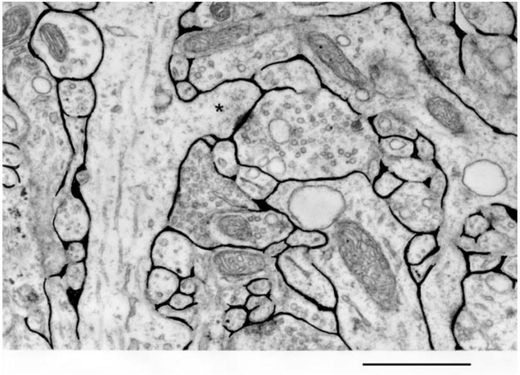


[Aspelund et al, Louveau et al (2015)]
Image courtesy of Kipnis (2016)

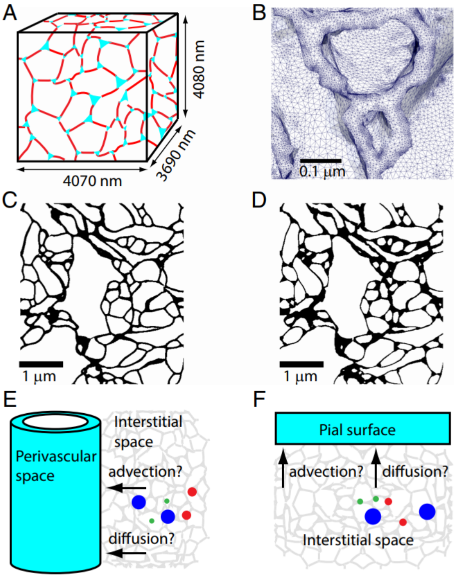


[Paolo Mascagni, *Vasorum Lymphaticorum Corporis Humani Historia et Ichnographia* (1787)]

Diffusion in the extracellular space is a driver for solute transport

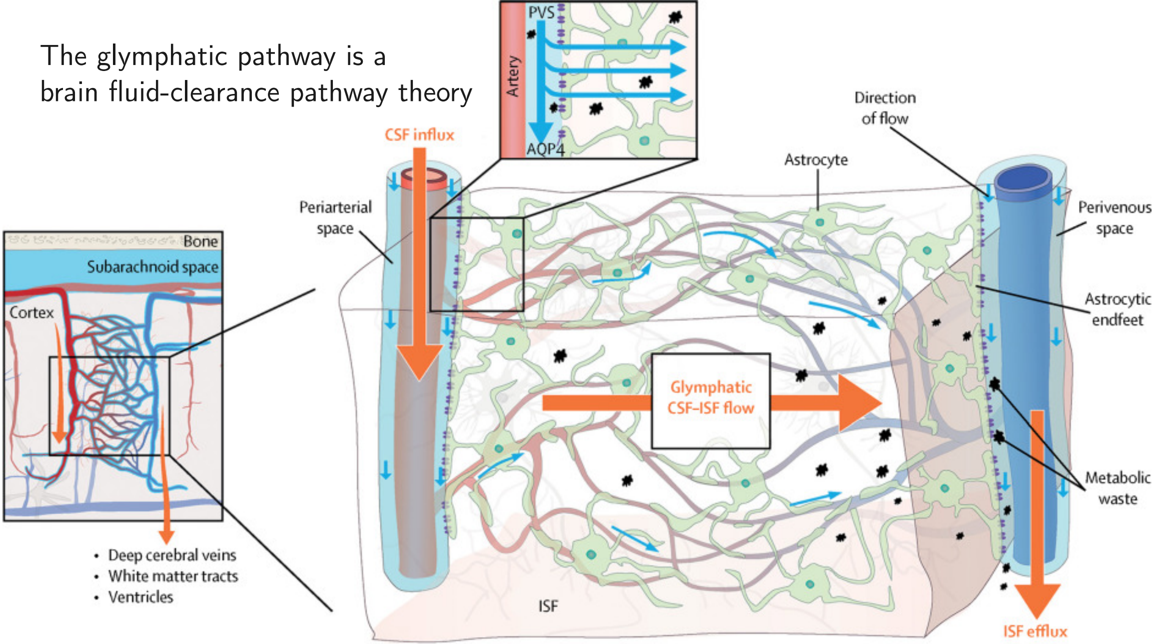


Scale bar: 1 μm



[Nicholson (2001) (Fig. 2); Holter et al (2017) (Fig. 1)]

The glymphatic pathway is a brain fluid-clearance pathway theory



[Iliff et al (2012); Rasmussen et al (2018) (Fig. 1)]

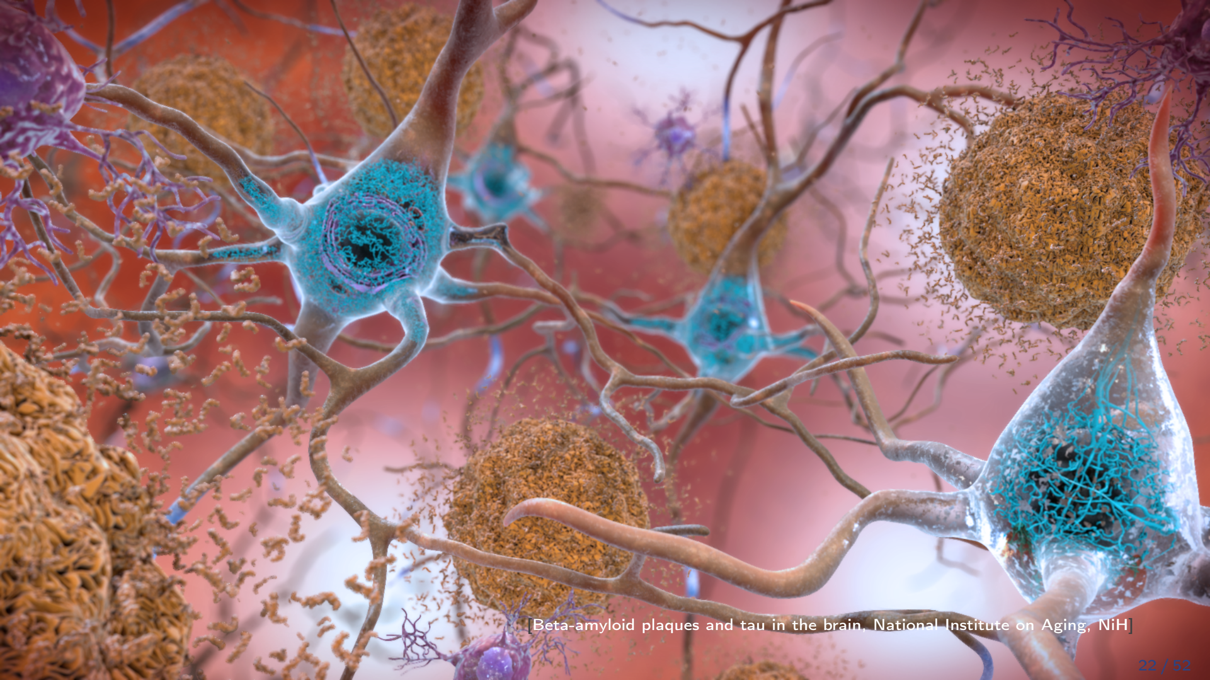
Review > Acta Neuropathol. 2018 Mar;135(3):387-407. doi: 10.1007/s00401-018-1812-4. Epub 2018 Feb 10.

The role of brain barriers in fluid movement in the CNS: is there a 'glymphatic' system?

N Joan Abbott [1], Michelle E Pizzo [2] [3], Jane E Preston [4], Damir Janigro [5] [6], Robert G Thorne [7] [8] [9] [10] [11] [12]

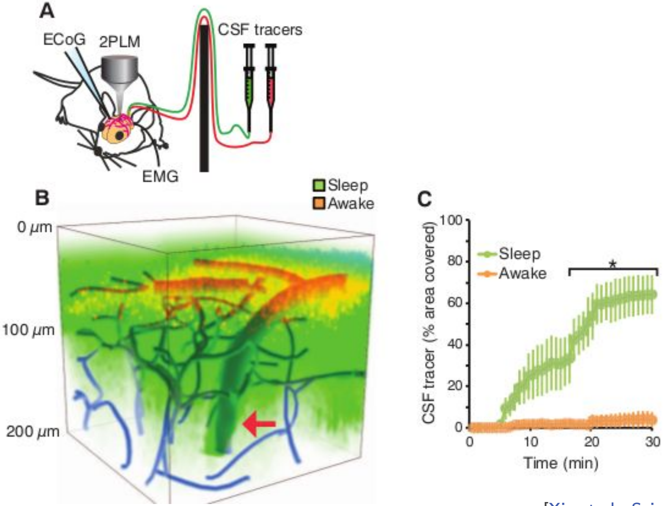
Affiliations + expand

PMID: 29428972 DOI: 10.1007/s00401-018-1812-4



[Beta-amyloid plaques and tau in the brain, National Institute on Aging, NiH]

Tracer experiments in mice indicate an increase in extracellular space volume and more rapid tracer transport during sleep



[Xie et al., Science, 2013]

FEATURE BIOMEDICINE, NEUROSCIENCE, MENTAL HEALTH

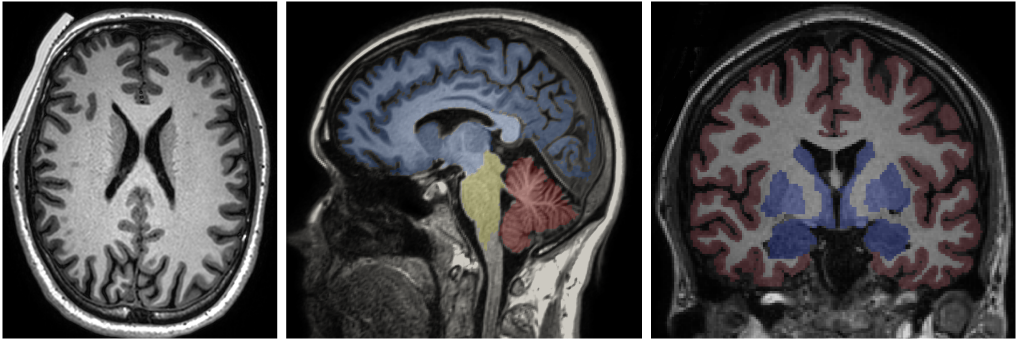
The brain may clean out Alzheimer's plaques during sleep

If sleep deprivation puts garbage removal on the fritz, the memory-robbing disease may develop

BY LAURA BEIL 6:00AM, JULY 15, 2018

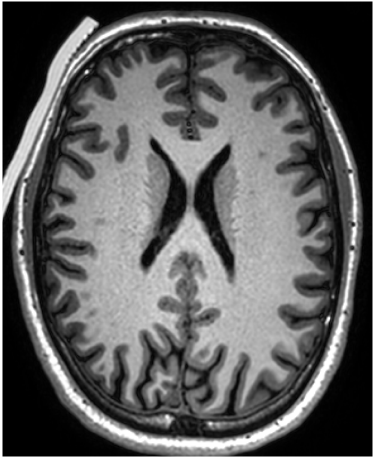
A very brief introduction to magnetic resonance imaging (MRI)

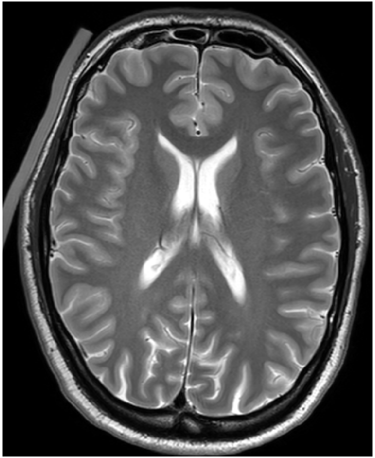
T1-weighted MRI reveals brain structure



Axial, sagittal and coronal cross-sections. T1w MRI: fat gives high signal intensity (light/white); fluids give low signal intensity (dark/black).

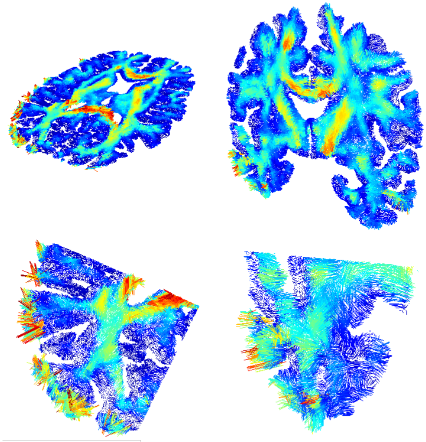
T2-weighted MRI reveals brain structure and fluids





T1w (left) versus T2w (right). In T2w MRI: fluids gives high signal intensity (light/white)

Diffusion-tensor MRI reveals water movement and directionality



In DTI: high signal intensity indicates high degree of anisotropy

Viewing and working with MRI data sets in DICOM format

Medical images are often stored in the DICOM file format: a collection of image files arranged in sequences. A DICOM viewer is useful for working with DICOM files.

Many possibilities including the basic DicomBrowser

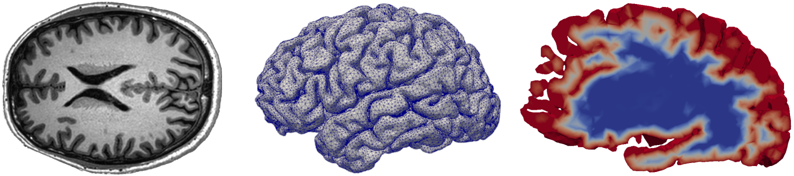
```
$ sudo apt-get install dicombrowser                    (my Ubuntu 18.04)
$ DicomBrowser &
```

Video example: downloading and viewing the mri2fem DICOM data set

A software ecosystem: from MRI to finite elements

Recommended software components

- Python3 for everything
- FreeSurfer for segmentation: https://surfer.nmr.mgh.harvard.edu/
- NiBabel for image manipulations: https://nipy.org/nibabel/
- SVM-Tk for meshing: https://github.com/SVMTK/SVMTK
- meshio for mesh conversions: https://github.com/nschloe/meshio
- FEniCS for finite elements : https://fenicsproject.org/
- ParaView for visualization: https://www.paraview.org/



A model problem: diffusion of solutes

Aim: to model and simulate the diffusion of a solute in brain regions

Model problem: diffusion equation

Find the concentration $u = u(t, x)$ at spatial points $x \in \Omega$ and time points $t > 0$ such that

$$
\begin{aligned}
u_t - \operatorname{div} D \operatorname{grad} u &= f && \text{in } (0, T] \times \Omega, && \text{(1a)} \\
u &= u_d && \text{on } (0, T] \times \partial\Omega, && \text{(1b)} \\
u(0, \cdot) &= u_0 && \text{in } \Omega. && \text{(1c)}
\end{aligned}
$$

From T1 images to a finite element mesh

We follow these three steps to generate a mesh from T1 images

To generate a mesh from an MRI data set including T1-weighted images, we follow three main steps:

1. extract a T1-weighted image series from the MRI dataset using DicomBrowser;
2. create (boundary) surfaces from the T1-weighted images using FreeSurfer;
3. generate a volume mesh of the interior of these using SVM-Tk.

Step 2: Using FreeSurfer to segment images and create surfaces

FreeSurfer offers the command `recon-all` to segment the brain images and reconstruct surfaces (parcellations, pial surface, white matter surface etc.)

```
$ cd mri2fem-dataset
$ cd dicom/ernie/T13D
$ recon-all -subjid ernie -i IM_0162 -all
```

This command is compute-intensive, with run times likely of 12–24 hours.
Key outputs (`mri2fem-dataset/freesurfer/ernie`) are

- `/stats`: contains files providing statistics derived during segmentation.
- `/mri`: contains volume files generated during segmentation
- `/surf`: contains surface files generated during segmentation

Video example: viewing the FreeSurfer output

```
$ cd mri2fem-dataset/freesurfer/ernie/surf
$ freeview # Open lh.pial
$
$ mris_convert ./lh.pial pial.stl
$ paraview # Open lh.pial.stl
```

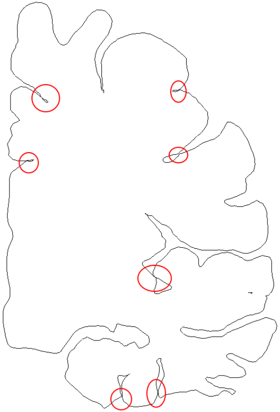
The surfaces may need enhancement to be suitable for finite element meshes

In practice, brain surfaces generated from T1 images

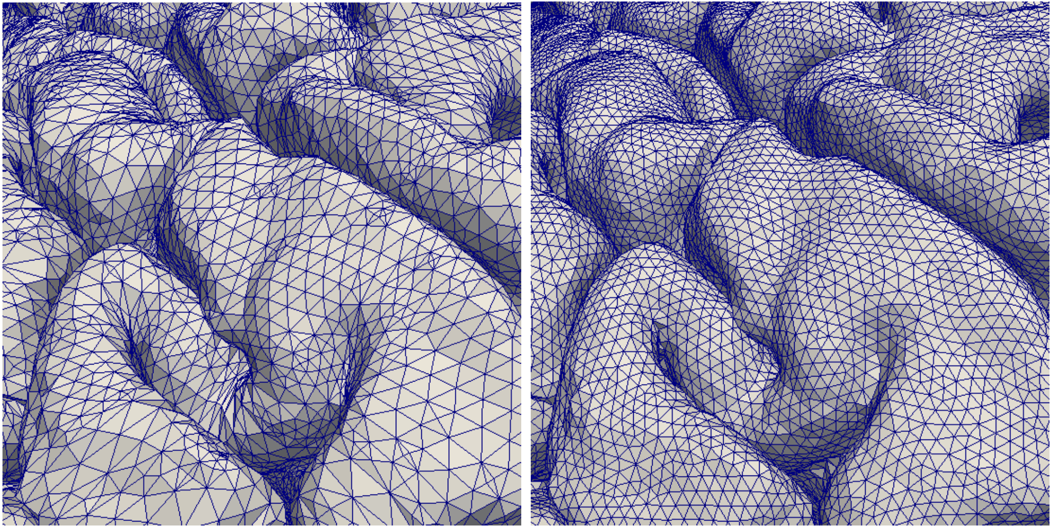
- may have unphysiologically sharp corners,
- may include triangles with very large aspect ratios,
- have topological defects such as holes, and
- may self-intersect or overlap with other surfaces.

Result: Low quality meshes (if any).

Fix: Enhance surface quality prior to meshing

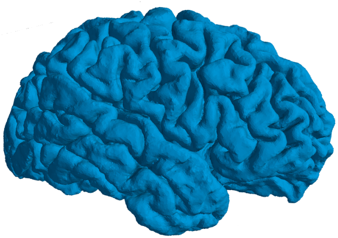


SVM-Tk (wrapping CGAL) includes utilities for remeshing surfaces

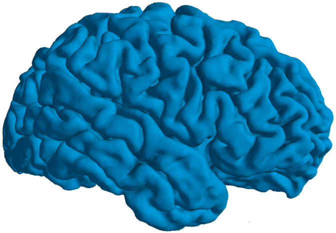


[Mardal et al (2021, Chapter 3.2.1); mri2fem/chp3/remesh_surface.py]

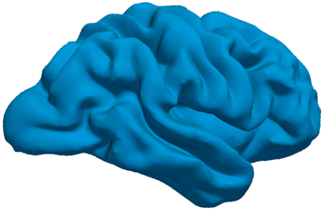
SVM-Tk includes utilities for smoothing surfaces



Original pial surface



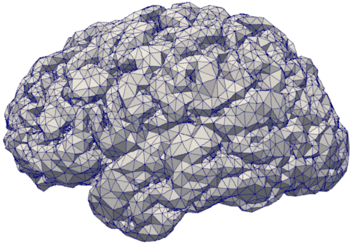
after Taubin smoothing

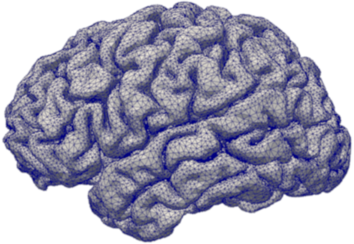


after over-smoothing.

[Mardal et al (2021, Chapter 3.2.2); mri2fem/chp3/smooth_surface.py]

SVM-Tk is designed to create brain volume meshes from surfaces





```python
import SVMTK as svmtk

def create_volume_mesh(stlfile, output, n=16):
    # Load input file
    surface = svmtk.Surface(stlfile)

    # Generate the volume mesh
    domain = svmtk.Domain(surface)
    domain.create_mesh(n)

    # Write the mesh to the output file
    domain.save(output)

# Create mesh
create_volume_mesh("lh.pial.stl", "lh.mesh")
```

[Mardal et al (2021, Chapter 3.1.3); mri2fem/chp3/surface_to_mesh.py]

Video example: creating a mesh of the left hemisphere

Numerical simulation of diffusion over the left hemisphere

Solving the diffusion equation with implicit Euler and finite elements (I)

Recall our diffusion equation:

$$u_t - \operatorname{div} D \operatorname{grad} u = f \text{ in } (0,T] \times \Omega,$$

Define discrete times:

Compute approximate solutions u_h^n of (1) such that $u_h^n \approx u(t^n)$ for each n.

We do a first-order backward difference approximation in time

and obtain:

$$\frac{1}{\tau_n}(u^n - u^{n-1}) - \operatorname{div} D \operatorname{grad} u^n = f(t^n) \quad \text{in } \Omega. \tag{2}$$

Solving the diffusion equation with implicit Euler and finite elements (II-)

$$\frac{1}{\tau_n}(u^n - u^{n-1}) - \operatorname{div} D \operatorname{grad} u^n = f(t^n) \quad \text{in } \Omega.$$

Let V_h be continuous piecewise k-polynomials relative to our mesh defining Ω.

Derive weak formulation:

Solving the diffusion equation with implicit Euler and finite elements (II)

Let V_h be continuous piecewise k-polynomials relative to our mesh defining Ω.

Multiply by test functions $\phi \in V_h$, integrate by parts, and shuffle to obtain the weak formulation:

Find the discrete solution $u_h^n \in V$ at each time $n = 1, \dots, N$ such that

$$\langle u_h^n, \phi \rangle + \tau_n \langle \operatorname{grad} u_h^n, \operatorname{grad} \phi \rangle = \langle u_h^{n-1}, \phi \rangle + \tau_n \langle f^n, \phi \rangle,$$

for all $\phi \in V_h$.

where

$$\langle u, \phi \rangle = \int_\Omega u \, \phi \, \mathrm{d}x.$$

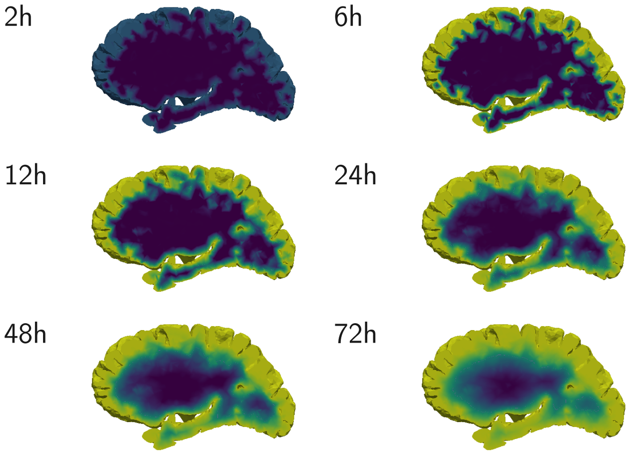
[The FEniCS tutorial (2016); Mardal et al (2021, Chapter 3.3.3); mri2fem/chp3/diffusion.py]

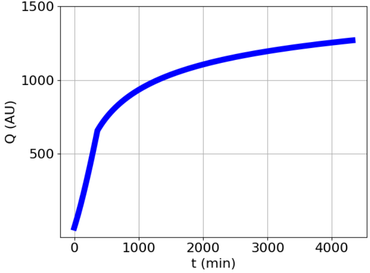
Solving the diffusion equation using FEniCS

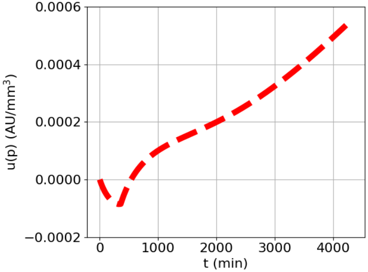
```
# Read the mesh
mesh = Mesh()
file = XDMFFile(MPI.comm_world, "ernie.xdmf") # mm
file.read(mesh)
...
# Define the finite element spaces and functions
V = FunctionSpace(mesh, "Lagrange", 1)
u = TrialFunction(V)
...
# Define the variational system to be solved at each time
a = (u*v + tau*D*dot(grad(u), grad(v)))*dx
L = (u_*v + tau*f*v)*dx
...
# Solve at each time step
for n in range(1, N+1):
    ...
    bc.apply(A, b)
    solve(A, u.vector(), b, "gmres", "amg")
```

[The FEniCS tutorial (2016); Mardal et al (2021, Chapter 3.3.3); mri2fem/chp3/diffusion.py]

Simulated tracer concentrations after injection into the SAS







Video example: simulating diffusion using FEniCS

Igor, bring me the brain!

Want to give it a try? Natural first steps:

1. Download the slides from this lecture: https://github.com/meg-simula/mri2fem-lectures.
2. Download the mri2fem data set and software from Zenodo and inspect the contents using the tools discussed.
3. Download the book: Mardal et al (2021): https://github.com/kent-and/mri2fem.
4. Install software dependencies following the instructions in Chapter 2 of Mardal et al (2021).
5. Try running some of the sample code in Chapter 3 of Mardal et al (2021).
6. Simulate something other than diffusion? Give it a try!