A cerebral circulation model for *in silico* clinical trials of ischaemic stroke

Tamás I. Józsa, Wahbi K. El-Bouri and Stephen J. Payne

UNIVERSITY OF OXFORD

tamas.jozsa@eng.ox.ac.uk

In SIlico clinical trials for treatment of acute Ischemic STroke

Lomonosov Moscow State University

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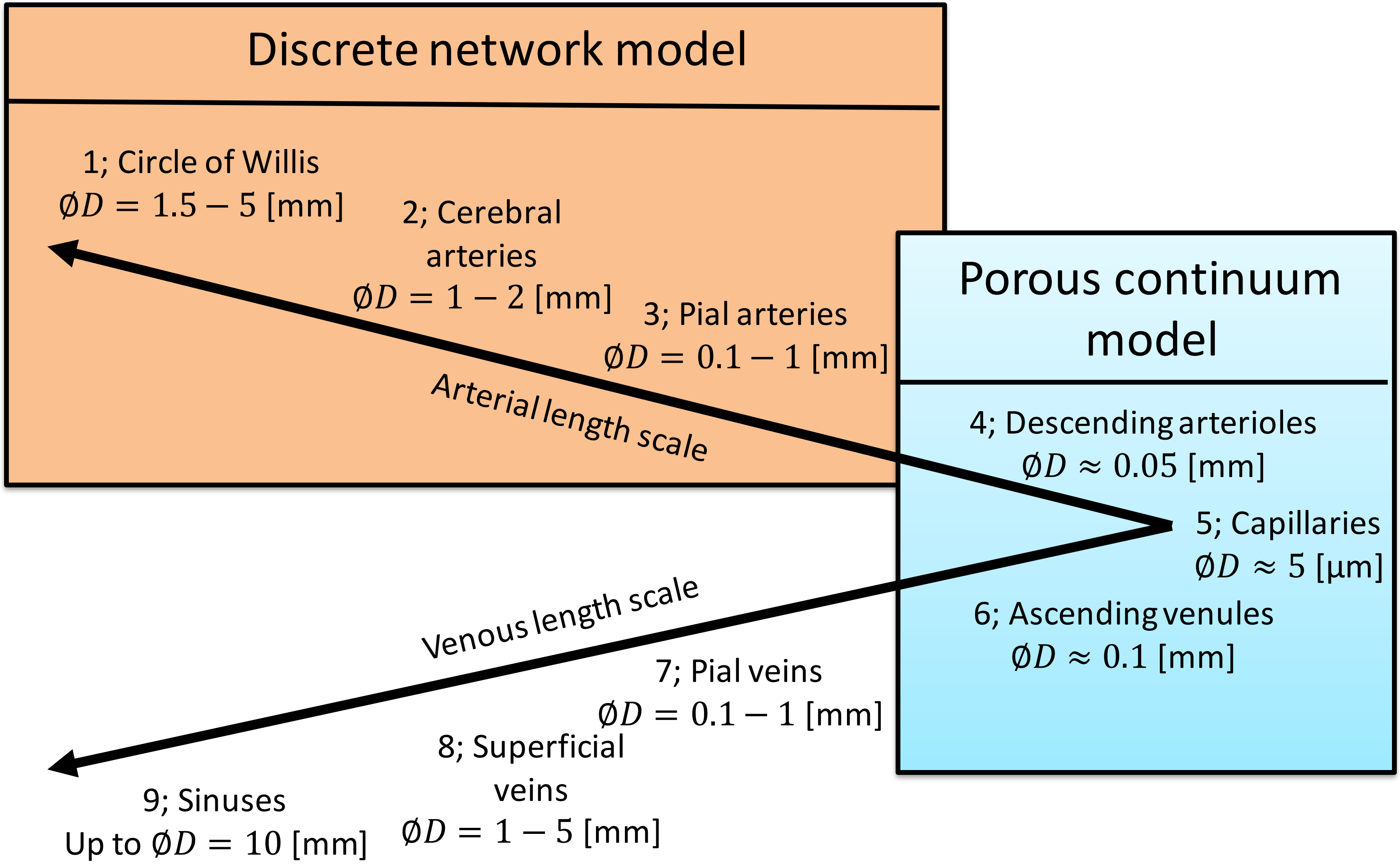
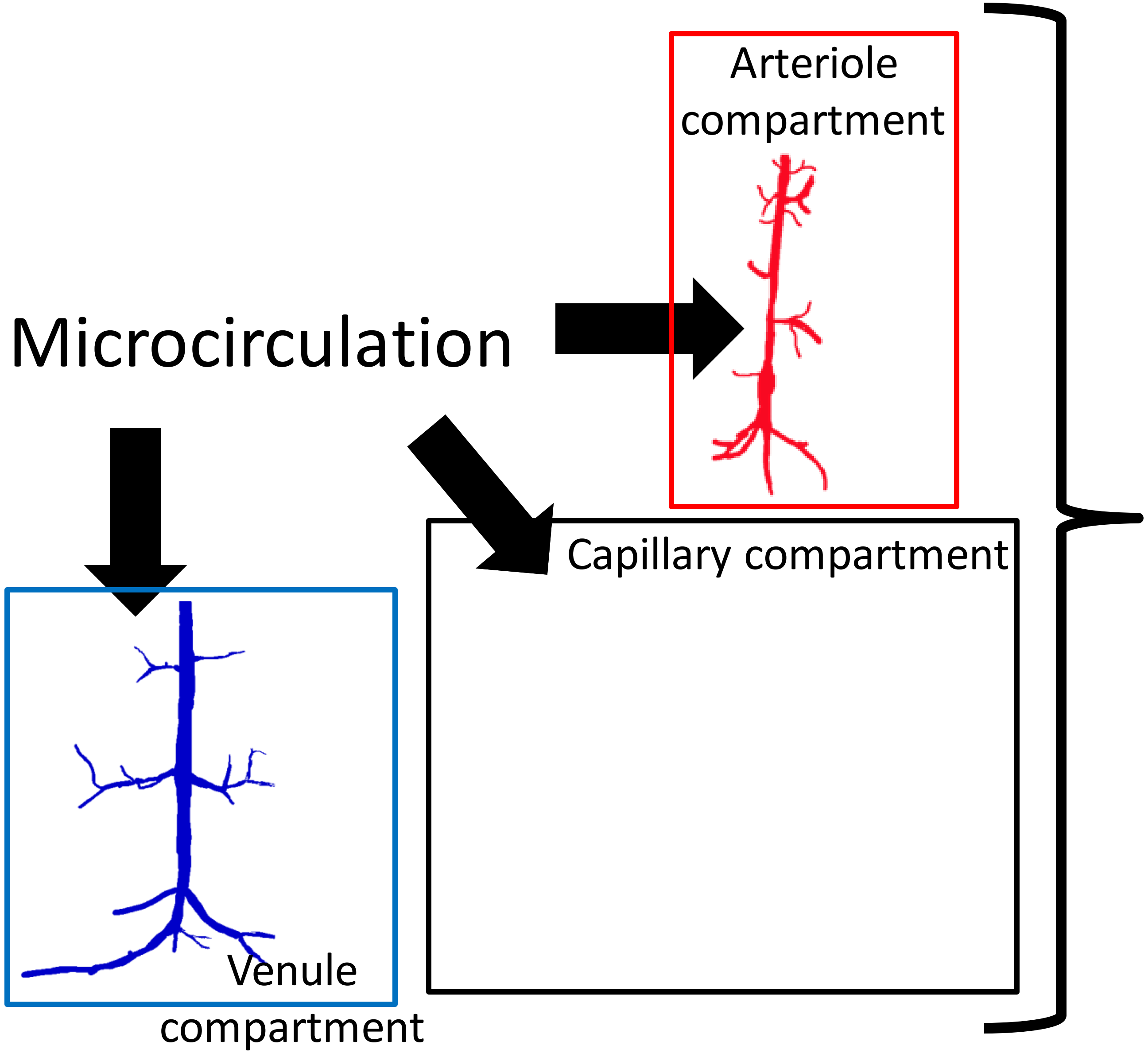
Challenges of human cerebral blood flow modelling



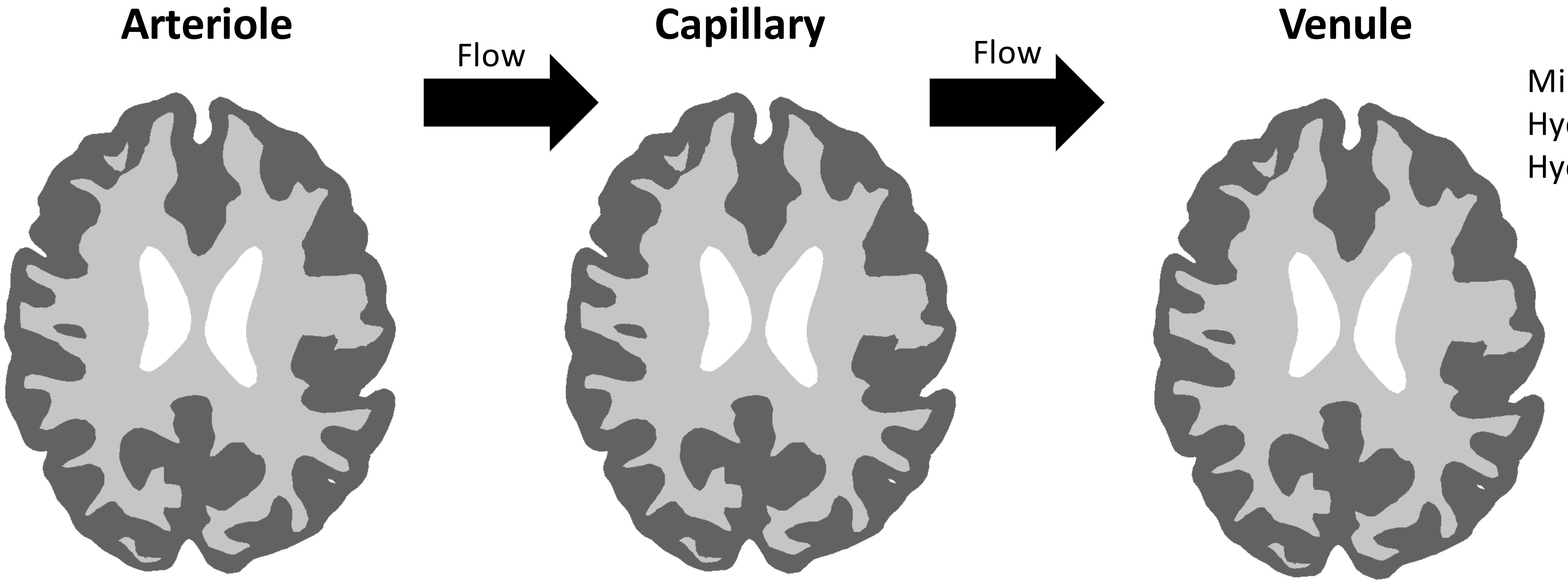
Porous compartments



Each compartment is modelled as a porous medium.

Instead of modelling individual vessels, spatially averaged blood flow is computed in the compartments and between them.

Governing equations



Michler et al. (2013), Hyde et al. (2013), Hyde *et al.* (2014)

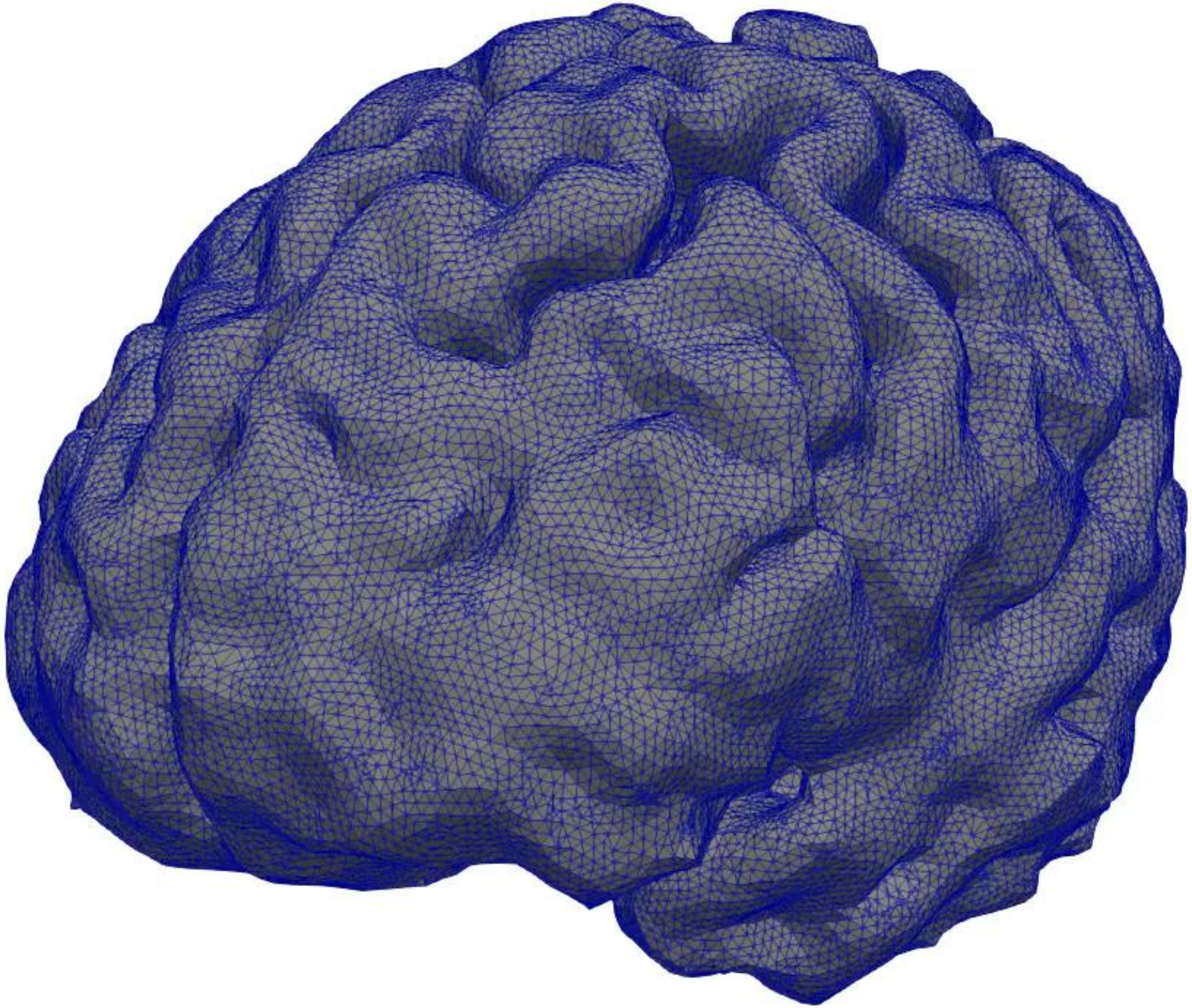
$$\nabla \cdot (\boldsymbol{K_a} \nabla p_a) - \beta_{a,c}(p_a - p_c) = 0$$
$$\nabla \cdot (\boldsymbol{K_c} \nabla p_c) + \beta_{a,c}(p_a - p_c) - \beta_{c,v}(p_c - p_v) = 0$$
$$\nabla \cdot (\boldsymbol{K_v} \nabla p_v) + \beta_{c,v}(p_c - p_v) = 0$$

a → arteriole compartment
c → capillary compartment
v → venule compartment

Fast and portable open source finite element software: FEniCS PROJECT

Logg & Wells (2010)

Brain geometry



Garcia-Gonzalez *et al.* (2018)

Model parameters

Arteriole

Capillary

Venule

Reference direction parallel to the axis of penetrating vessels $\bar{e}_{\mathrm{ref}}$

$$\boldsymbol{K}_{\boldsymbol{a}}^{\mathbf{ref}} = \begin{bmatrix} k_a & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\boldsymbol{K}_{\boldsymbol{c}}^{\mathbf{ref}} = \begin{bmatrix} k_{\mathrm{c}} & 0 & 0 \\ 0 & k_{\mathrm{c}} & 0 \\ 0 & 0 & k_{\mathrm{c}} \end{bmatrix}$$

$$\boldsymbol{K}_{\boldsymbol{v}}^{\mathbf{ref}} = \begin{bmatrix} k_{\mathrm{v}} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

In grey matter

$k_{\mathrm{a}} = 2.27$

$k_{\mathrm{c}} = 4.28 \times 10^{-4}$

$k_v = 7.78$

$[\mathrm{mm}^3\ \mathrm{s}\ \mathrm{kg}^{-1}]$

In white matter (estimation)

$k_{\mathrm{a}} = 0.75$

$k_{\mathrm{c}} = 1.43 \times 10^{-4}$

$k_v = 2.59$

$[\mathrm{mm}^3\ \mathrm{s}\ \mathrm{kg}^{-1}]$

$\beta_{\mathrm{a,c}} = 7.5 \times 10^{-6}$

$\beta_{\mathrm{c,v}} = 15 \times 10^{-6}$

$[\mathrm{Pa/s}]$

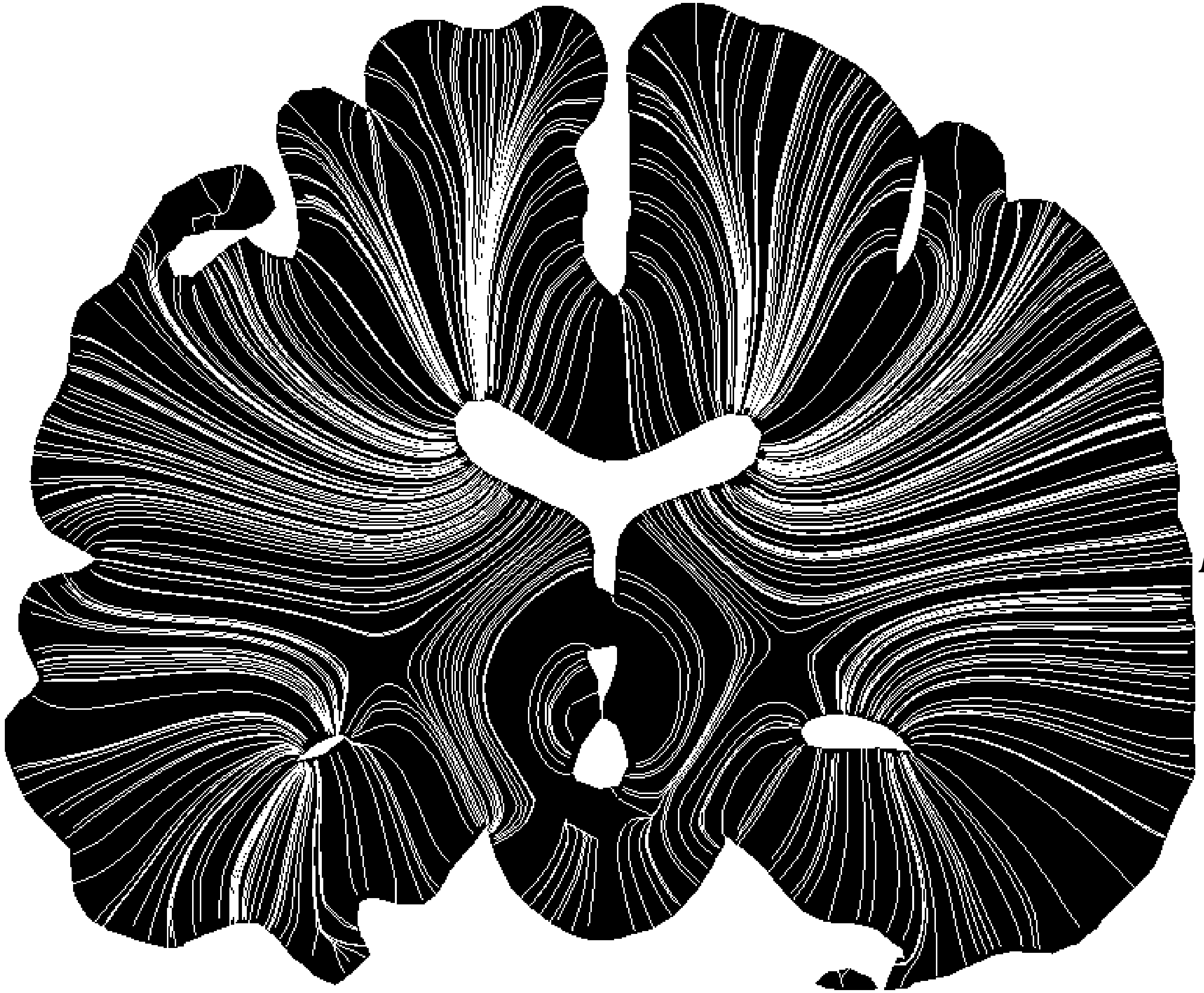
Parameter optimisation is in progress!

El-Bouri and Payne (2015, 2016, 2018)

Adjusting the permeability tensor

Arterioles/venules penetrate normal to the surface

Characteristic direction of penetrating vessels ($\bar{e}_{\mathrm{local}}$)



$$\nabla^2 a = 0$$

$$\bar{e}_{\mathrm{local}} = \nabla a$$

$$\bar{v} = \bar{e}_{\mathrm{ref}} \times \bar{e}_{\mathrm{local}}$$

$$[\bar{v}]_\times = \begin{bmatrix} 0 & -v_z & v_y \\ v_z & 0 & -v_x \\ -v_y & v_x & 0 \end{bmatrix}$$

$$\boldsymbol{R} = (\bar{e}_{\mathrm{ref}} \cdot \bar{e}_{\mathrm{local}})\boldsymbol{I} + |\bar{v}|[\bar{v}]_\times + (1 - \bar{e}_{\mathrm{ref}} \cdot \bar{e}_{\mathrm{local}})(\bar{v} \otimes \bar{v})$$

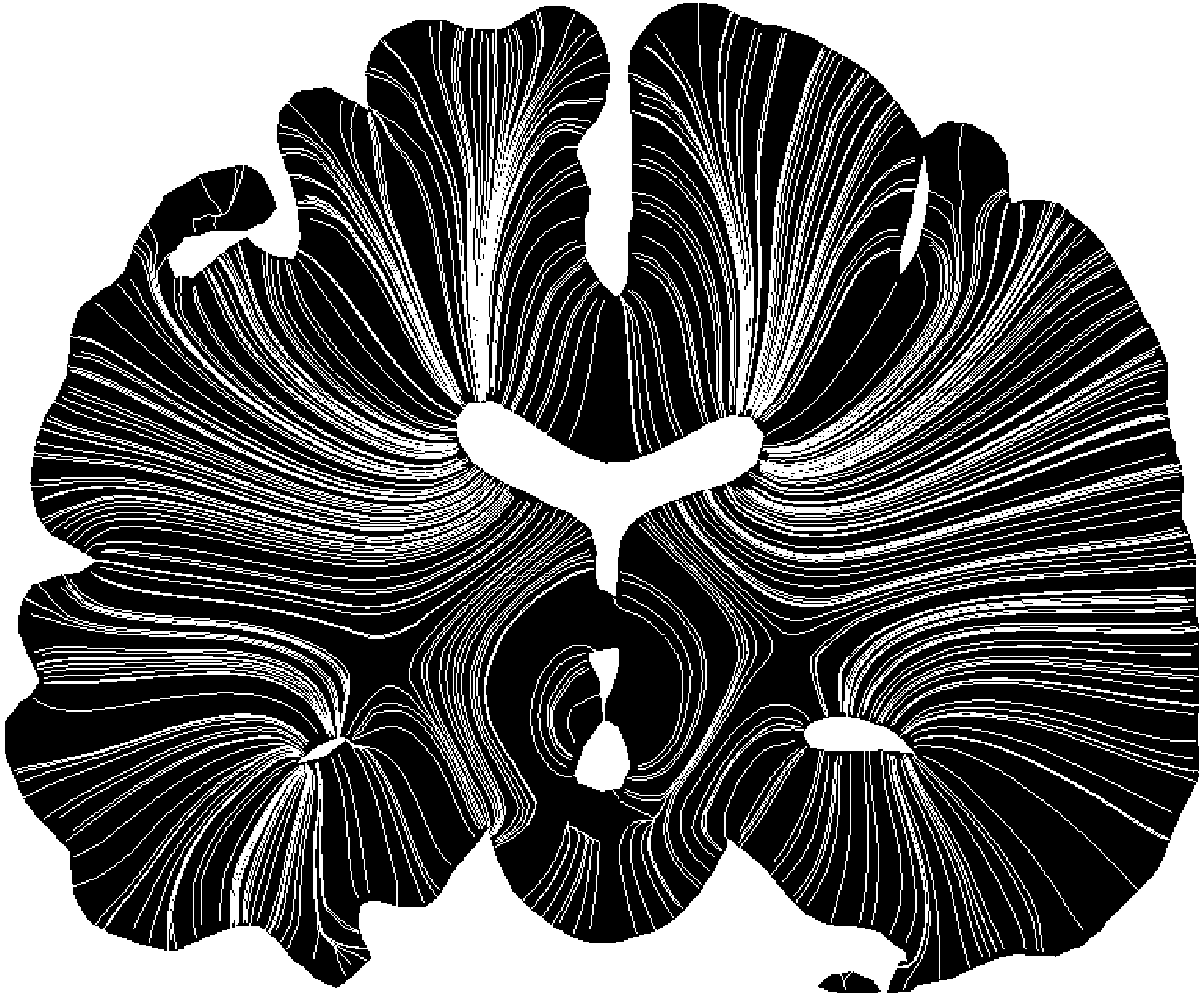
$$\boxed{\boldsymbol{K_i^{local}} = \boldsymbol{R}\boldsymbol{K}_i^{\mathbf{ref}}\boldsymbol{R}^{\mathrm{T}}}$$

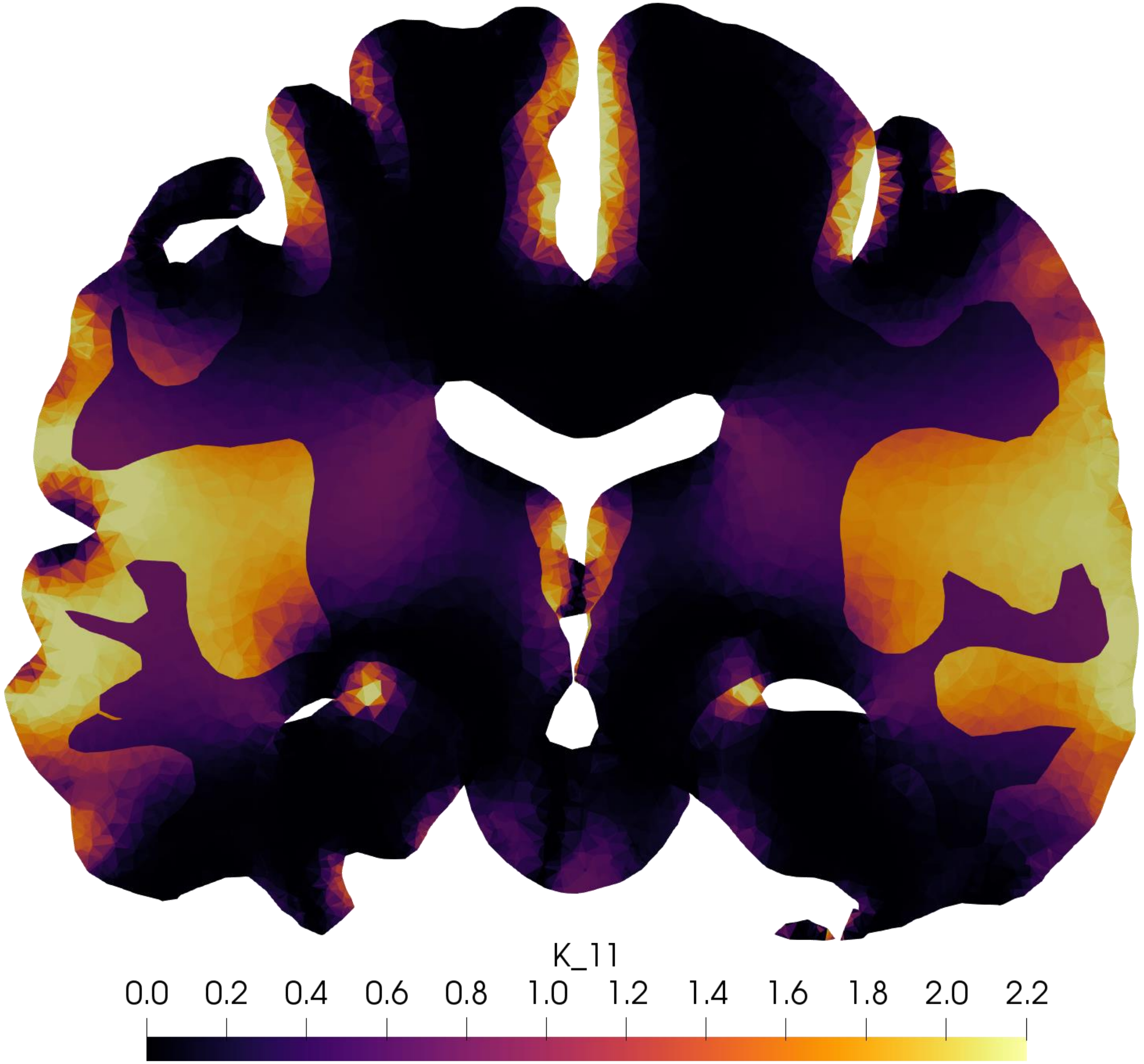
Inhomogeneous <u>and anisotropic</u> permeability

Adjusting the permeability tensor

Arterioles/venules penetrate normal to the surface

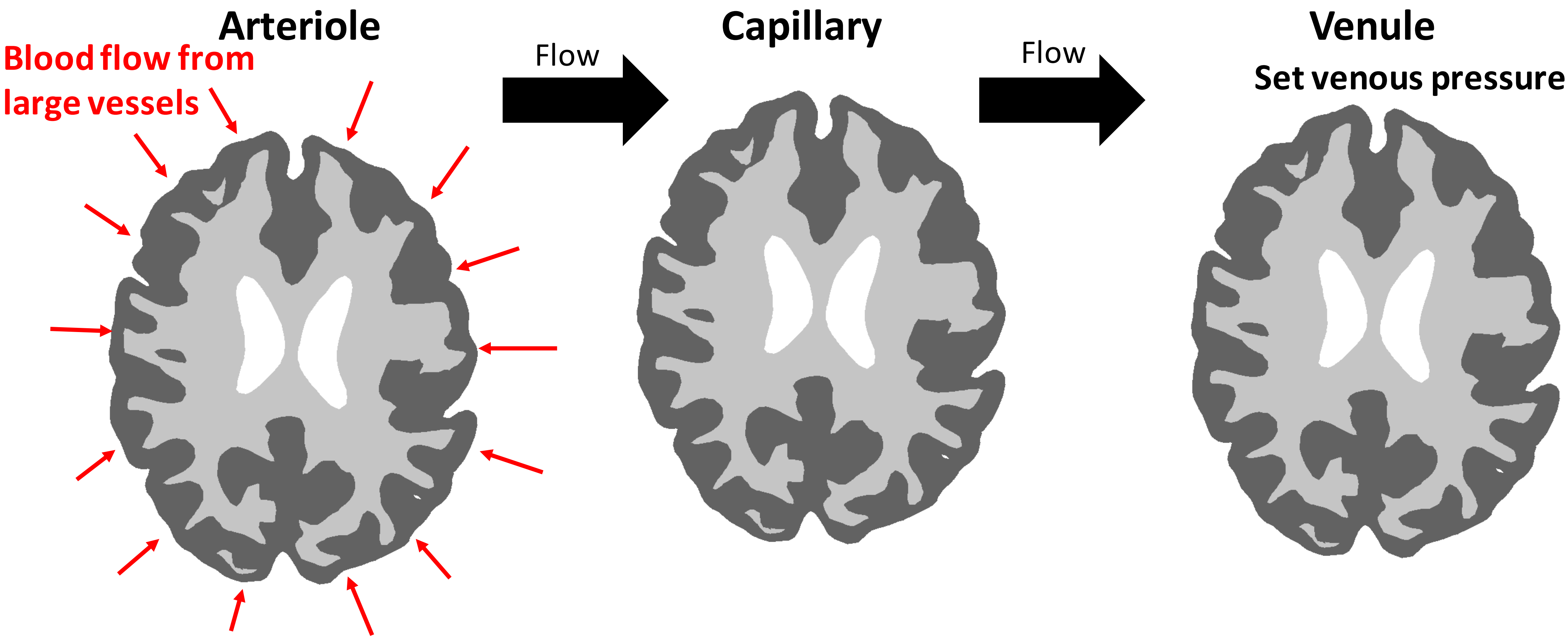
Characteristic direction of penetrating vessels ($\bar{e}_{\mathrm{local}}$)





Inhomogeneous <u>and anisotropic</u> permeability

Boundary conditions I.



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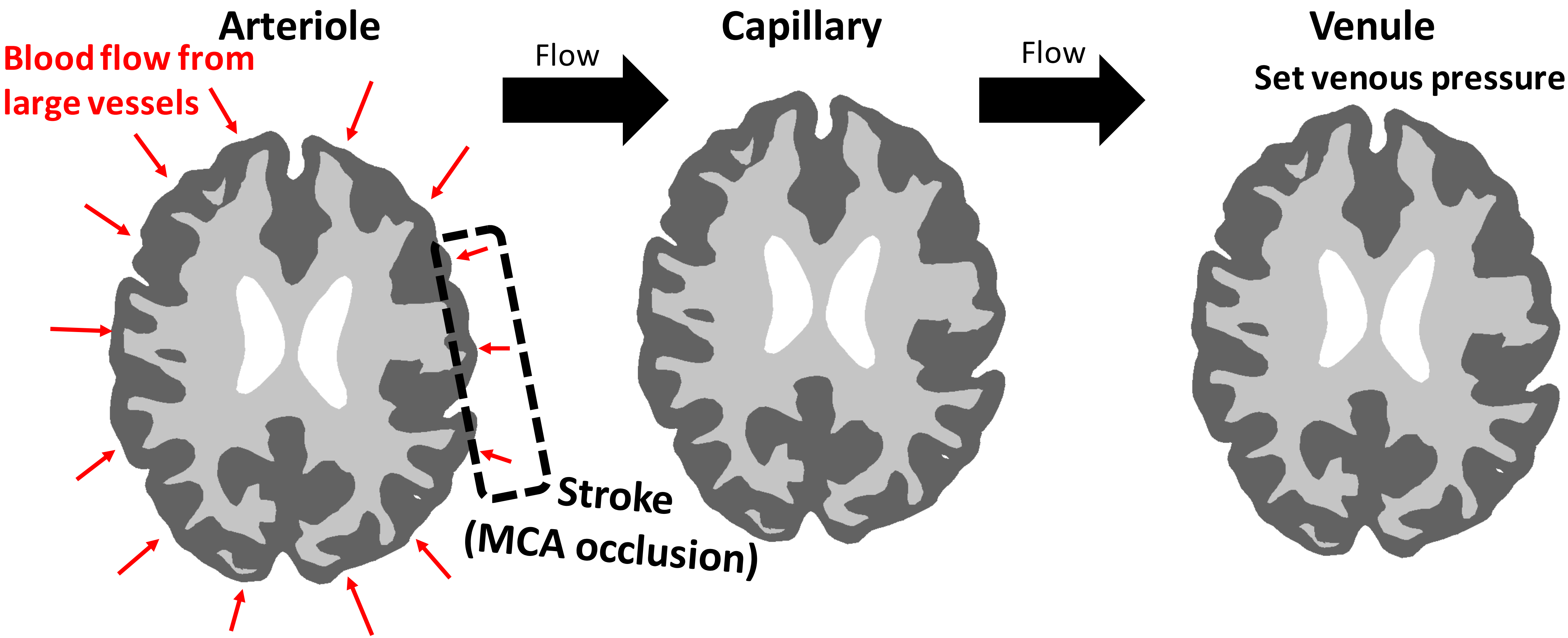
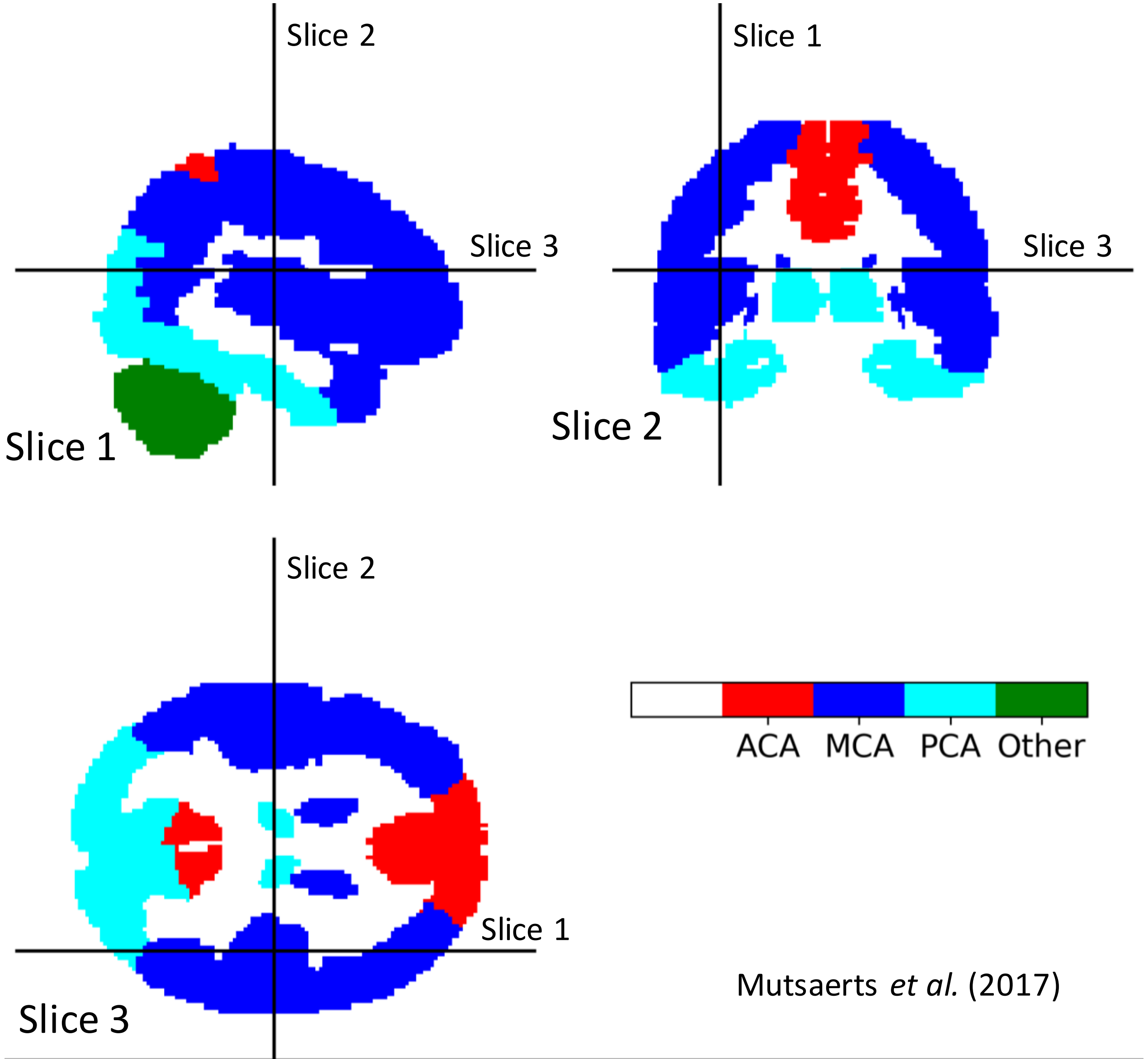


Boundary conditions II.

Vessel encoded arterial spin labelling MRI



Mutsaerts *et al.* (2017)

Mapping

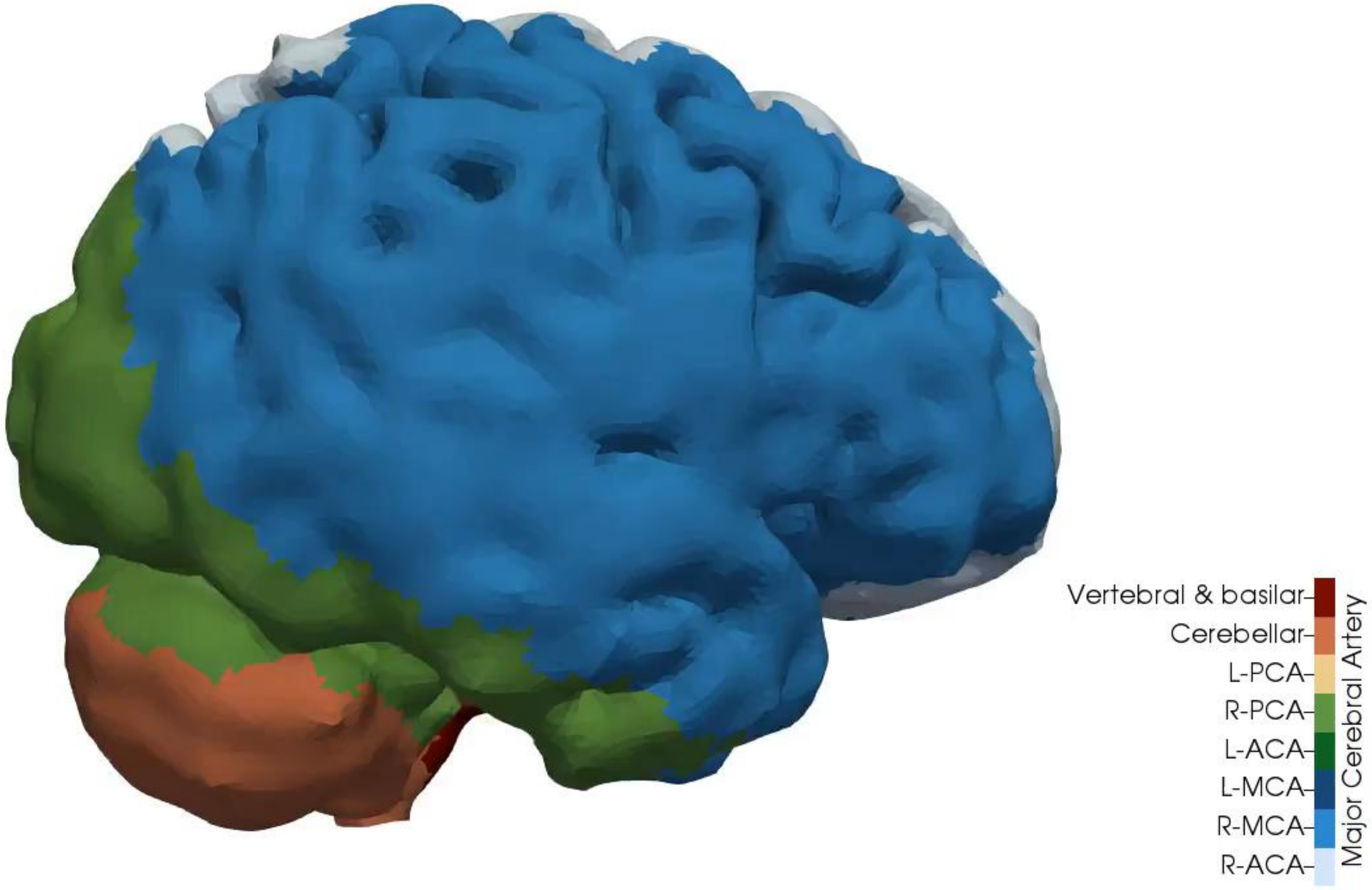
Boundary conditions III.

Vessel encoded arterial spin labelling MRI

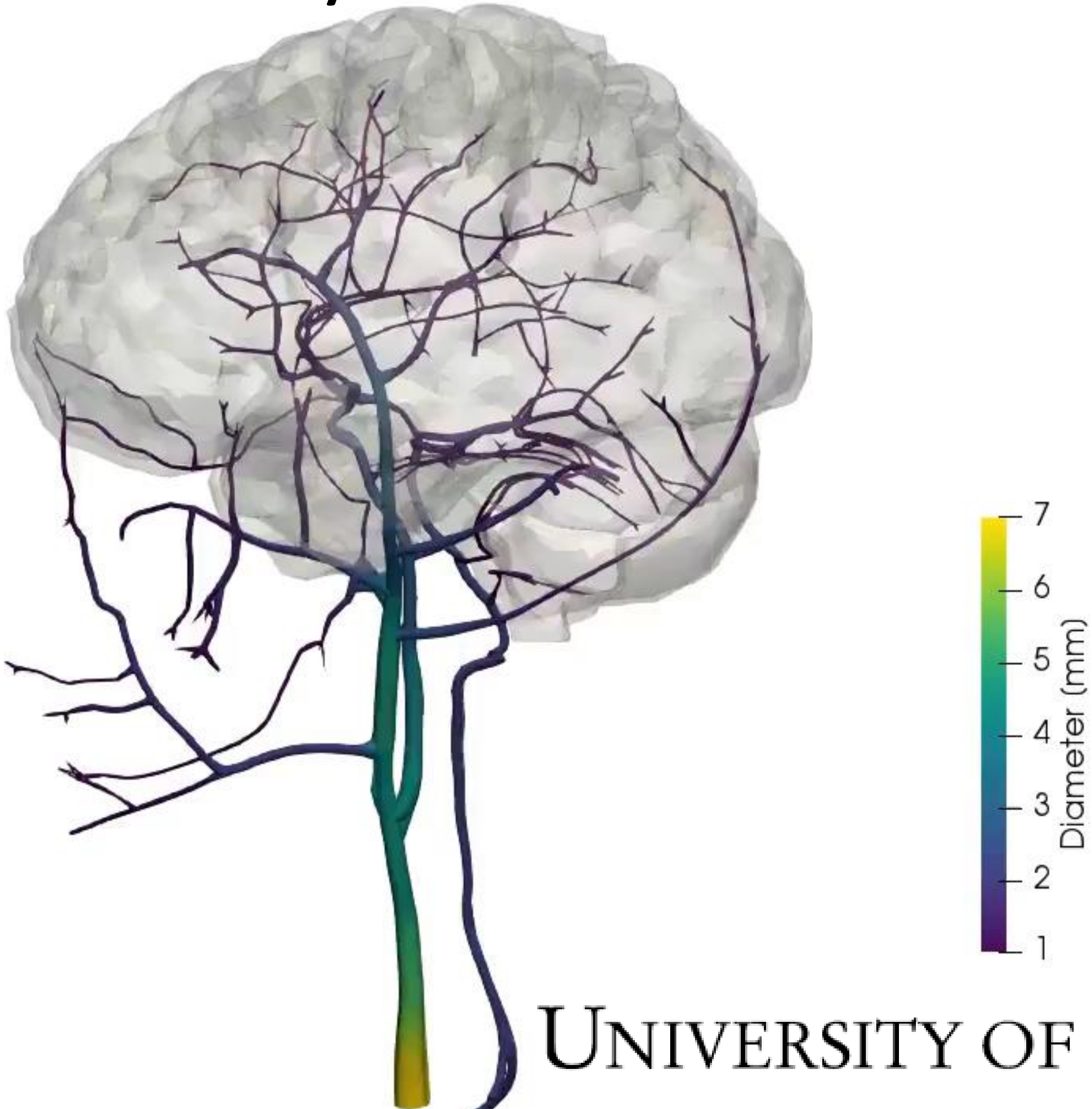
- These territories are further divided:

  8 vessel regions → 120 subregions

- A network model computes blood flow through each region which is the input of the porous microcirculation model



Boundary conditions IV.



Blanco *et al.* (2015)

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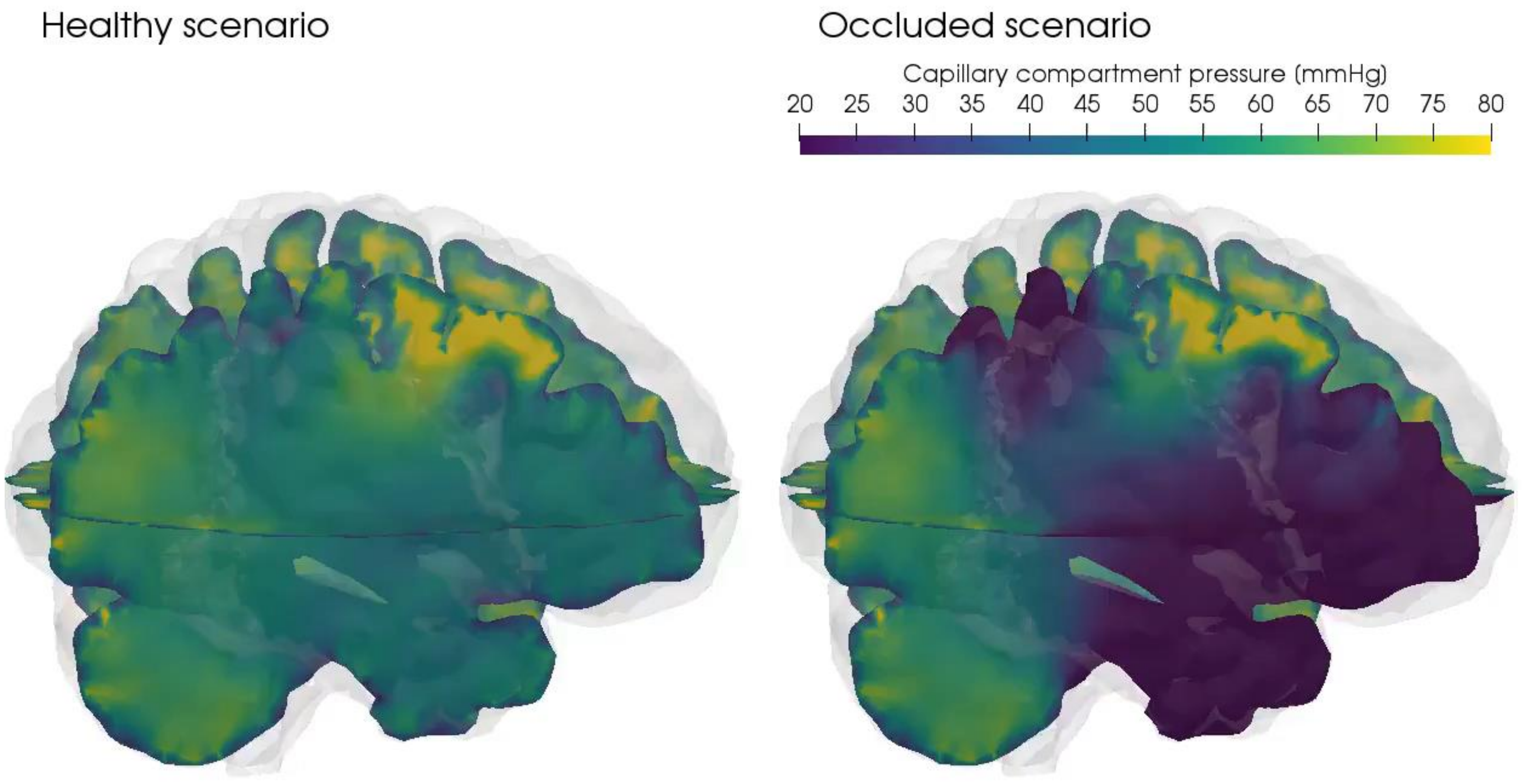
Results from the blood flow model

Outputs: volume averaged pressure and blood flow velocity in each compartment



Future tasks

- **Parameter optimization to match CT perfusion images in the baseline (healthy) scenario**

Coupling small-scale and large-scale models

For more details see Padmos *et al.* on Friday, 10:50, Kelvin Lecture Theatre

- **Oxygen transport, metabolism and cell death model development**

For more details see Bing *et al. on* Friday, 11:05, Kelvin Lecture Theatre

- **Microthrombi transport and impact of micro-occlusions**
- **Treatment modelling (thrombectomy and thrombolysis)**

For more details see Petkantchin *et al.* and Luraghi *et al.* today at 12:05 and 14:50 here

- **Extensive validation based on the Mr Clean clinical trial**
    - Infarct location & volume