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Upscaling mass transfer in brain capillary networks

Vincent Doyeux, Yohan Davit, Michel Quintard, Sylvie Lorthois

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Upscaling mass transfer in brain capillary networks

Vincent Doyeux, Yohan Davit, Michel Quintard, Sylvie Lorthois

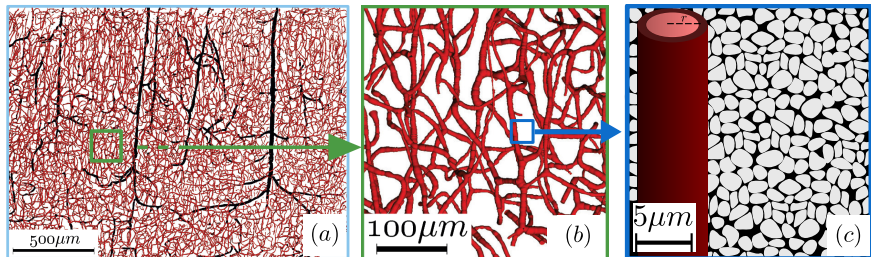
Fluid Mechanics Institute of Toulouse (IMFT) - France



Hybrid continuous/network models for large scale simulation

Simulating Mass Transfer in the brain: a multi-scale problem

- Multi-scale problem (arterio-venous, capillary, parenchyma)
- Continuous representation of Parenchyma (Nicholson 2001, Kojic 2017, Holter 2017)
- Still need to explicitly resolve the vessels
- **Upscale the capillary bed, including vessels and parenchyma**
- Coupling with explicit arterio-venous tree is different for the capillaries and parenchyma. **Two concentrations necessary.**



Macroscopic scale

Microscopic scale

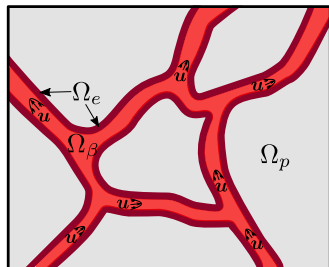
Sub-Microscopic scale

- 1 Homogenization - Equations
- 2 Fictitious Domain Framework
- 3 Verification

Mass transfer model at capillary scale

Hypotheses

- Parenchyma and endothelium are **purely diffusive** domains
- Parenchyma + endothelium = tissue,
 $\Omega_p \cup \Omega_e = \Omega_t$
- D_t spacially varying (small in Ω_e)
- Red blood cells are neglected



Two-phase capillary bed model

$$\begin{aligned}
 \partial_\tau c_\beta + \mathbf{u} \cdot \nabla c_\beta - D_v \Delta c_\beta &= 0 & \text{in } \Omega_\beta \\
 \partial_\tau c_t - D_t \Delta c_t &= 0 & \text{in } \Omega_t \\
 c_\beta &= c_t & \text{on } \partial\Omega_{\beta t} \\
 D_v \nabla c_\beta \cdot \mathbf{n} &= D_t \nabla c_t \cdot \mathbf{n} & \text{on } \partial\Omega_{\beta t}
 \end{aligned}$$

Upscaled representation of the capillary domain

Upscaled model for the two concentrations

$$\begin{aligned} \varepsilon_\beta \partial_\tau \langle c_\beta \rangle^\beta + (\varepsilon_\beta \langle \mathbf{u} \rangle^\beta - \mathbf{u}_{\beta\beta}) \cdot \nabla \langle c_\beta \rangle^\beta - \mathbf{u}_{\beta t} \cdot \nabla \langle c_t \rangle^t + \tau_m (\langle c_\beta \rangle^\beta - \langle c_t \rangle^t) \\ = \nabla \cdot (\mathbf{K}_{\beta\beta} \nabla \langle c_\beta \rangle^\beta) + \nabla \cdot (\mathbf{K}_{\beta t} \nabla \langle c_t \rangle^t) \end{aligned}$$

$$\begin{aligned} \varepsilon_t \partial_\tau \langle c_t \rangle^t - \mathbf{u}_{tt} \cdot \nabla \langle c_t \rangle^t - \mathbf{u}_{t\beta} \cdot \nabla \langle c_\beta \rangle^\beta + \tau_m (\langle c_t \rangle^t - \langle c_\beta \rangle^\beta) \\ = \nabla \cdot (\mathbf{K}_{tt} \nabla \langle c_t \rangle^t) + \nabla \cdot (\mathbf{K}_{t\beta} \nabla \langle c_\beta \rangle^\beta) \end{aligned}$$

- Equations solved on a domain without explicit representation of vessels
- Presence of capillary network taken into account through effective coefficients

Volume averaging

Averaging equations

$$\begin{aligned} \langle \partial_\tau c_\beta + \mathbf{u} \cdot \nabla c_\beta - D_v \Delta c_\beta \rangle &= 0 & \text{in } \Omega_\beta \\ \langle \partial_\tau c_t - D_t \Delta c_t \rangle &= 0 & \text{in } \Omega_t \end{aligned}$$

Decomposition in averaged and deviation

$$\begin{aligned} c_\beta &= \langle c_\beta \rangle^\beta + \tilde{c}_\beta & \langle \tilde{c}_\beta \rangle &= 0 \\ c_t &= \langle c_t \rangle^t + \tilde{c}_t & \langle \tilde{c}_t \rangle &= 0 \end{aligned}$$

- We obtain equations on $\langle c_\beta \rangle^\beta$ and $\langle c_t \rangle^t$
- Equations depend on deviation terms \tilde{c}_β and \tilde{c}_t
- Need closure equations on \tilde{c}_β and \tilde{c}_t .
- Subtracting equations on the mean to microscopic equations leads to equations on \tilde{c}_β and \tilde{c}_t .

Deviation terms as linear combination of averaged values and their gradients

$$\begin{aligned} \tilde{c}_\beta &= \mathbf{b}_{\beta\beta} \cdot \nabla \langle c_\beta \rangle^\beta + \mathbf{b}_{\beta t} \cdot \nabla \langle c_t \rangle^t - s_\beta \left(\langle c_\beta \rangle^\beta - \langle c_t \rangle^t \right) \\ \tilde{c}_t &= \mathbf{b}_{t\beta} \cdot \nabla \langle c_\beta \rangle^\beta + \mathbf{b}_{tt} \cdot \nabla \langle c_t \rangle^t - s_t \left(\langle c_\beta \rangle^\beta - \langle c_t \rangle^t \right) \end{aligned}$$

Volume averaging

Decomposition of deviation terms

$$\begin{aligned}\tilde{c}_\beta &= \mathbf{b}_{\beta\beta} \cdot \nabla \langle c_\beta \rangle^\beta + \mathbf{b}_{\beta t} \cdot \nabla \langle c_t \rangle^t - \mathbf{s}_\beta \left(\langle c_\beta \rangle^\beta - \langle c_t \rangle^t \right) \\ \tilde{c}_t &= \mathbf{b}_{t\beta} \cdot \nabla \langle c_\beta \rangle^\beta + \mathbf{b}_{tt} \cdot \nabla \langle c_t \rangle^t - \mathbf{s}_t \left(\langle c_\beta \rangle^\beta - \langle c_t \rangle^t \right)\end{aligned}$$

Effective coefficients associated

$$\begin{aligned}\mathbf{u}_{\beta\beta} &= \langle \tilde{\mathbf{u}}_{\mathbf{s}_\beta} \rangle - \frac{D_\beta}{V} \int_{\partial\Omega_{\beta t}} \mathbf{n}_{\beta t} \mathbf{s}_\beta dA \\ \tau_m &= \frac{1}{V} \int_{\partial\Omega_{\beta t}} \mathbf{n}_{\beta t} \cdot D_\beta \nabla \mathbf{s}_\beta dA\end{aligned}$$

Closure problem on s_β and s_t coefficients:

$$\begin{aligned}-\nabla \cdot (D_\beta \nabla \mathbf{s}_\beta) - \varepsilon_\beta \tau_m + \mathbf{u} \cdot \nabla \mathbf{s}_\beta &= 0 && \text{on } \Omega_\beta \\ -D_t \Delta \mathbf{s}_t - \varepsilon_t \tau_m &= 0 && \text{on } \Omega_t \\ \tau_m - \frac{1}{V} \int_{\partial\Omega_{\beta t}} (\mathbf{n} \cdot D_\beta \nabla \mathbf{s}_\beta) dV &= 0 \\ \mathbf{n} \cdot D_\beta \nabla \mathbf{s}_\beta - \mathbf{n} \cdot D_t \nabla \mathbf{s}_t &= 1 && \text{on } \partial\Omega_{\beta t} \\ &= 0 && \text{on } \partial\Omega_{\beta t} \\ \langle \mathbf{s}_\beta \rangle^\beta &= 0 \\ \langle \mathbf{s}_t \rangle^t &= 0\end{aligned}$$

Take-home idea

Obtaining the effective coefficients necessitates to **solve PDEs on a Representative Elementary Volume of the micro-structure**

Computational Framework

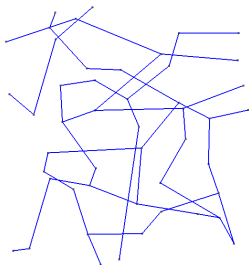
Solution proposed:

- C++/Parallel Finite element library ¹FEEL++
- Use a distance function field to capture the domain geometries
 - ▶ Mesh adaptation from distance function
 - ▶ Sub-domain localization to solve Stokes problem
 - ▶ Fictitious domain to solve advection/diffusion problem

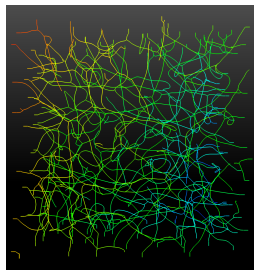
¹Prud'homme et. al. (2016), feelpp.org

- 1 Homogenization - Equations
- 2 Fictitious Domain Framework
- 3 Verification

Network geometries



$(150 \mu\text{m})^3$ network.
Secomb (2000)



$(300 \mu\text{m})^3$ network.
Ross (2005), Tsai (2009), Kleinfeld (2011),
Kaufhold 2012, Blinder (2013)

- Segment networks extracted from biological images (center-line detection)
- Need to mesh inner and outer domains (vessels and tissue)
- Difficult to mesh automatically with CAD software (design of bifurcations)
- Geometry representation needs to be robust and automated
- Solution: use a fictitious domain method

Levelset field

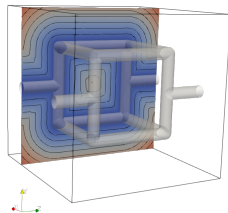
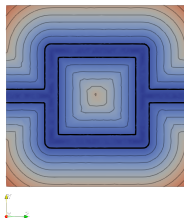
Defining ϕ_i , the distance field to centerline S_i of a vessel of radius r_i
 The distance field to the closest vessel boundary of the network is:

$$\phi(\mathbf{x}) = \min_{i=0}^{\text{Nb Vessels}} \text{dist}(\mathbf{x}, S_i) - r_i$$



Properties of ϕ :

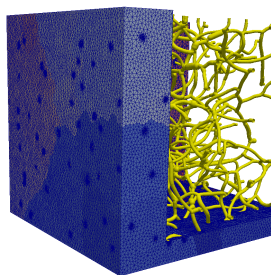
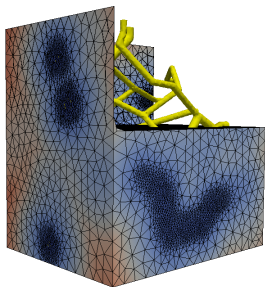
- $\phi(\mathbf{x}) < 0$ if $\mathbf{x} \in \Omega_\beta$
- $\phi(\mathbf{x}) > 0$ if $\mathbf{x} \in \Omega_t$
- $\phi(\mathbf{x}) = 0$ if $\mathbf{x} \in \partial\Omega_{\beta t}$



Mesh adaptation from distance function

Target mesh size field calculated from levelset field

$$h(\mathbf{x}) = \begin{cases} h_{\min}, & |\phi(\mathbf{x})| \leq R_1, \\ \alpha|\phi(\mathbf{x})| + \beta, & R_1 \leq |\phi(\mathbf{x})| \leq R_2, \\ h_{\max}, & |\phi(\mathbf{x})| \geq R_2 \end{cases}$$



Transport equations

Two domain problem

$$\begin{aligned} \partial_\tau c_\beta + \mathbf{u} \cdot \nabla c_\beta - D_\nu \Delta c_\beta &= 0 & \text{in } \Omega_\nu \\ \partial_\tau c_t - D_t \Delta c_t &= 0 & \text{in } \Omega_t \end{aligned}$$

$$\begin{aligned} c_\beta &= c_t & \text{on } \partial\Omega_{\beta t} \\ D_\beta \nabla c_\beta \cdot \mathbf{n} &= D_t \nabla c_t \cdot \mathbf{n} & \text{on } \partial\Omega_{\beta t} \end{aligned}$$

Prescribed B.Cs for c_β on $\partial\Omega_\beta \setminus \partial\Omega_{\beta t}$

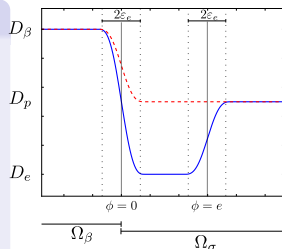
Prescribed B.Cs for c_t on $\partial\Omega_t \setminus \partial\Omega_{\beta t}$

One domain problem with spacialized coefficients

$$\partial_\tau c + \mathbf{u} \cdot \nabla c - D(\phi) \Delta c = 0 \quad \text{in } \Omega$$

Prescribed B.Cs for c on $\partial\Omega$

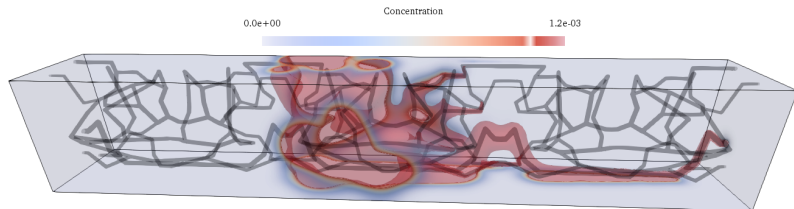
- Velocity \mathbf{u} is obtained by solving Stokes equation on the vessel domain only.
- Diffusion coefficient spatialized to take into account the BBB.



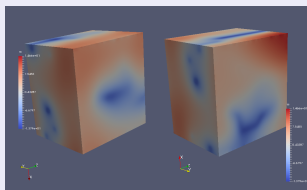
PDEs solved by our framework

The frameworks of fictitious network allows to solve:

The microscopic problem (DNS)



Closure equations to get the effective coefficients



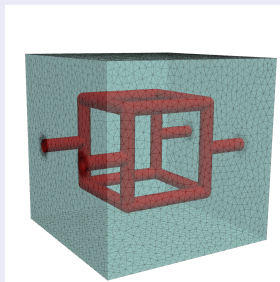
Upscaled model

- Monolithic solver used for the upscaled model
- Mesh is a simple box

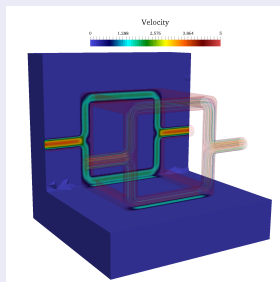
- 1 Homogenization - Equations
- 2 Fictitious Domain Framework
- 3 Verification**

Test Case, order 3 network.

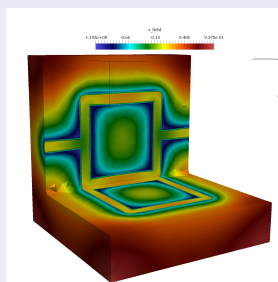
Representative Elementary Volume, size $(2 \times 2 \times 2)$



Geometry and mesh.



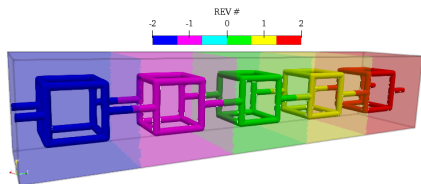
Velocity field.



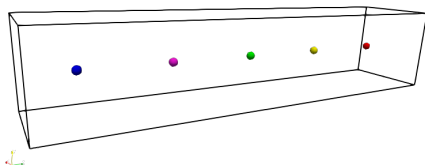
Closure variable

Comparison DNS - Homogenized model

Direct Numerical Simulation (DNS)



Darcy Scale



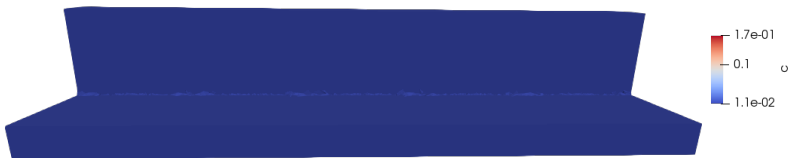
DNS

- Number of elements (tetrahedrons): 8.5×10^6
- Computational Cost: 1h on 100 cores

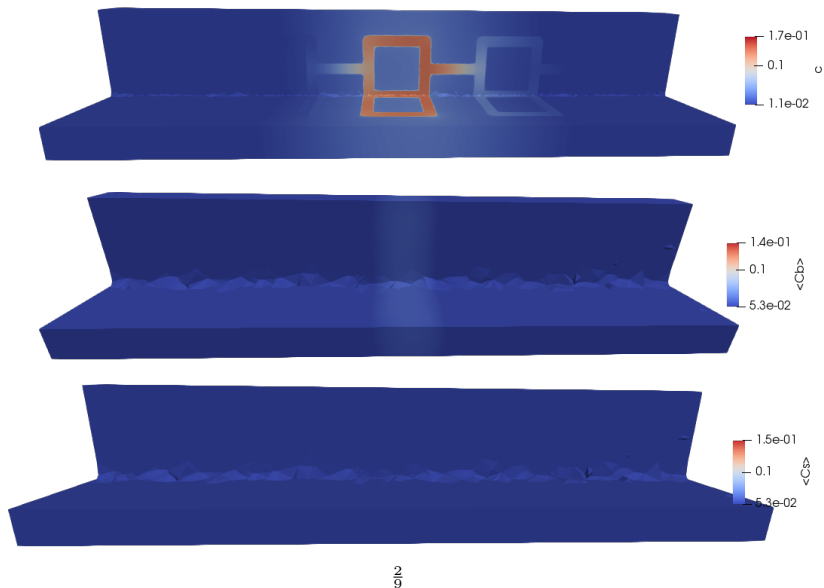
Darcy Scale

- Number of elements (tetrahedrons): 3×10^4
- Computational Cost: 10 min on 20 cores

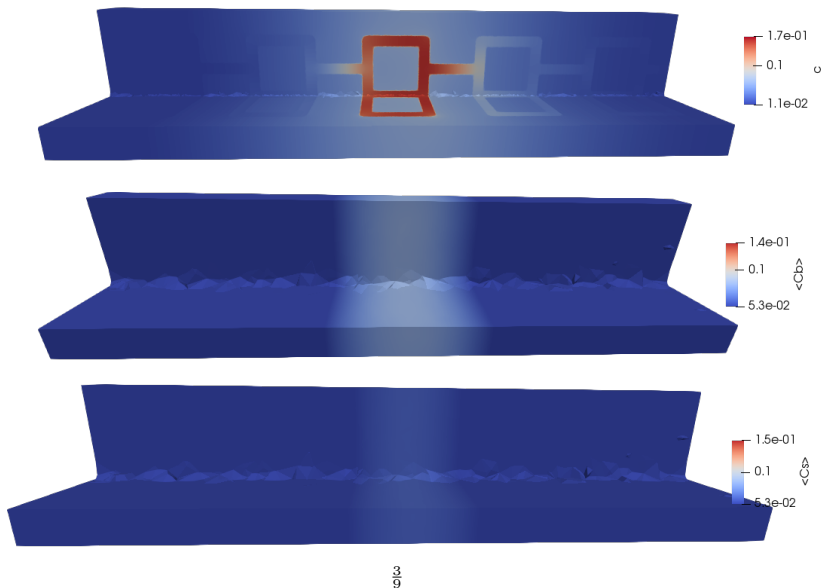
Simulation Visualization



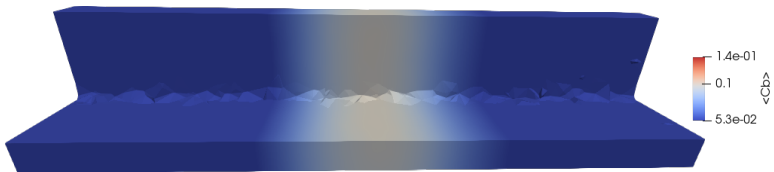
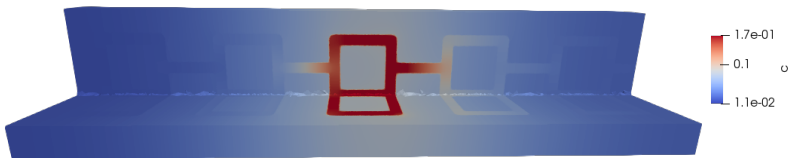
Simulation Visualization



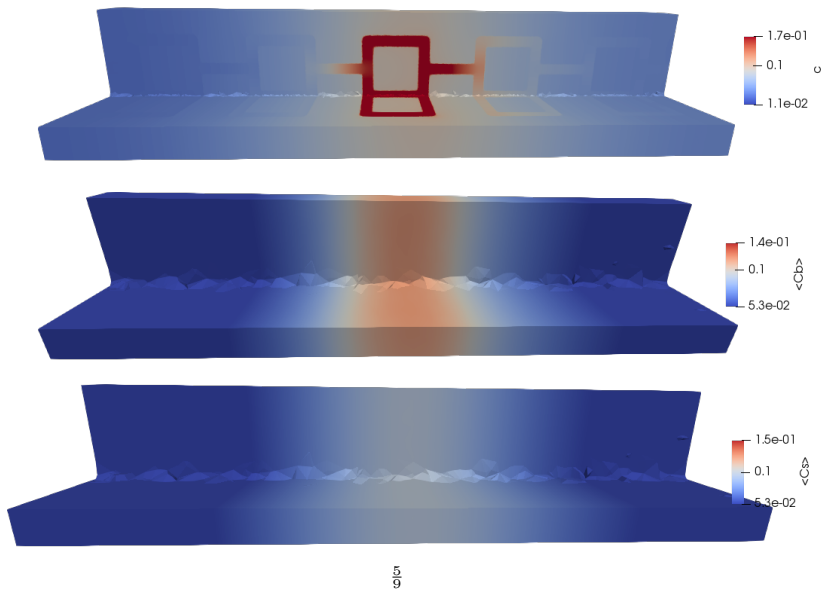
Simulation Visualization



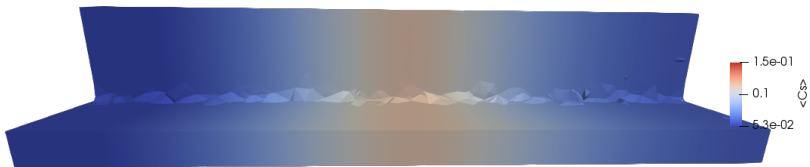
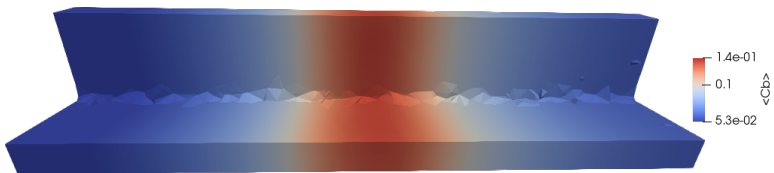
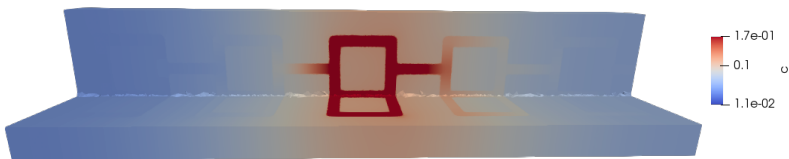
Simulation Visualization



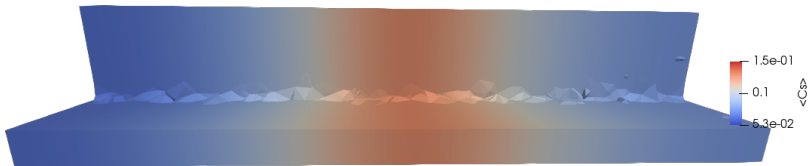
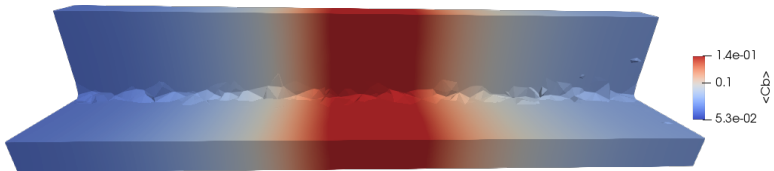
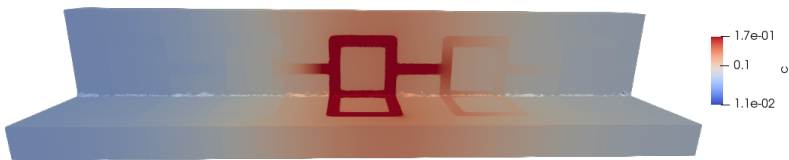
Simulation Visualization



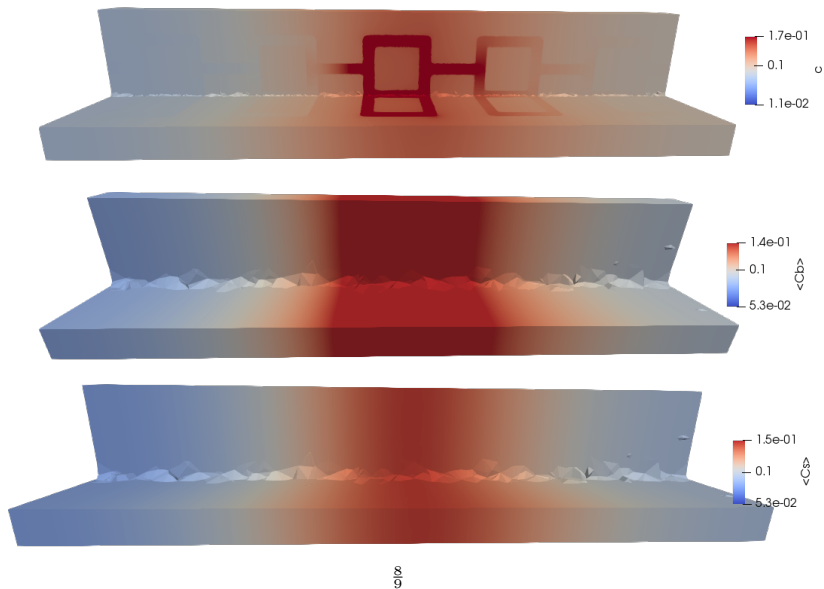
Simulation Visualization



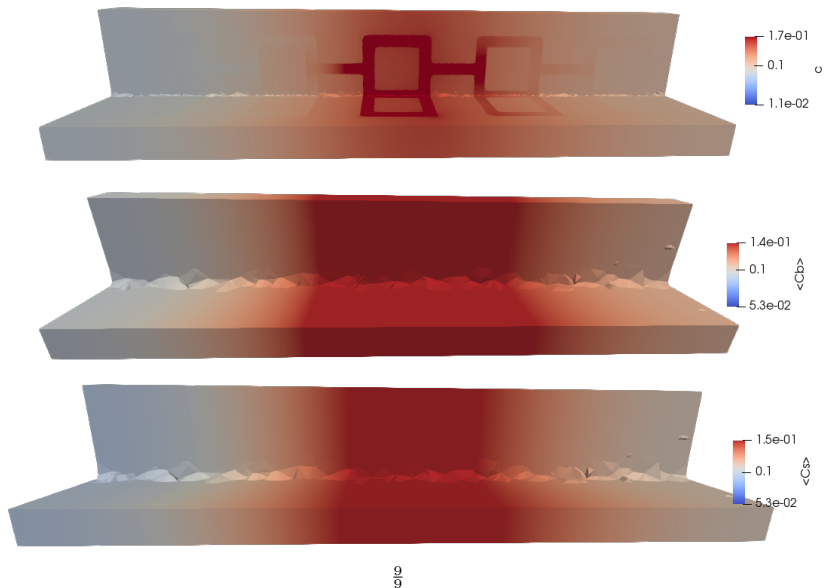
Simulation Visualization



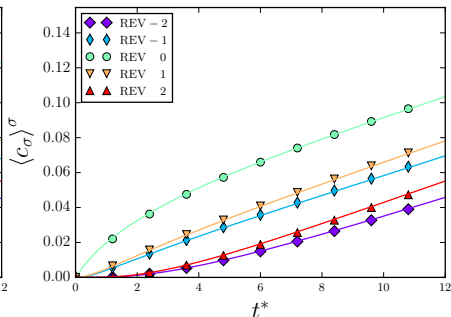
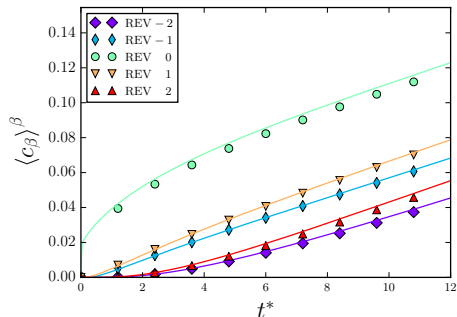
Simulation Visualization



Simulation Visualization



Quantitative comparison

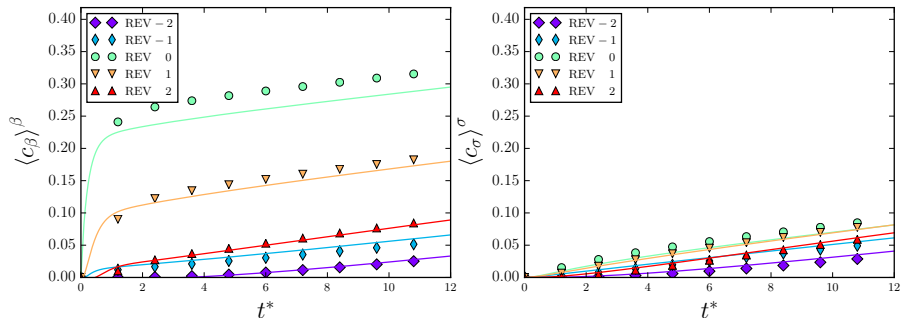


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

Quantitative comparison

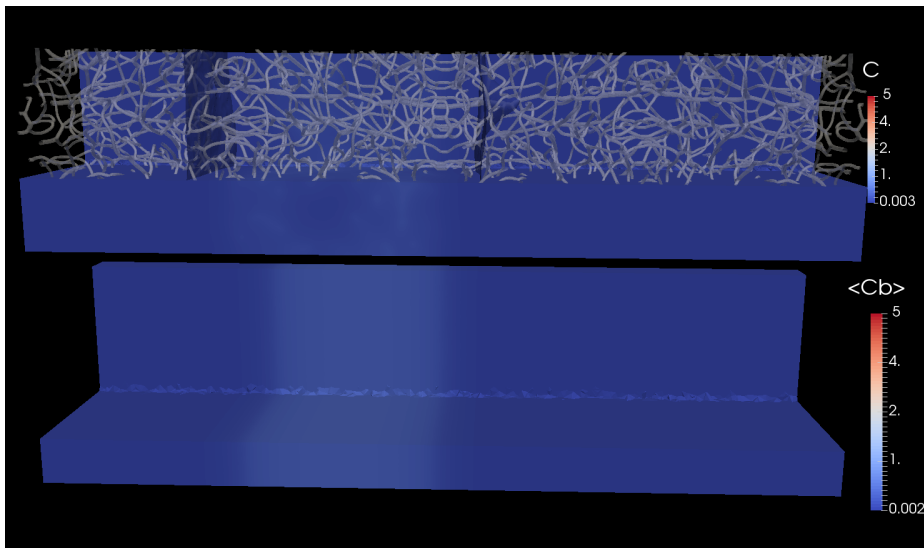


$$P_e^{\text{REV}} = 10, K_m = 3 \times 10^{-4}$$

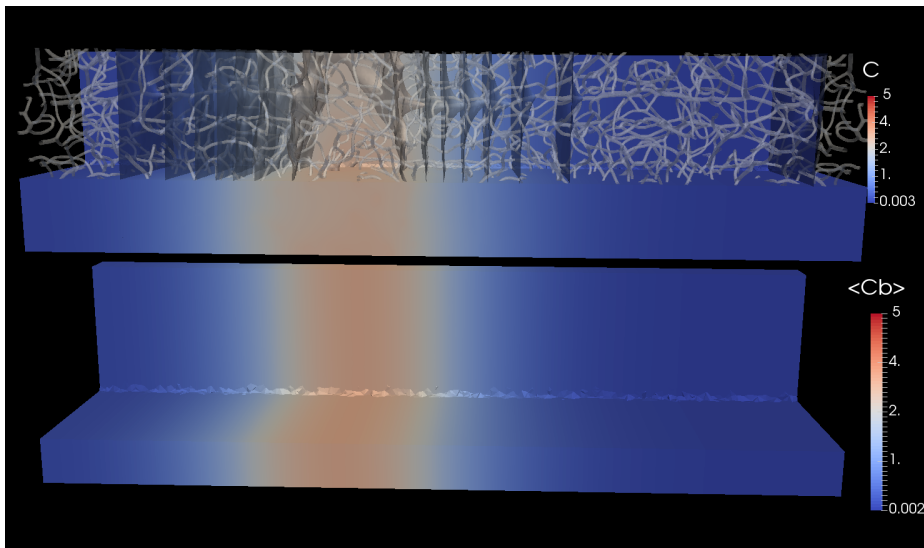
Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

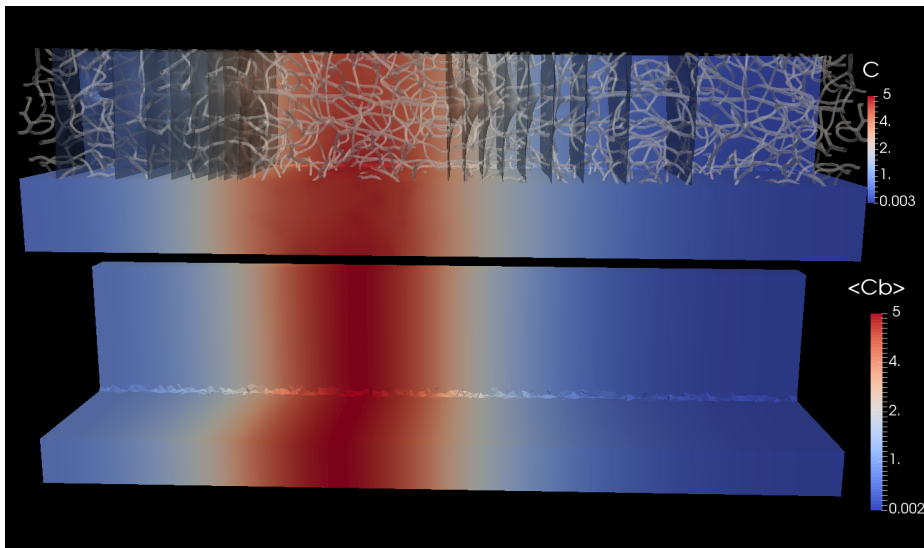
Anatomical Network

 $\frac{1}{4}$

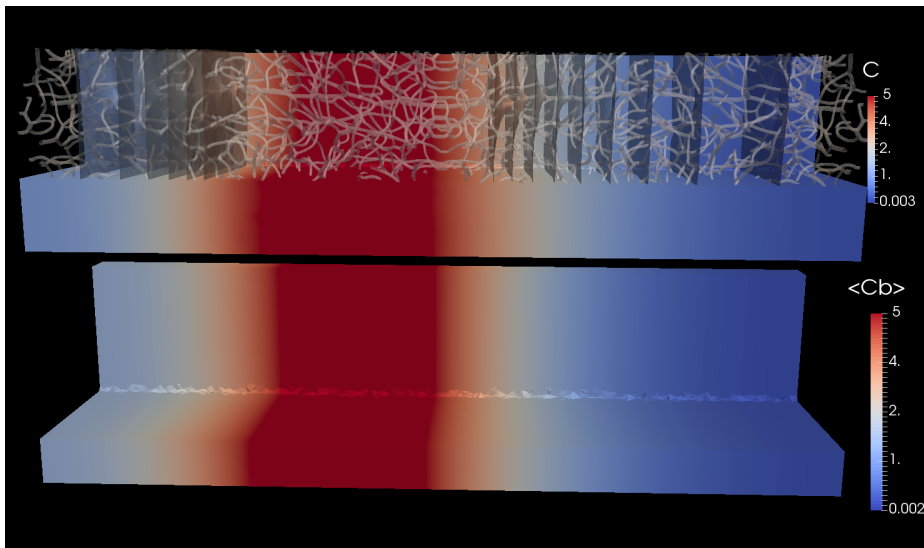
Anatomical Network



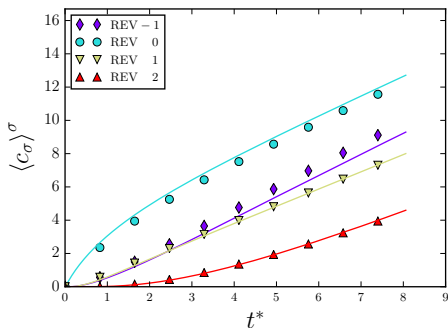
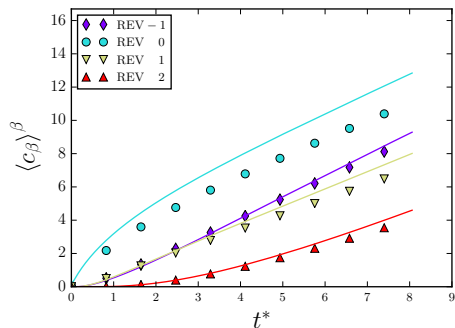
Anatomical Network



Anatomical Network



Quantitative comparison



$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

Conclusion and perspective

Conclusion

- Two-phase representation of the capillaries and tissue
- Successful upscaling of the capillary bed
- Framework using fictitious domain for DNS and Closure equations

In the future...

- Coupling with arterio-venous tree (1D-3D) or (3D-3D)
- Include the RBCs
- Include non linear consumption in tissue (Michaelis-Menten like)

Thank you!

Use of the distance function

Distance function used to:

- define a sub-domain:

$$\Omega_{vh} \subset \Omega_h, \quad \Omega_{vh} = \bigcup_i \left(\Omega_{e_i} \mid \pi_{\Omega_{e_i}}^{P_{dh}^0}(\phi) < 0 \right)$$

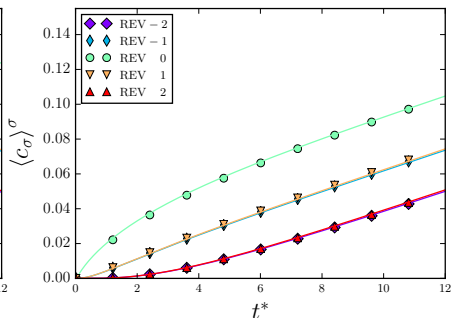
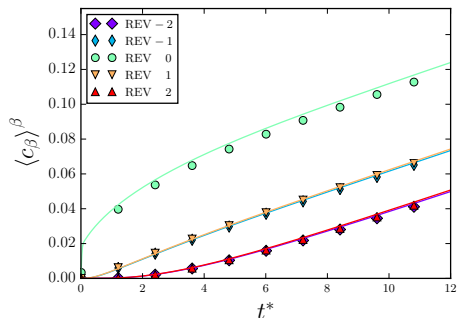
An example of projection function on a elements is given by:

$$\pi_{\Omega_{e_i}}^{P_{dh}^0} = \begin{cases} -1, & \text{if } \phi < 0 \text{ on at least one dof of } \Omega_{e_i} \\ 1 & \text{else} \end{cases}$$

- define continuously quantities having a different value in the domains thanks to a smoothed Heaviside function (level set method):

$$H_\varepsilon(\phi) = \begin{cases} 0, & \phi \leq -\varepsilon, \\ \text{smooth variations,} & -\varepsilon \leq \phi \leq \varepsilon, \\ 1, & \phi \geq \varepsilon \end{cases}$$

All results, order 3

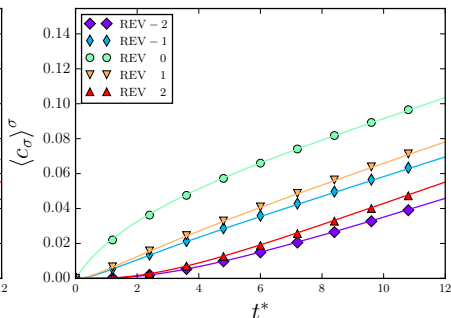
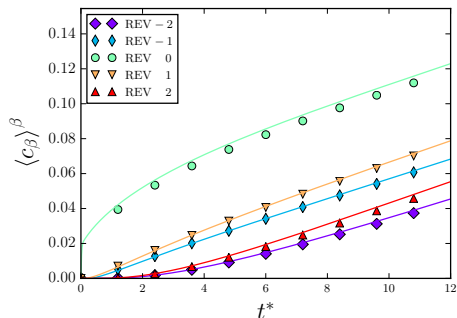


$$P_e^{\text{REV}} = 0.1, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

All results, order 3

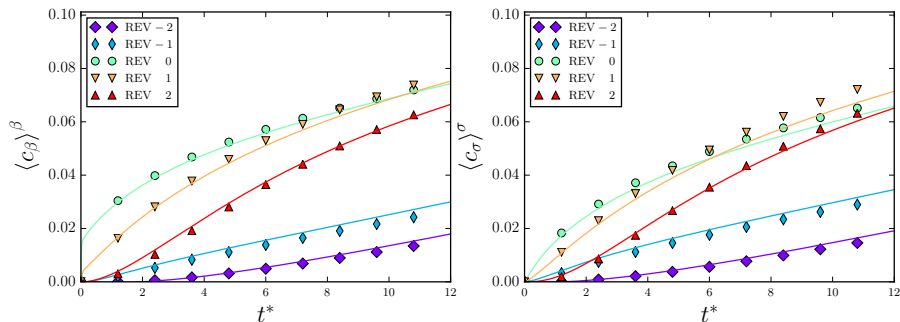


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

All results, order 3

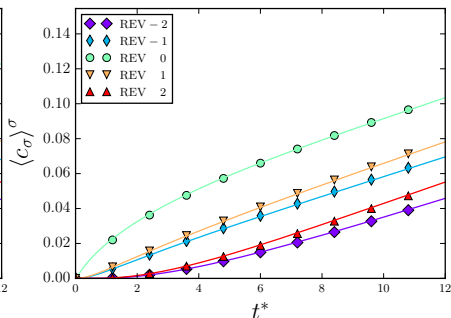
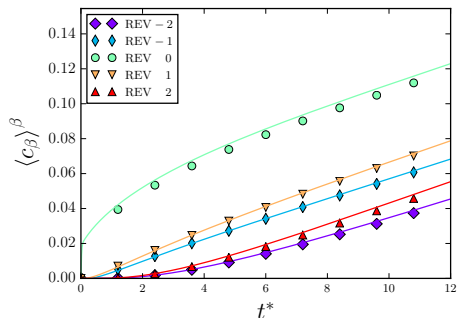


$$P_e^{\text{REV}} = 10, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

All results, order 3

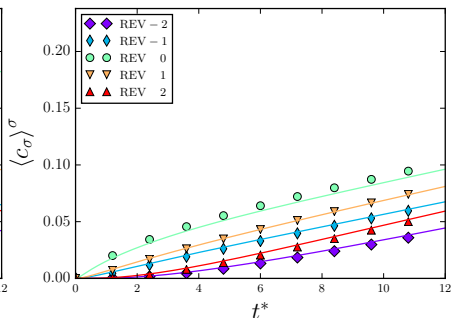
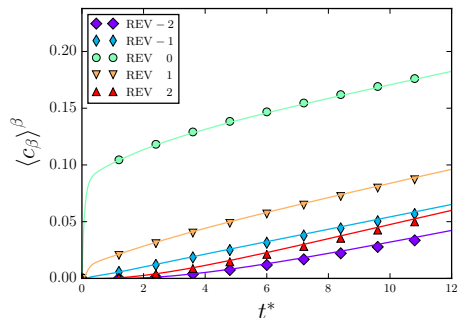


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

All results, order 3

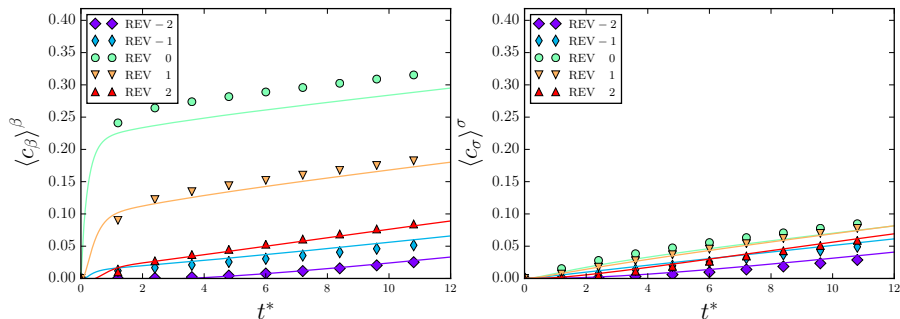


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-3}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$

All results, order 3



$$P_e^{\text{REV}} = 10, K_m = 3 \times 10^{-4}$$

Adimensional coefficients

- Péclet number $P_e^{\text{REV}} = \frac{\langle \mathbf{u} \rangle_z^\beta L^{\text{REV}}}{D_v}$
- Membrane Permeability $K_m^* = \frac{D_e r}{D_v e}$