



**HAL**  
open science

## Upscaling mass transfer in brain capillary networks

Vincent Doyeux, Yohan Davit, Michel Quintard, Sylvie Lorthois

► **To cite this version:**

Vincent Doyeux, Yohan Davit, Michel Quintard, Sylvie Lorthois. Upscaling mass transfer in brain capillary networks. ECCM-ECFD 2018 (6th European Conference on Computational Mechanics (Solids, Structures and Coupled Problems) (ECCM 6) and the 7th European Conference on Computational Fluid Dynamics (ECFD 7), Jun 2018, Glasgow, United Kingdom. pp.0. hal-03656518

**HAL Id: hal-03656518**

**<https://hal.science/hal-03656518v1>**

Submitted on 2 May 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



## Open Archive Toulouse Archive Ouverte

OATAO is an open access repository that collects the work of Toulouse researchers and makes it freely available over the web where possible

This presentation is published in: <http://oatao.univ-toulouse.fr/20439>

**To cite this version:**

Doyeux, Vincent and Davit, Yohan and Quintard, Michel and Lorthois, Sylvie. Upscaling mass transfer in brain capillary networks. (2018) In: ECCM-ECFD 2018 (6th European Conference on Computational Mechanics (Solids, Structures and Coupled Problems) (ECCM 6) and the 7th European Conference on Computational Fluid Dynamics (ECFD 7), 11-15 June 2018 (Glasgow, United Kingdom). (Unpublished)

Any correspondence concerning this service should be sent to the repository administrator: [tech-oatao@listes-diff.inp-toulouse.fr](mailto:tech-oatao@listes-diff.inp-toulouse.fr)

# Upscaling mass transfer in brain capillary networks

Vincent Doyeux, Yohan Davit, Michel Quintard, Sylvie Lorthois

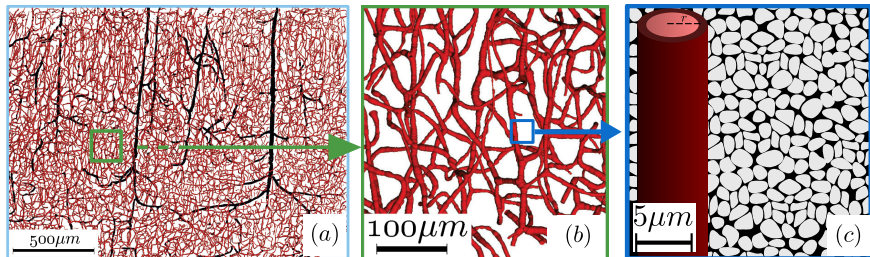
Fluid Mechanics Institute of Toulouse (IMFT) - France



## 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

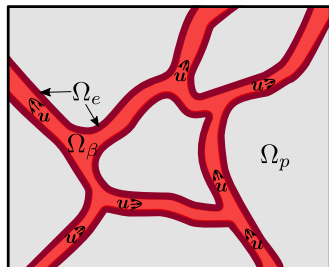
Sub-Microscopic scale

- 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  $\Omega_e$ )
- Red blood cells are neglected



### Two-phase capillary bed model

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

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

## 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  $\tilde{c}_\beta$  and  $\tilde{c}_t$
- Need closure equations on  $\tilde{c}_\beta$  and  $\tilde{c}_t$ .
- Subtracting equations on the mean to microscopic equations leads to equations on  $\tilde{c}_\beta$  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 $s_\beta$ 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:

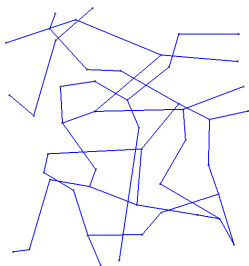
- C++/Parallel Finite element library <sup>1</sup>FEEL++
- Use a distance function field to capture the domain geometries
  - ▶ Mesh adaptation from distance function
  - ▶ Sub-domain localization to solve Stokes problem
  - ▶ Fictitious domain to solve advection/diffusion problem

---

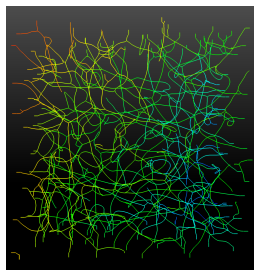
<sup>1</sup>Prud'homme et. al. (2016), [feelpp.org](http://feelpp.org)

- 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

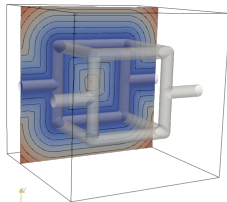
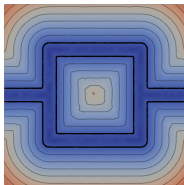
Defining  $\phi_i$ , the distance field to centerline  $S_i$  of a vessel of radius  $r_i$   
 The distance field to the closest vessel boundary of the network is:

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



Properties of  $\phi$ :

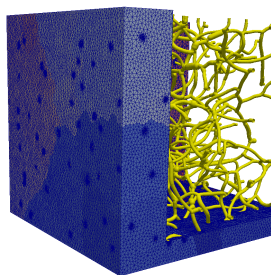
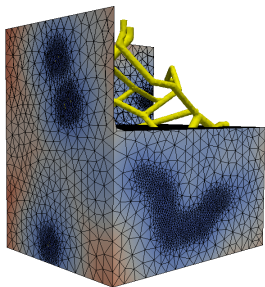
- $\phi(\mathbf{x}) < 0$  if  $\mathbf{x} \in \Omega_\beta$
- $\phi(\mathbf{x}) > 0$  if  $\mathbf{x} \in \Omega_t$
- $\phi(\mathbf{x}) = 0$  if  $\mathbf{x} \in \partial\Omega_{\beta t}$



## 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  $c_\beta$  on  $\partial\Omega_\beta \setminus \partial\Omega_{\beta t}$

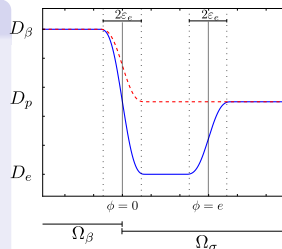
Prescribed B.Cs for  $c_t$  on  $\partial\Omega_t \setminus \partial\Omega_{\beta t}$

## 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  $\partial\Omega$

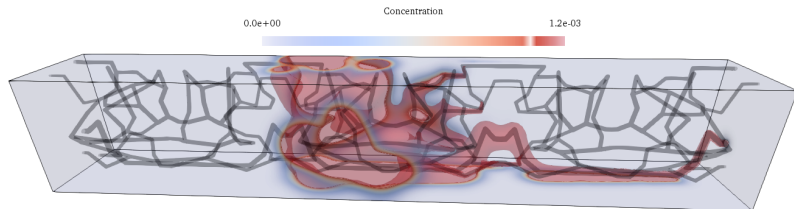
- Velocity  $\mathbf{u}$  is obtained by solving Stokes equation on the vessel domain only.
- Diffusion coefficient spatialized to take into account the BBB.



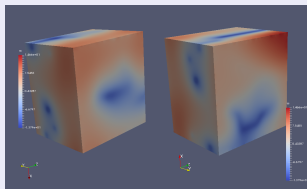
## PDEs solved by our framework

The frameworks of fictitious network allows to solve:

### The microscopic problem (DNS)



### Closure equations to get the effective coefficients



### Upscaled model

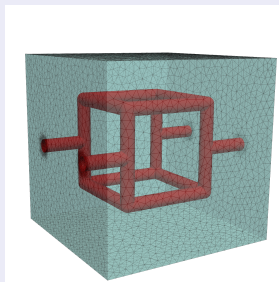
- Monolithic solver used for the upscaled model
- Mesh is a simple box



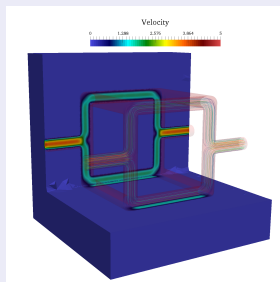
- 1 Homogenization - Equations
- 2 Fictitious Domain Framework
- 3 Verification**

# Test Case, order 3 network.

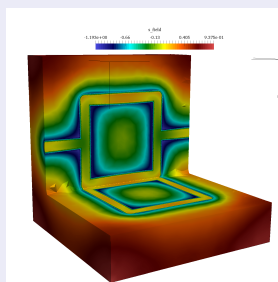
## Representative Elementary Volume, size $(2 \times 2 \times 2)$



Geometry and mesh.



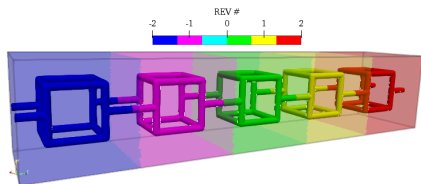
Velocity field.



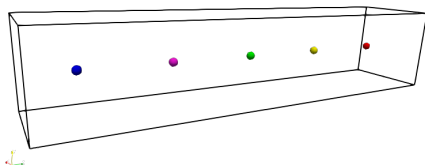
Closure variable

# Comparison DNS - Homogenized model

## Direct Numerical Simulation (DNS)



## Darcy Scale



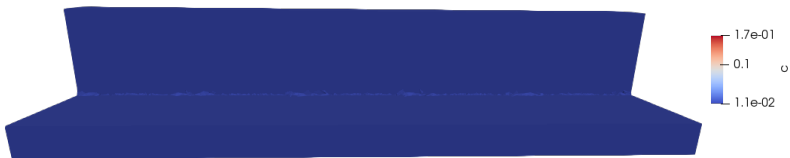
## DNS

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

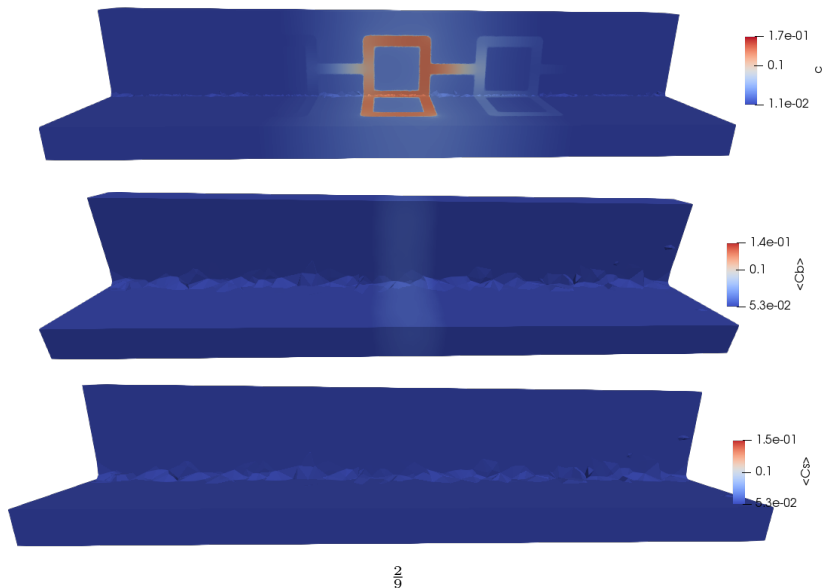
## Darcy Scale

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

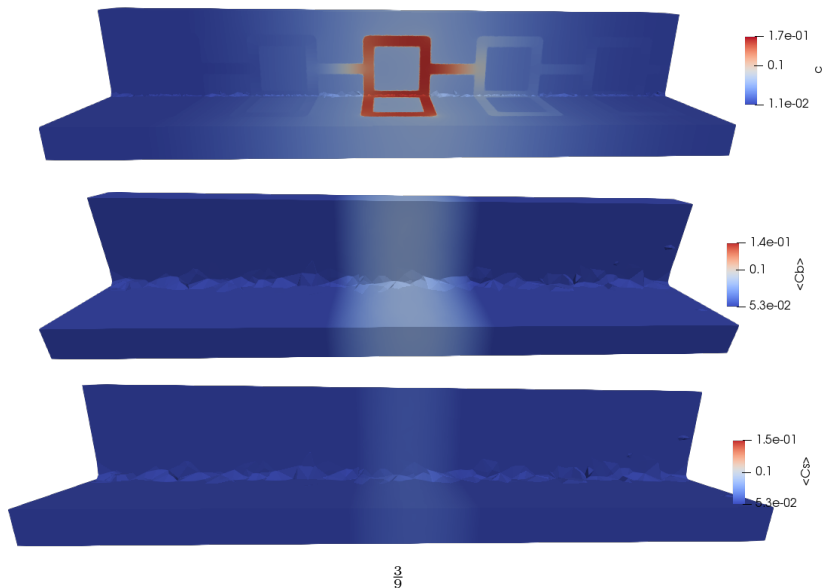
## Simulation Visualization



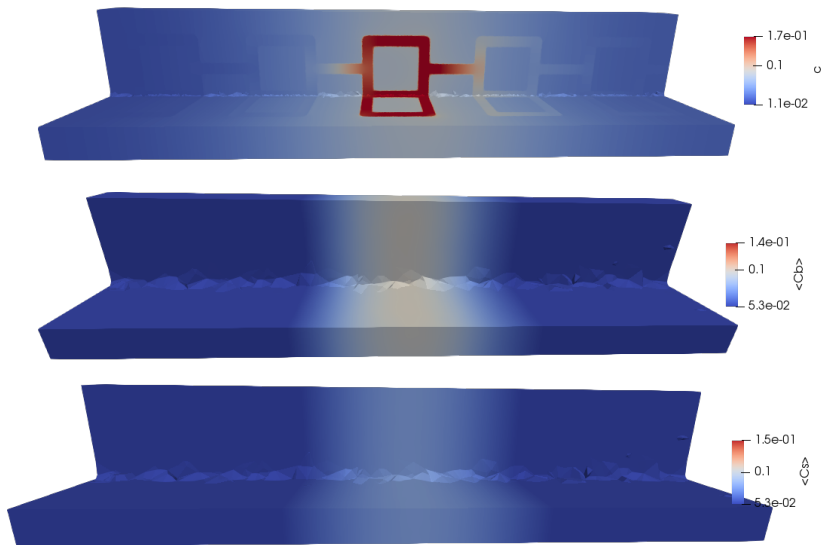
## Simulation Visualization



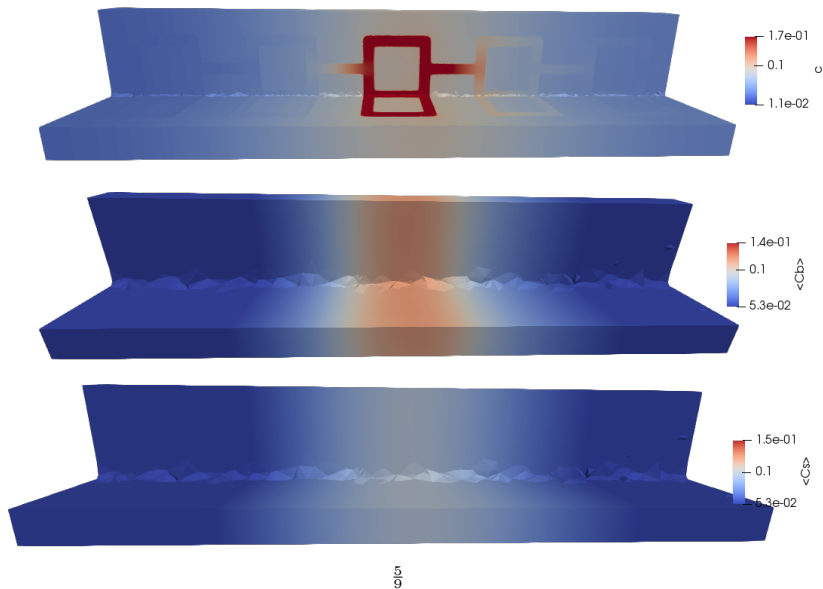
## Simulation Visualization



## Simulation Visualization

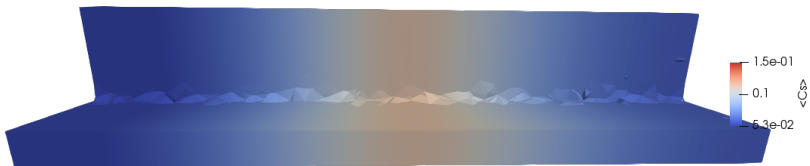
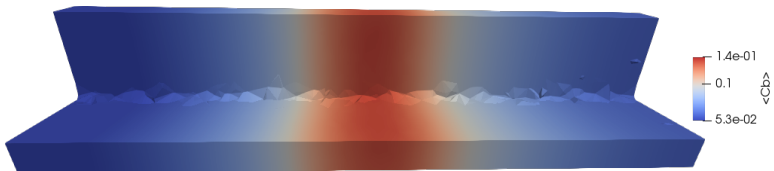
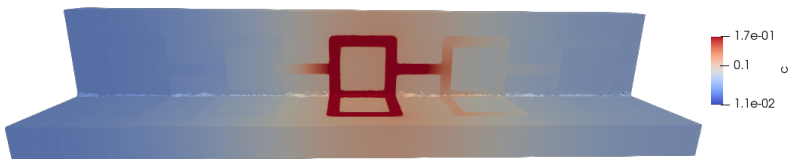


## Simulation Visualization

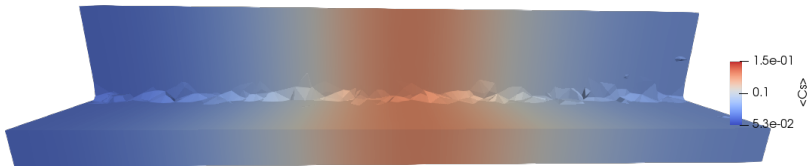
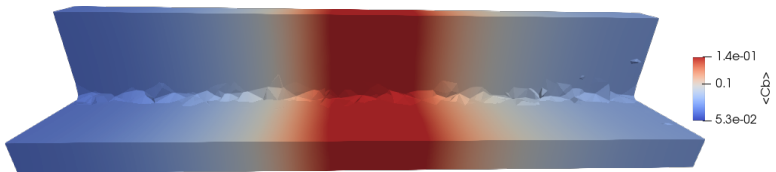
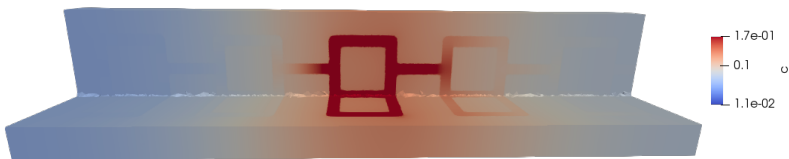




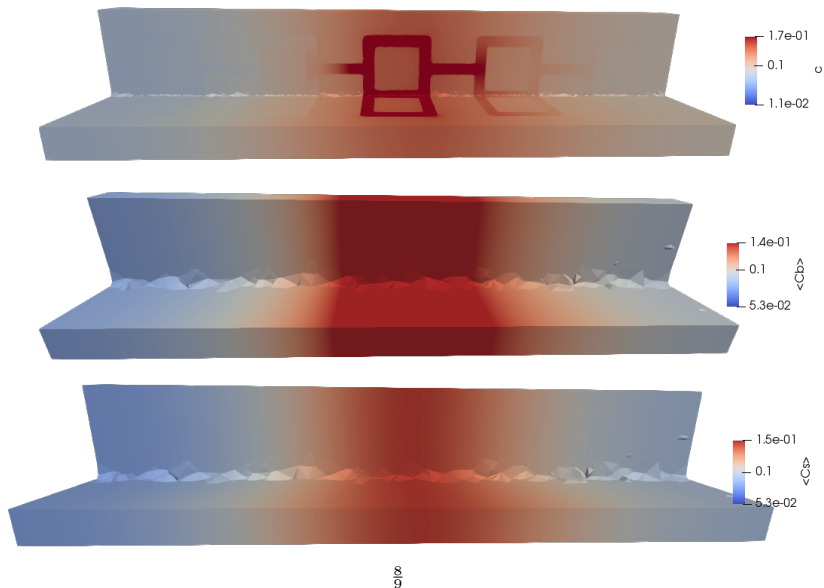
## Simulation Visualization



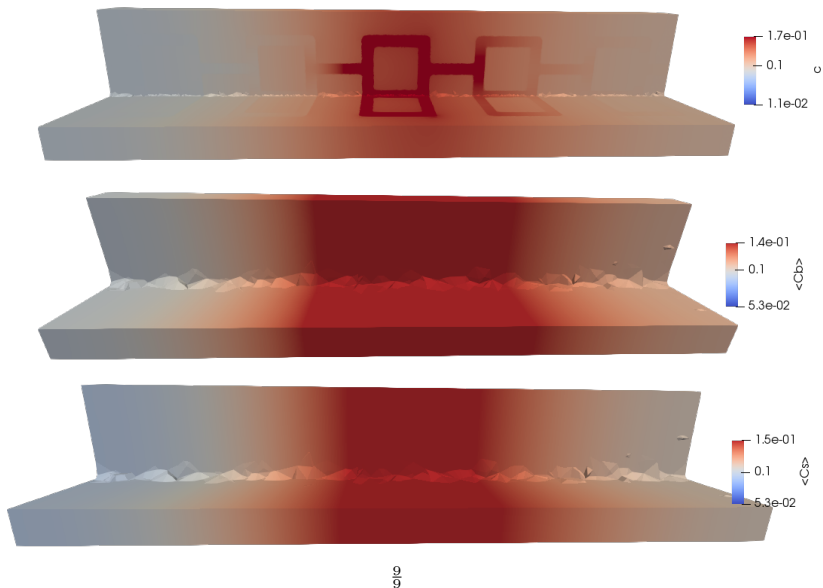
## Simulation Visualization



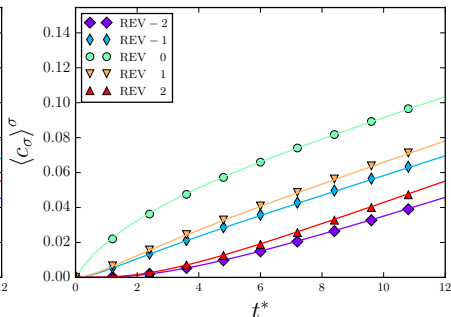
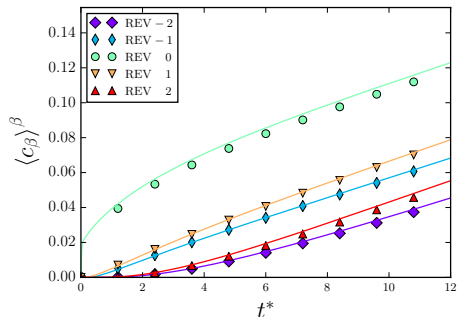
## Simulation Visualization



## Simulation Visualization



## Quantitative comparison

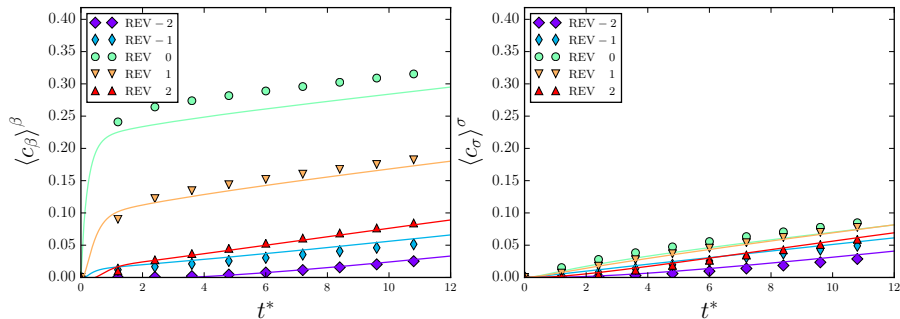


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

## 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

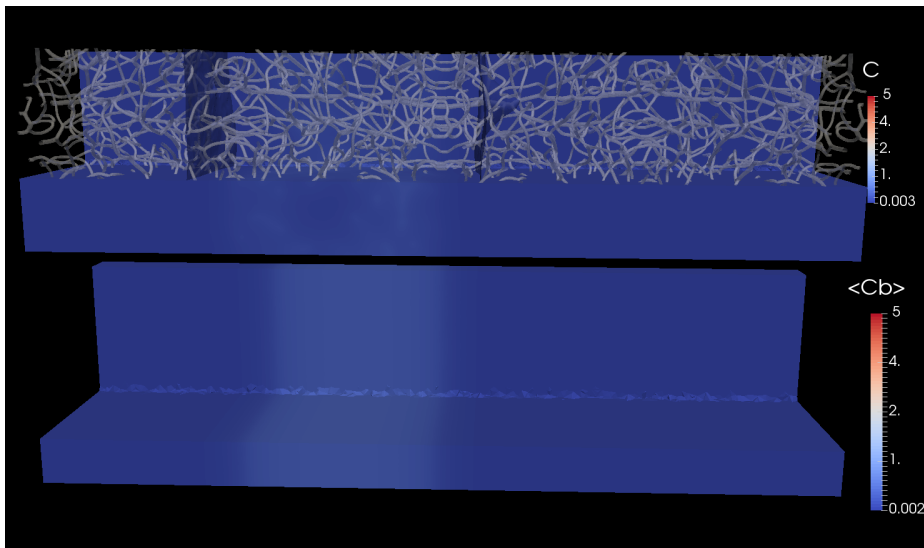


$$P_e^{\text{REV}} = 10, K_m = 3 \times 10^{-4}$$

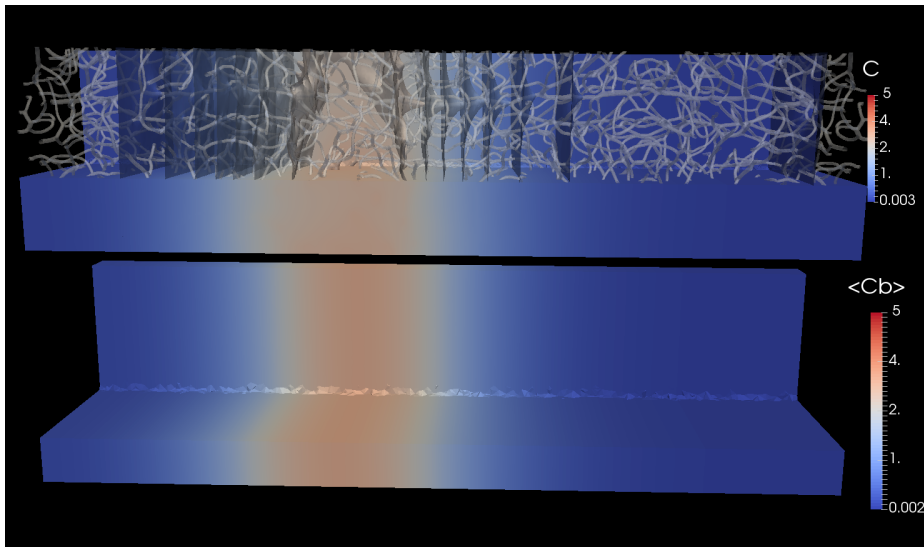
## Adimensional coefficients

- 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

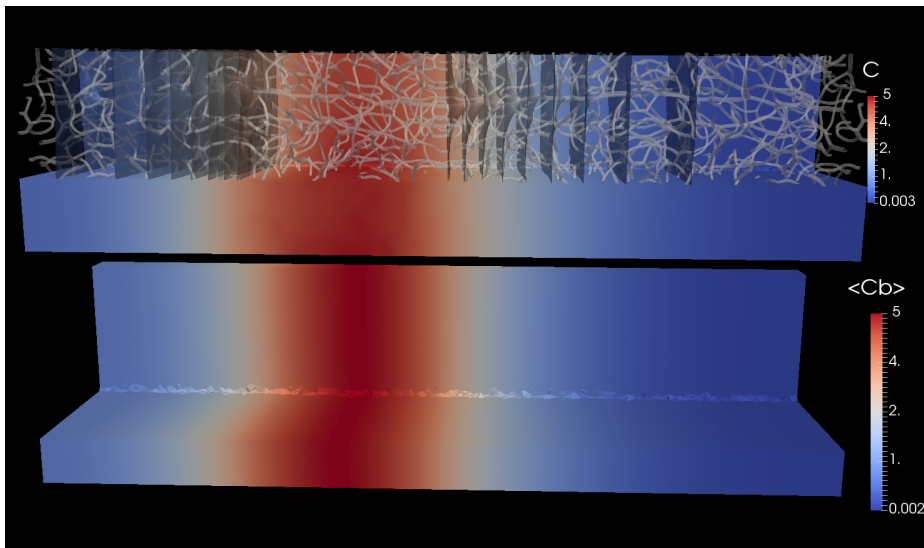
 $\frac{1}{4}$

# Anatomical Network

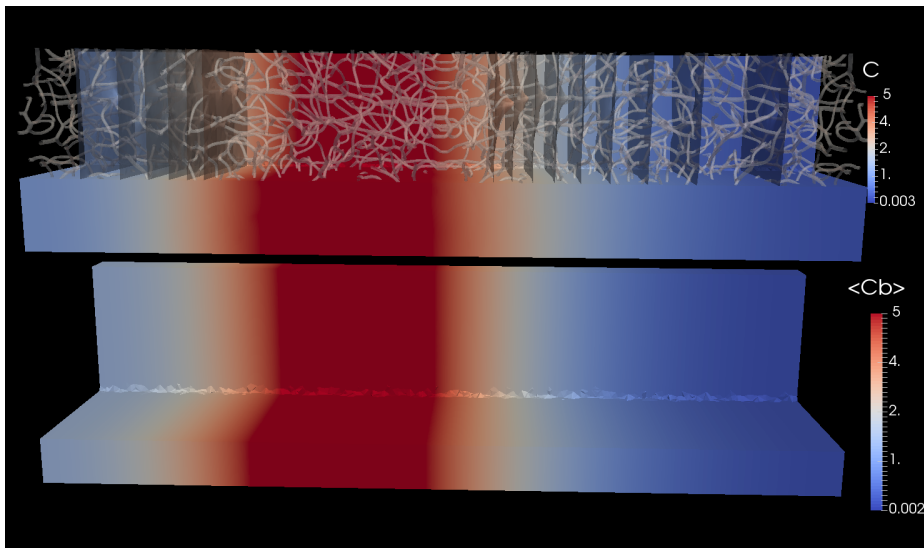




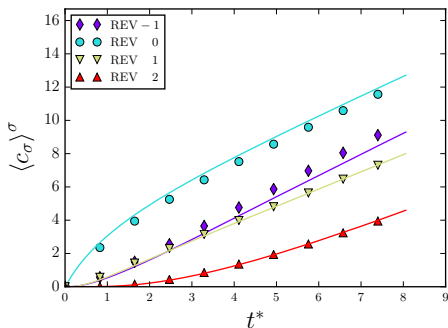
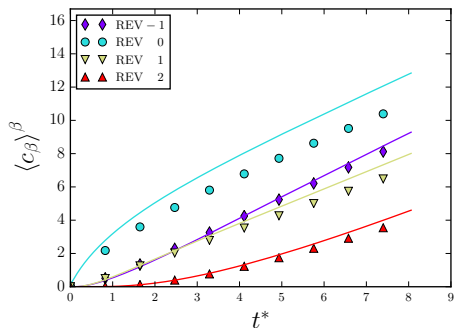
# Anatomical Network



# 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:

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

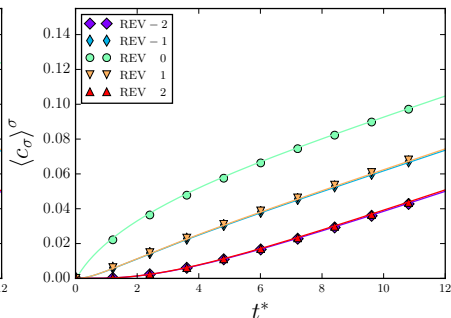
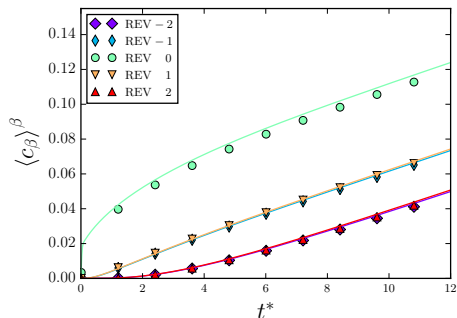
An example of projection function on a elements is given by:

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

- 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

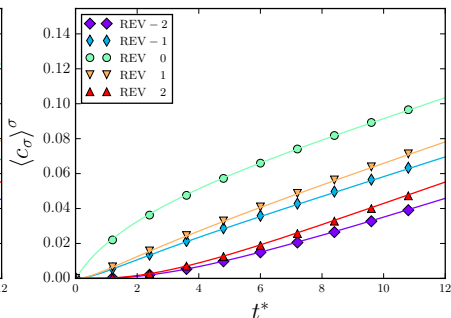
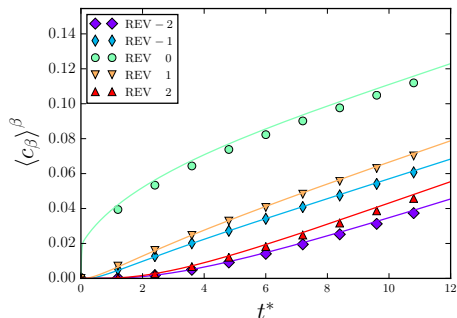


$$P_e^{\text{REV}} = 0.1, K_m = 3 \times 10^{-2}$$

## 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



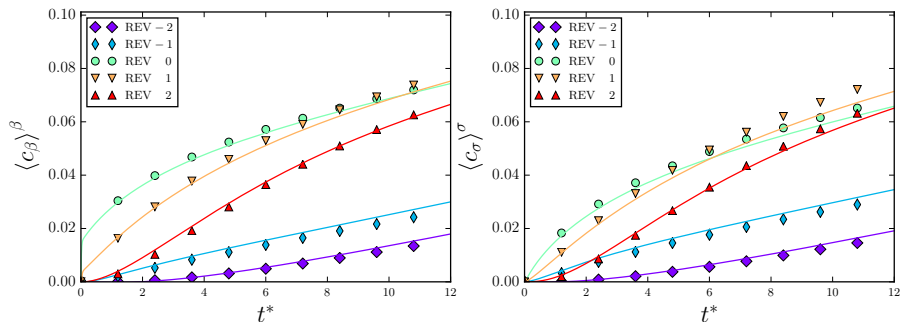
$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

## 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

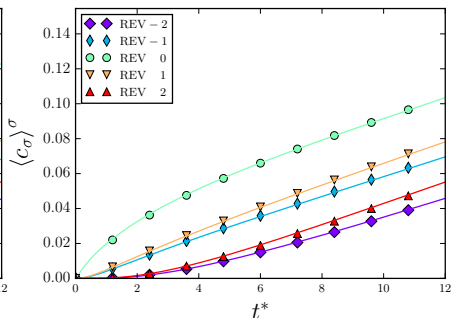
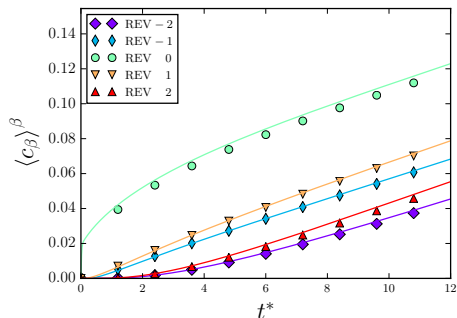


$$P_e^{\text{REV}} = 10, K_m = 3 \times 10^{-2}$$

## 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

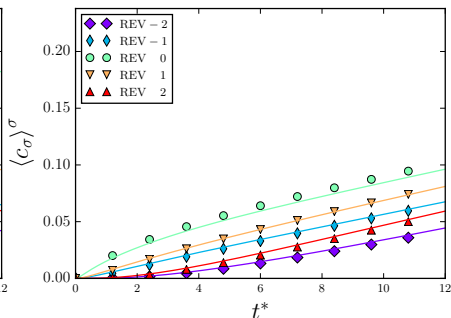
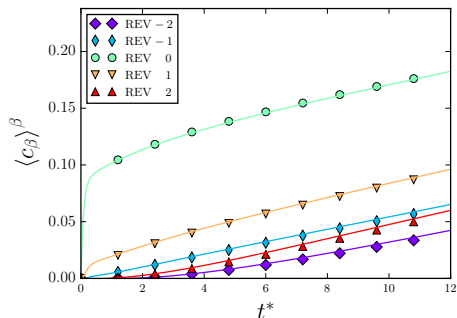


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-2}$$

## 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

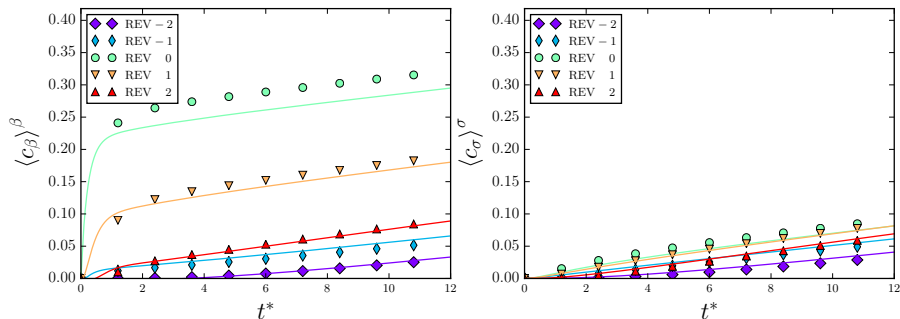


$$P_e^{\text{REV}} = 1, K_m = 3 \times 10^{-3}$$

## 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  $K_m^* = \frac{D_e r}{D_v e}$