Multiscale Modeling of the Hepatic Perfusion

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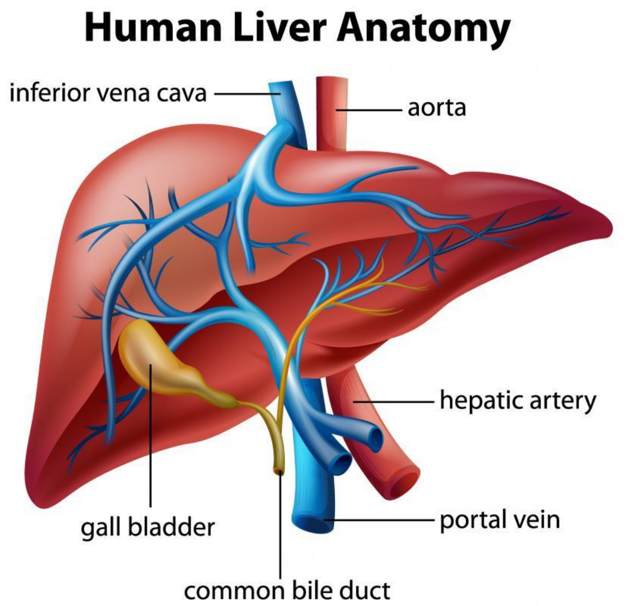
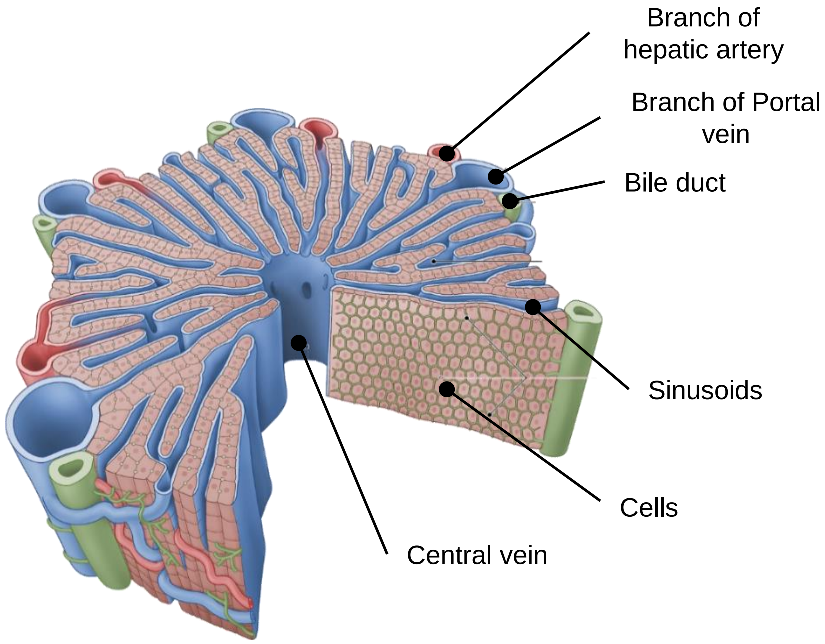
Plan

- **Context**
- *Methodology*
- *Some results and perspectives*





Blood supply

- Portal vein (≈70%): nutrient-rich blood
- Hepatic artery (≈30%): Oxygen-rich blood

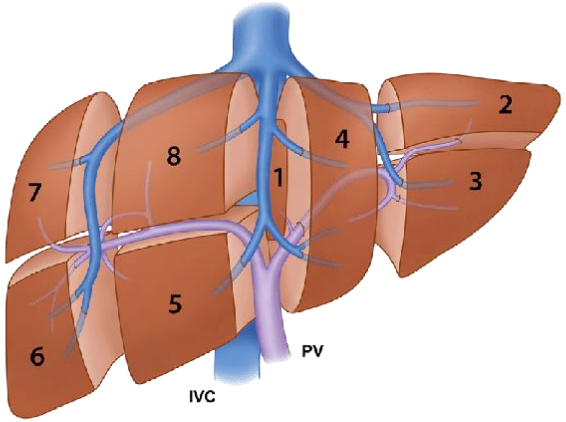
Outgoing blood

- Hepatic vein: deoxygenated and filtered blood

Hepatic lobule

- Portal triad (3 capillaries)
- Central Vein (toward Hepatic vein)
- Sinusoids with fenestrations

Liver modeling contribution

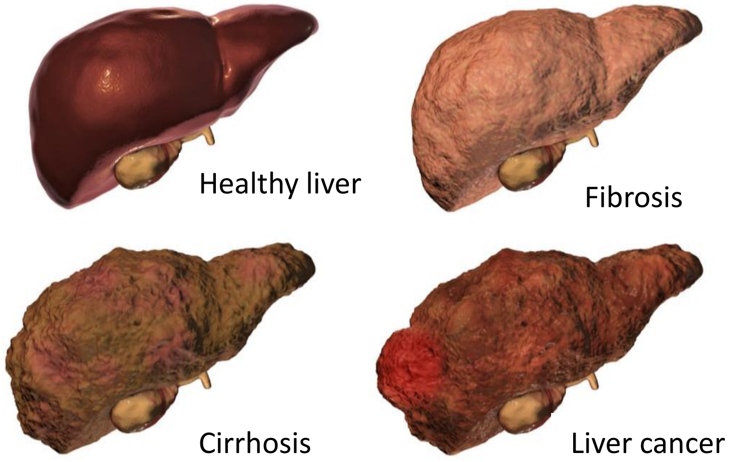


Provide quantitative information

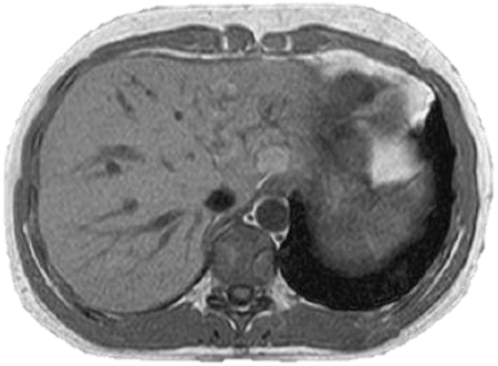
- Blood flow
- Local pressure

Help to understand pathological mechanism

- Effect of structural alteration on blood flow
- Relationship between macro and micro-circulations

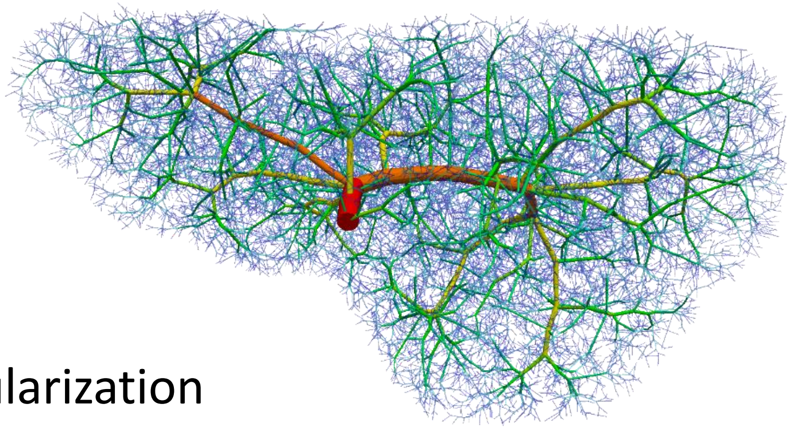


Liver modeling barriers



Resolution of imaging technics

- ≈ 1 mm
- Vessels under 1mm are not detected

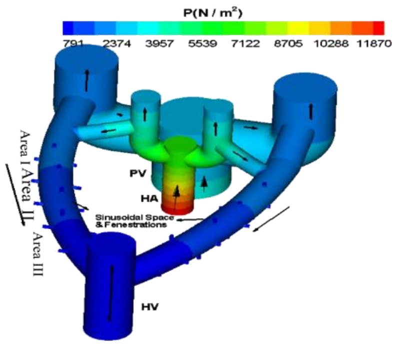


Multiscale vascular trees

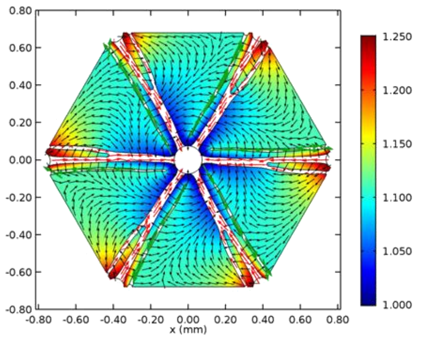
- From **10** to $\mathbf{10^{-3}}$ mm
- Complexity of the reconstruction of the entire tree
- Complexity of the implementation of the entire vascularization

Examples of models

Micro-perfusion models

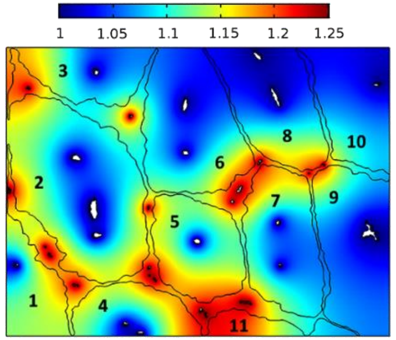


Rani et al. 2006
- Flow in the lobule
- Non Newtonian fluid



(d) Model B, Brinkman solution, $T_{bb} = 1.0$

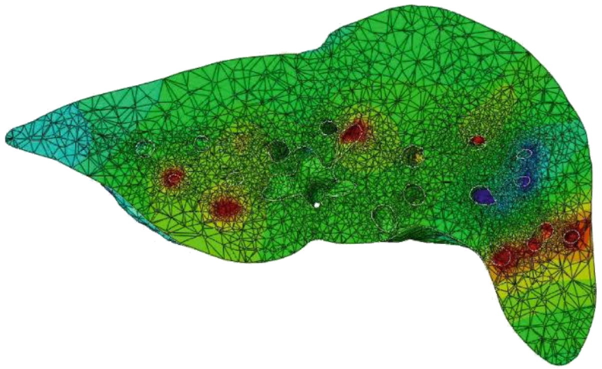
Mosharaf-Dehkordi et al. 2006
- Flow in the lobule
- Porous media + FSI



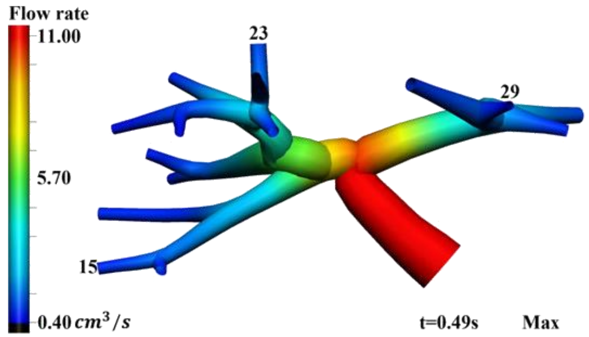
(a) Pressure field, $k_n = 1$

Ahmadi-Badjani et al. 2017
- Flow in the lobule
- Porous media + solid deformation

Organ-scale models



Lebre et al. 2017
- Flow in the liver
- Porous media

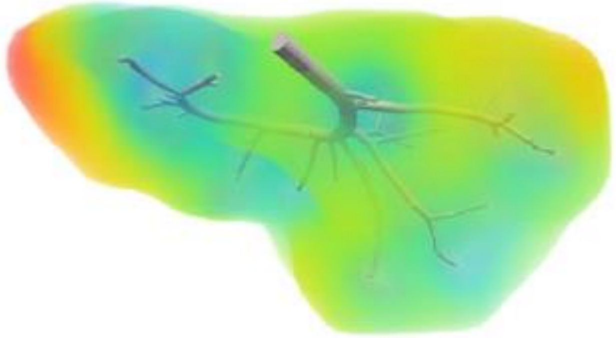


Ma et al. 2019
- Flow in the principal vessels
- Newtonian fluid

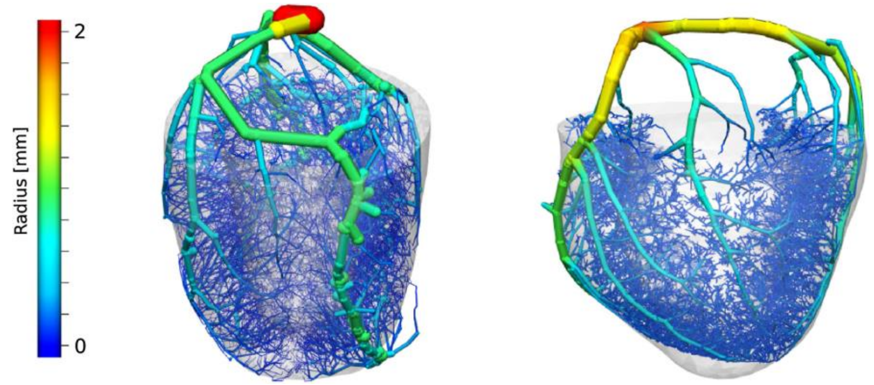
There is a strong relationship between the two scales!

Multiscale models: Multi-compartment flow

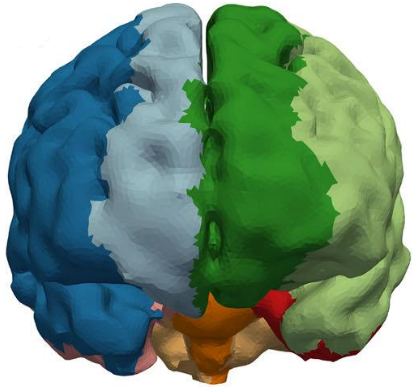
- **A model to describe the perfusion in high vascularized tissues**



Rohan et al. 2018
Hepatic perfusion



Hyde et al. 2014
cardiac perfusion



Jozsa et al. 2021
Cerebral perfusion

Plan

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- ***Methodology***
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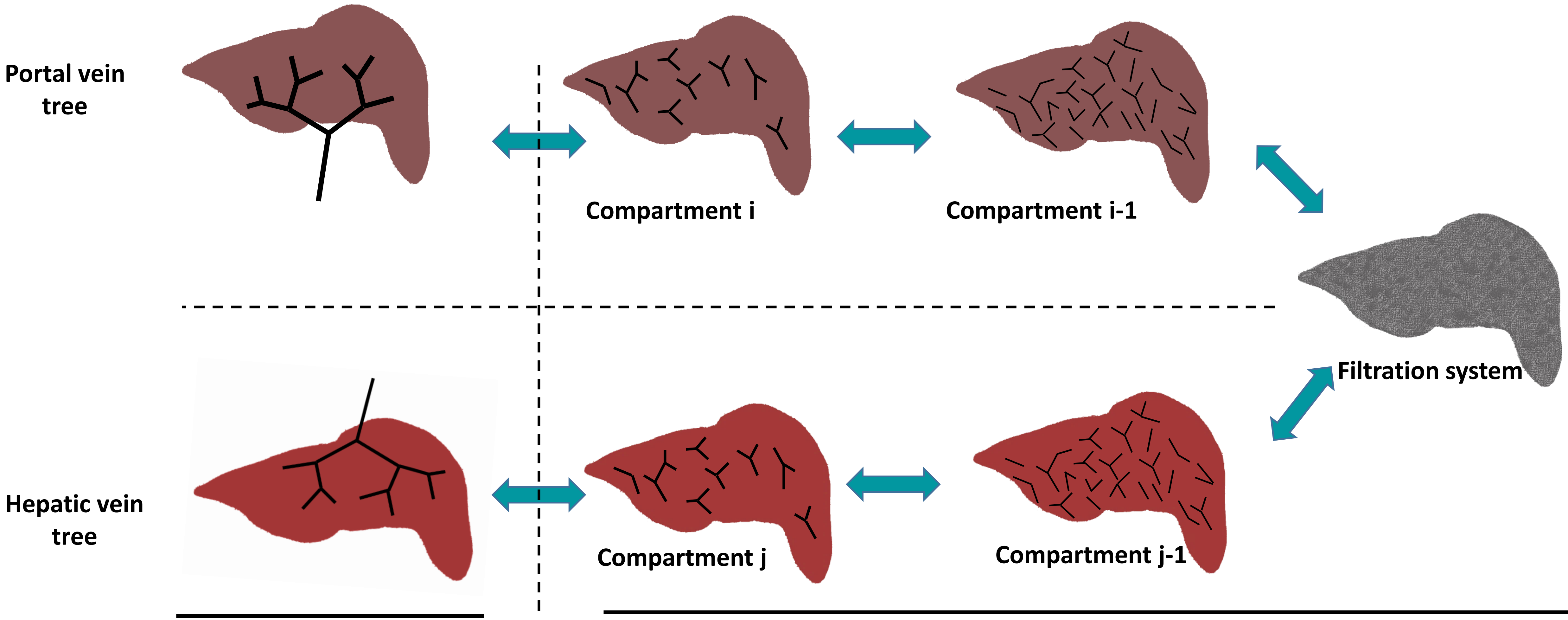
Multi-compartment model applied to the liver



Flow in the principal vessels
1D fluid flow

Flow in the parenchyma
3D multi-compartment porous flow: A superposition of *N* coupled porous media with different permeability

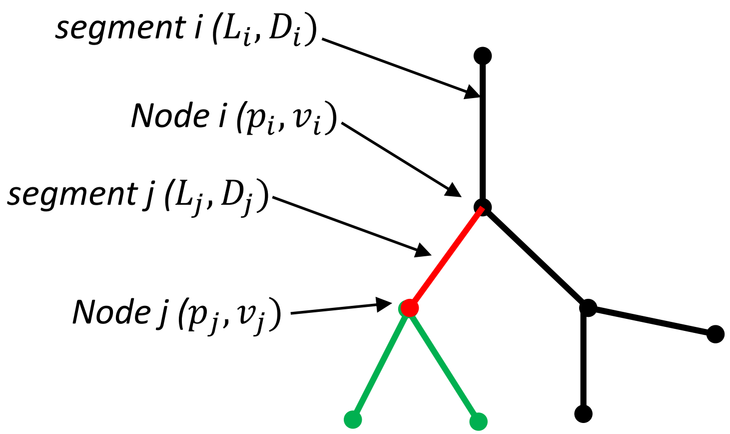
Flow between compartments

1D flow in large vessels

- **Bernoulli with head loss**

For each segment *j* limited by the nodes *i* and *j*

$$\frac{1}{2}\rho v_i^2 + p_i = \frac{1}{2}\rho v_j^2 + p_j + 32\mu\frac{L_j}{D_j}v_j$$



- **Conservation of the mass**

For each node j linking s segments

$$\sum_k^s A_k v_k = 0$$

- **Fluid properties**

ρ: Blood density
μ: Blood viscosity

- **Network parameters**

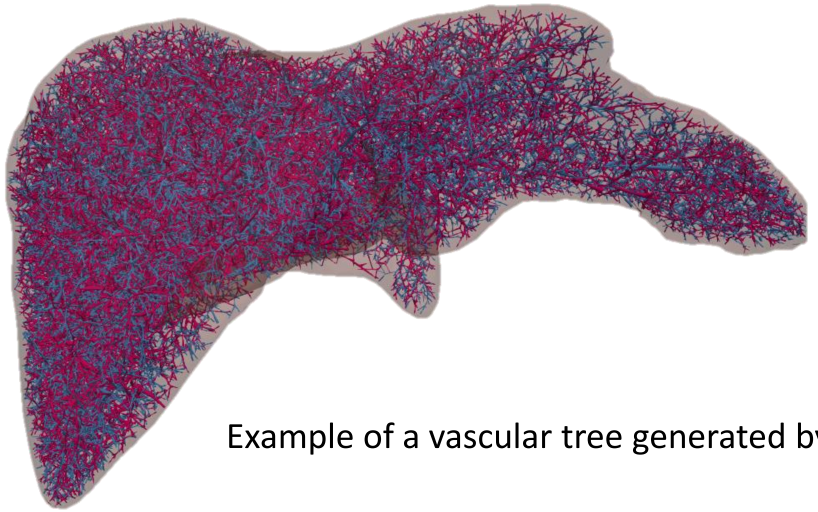
L_i: Length of the segment i
D_i: Diameter of the segment i

- **Unknowns**

p_i: Pressure in the node i
v_i: Velocity in the node i

3D Multi-compartment flow

- **Virtual vascular trees: generated using Constrained Constructive Optimization algorithm (CCO)**



Example of a vascular tree generated by CCO

For each compartment i of *the tree* T

$$\nabla.\left(-k_{T,i}\vec{\nabla}p_{T,i}\right) + \sum_{j}^{N} \beta_{ij}\left(p_{T,i} - p_{T,j}\right) = 0$$

- **Medium parameters**

$k_{T,i}$: Permeability of the compartment i of the Tree T

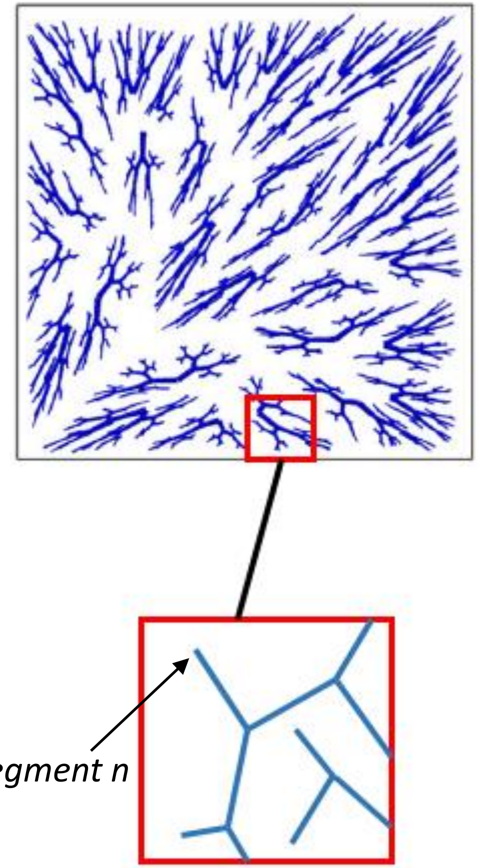
β_{ij}: Coupling coefficient between the compartments i and j

$\boldsymbol{\beta_{ij} = 0 \quad \text{if } |i - j| > 1}$

- **Unknowns**

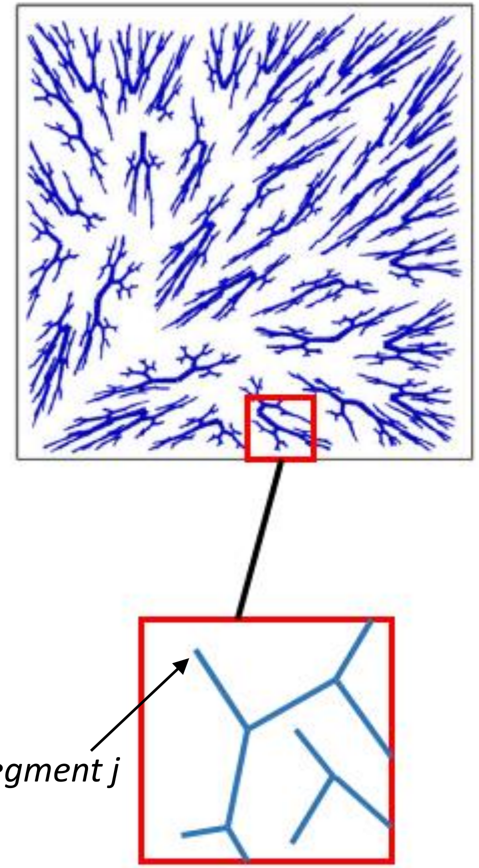
$p_{T,i}(x,y,z)$: Pressure of the compartment i of the Tree T

Parametrization of the multi-compartment porous media



- **For each compartment *i* of a vascular tree *T***
  - ➢ Split the medium volume into elementary volumes
  - ➢ Browse all the elementary volumes
  - **For each elementary volume *m***
    - ➢ Find the segments included in the elementary volume
    - **For each segment *n* included in the elementary volume *m we define***
      - ➢ V_n: segment volume
      - ➢ P_n: Mean fluid pressure in the segment *j*
      - ➢ Q_n: Fluid flow in the segment *j*
      - ➢ d_n: segment diameter
      - ➢ l_n: segment length
      - ➢ s_{xn}, s_{yn}, s_{zn}: Coordinate difference between the two points limiting the segment in the 3 directions
    - **Compute**
      - ➢ $\boldsymbol{Q^{mij} = \sum_n Q_n}$ Fluid flow crossing the segments linking I and j in the elementary volume *m*
      - ➢ $\boldsymbol{P^{mi} = \frac{\sum_n P_n V_n}{\sum_n V_n}}$: Mean fluid pressure in the elementary volume *i*

Parametrization of the multi-compartment porous media



- **The permeability tensor of the compartment i in the elementary volume *m*:**

$$K_{ab}^{mi} = \frac{\pi}{128\mu . V_m . \xi_0} \sum_n \frac{d_n^4 . s_{an} . s_{bn}}{l_n} \qquad a, b = (x, y, z)$$

- **The coupling coefficient between two compartments i and j in the elementary volume m:**

$$\beta_{ij}^{m} = \frac{|\boldsymbol{Q}^{mij}|}{|\boldsymbol{P}^{mi} - \boldsymbol{P}^{mj}|}$$

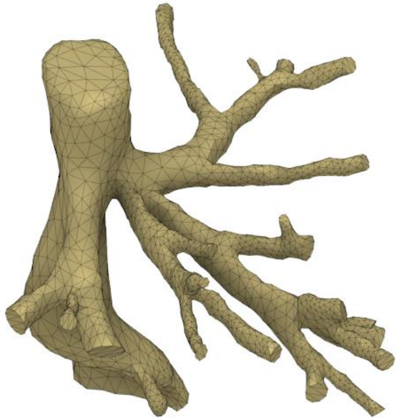
K^{mi} and β_{ij}^{m} were defined in the center of each elementary volume m

Linear interpolation → $K^{i}(x, y, z)$ and $\beta_{ij}^{m}(x, y, z)$

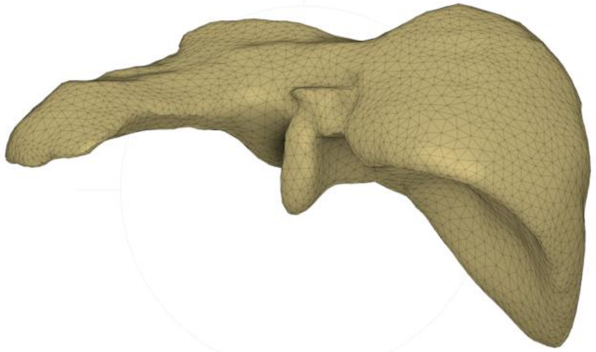
Geometries

- **Image processing of CT-Scan sequences**

Portal vein

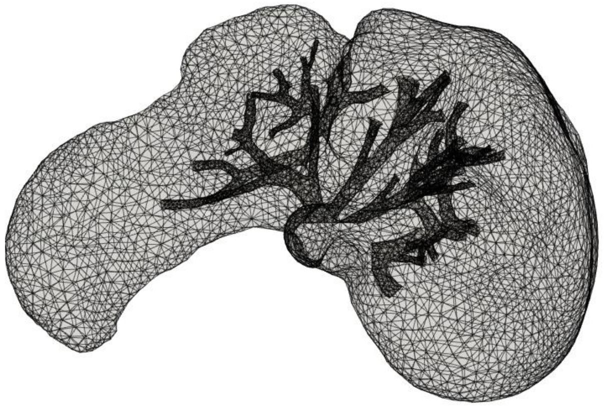


Hepatic vein

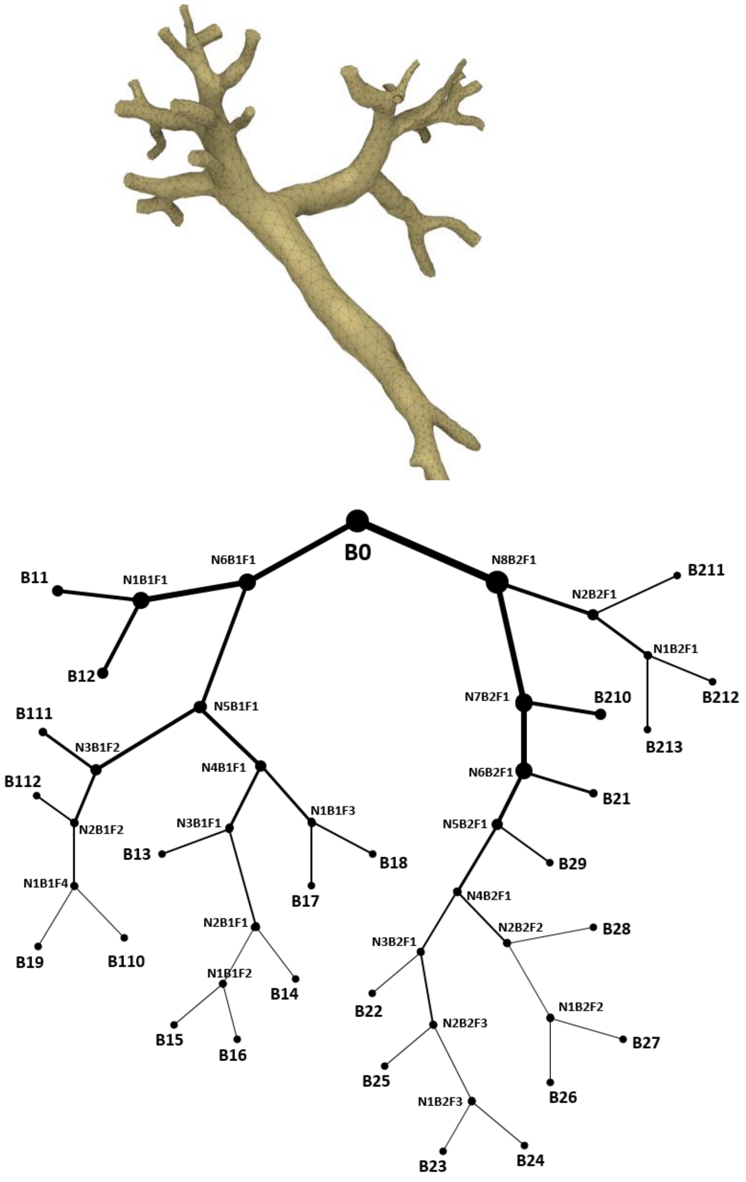


Liver

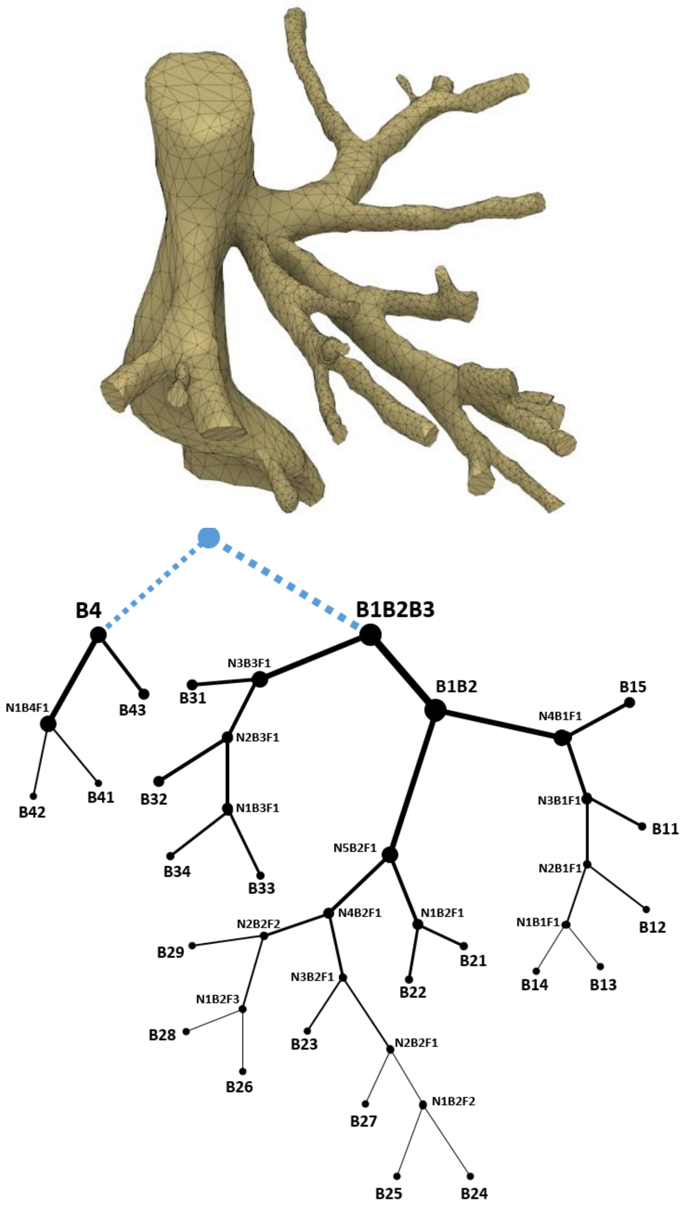
- **Geometry processing + meshing**



Modeling the 1D-flow problem



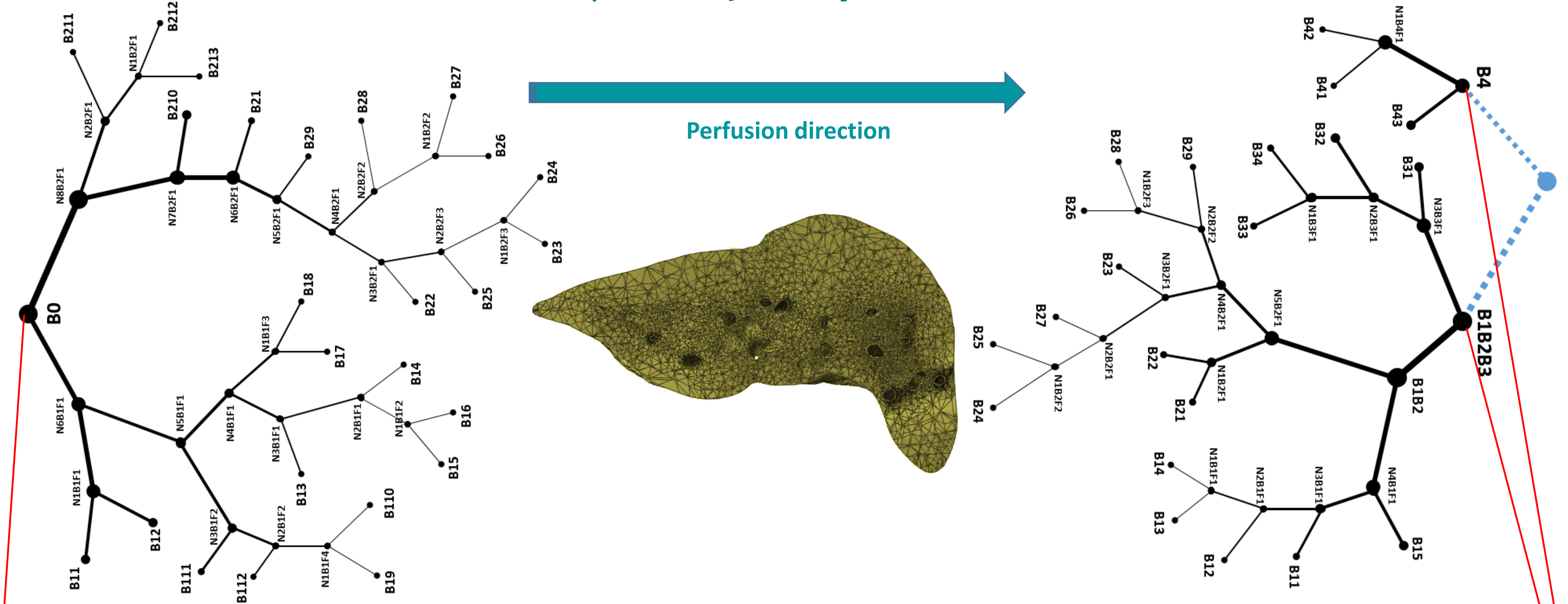
Portal vein



Hepatic vein

- Portal vein:
  - 49 nodes
  - 48 segments
  - 25 terminal nodes
- Hepatic vein:
  - 40 nodes
  - 38 segments
  - 21 terminal nodes
- Total:
  - 89 nodes
  - 46 terminal nodes
  - 178 Unknowns

System resolution: 178 unknowns (velocity and pressure in each node)



72 Equations:
48 Bernoulli + 24 Mass conservation

57 Equations:
38 Bernoulli + 19 Mass conservation

BC: Input velocity

132 Equations ---- 178 Unknowns: **46 Equations needed**

BC: 2 Output pressures

Relations between terminal nodes pressures and velocities

Let N_t be the number of the terminal segments of the two trees, We need to write the velocities in the terminal nodes in the following form:

$$v_i = \sum_{j}^{N_t} \alpha_{ij} p_j \quad \rightarrow \quad (v_1, \dots, v_{N_t})^T = \begin{pmatrix} \alpha_{11} & \cdots & \alpha_{1N_t} \\ \vdots & \ddots & \vdots \\ \alpha_{N_t 1} & \cdots & \alpha_{N_t N_t} \end{pmatrix} (p_1, \dots, p_{N_t})^T$$

We perform N_t simulation with the multi-compartment liver model:

- **For j=1 to N_t**

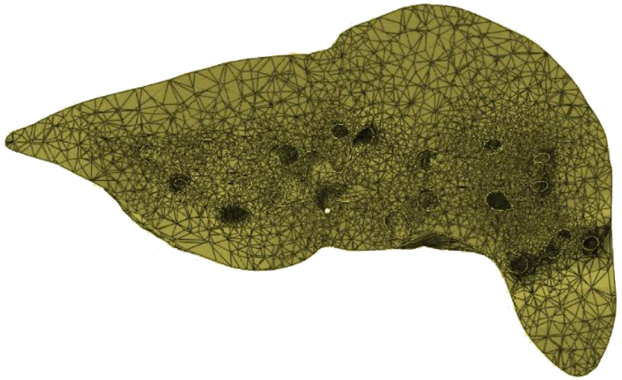
1/ $(p_1, \dots, p_{N_t})^T = (0, \dots, 0)^T$

2/ $p_j = 1;$

3/Compute the multi-compartment model:

$$\nabla.\left(-k_{T,i} \vec{\nabla} p_{T,i}\right) + \sum_{j}^{N} \beta_{ij}\left(p_{T,i} - p_{T,j}\right) = 0$$

4/find $(v_1, \dots, v_{N_t})^T \quad \rightarrow \alpha_{ij}$



- Provides the remaining 46 equations

Resolution of the system

- **86 Bernoulli with head loss**

$$\frac{1}{2}\rho v_i^2 + p_i = \frac{1}{2}\rho v_j^2 + p_j + 32\mu \frac{L_j}{D_j} v_j$$

- **43 Conservation of the mass**

$$\sum_k^S A_k v_k = 0$$

- **46 Terminal pressures and velocities relations**

$$v_i = \sum_j^{N_t} \alpha_{ij} p_j$$

- **3 Boundary conditions**

$$v_{in} = v_{PV} \qquad p_{out1} = p_{HV}$$
$$p_{out2} = p_{HV}$$

- **Equation system:** *Find the vector* $[U]$ *that satisfy*

$$[K_1][U] + [K_2][U^2] - [BC] = 0$$

$[U] = (p_1, \dots, p_{N_t}, v_1, \dots, v_{N_t})^T$: Unknowns vector

$[U^2] = (p_1^2, \dots, p_{N_t}^2, v_1^2, \dots, v_{N_t}^2)^T$

- A new method to couple the flow in the principal vessels and the flow in the liver

Plan

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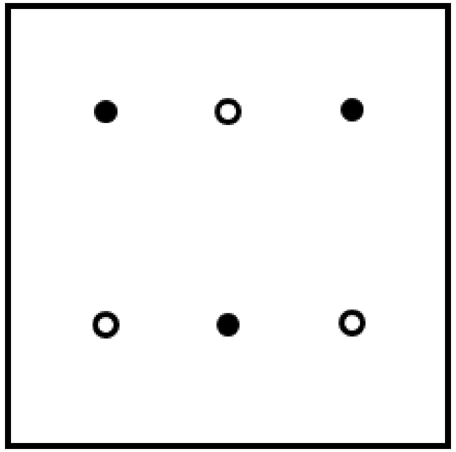
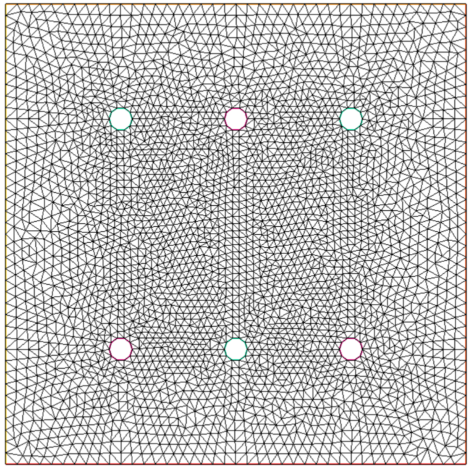
- ***Some results and perspectives***

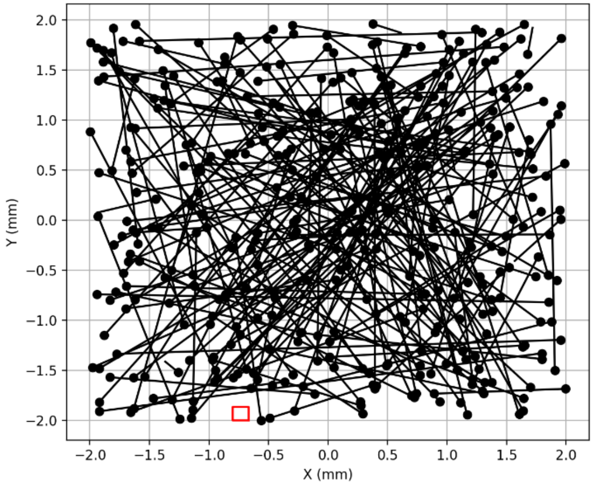
2D multi-compartment porous media with random vascular network (3 compartments)



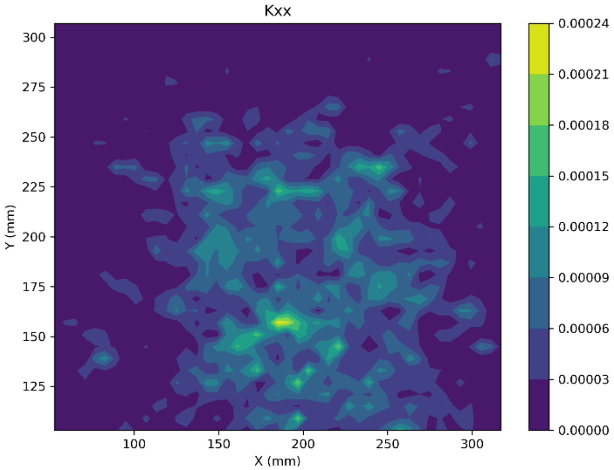
● **Inflow** ○ **Outflow**



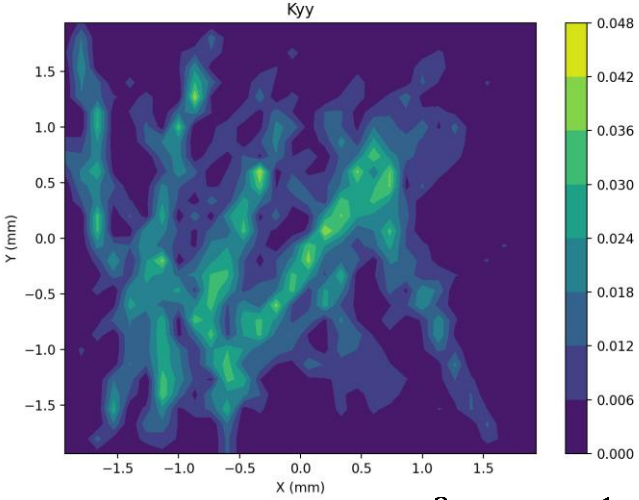
Mesh



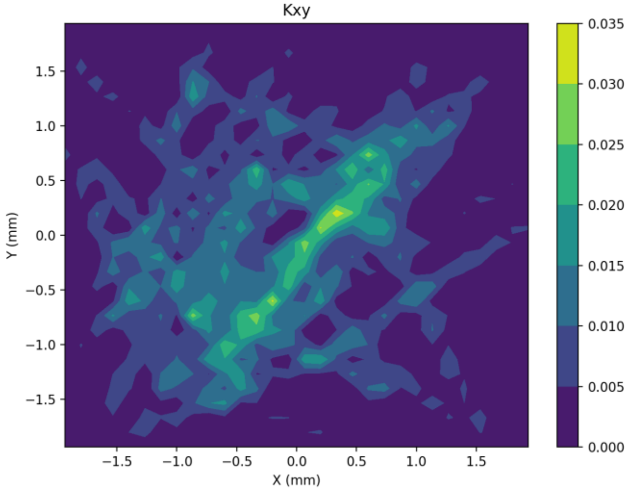
Random Network



Permeability $K_{xx}(m^2(Pa.s)^{-1})$
Compartment 1

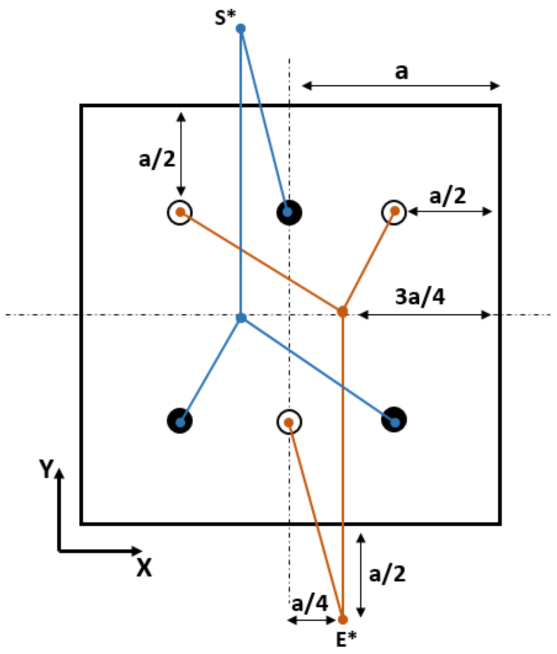


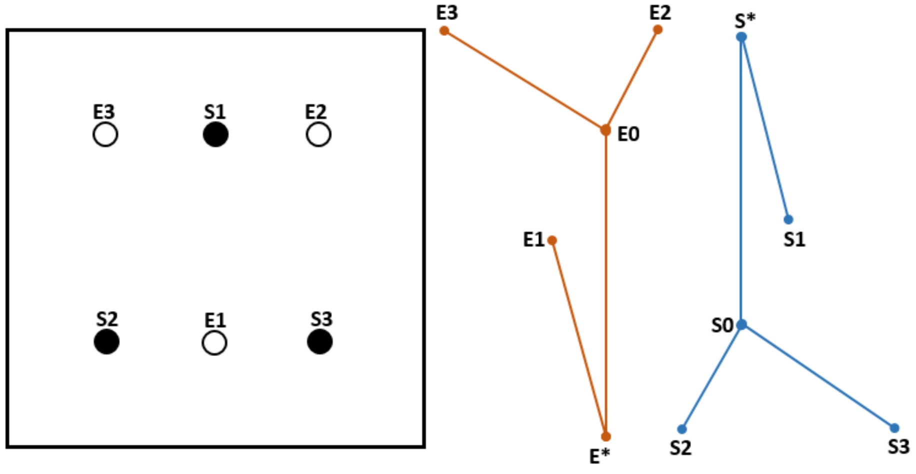
Permeability $K_{yy}(m^2(Pa.s)^{-1})$
Compartment 1



Permeability $K_{xy}(m^2(Pa.s)^{-1})$
Compartment 1

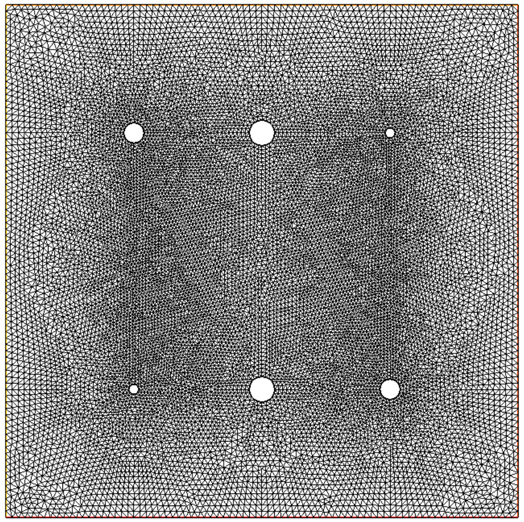
Coupling 1D and 3D multi-compartment flows in a 2D model





Inlet flow network

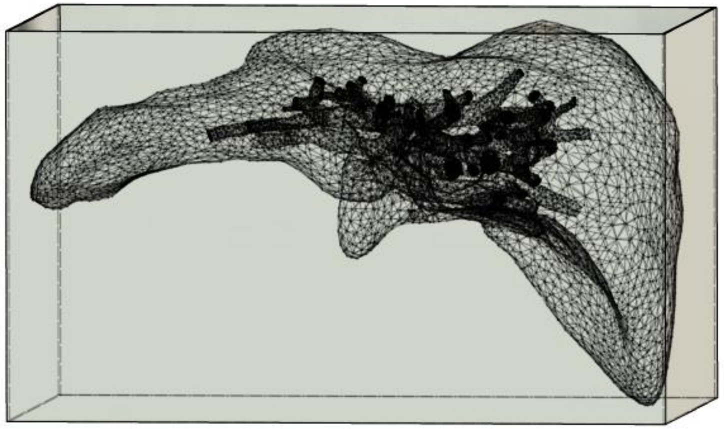
Outlet flow network

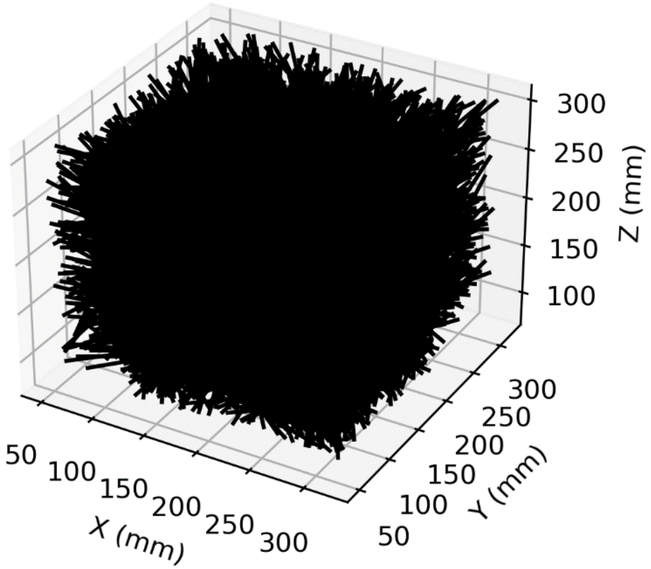


- The system converged with the Trust-region algorithm

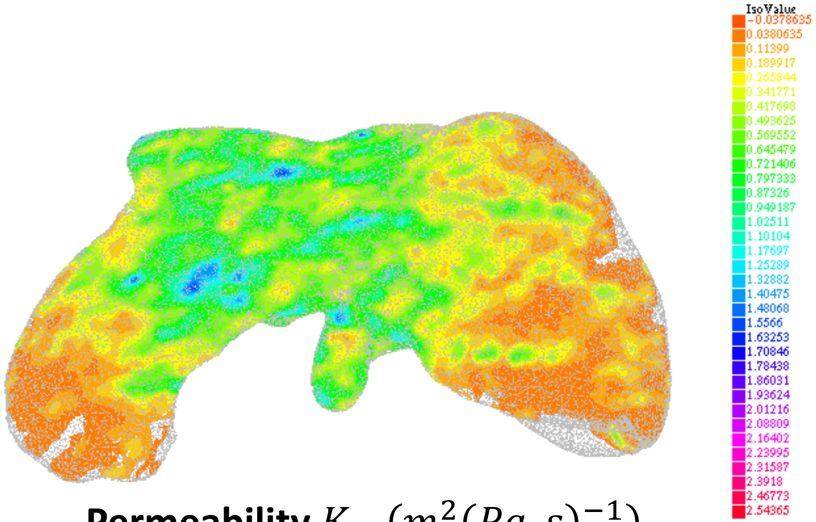
	E*	E0	E1	E2	E3	S3	S2	S1	S0	S*
Pressure (Pa)	821	769	404	404	402	401	400	398	113	50
Velocity (m/s)	0.1	0,06	0,24	0,24	0,04	0,03	0,25	0,24	0,06	0,1

Liver multi-compartment porous media with random vascular network (3 compartments)

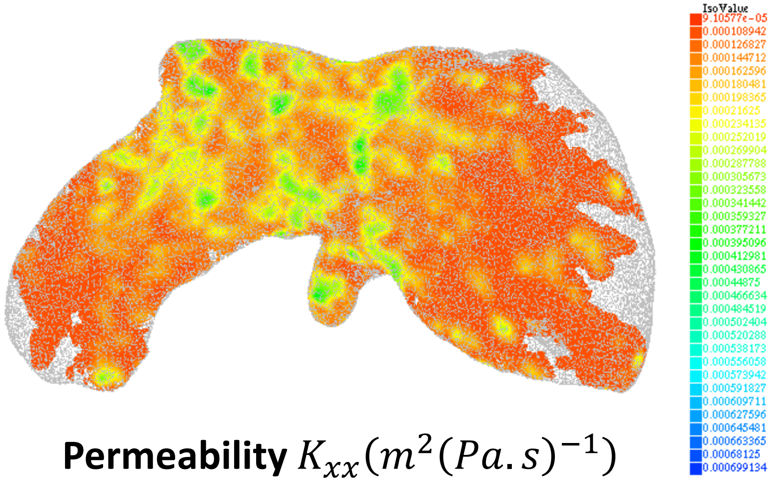




Random Network (10000 Fragments)



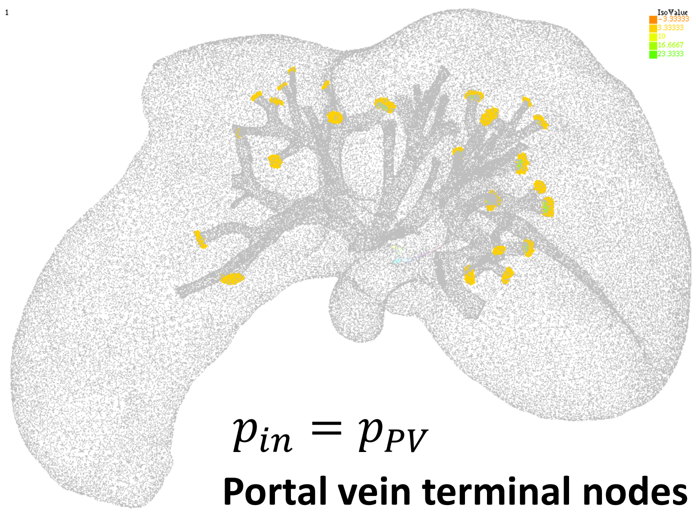
Permeability $K_{xx}(m^2(Pa.s)^{-1})$
Compartment 1



Permeability $K_{xx}(m^2(Pa.s)^{-1})$
Filtration system

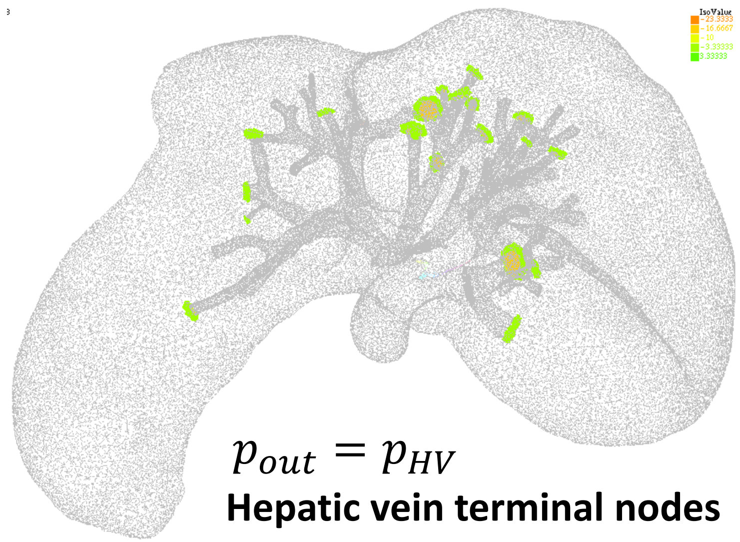
Liver multi-compartment porous media with random vascular network (3 compartments)

Boundary conditions in the terminal nodes



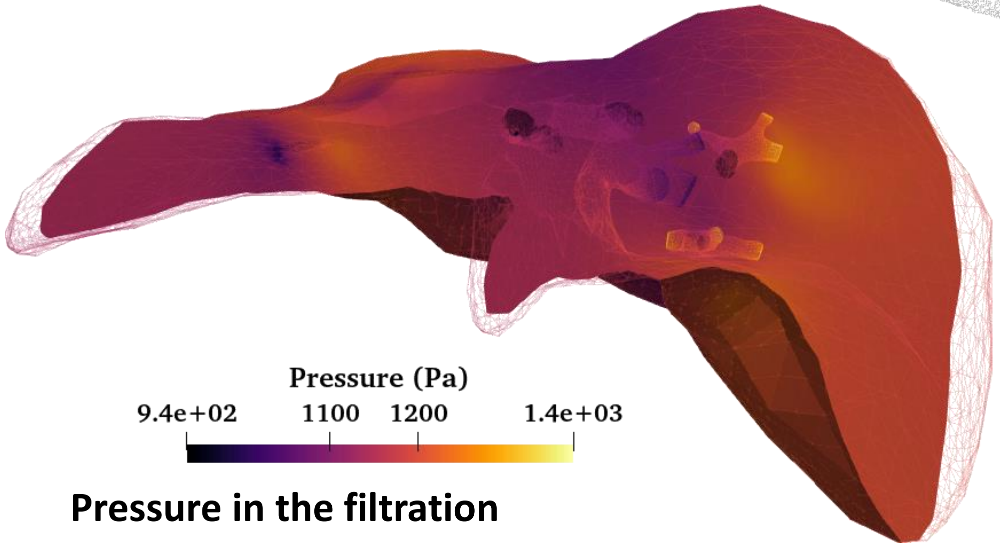
$p_{in} = p_{PV}$

Portal vein terminal nodes



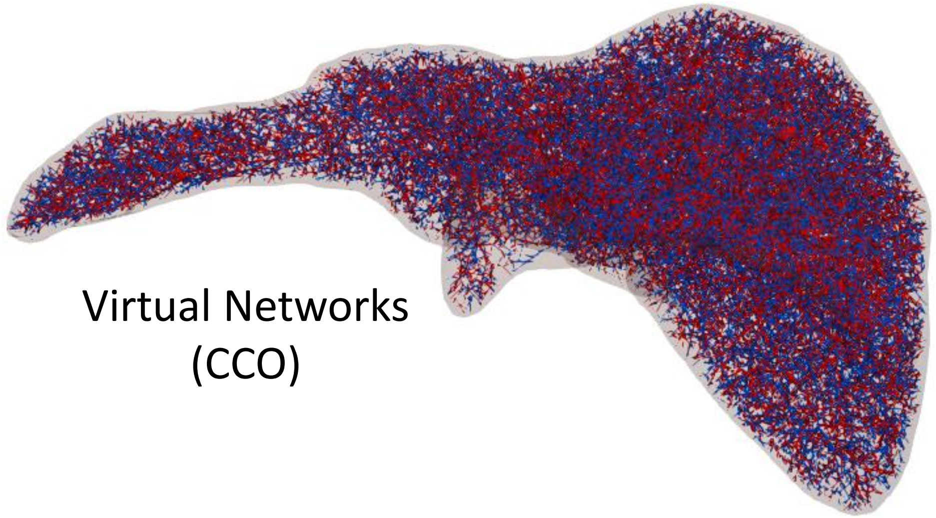
$p_{out} = p_{HV}$

Hepatic vein terminal nodes

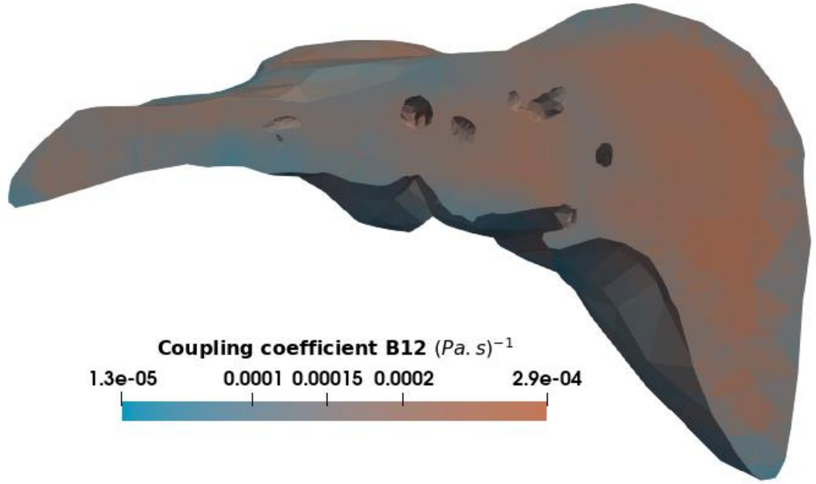


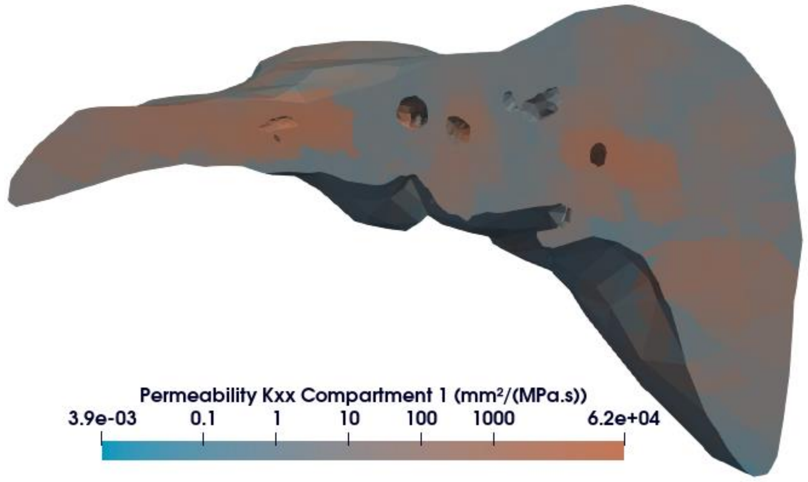
Pressure in the filtration system

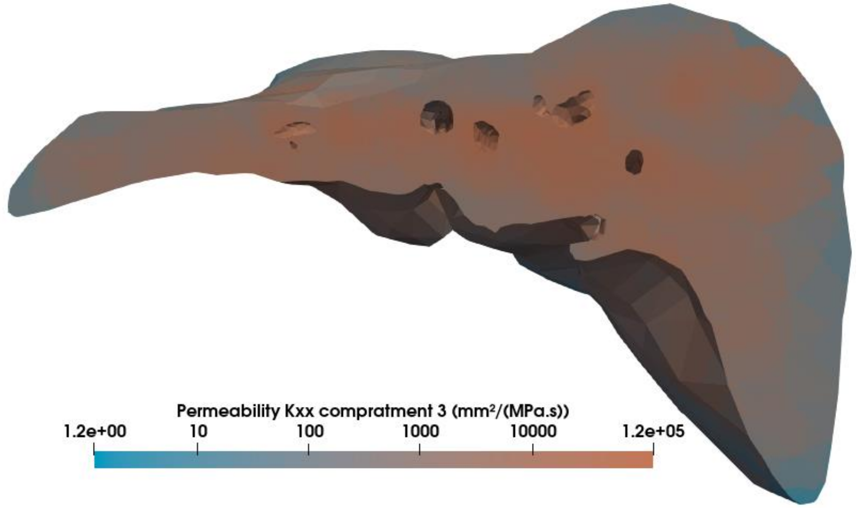
Liver multi-compartment porous media with realistic vascular network (3 compartments)



Virtual Networks
(CCO)







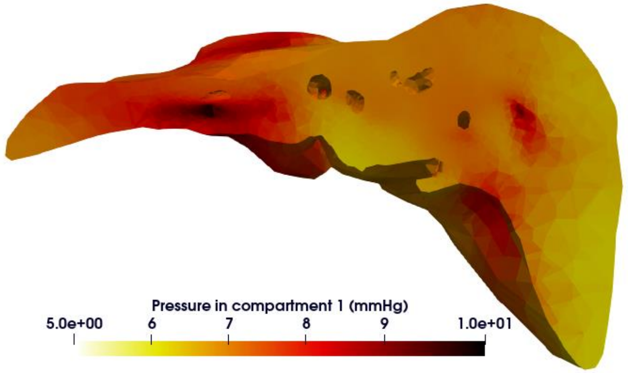
Liver muli-compartment porous media with realistic vascular network (3 compartments)

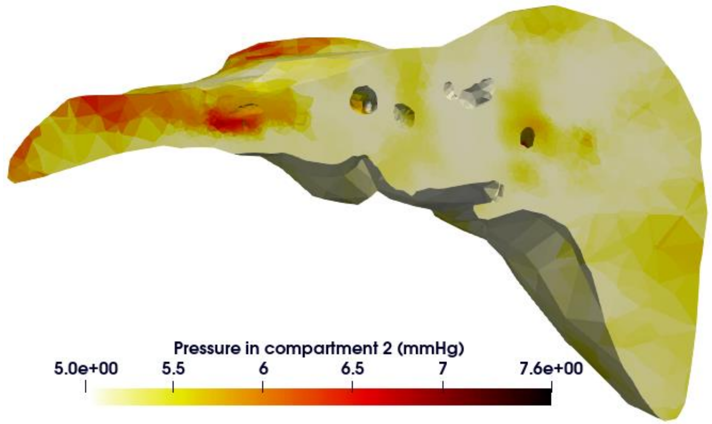
Compartment 1

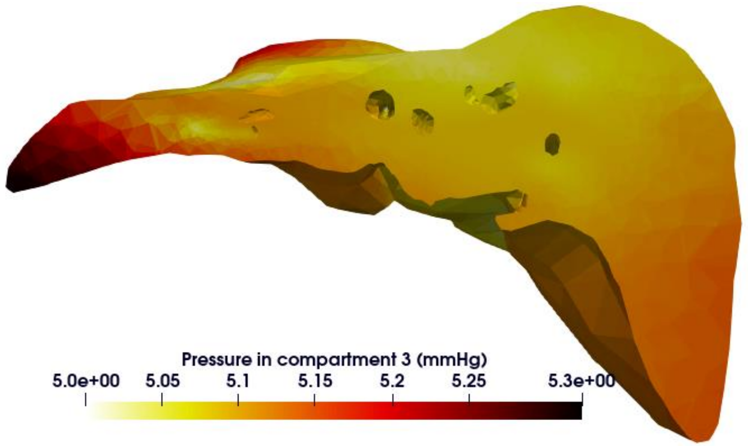
Filtration system

Compartment 3

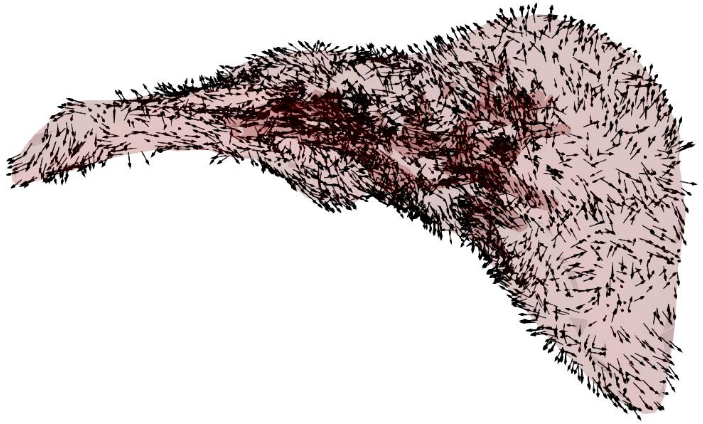
Pressure

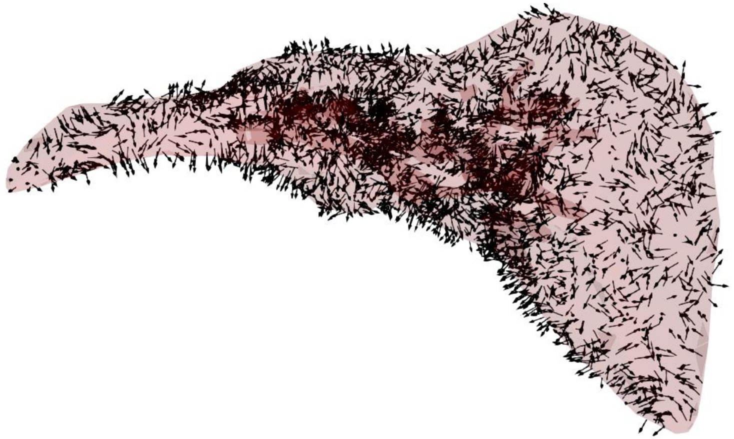


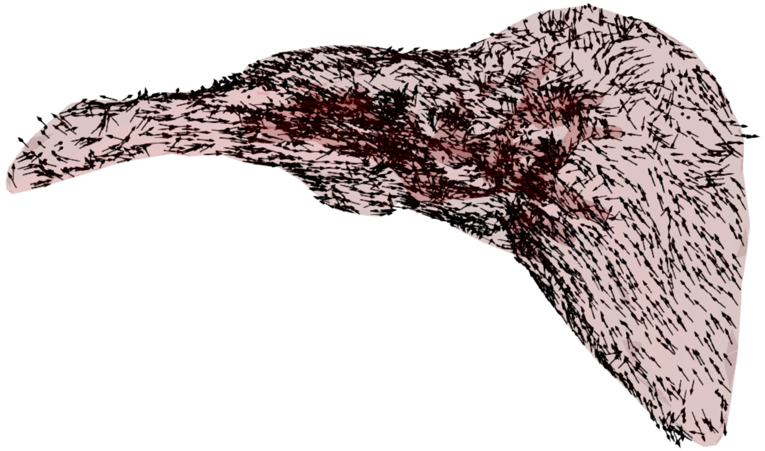




Velocity







Perspectives

- **Vessels geometry generation:**
  - A subjective process, may be different for different users
- **Porous media parametrization:**
  - Depends on the virtual network and the elementary volume
  - Possibility to find a singularity in the permeability tensor for some elementary volumes

  → Sensitivity studies (elementary volume, compartment number…)
- **Coupling method:**
  - May face optimization issues for a huge number of unknowns

  → Algorithm adaptation, resolution method
- **Validation of the model**
  - Find suitable and measurable internal quantities?