



A blood-brain-barrier microfluidic model with complexified vascular architecture to promote brain angiogenesis



Micro NanoFluidics - October 13, 2026

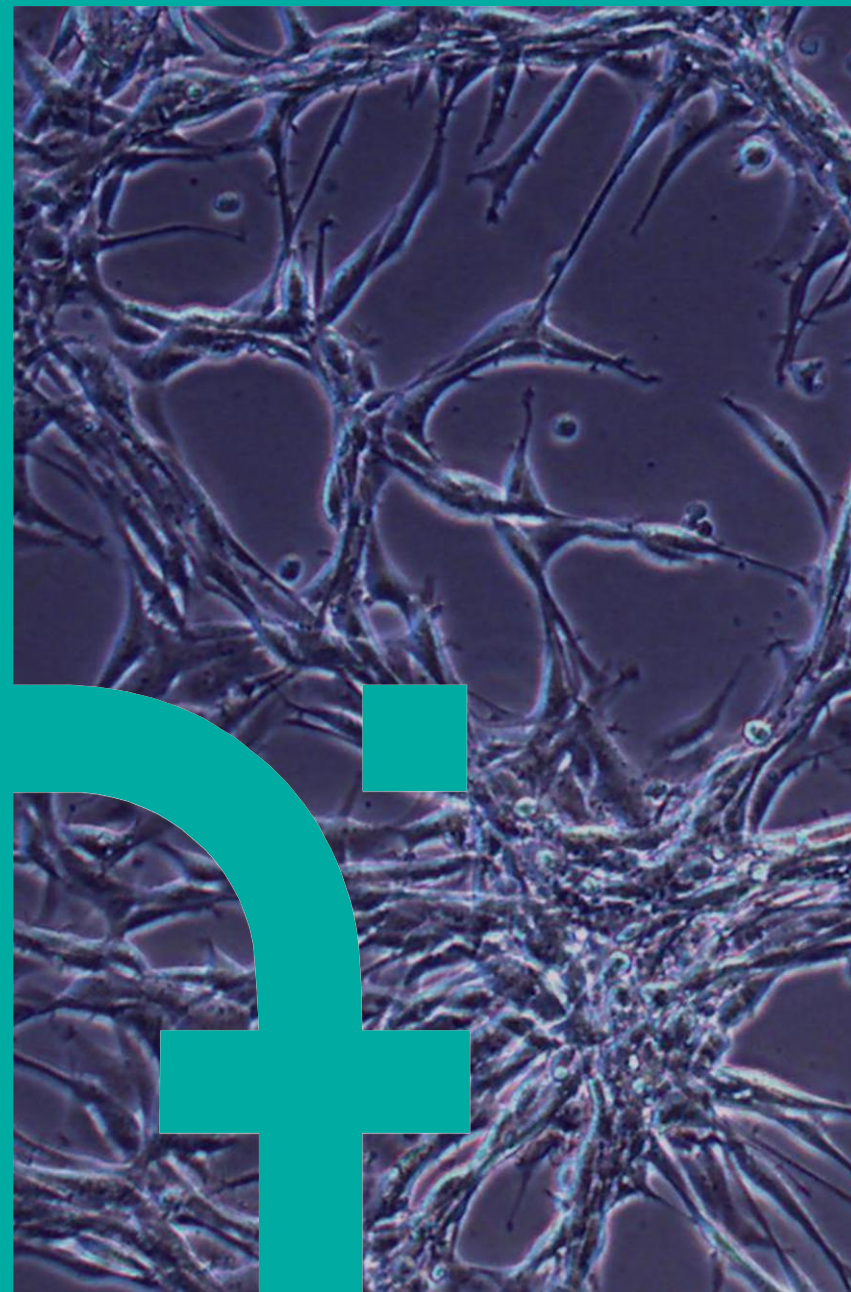
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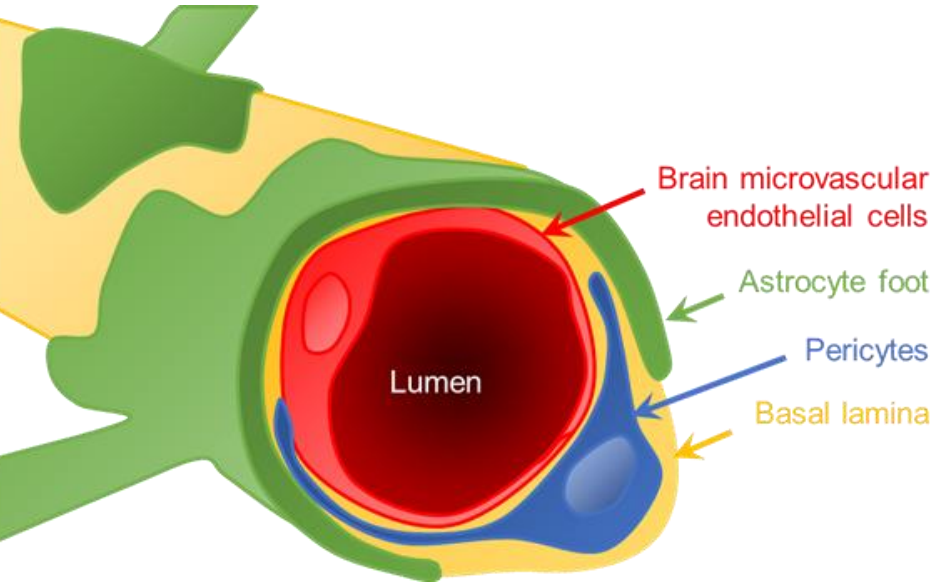
PhD supervised by Thérèse LEBLOIS and Agathe FIGAROL

Funding ANR SIBorG (ANR-23-CE52-0001)

thomas.sivier@femto-st.fr



Context: blood-brain-barrier



The blood brain barrier (BBB):

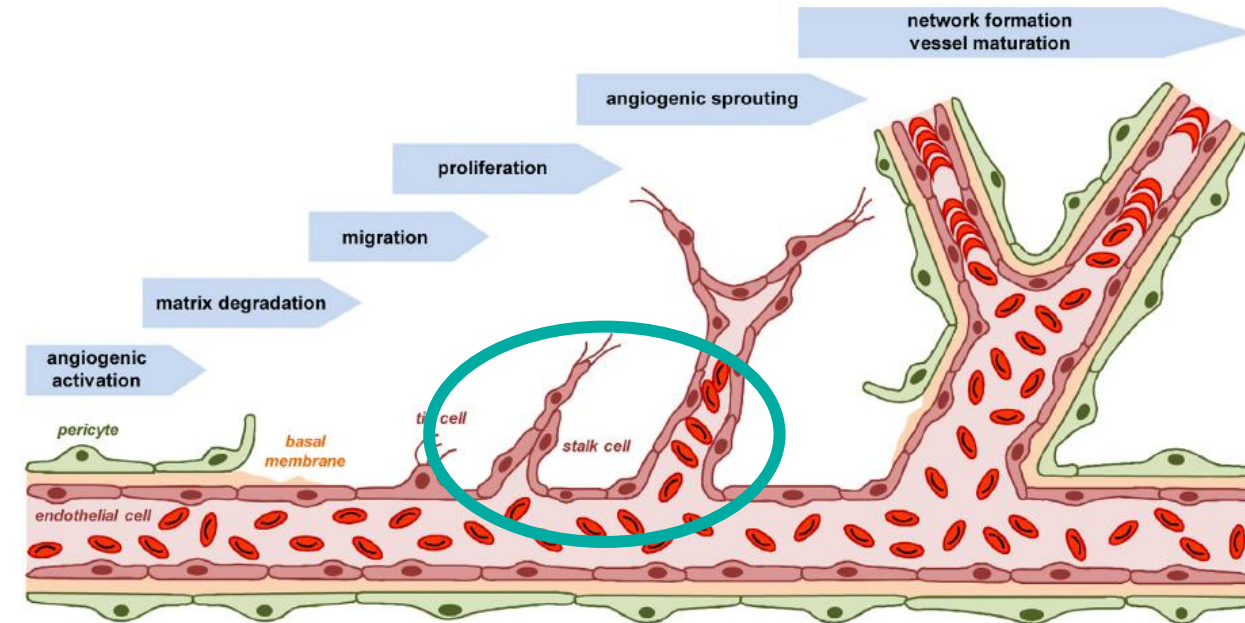
- Physical and metabolic barrier inside blood vessels
- Protection from external aggression
- Blood filtration → allows the passage of waste, nutrients, O₂, CO₂

Angiogenesis = development of new blood vessels from pre-existing ones

- Occurs through endothelial cells sprouting

→ Involved in physiological and pathological situations

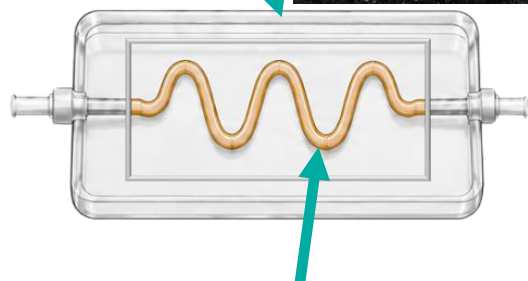
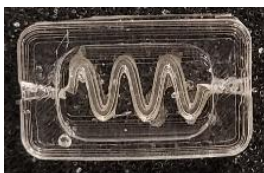
Objective: to develop a BBB microfluidic model with a macrovascularization to promote microvascularisation through brain angiogenesis



The BBB-on-chip model

Design:

- PDMS mold

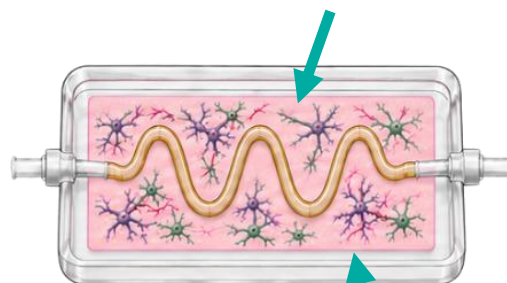
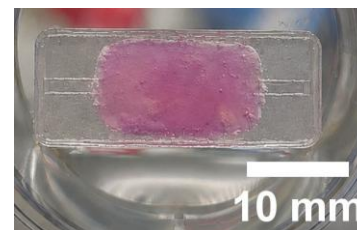


Complex design as sacrificial template

- Dissolution of the template for channel formation

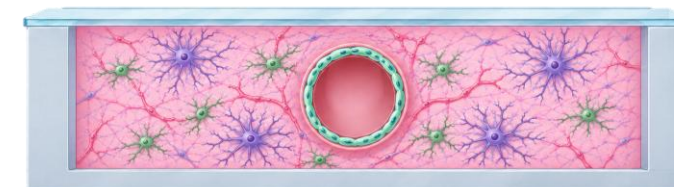
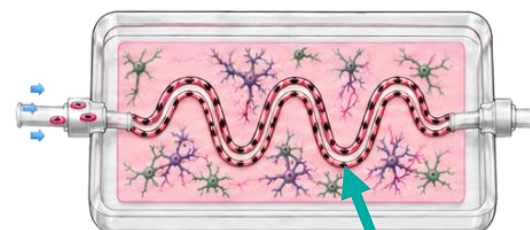
Hydrogel:

- Extracellular matrix
- 3D cell organisation
- Interactions
- Molded around sacrificial template



3D cell culture :

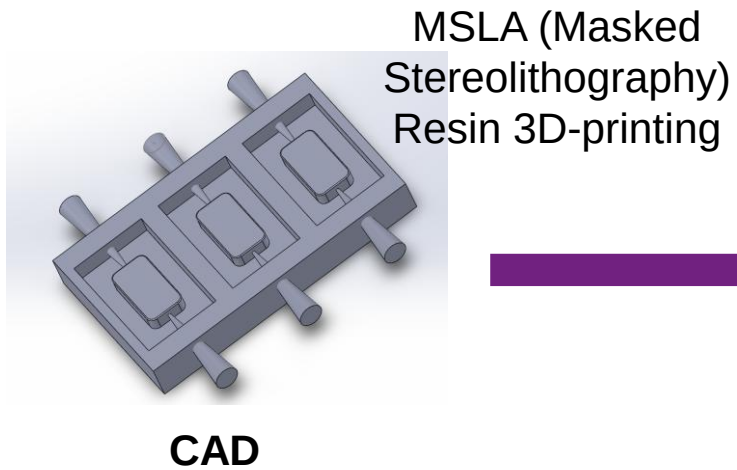
- Human astrocytes (HA)
- Human pericytes (HP)



MACRO and MICRO-vascularization:

- Endothelial monolayer all around the newest channel
- Cells auto-organization = **angiogenesis**

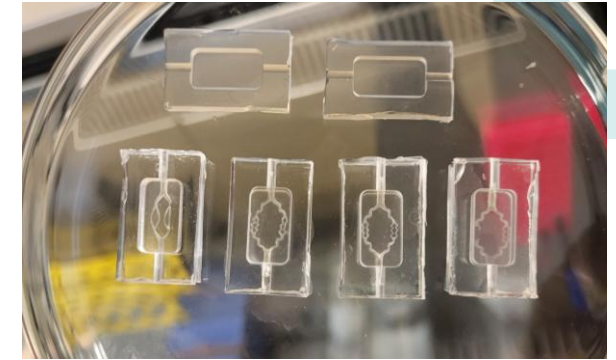
BBB-on-chip design



PDMS pouring

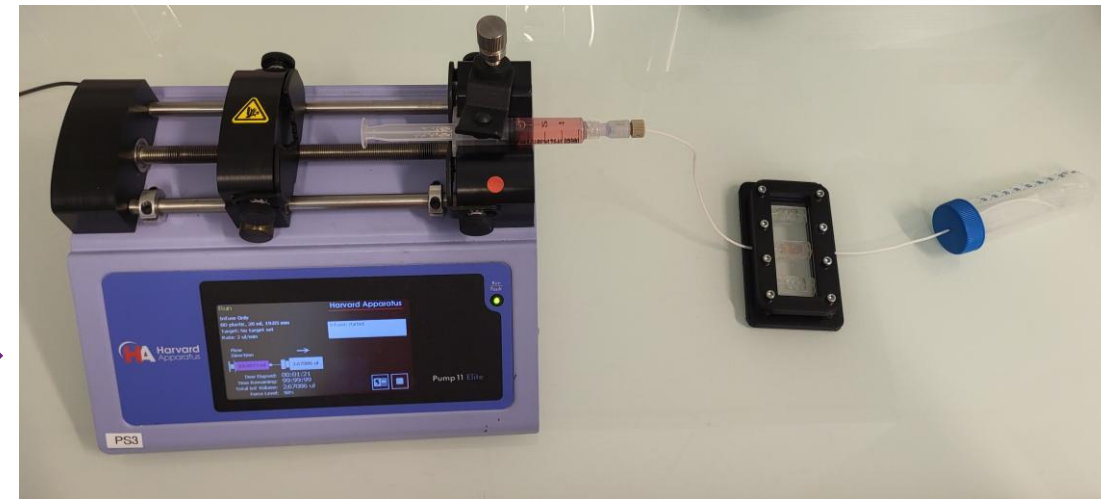


PDMS microchip



Lock and play device

Sealed but reversible
closure of the microchip with
glass cover and screws

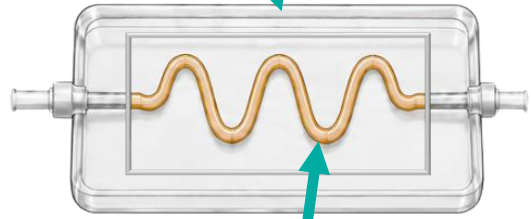
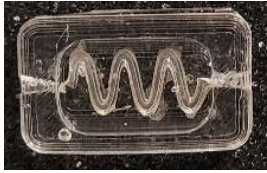


Perfusion setup

SIBorG project : BBB-on-chip fabrication

Design:

- PDMS mold

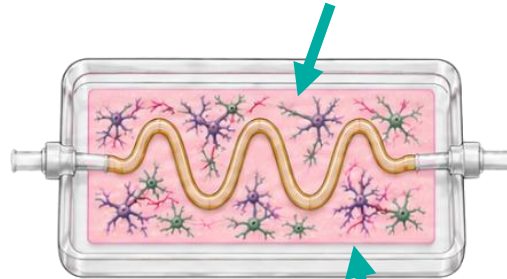
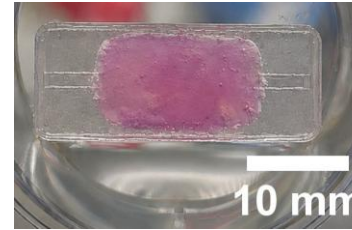


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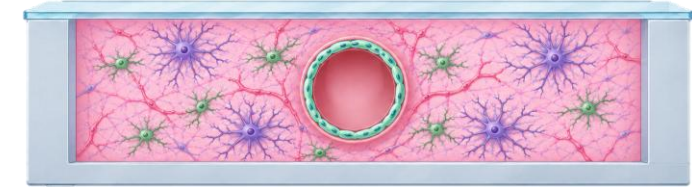
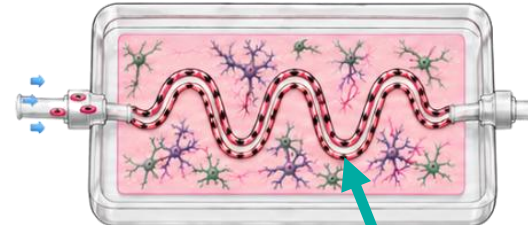
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3D cell culture :

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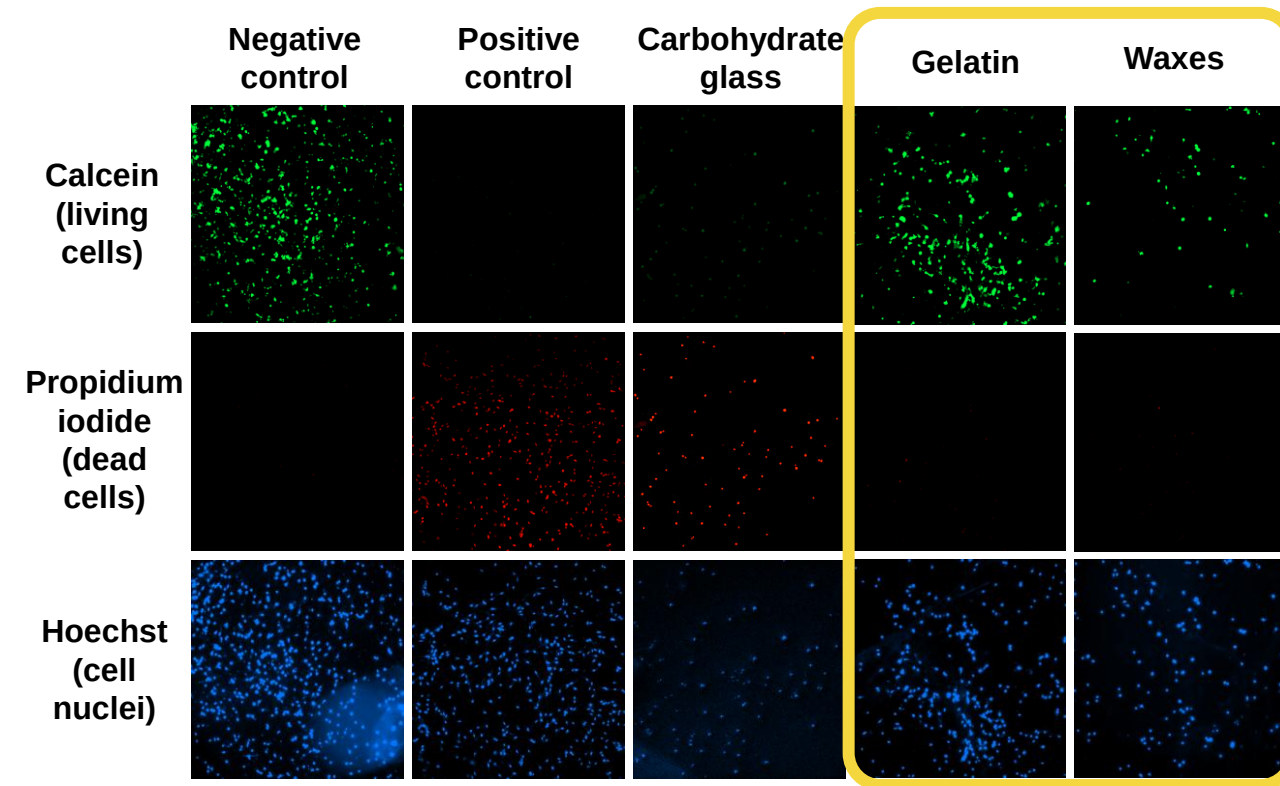
Sacrificial materials for vascular architecture complexification

3 sacrificial materials:

Carbohydrate glass

Gelatin

Polyester-paraffin waxes



Live-dead results

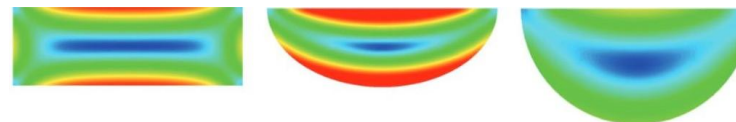
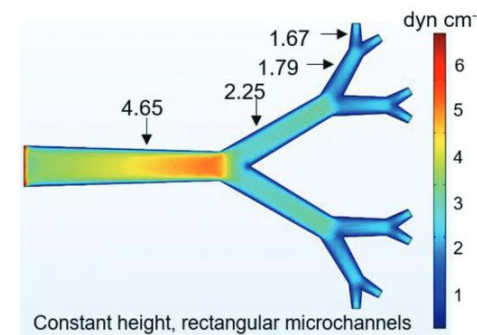
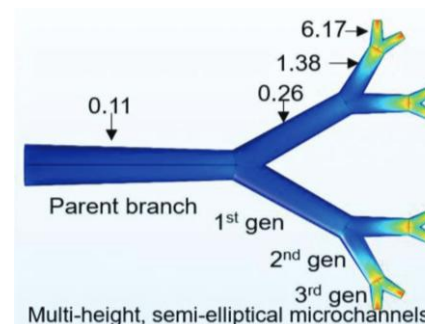
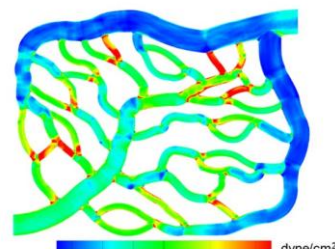
	Synthesis	Molding demolding in PDMS	Dissolution at 37°C
Carbohydrate glass	✓	✗	✓ with PBS
Gelatin	✓	✓	✓ with albumin 30%
Waxes	✓	✓	✗ with PBS (> 42°C)

Physico-chemical properties

→ Gelatin is the optimal sacrificial material

Designing the vascular network

Vessels	Wall shear stress (WSS)
Arteries	10 – 70 dyn/cm ²
Capillaries	5 – 23 dyn/cm ²



Emilie MOURIC
M2 internship

What is important?

Parameter	Value
Geometry	Semi-elliptic
WSS	5 to 6 dyn/cm ² in the smaller vessels
	Gradient
Tortuosity	Low to high

Limitations for WSS reproduction:

- Minimum diameter achievable
- Maximum flow rate that can be applied at the inlet without causing leaks
- Fluid that does not have the rheological properties of blood

→ Get as close as possible to physiological values to maximize angiogenesis

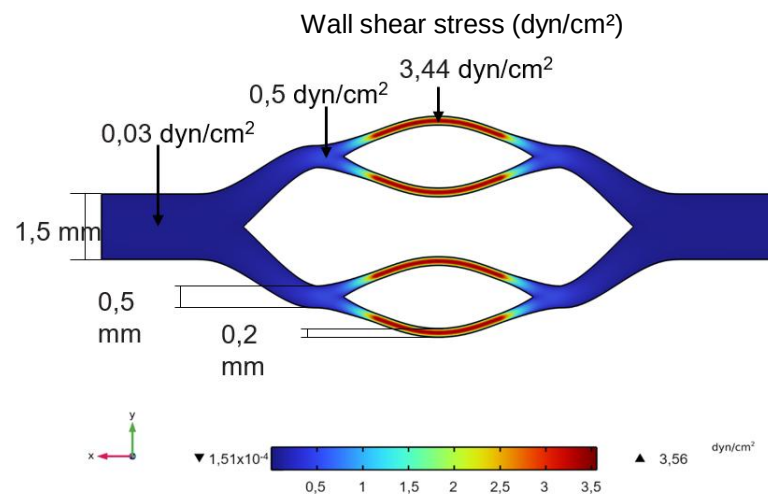
Designing the vascular network

3 designs developed:

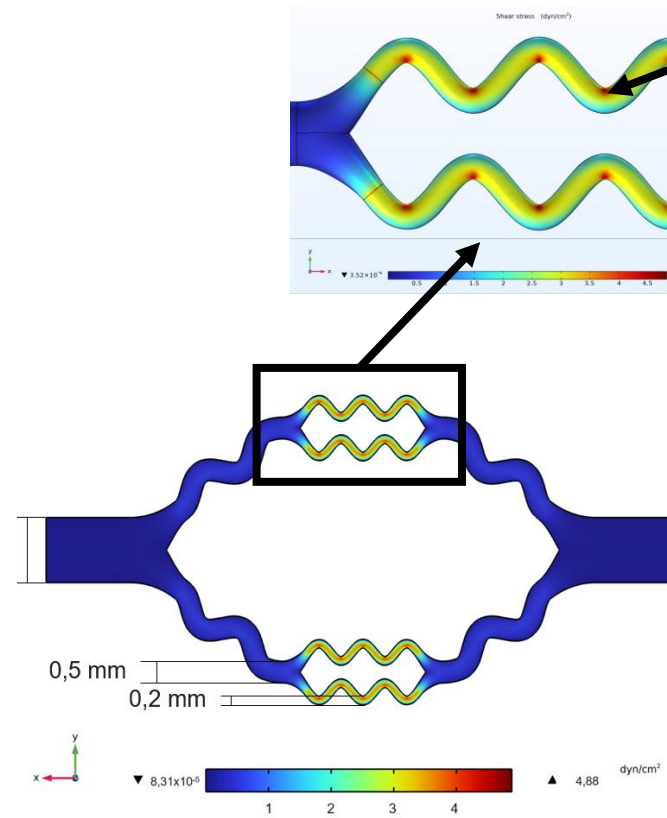
Sprouting is expected to occur at the apex of curvatures where shear stress is smaller



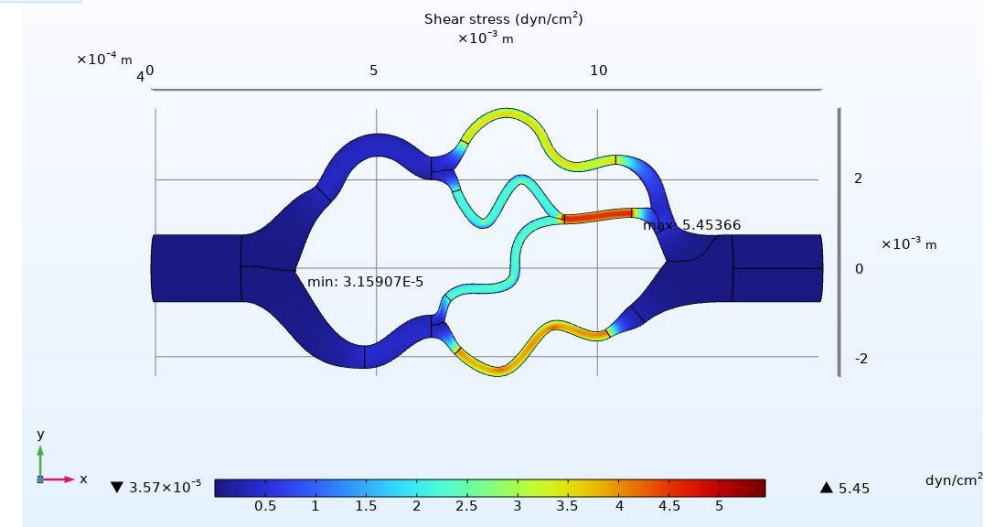
Emilie MOURIC
M2 internship



Simple hierarchical network



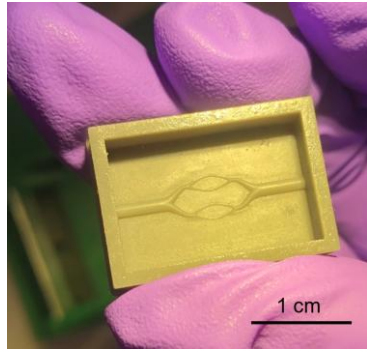
Complex hierarchical network



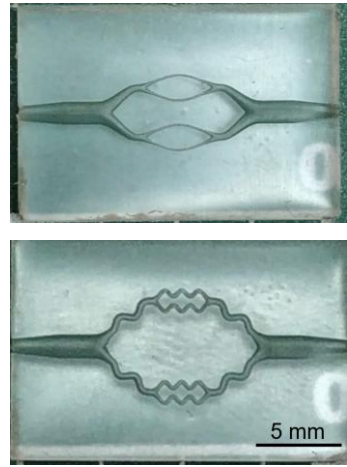
Tortuous hierarchical network

Fabrication of the vascular template

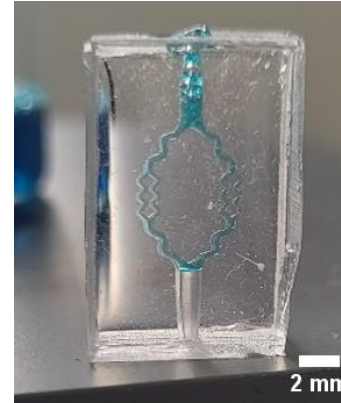
Negative mold
printed in resin



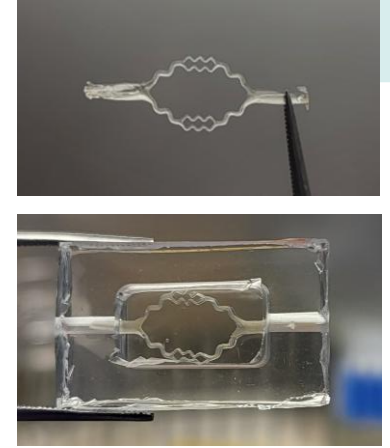
PDMS-PDMS mold



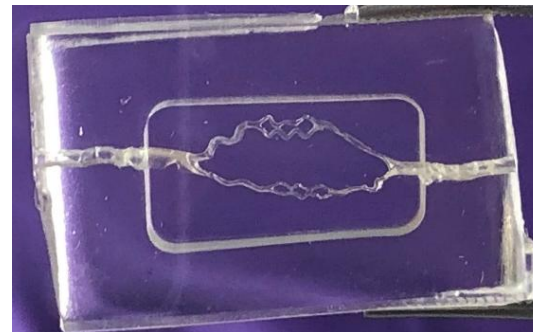
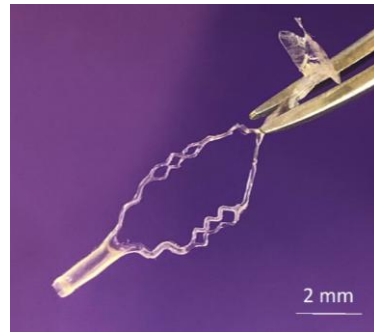
Gelatin pouring



Sacrificial template



But ...



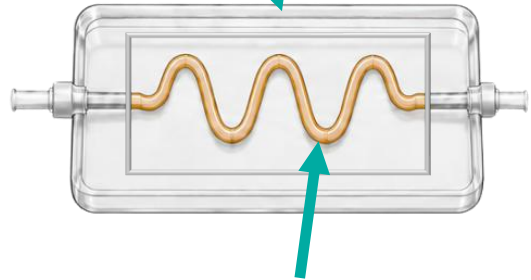
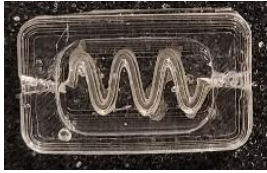
Weakness in the small channels

3D bioprinting
and changing
chip design?

SIBorG project : BBB-on-chip fabrication

Design:

- PDMS mold

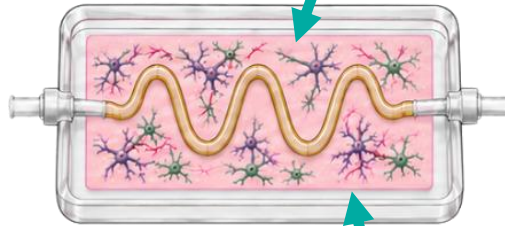
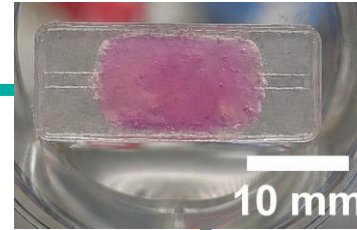


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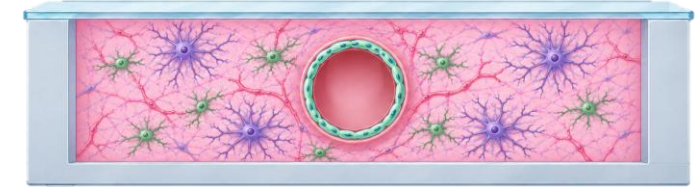
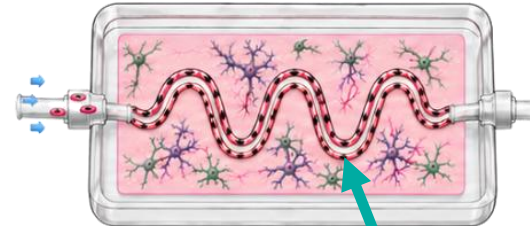
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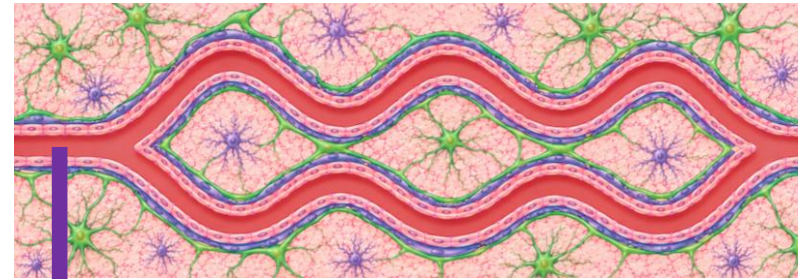
MACRO and MICRO-vascularization:

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Promote microvascularisation

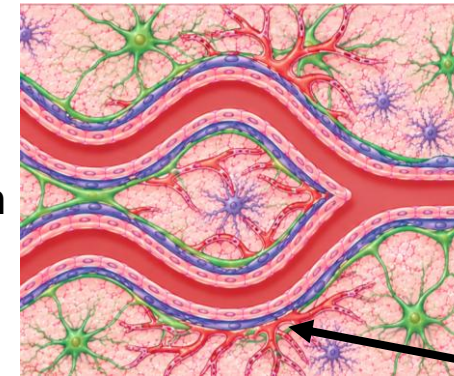
Hydrogel composition

Hyaluronic acid (mg/mL)	2,5
Collagen (mg/mL)	2,5
Fibrinogen (mg/mL)	5
Thrombin (U/mL)	1
HA (cell/mL)	$3,33 \cdot 10^6$
HP (cell/mL)	$0,83 \cdot 10^6$



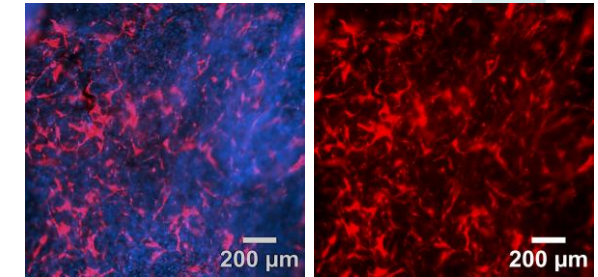
Perfusion

Microvascularization
= capillaries through
angiogenesis



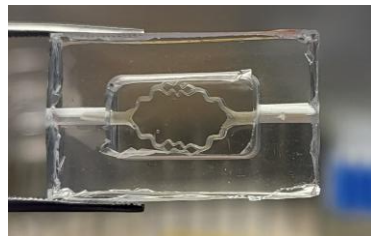
Macrovascularization
= arteriole

Hoechst
CD31

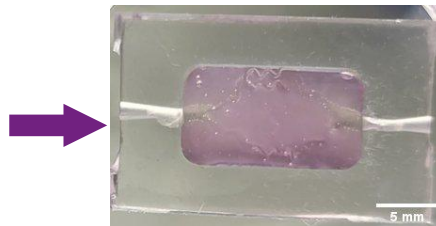


Early endothelial network formation

Sprouting



Gelatin in the chip



Hydrogel pouring + gelatin
dissolution
→ Channel formation

Endothelial cells
seeding inside
the channel



Medium perfusion in the channel for
microvascularization formation

Conclusion

Design and conception of the BBB-on-chip

- ✓ Model design: CAD → **PDMS microchip**
- ✓ 3 sacrificial materials assessed: carbohydrate glass, gelatin, polyester/paraffin waxes → **gelatin**
- ✓ Vasculature design simulations → **validation of 3 macrovascularization designs**
- ✓ Hydrogel composition → **early endothelial network formation**
- ✗ Template fabrication → **3D bioprinting and changing the chip design**
- ✗ Perfusion and dynamic culture for macrovascularization by arteriole formation, then microvascularisation through angiogenesis (capillaries formation)

Perspectives

- Validation of the BBB function: permeability and nanoparticles assays
- Instrumentation for real-time monitoring (pH, O₂)
- Addition of tumor cells for the development of a glioblastoma-on-chip model

THANK YOU FOR YOUR ATTENTION

ANY QUESTIONS?

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