

Artificial Microcirculation replicas using backside lithography for blood flow analysis

BioMP

BioMicrofluidics
& BioPhotonics
ies.univ-montp2.fr/biomp/

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Hemophysics

For physicists, blood is a **complex fluid**

Suspension of **highly deformable cells**

Shear thinning, viscosity \searrow shear rate

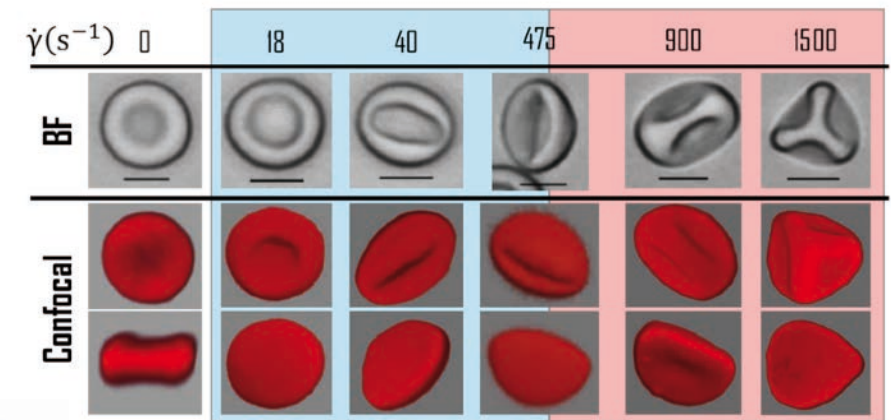
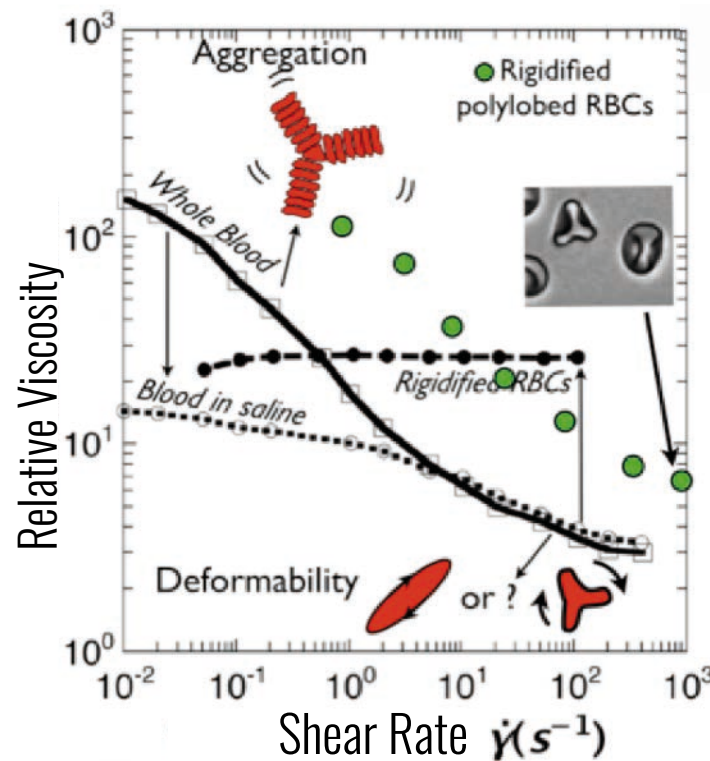
Aggregation / cell deformation

Cell free layer

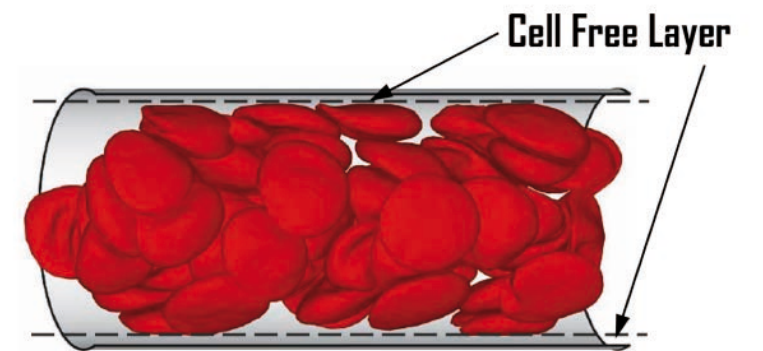
Margination / diffusion

Anti Weissenberg effect ?

Surface tension ?



L. Lanotte, M. Abkarian et al.
A new look on blood shear thinning PNAS (2016).



Rigidified RBCs : Stroke on a chip



Trilobe shape
Simulation
Yales2bio
S.MENDEZ, IMAG
Montpellier

... and blood flows in **complex vascular networks**

Vascular networks

From the heart to an
hierarchical network of

Arteries

Arterioles

Capillaries

Veinules

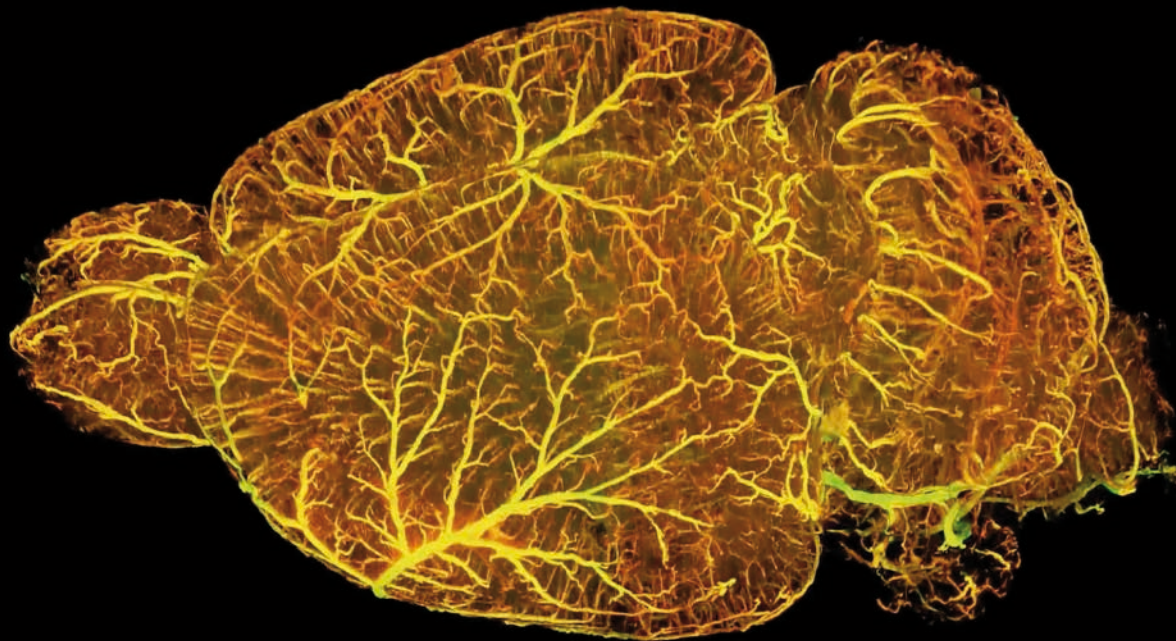
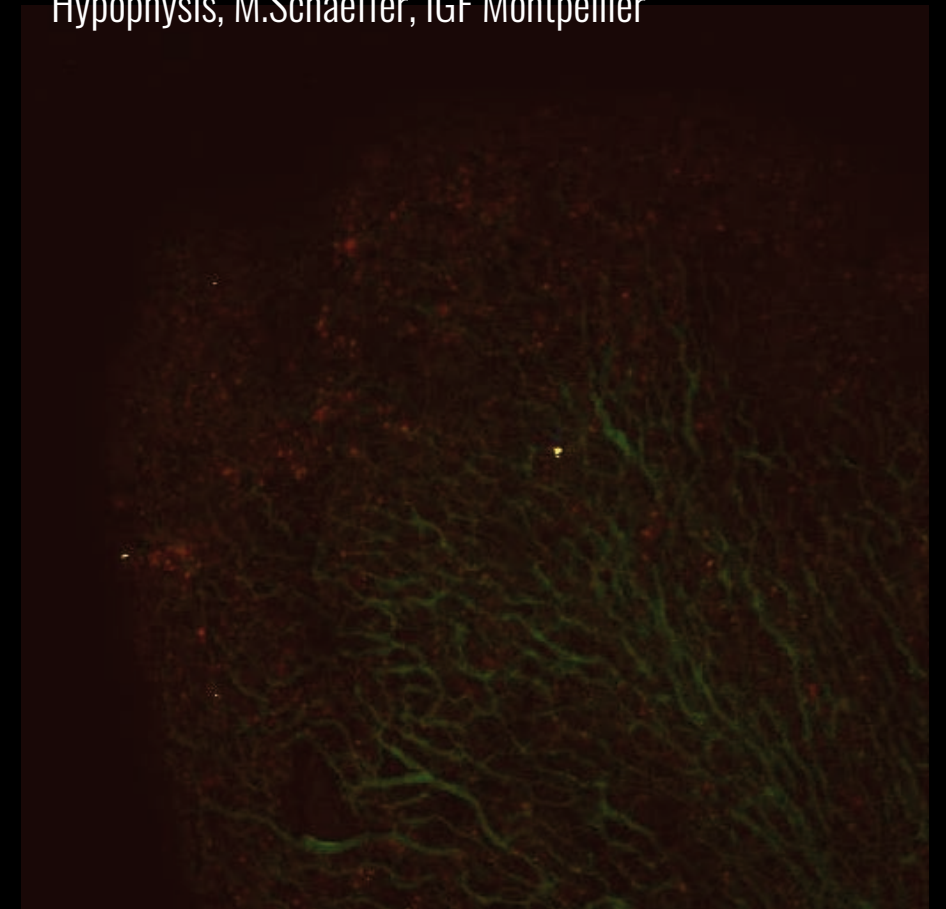
Veins

for an optimum perfusion of blood in
the tissues

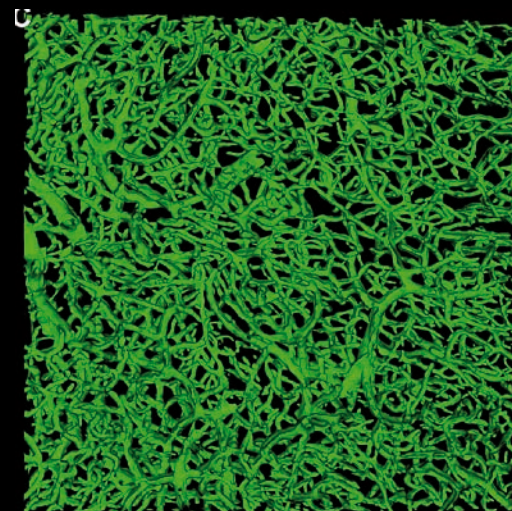
! Bifurcation, branches, loops and tortuosities

! Static or dynamic

Hypophysis, M.Schaeffer, IGF Montpellier



light-sheet microscopy + segmentation
M.I. Todorov et al. Automated analysis of whole
brain vasculature using machine learning, BiorXiv



600km of vessels in your brain

Vascular network

of a murine lymph node

1mm long

0,2 mm³

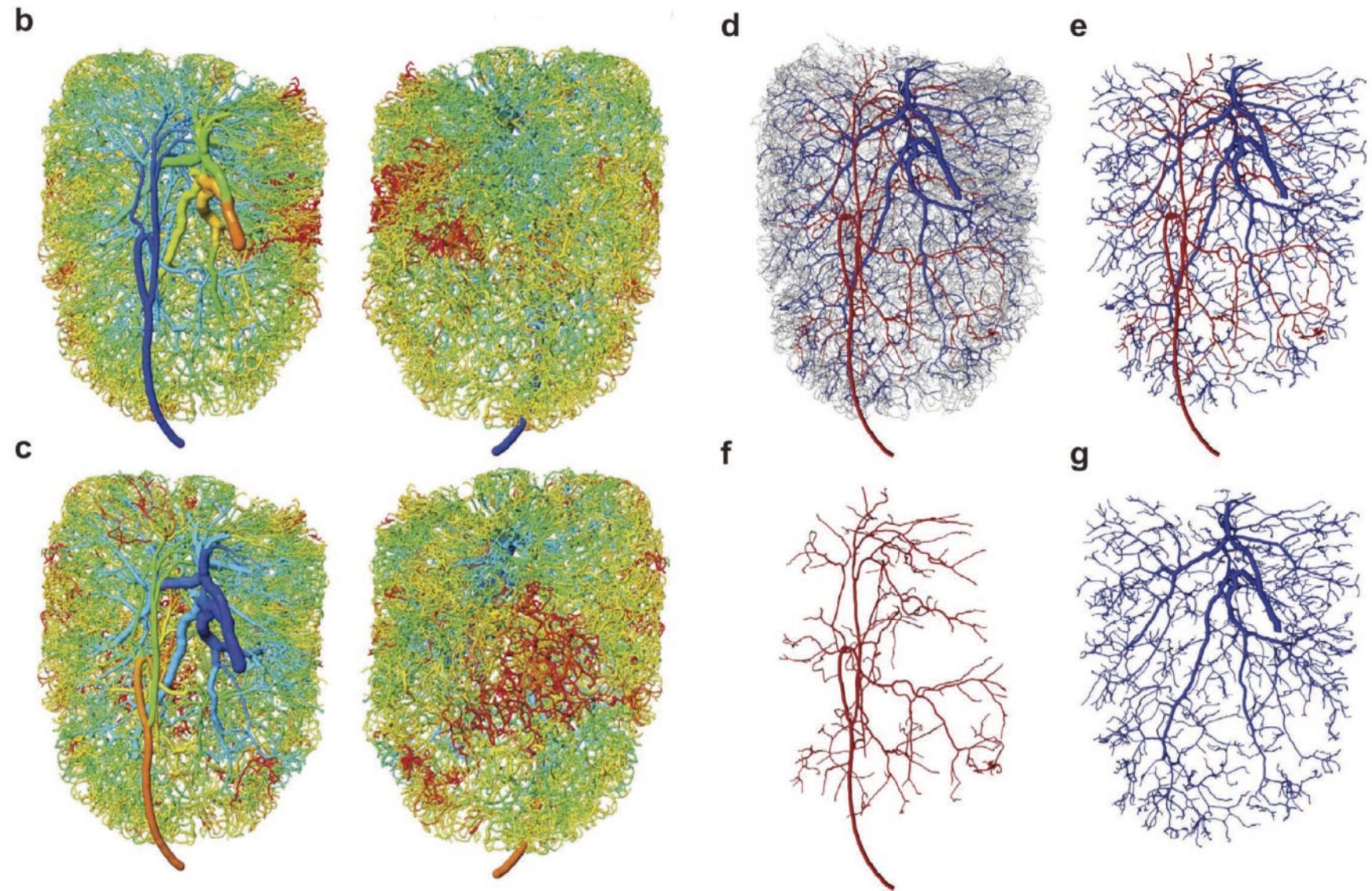
16 000 vessels

12 000 Nodes

90cm long network

One input

One output

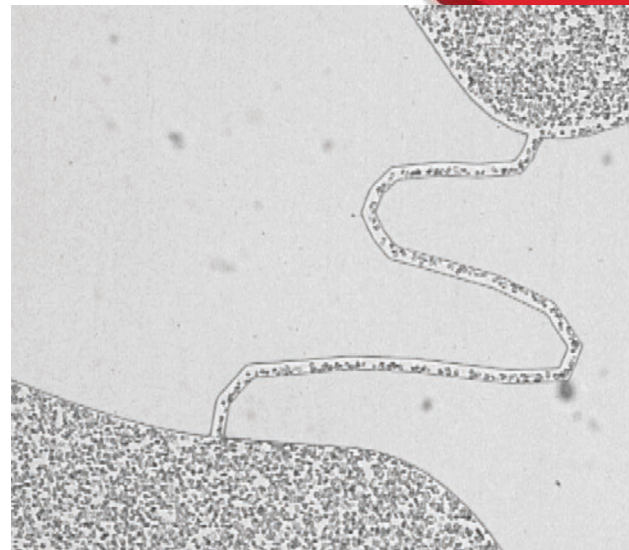
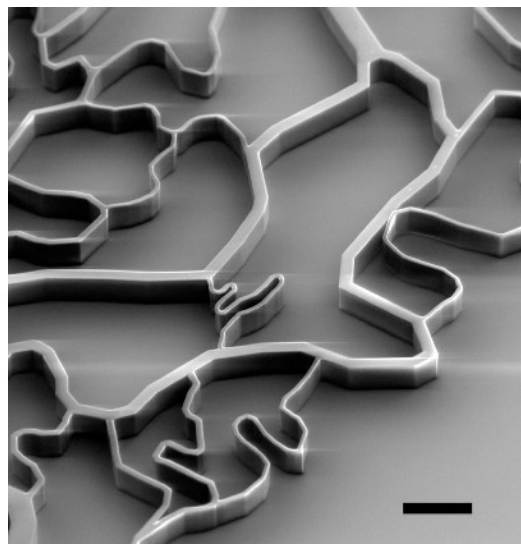


Organ-wide 3D-imaging and topological analysis of the continuous microvascular network in a murine lymph node P. Rod Dunbar, Sci. Rep. 5:16534

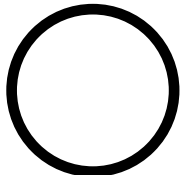
Difficult to reproduce in microfluidics....

Standard SU-8 / PDMS Microfluidics

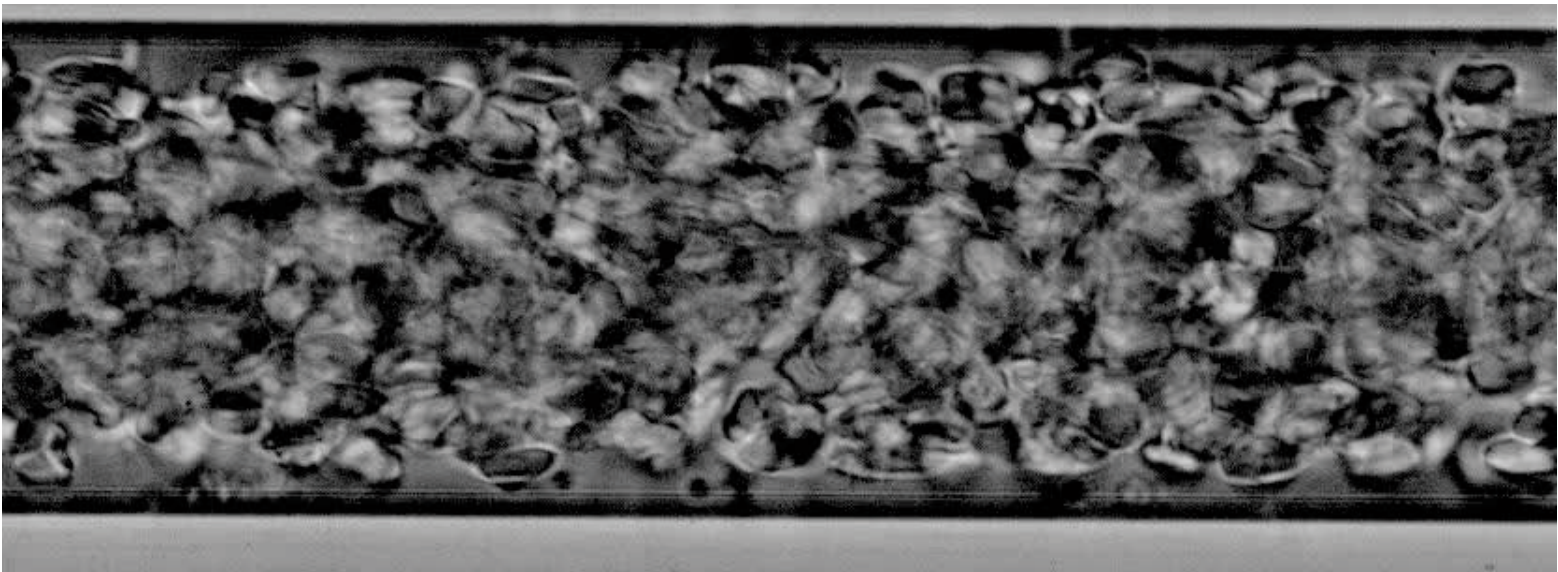
- same height everywhere
- rectangular section



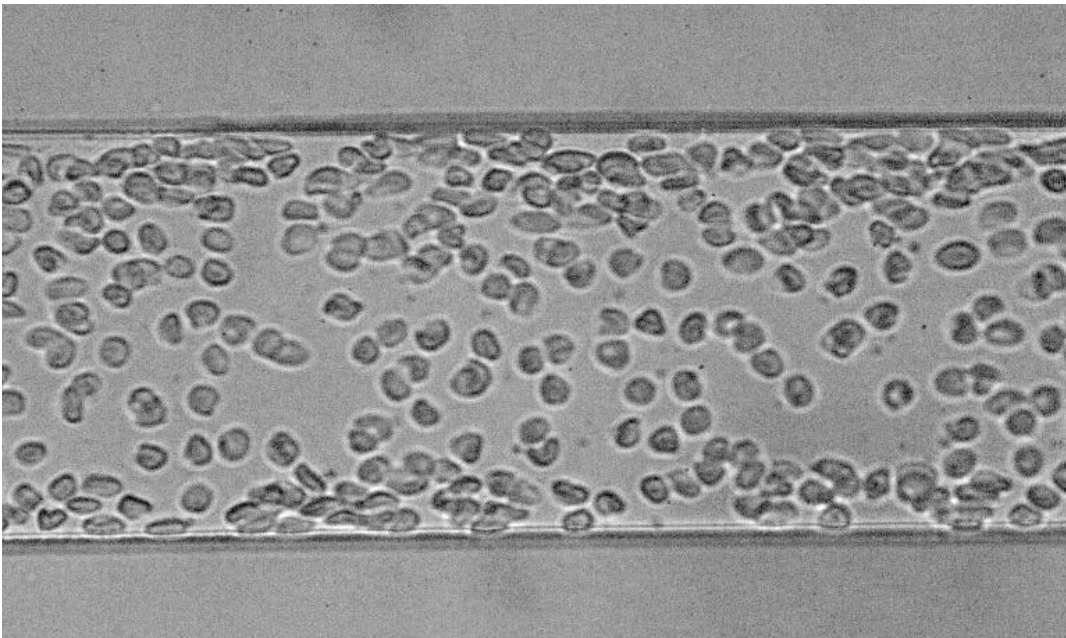
Blood flow in microfluidics



Glass capillary



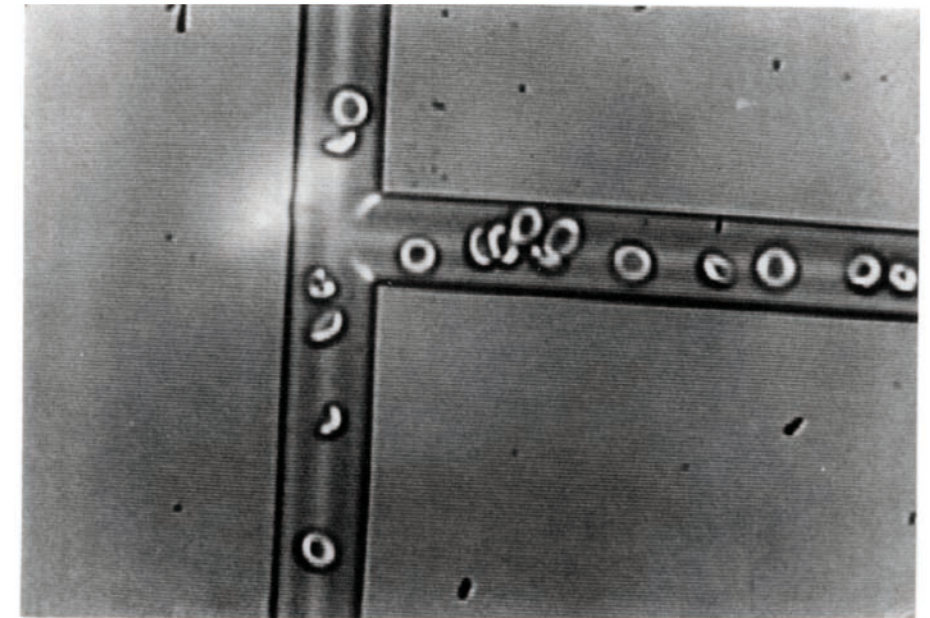
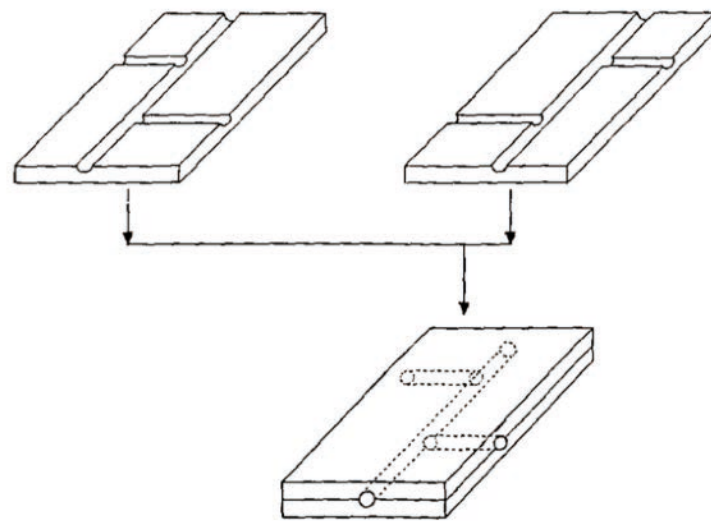
Microfluidic



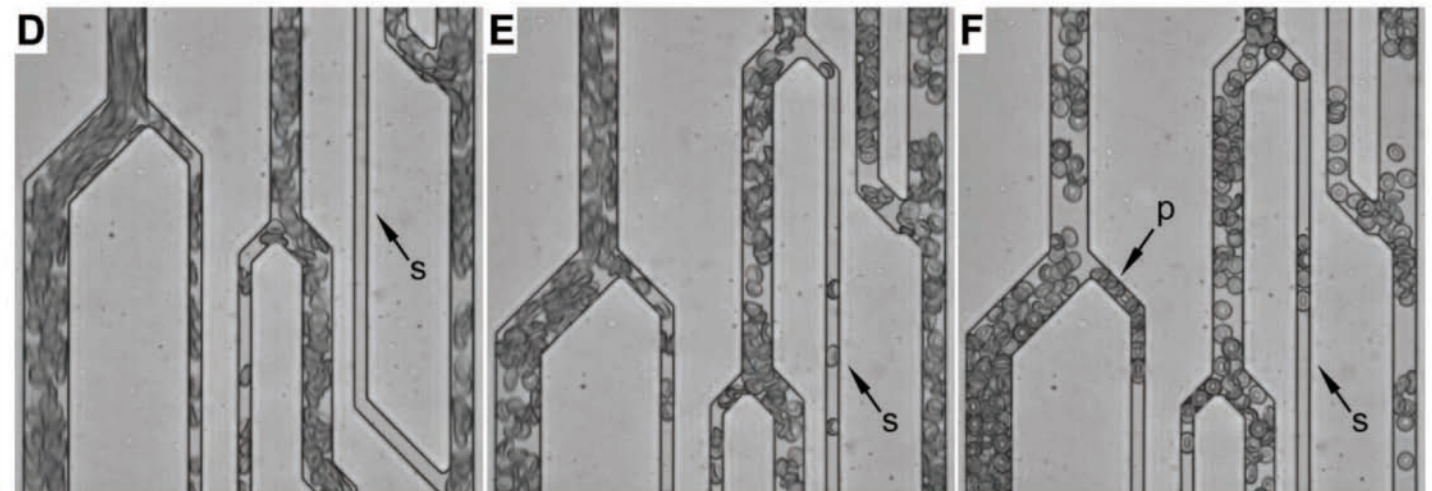
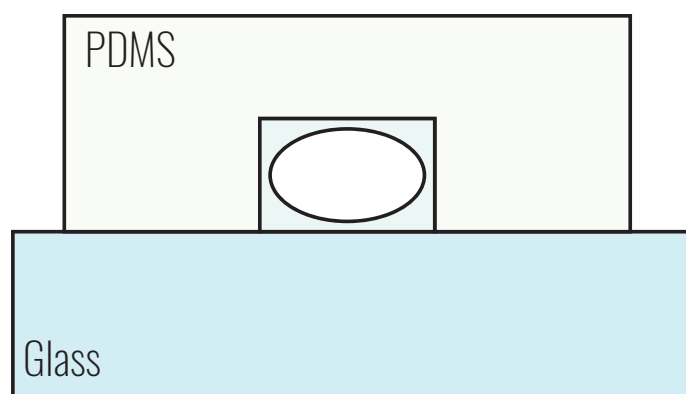
Slit like
channels
One cell layer

Microfluidics

G.R.Cokelet, Univ.Rochester



Serguey Shevkoplyas, Univ. Houston



Round channels, still same height...

Something more realistic

A 3D rendering of a red, wavy channel with a mesh-like structure in the center, connected to two larger red cylindrical structures. The channel is shown in a perspective view, with the mesh structure being a grid of rounded rectangular openings. The channel is connected to two larger red cylindrical structures, one on the left and one on the right. The background is a light gray gradient.

- Height gradation function of width
- ~~Circular~~ rounded channels

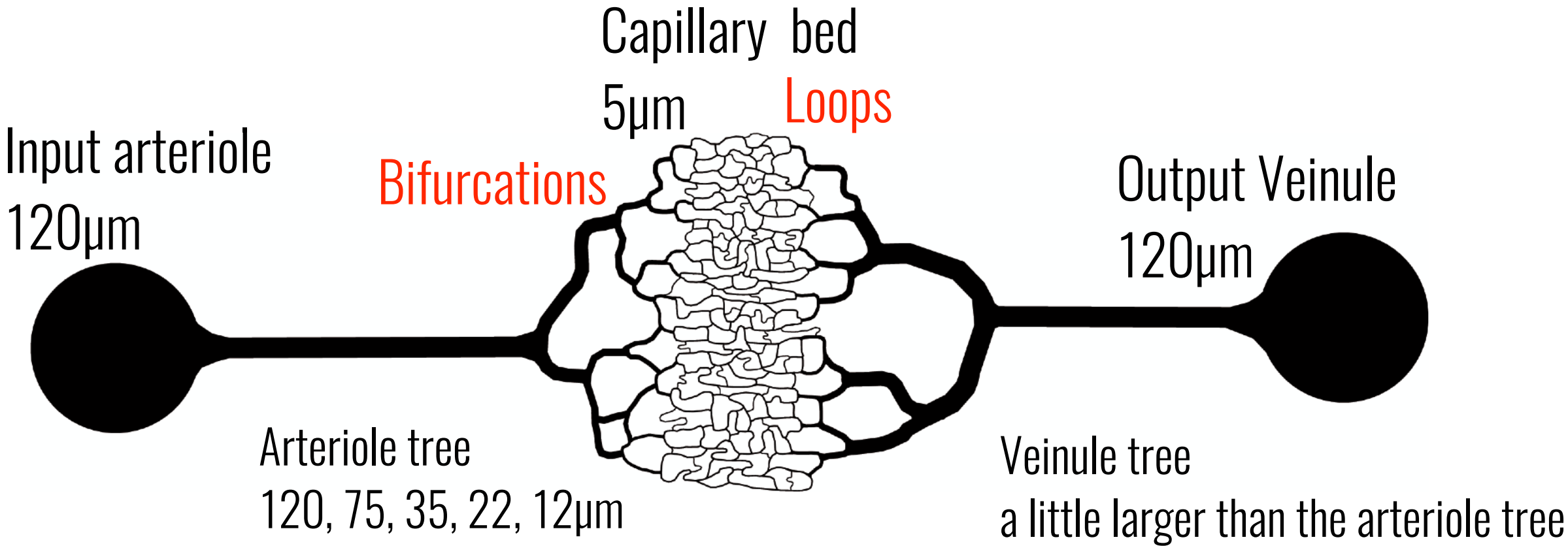
keep it simple.... One photomask, standard lithography equipment

Network design

First of all, a model of a 2D network



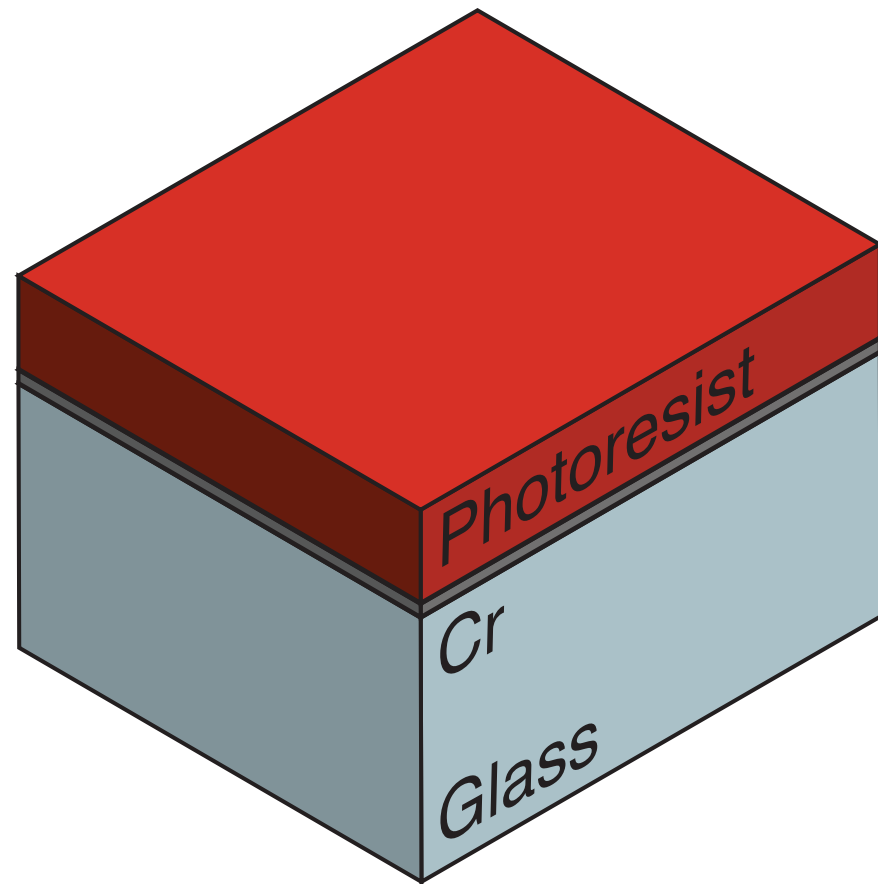
3D → 2D projection



Network statistics : Vessel sizes, length and number distribution, nodes and connectivity, loops, tortuosities

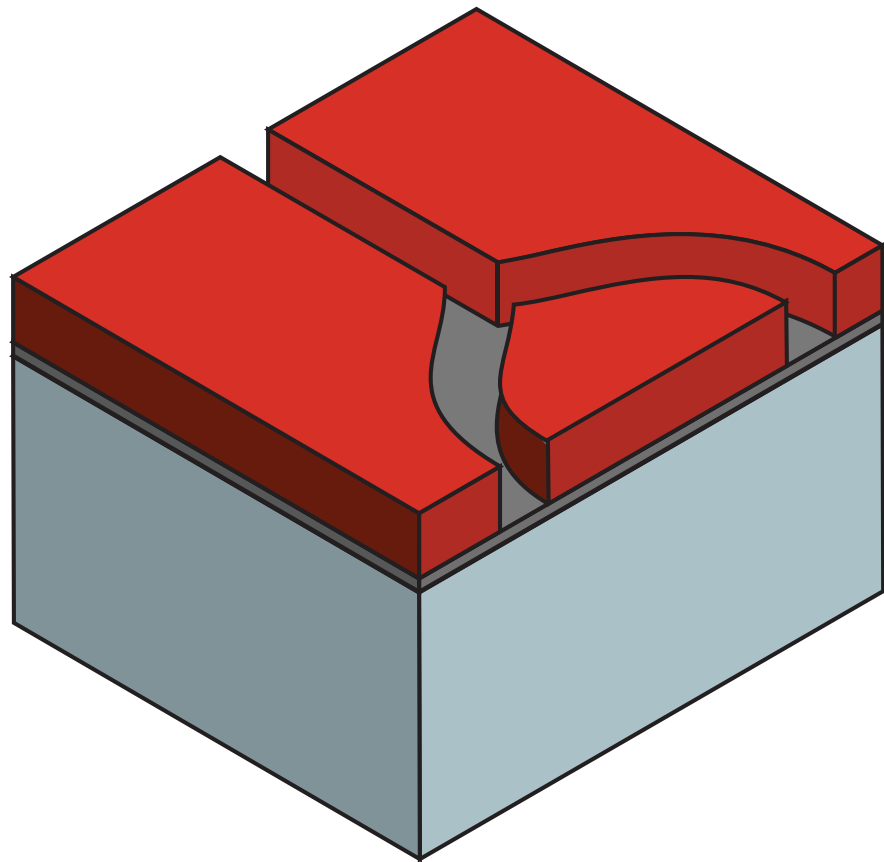
Now let's fabricate it

Microfabrication

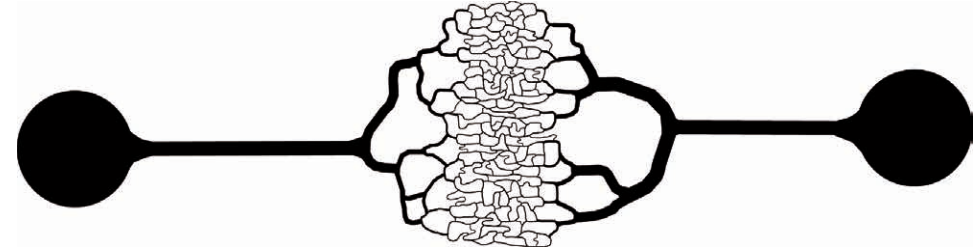


500 μ m glass
Piranha clean
100nm Cr evap
AZ2020 photoresist

Microfabrication



Lithography

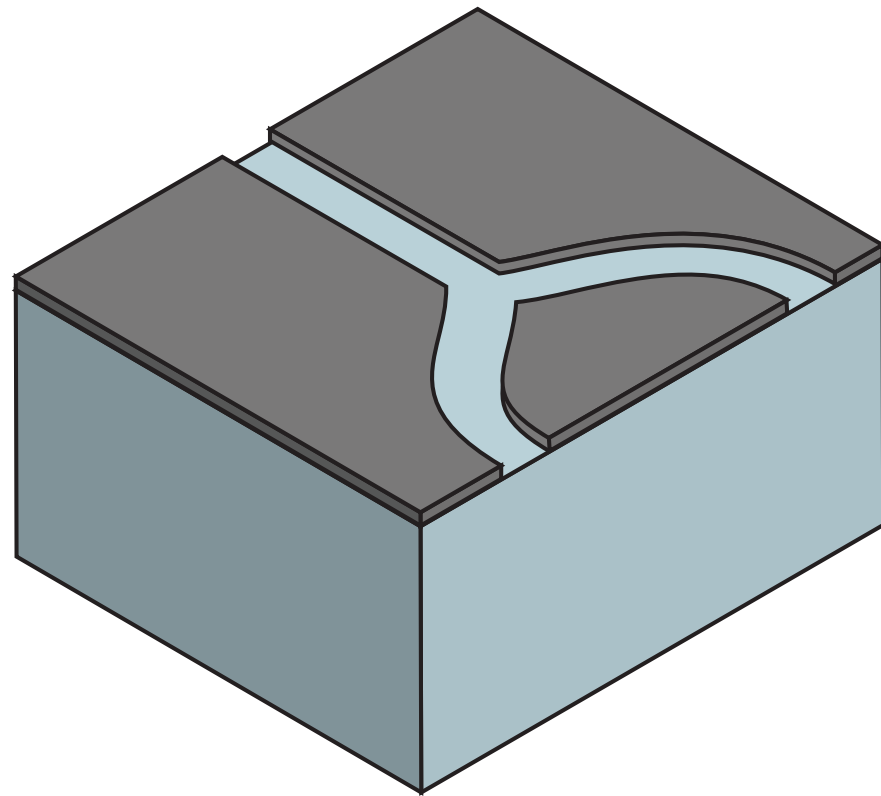


Spin coating

Baking

Development

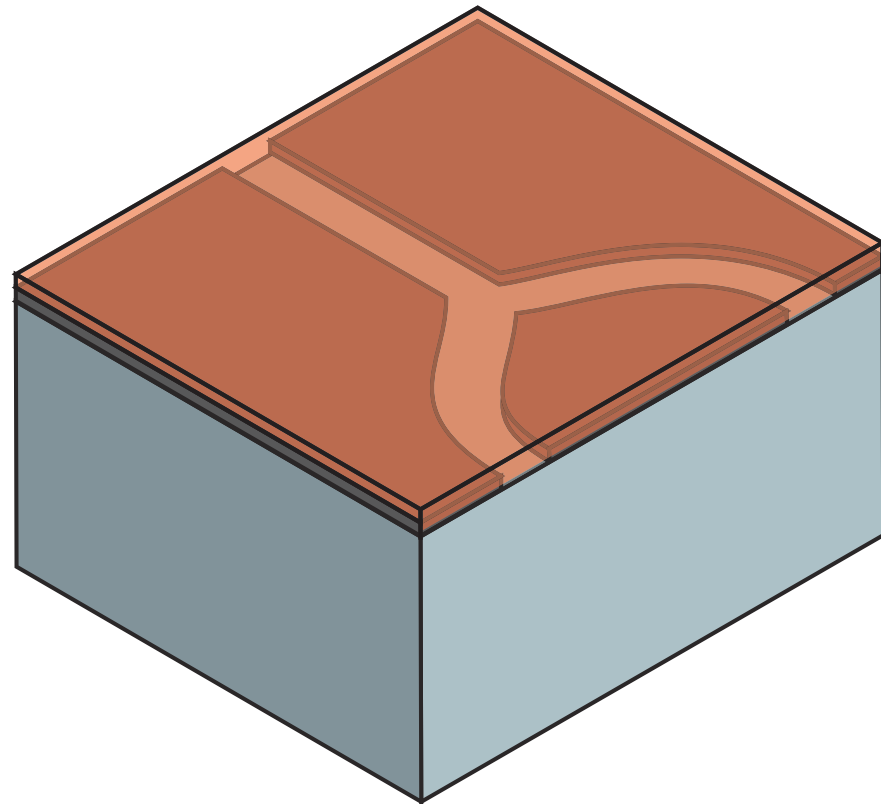
Microfabrication



Chrome wet etch

....now it looks like a photomask

Microfabrication



! bad adhesion of SU-8 on Cr

Adhesion layer

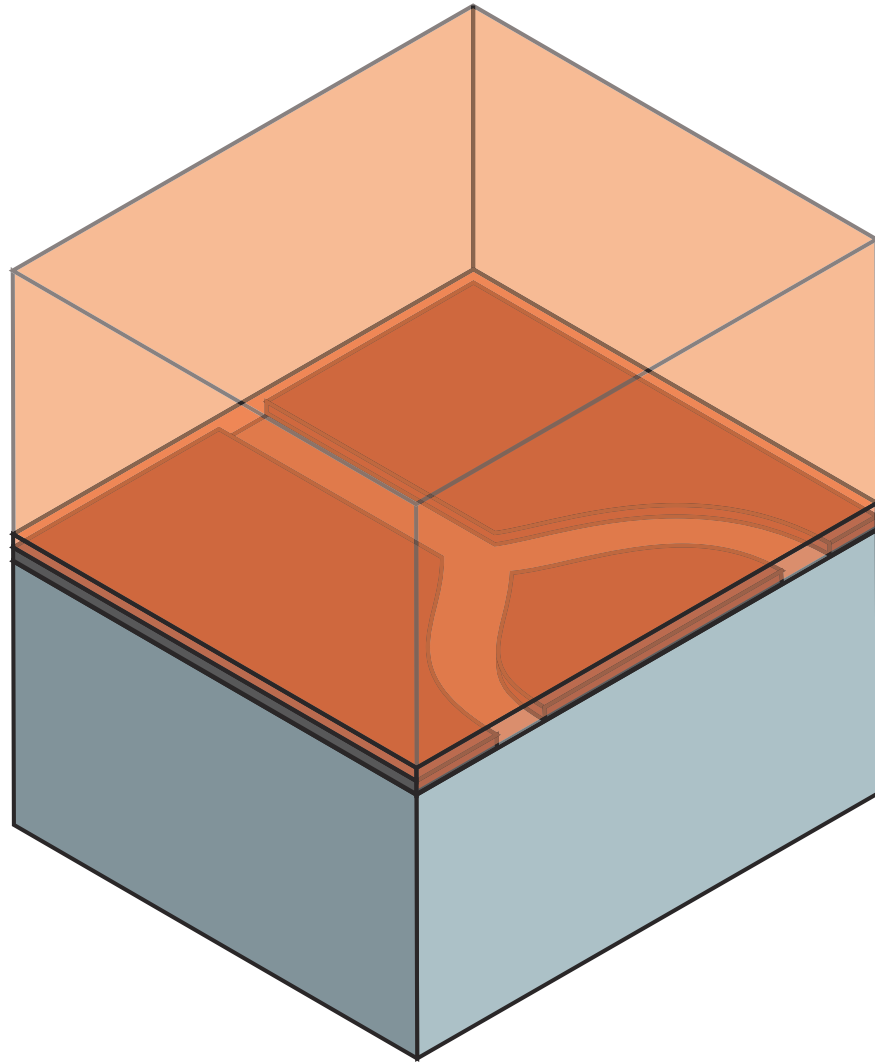
SU-8 2002 @5000rpm

Baking

Flood exposure

Post exposure Baking

Microfabrication



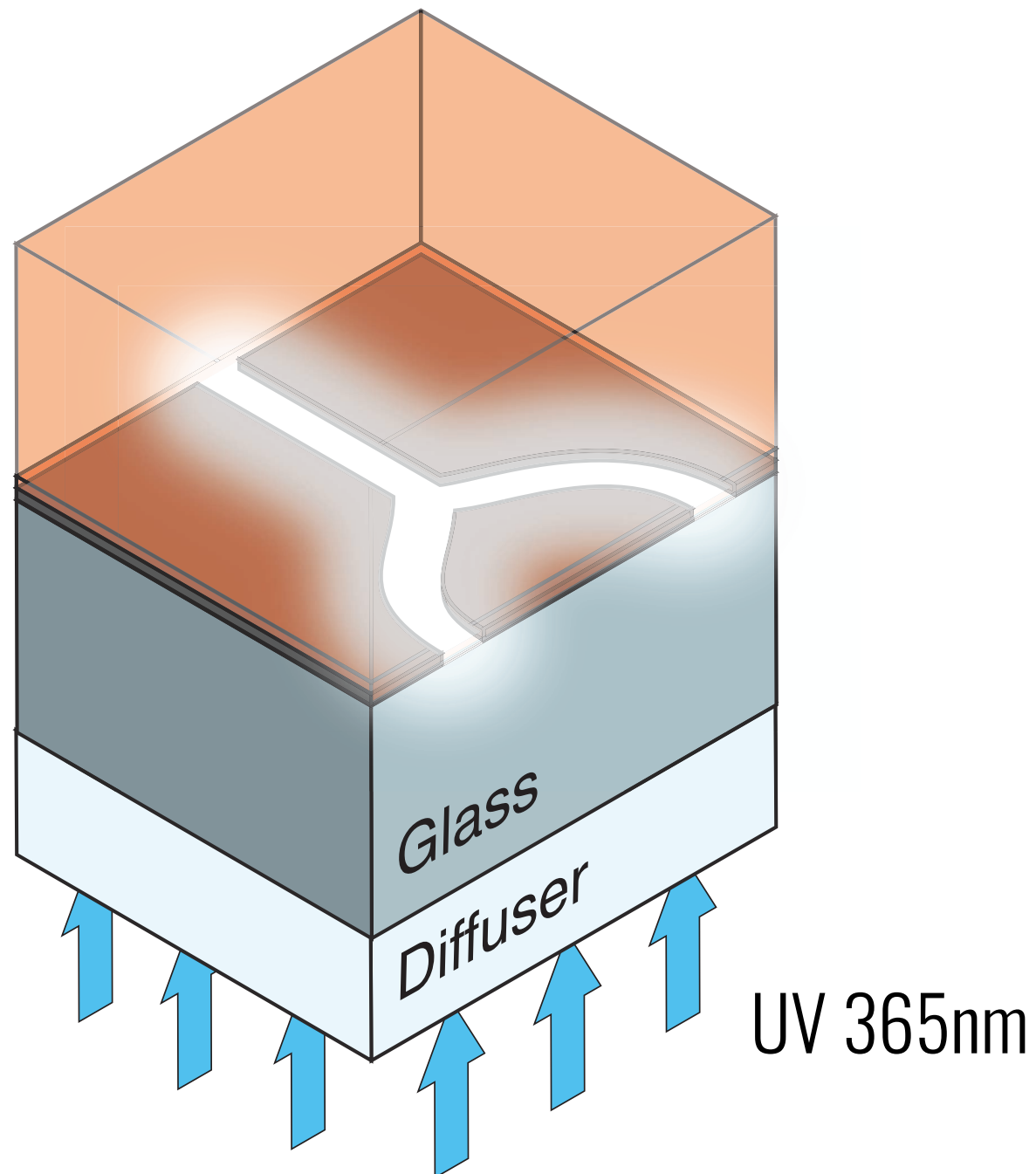
Thick SU8

No spincoating

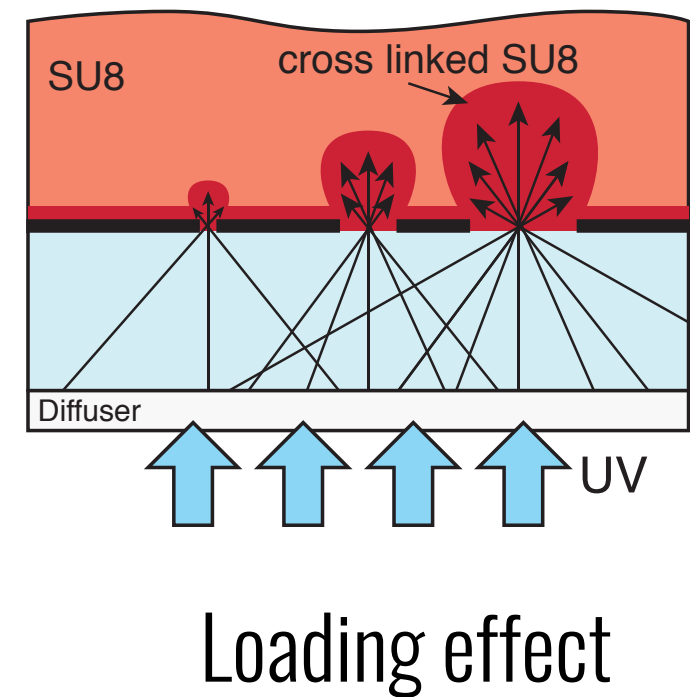
Thickness > largest opening
on the mask

Baking

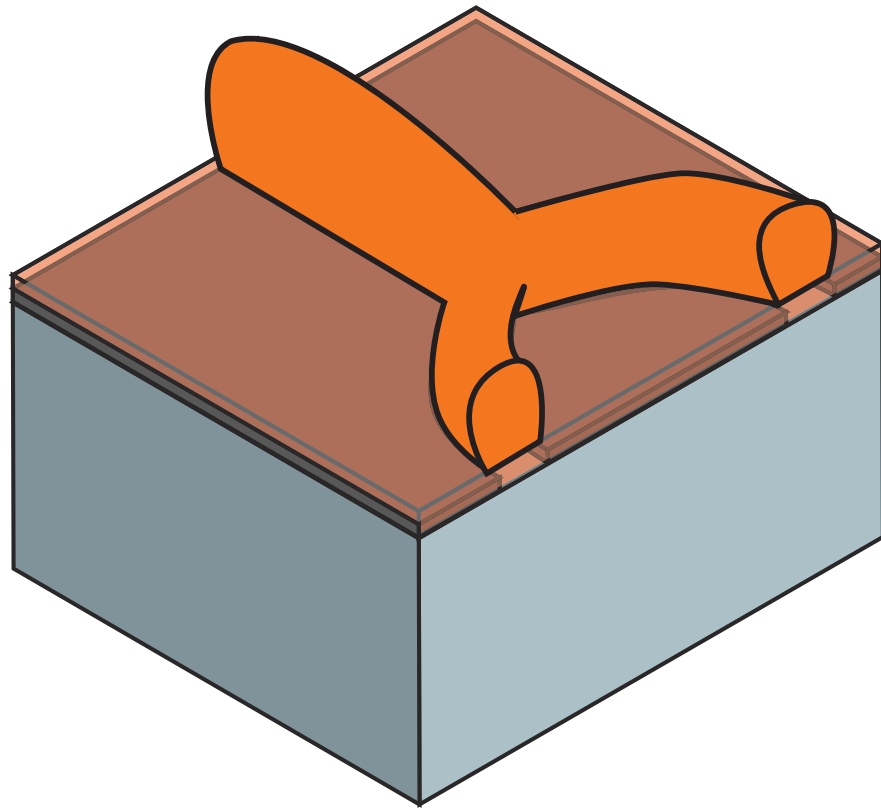
Microfabrication



Backside exposure
 160 mJ.cm^{-2}
Opal diffuser
! Glass thickness



Microfabrication

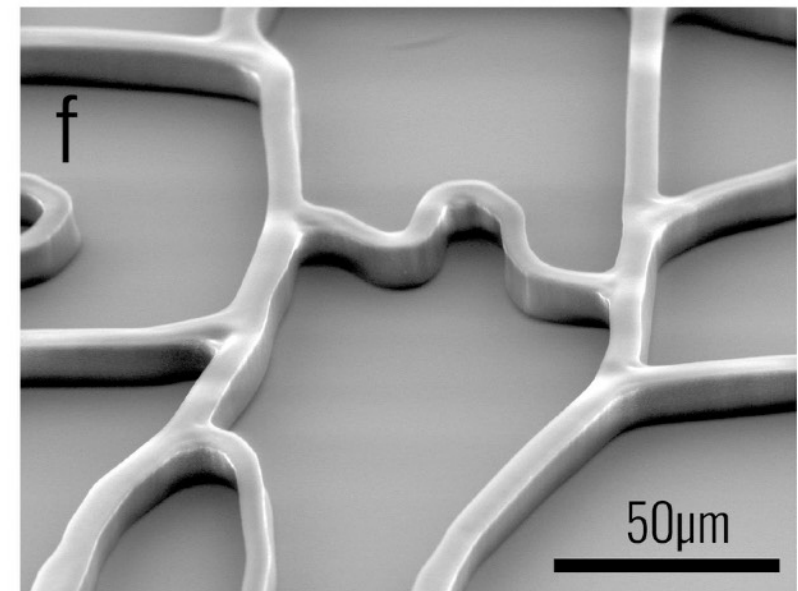
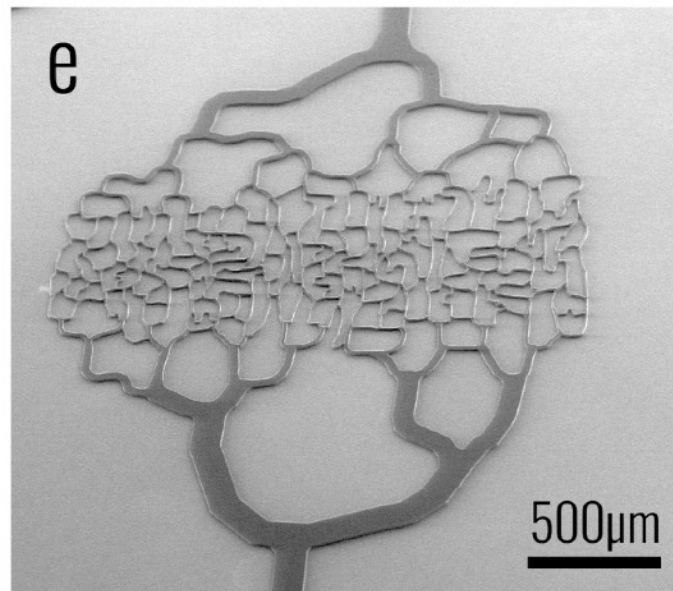
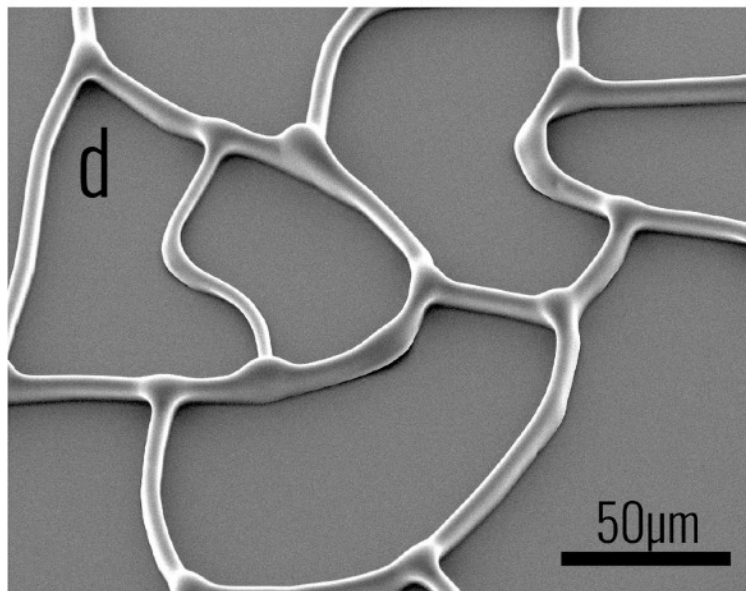
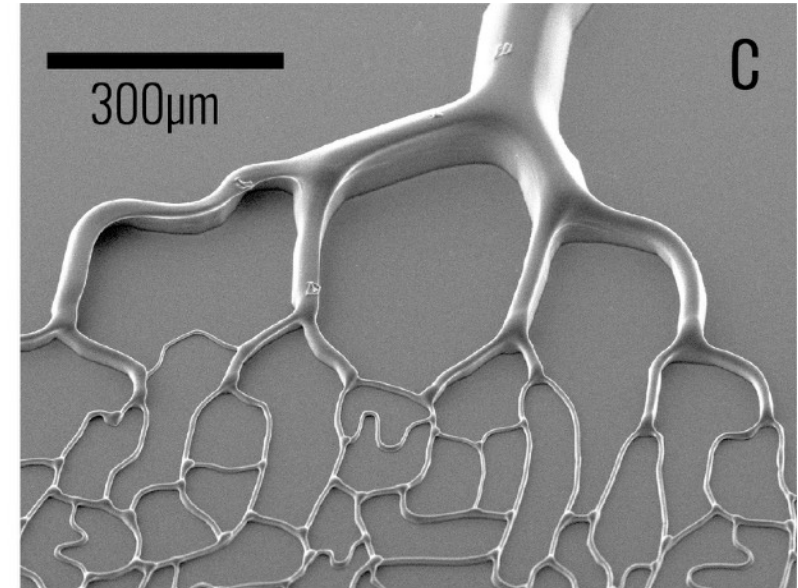
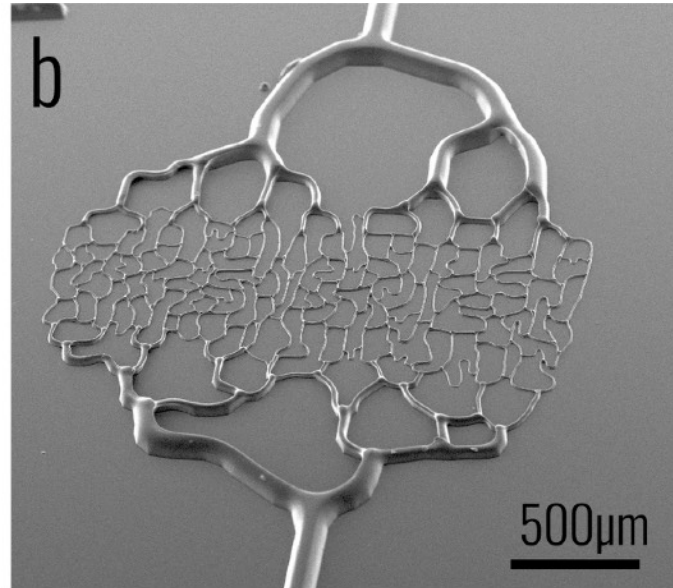
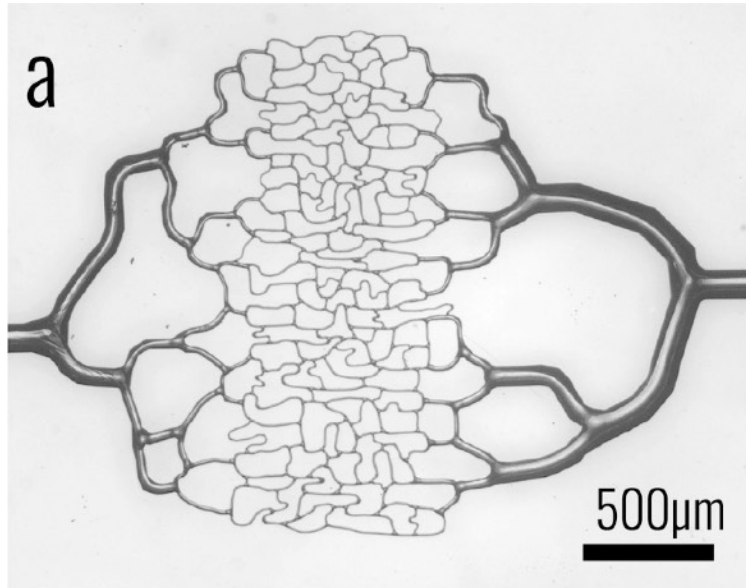


Development

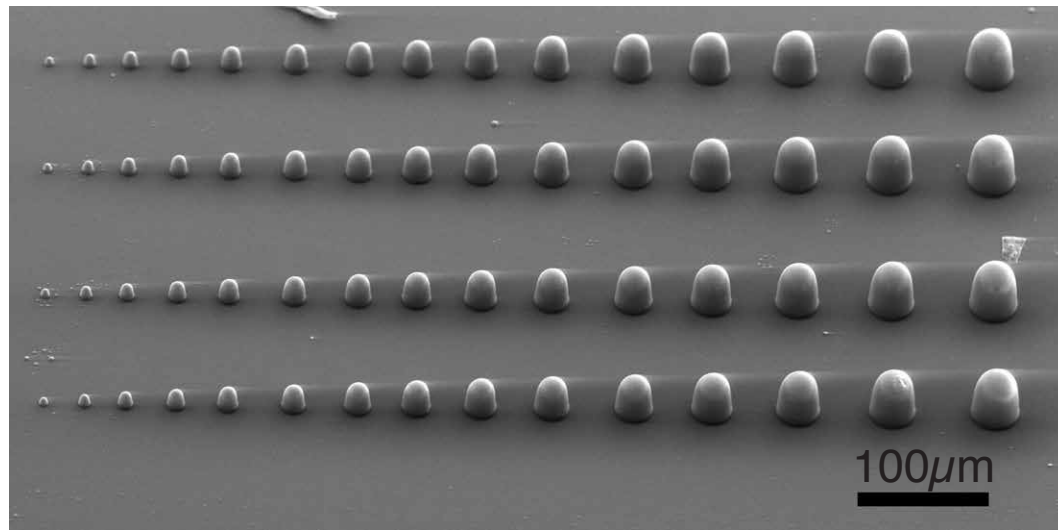
! Hard bake for smoothing

PDMS Casting

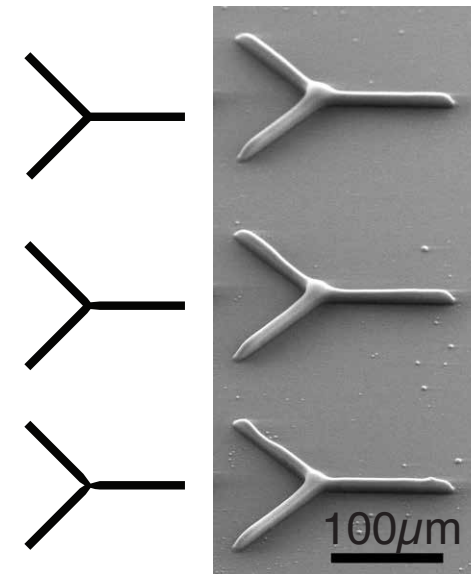
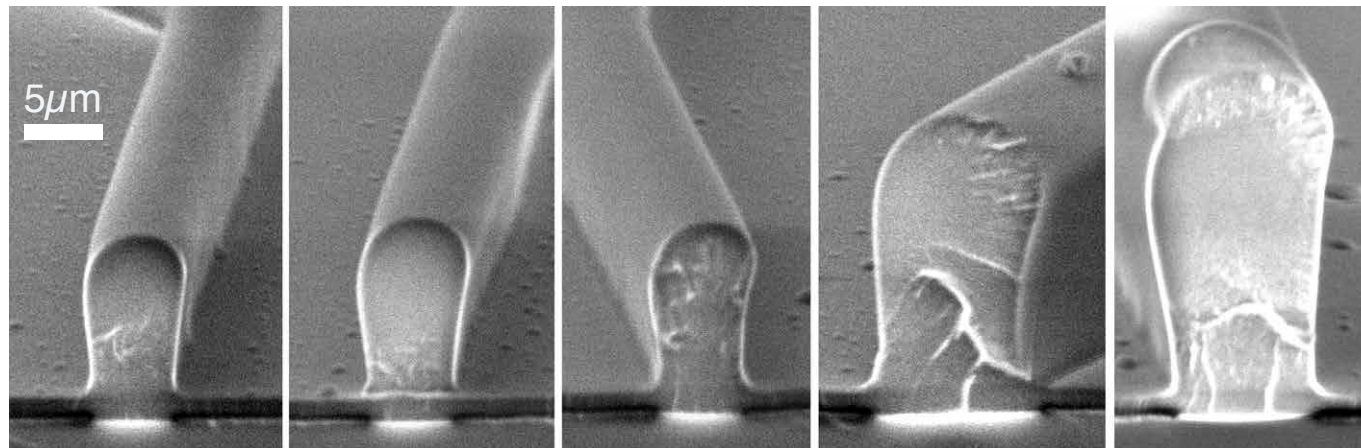
Microfabrication



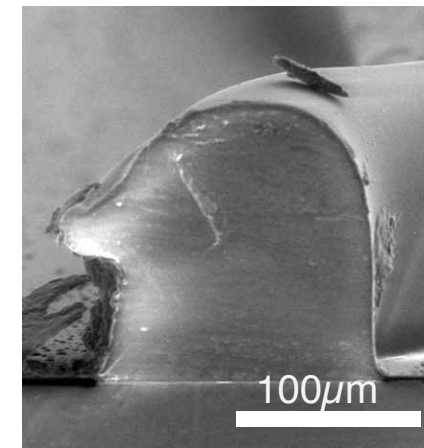
Cross sections & Bumps



Rounded shapes



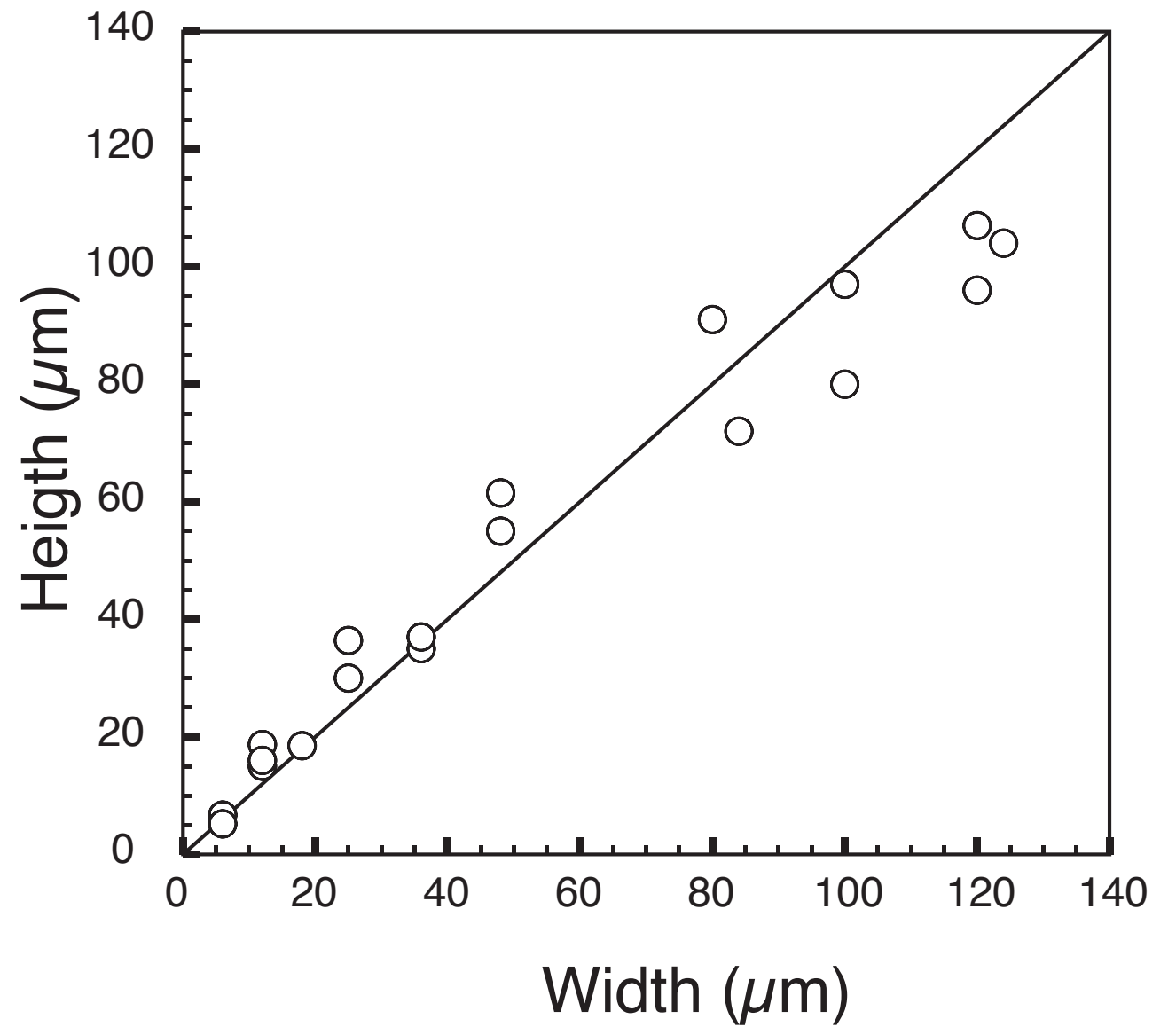
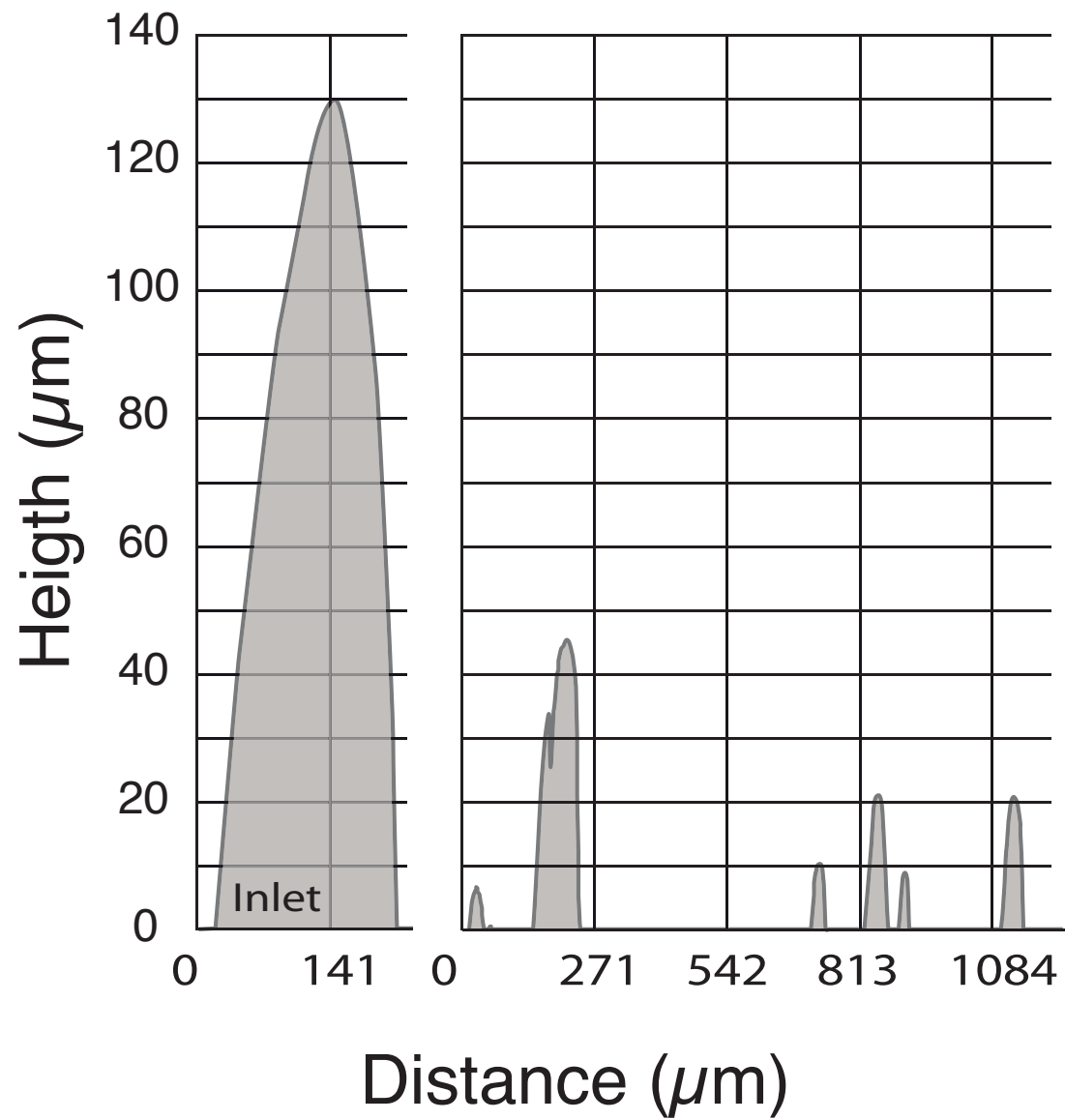
Bumps at nodes





Baguette vs Soft bread

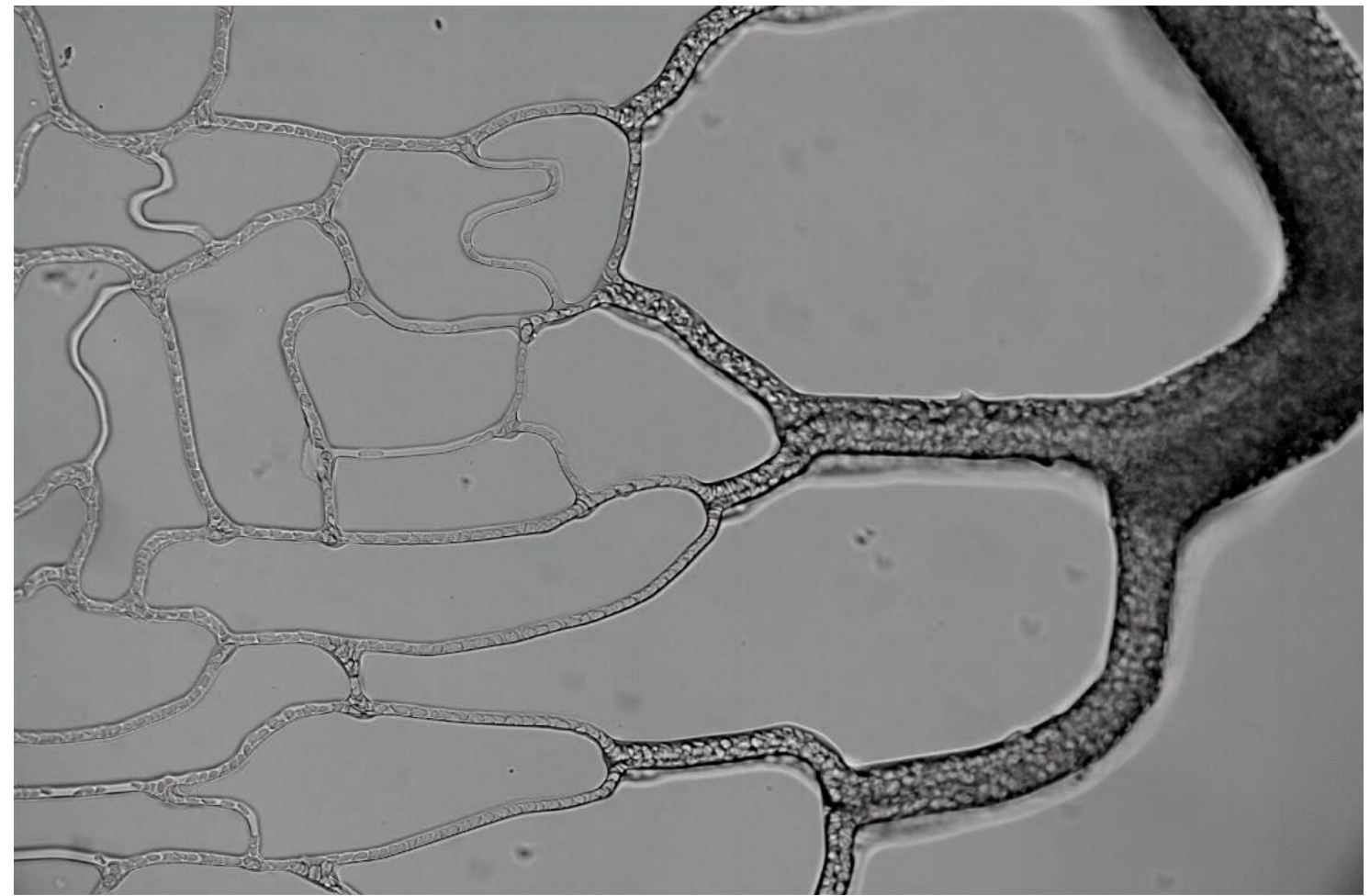
Height vs Width



Blood flows @ trees



Arteriole tree

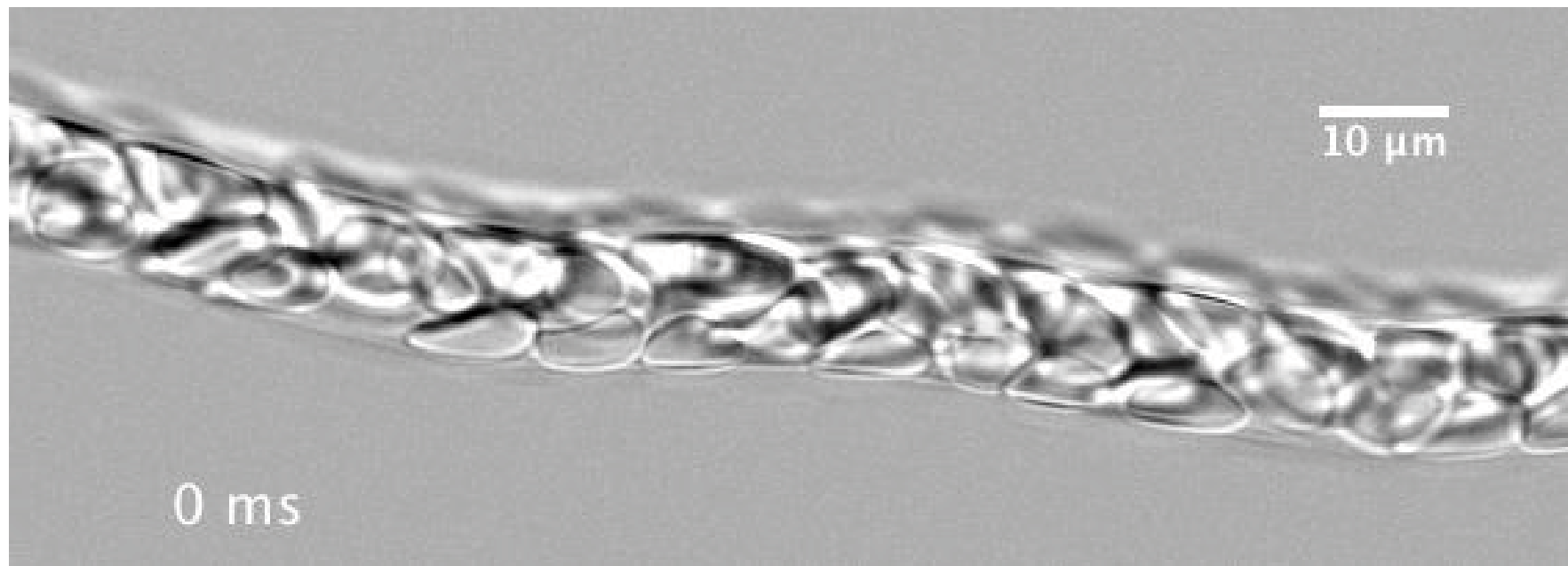
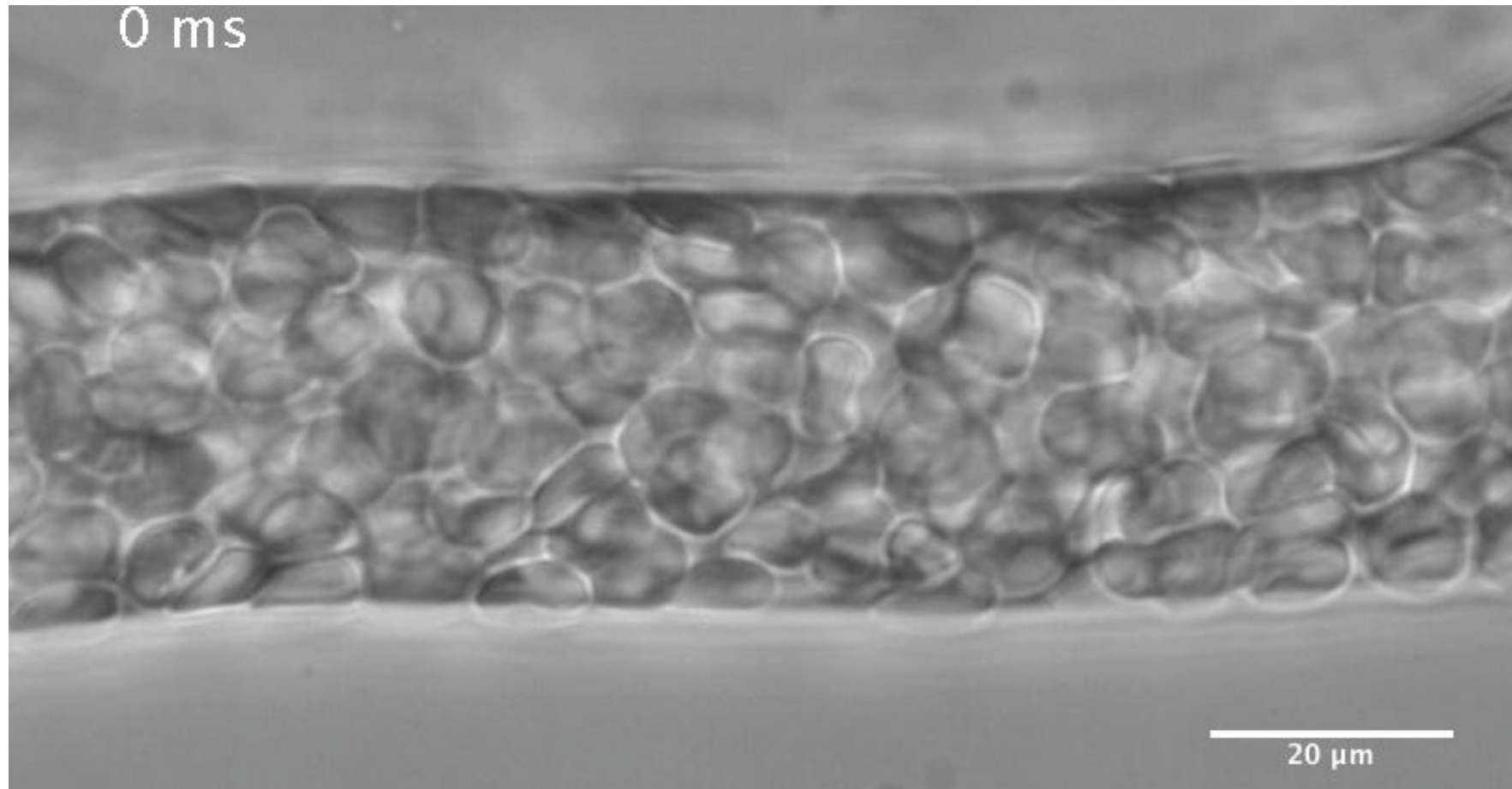


Veinule tree

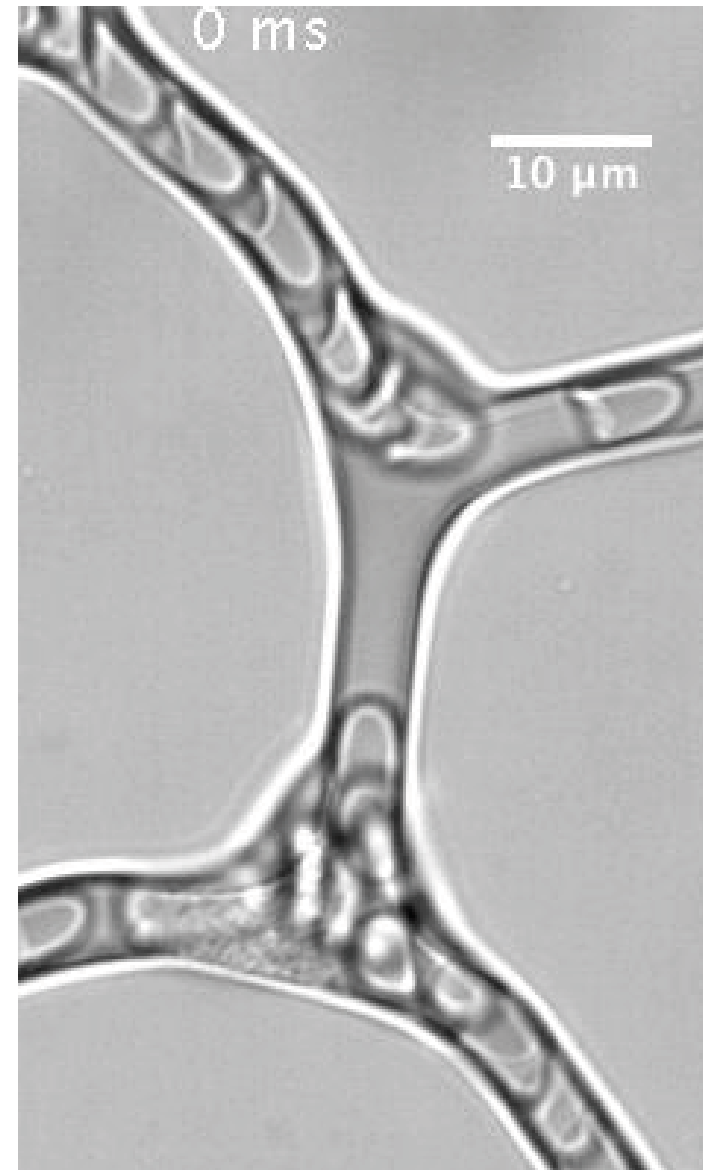
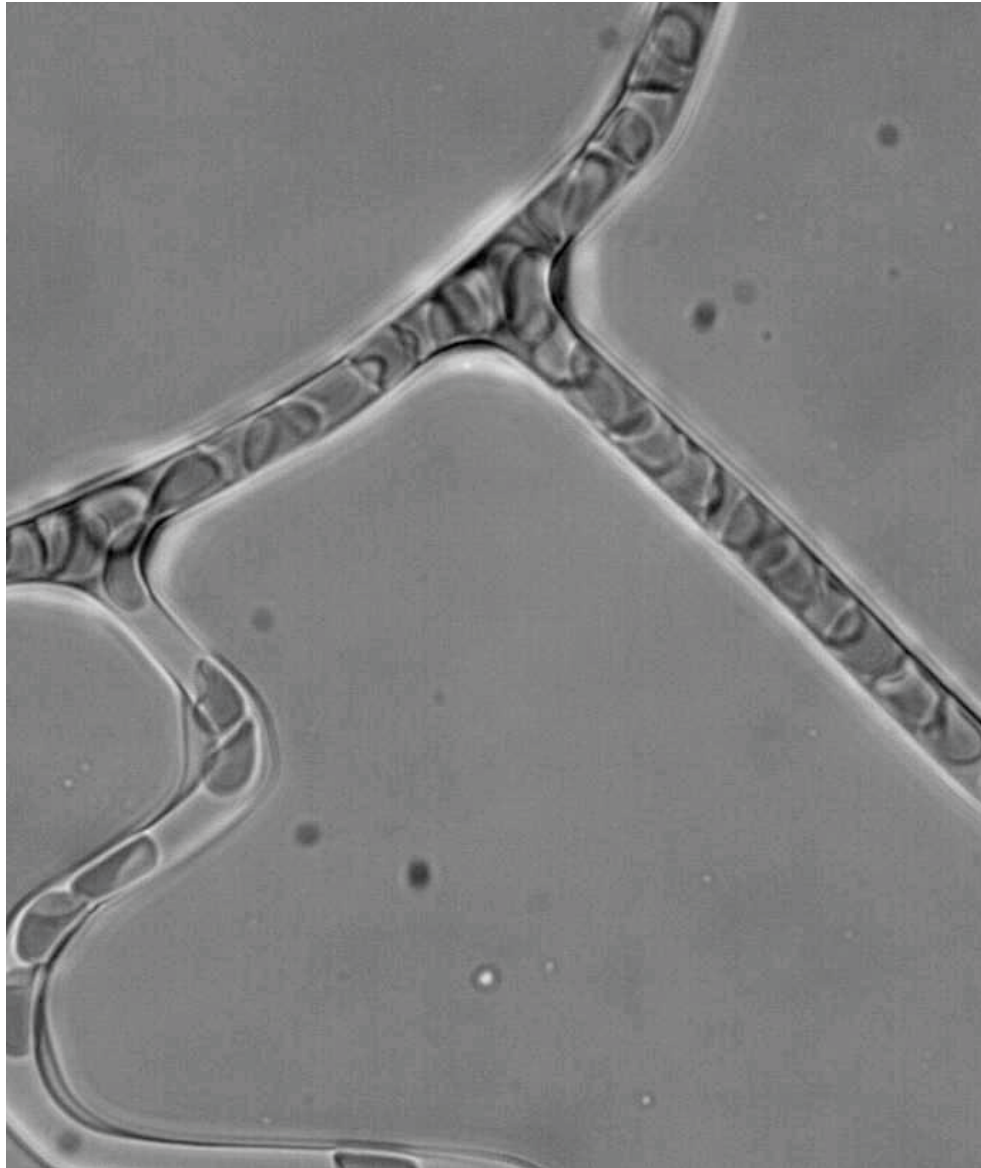
45% Ht washed blood in PBS/optiprep, 1-100 mbar pressure controlled

Blood flows @ arterioles

Cell compaction



Blood flows @ bifurcations and branches



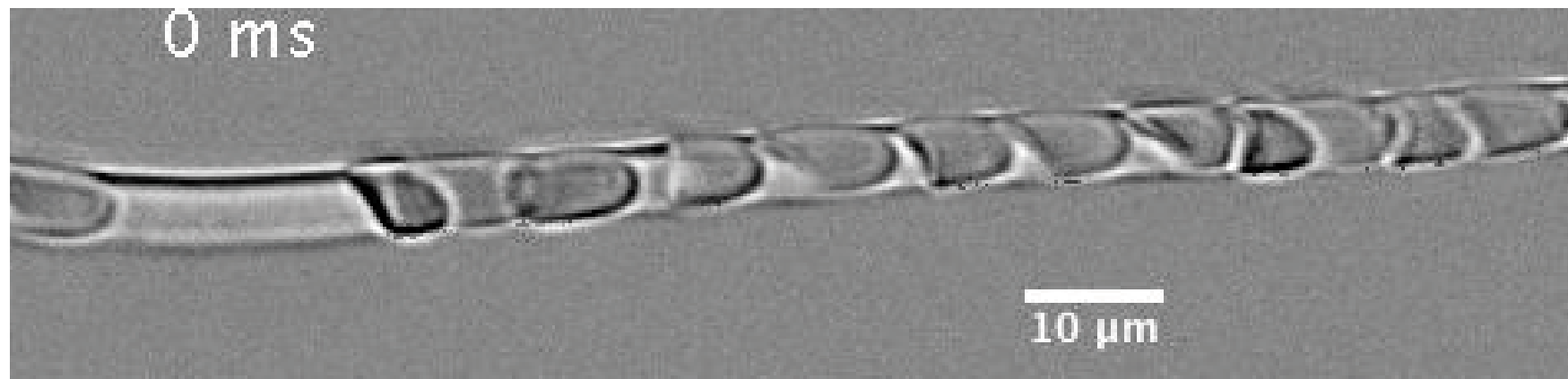
As observed in vivo :

Silent channels
change in flow
direction

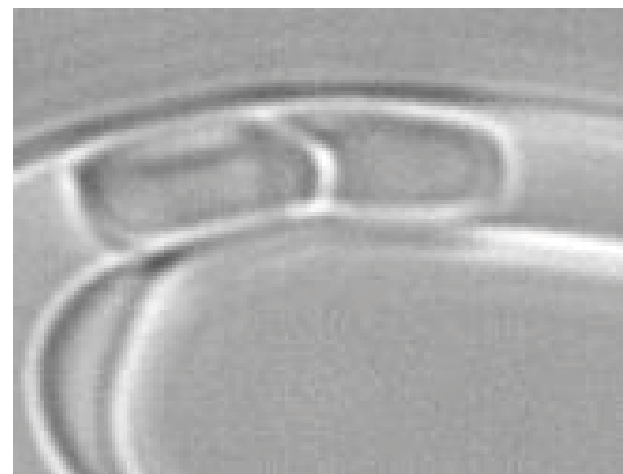
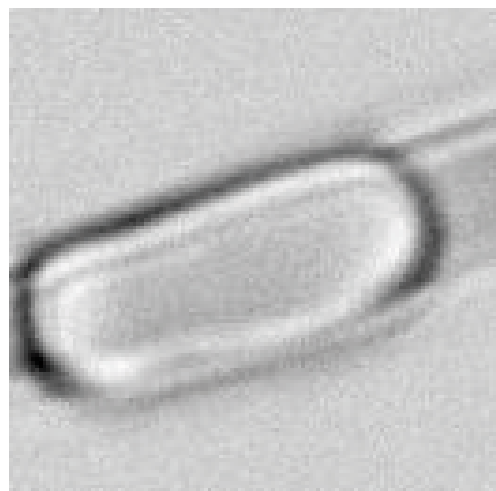
Local hematocrit

Inhomogeneity of the flow repartition and of the cell density

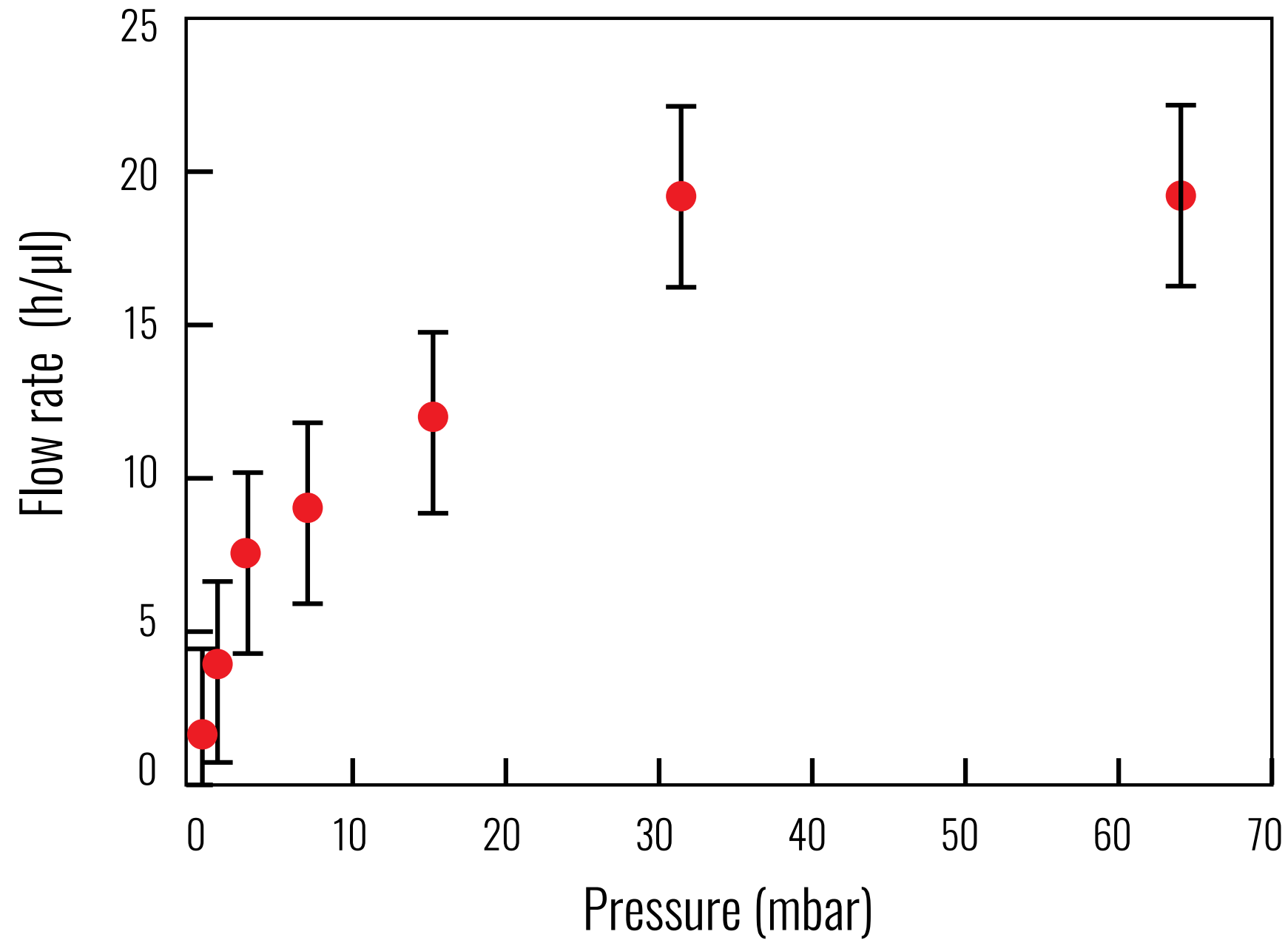
Blood flows @ capillaries



Parachutes, dynamic rouleaux, clustering, tank treading



Flow rate vs Pressure



non linear ???

Conclusions

Replicas of microcirculation vascular networks

One mask process

Back side exposure with Opal diffuser

Height gradation

Rounded channel

Aknowledgments



Benoît CHARLOT
Sebastien MEANCE
Vincent GIROD



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Manouk
ABKARIAN
Viviana CLAVERIA
Luca Lanotte



Hemphys summer school
october 6-9 2020

[https://
hemphys.sciencesconf.org/](https://hemphys.sciencesconf.org/)

National center for
scientific research



National Institute
for medical
research

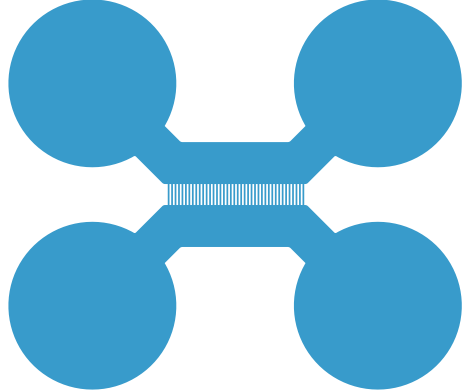


MONTPELLIER UNIVERSITÉ D'EXCELLENCE



RheoBlood

neurofluidics



neuroscience & microfluidics
November 27-28, 2019. Montpellier, France

neurofluidics.org