

Lab on a Chip and Microfluidics

Benoît CHARLOT

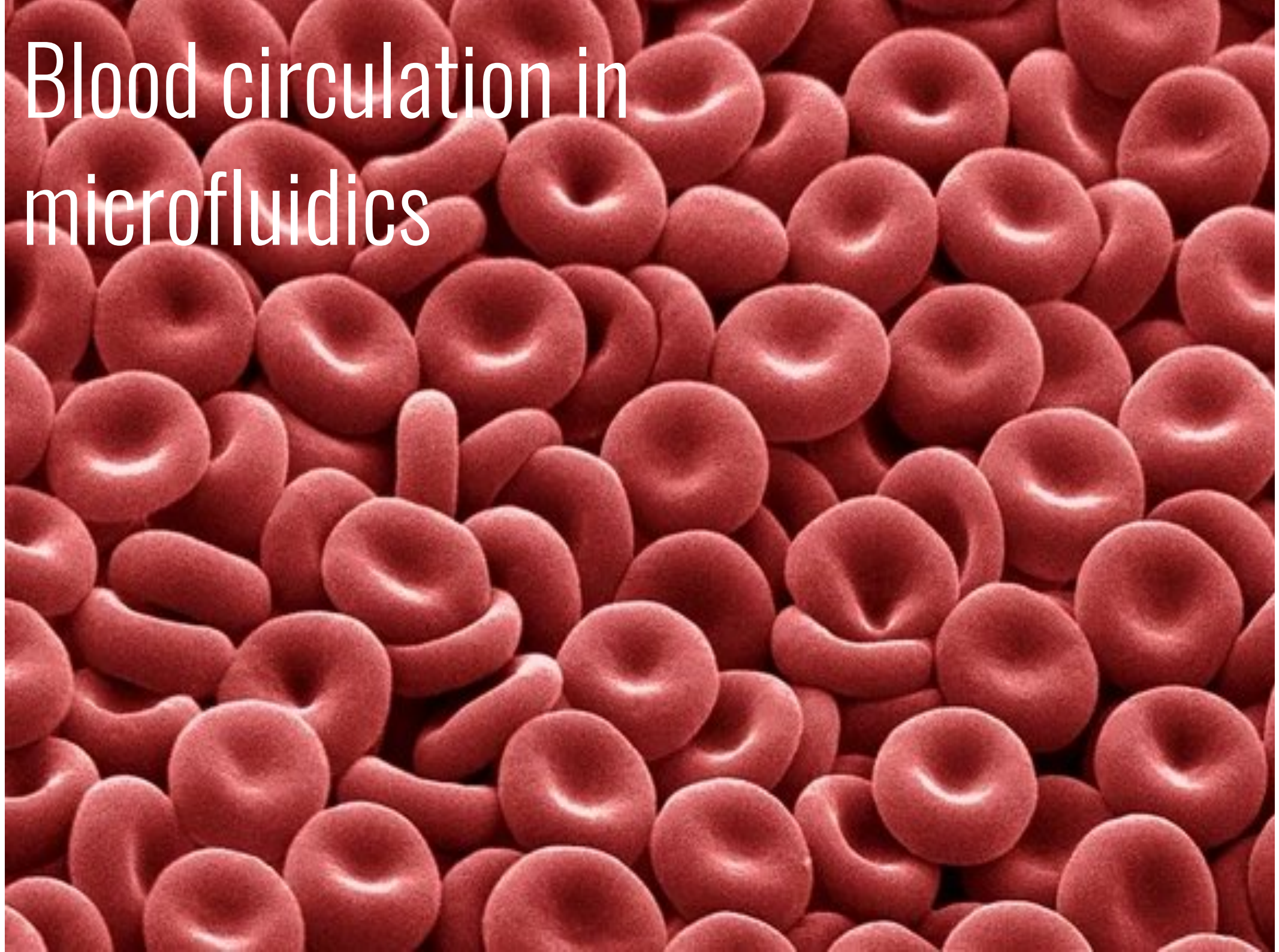
<http://www.ies.univ-montp2.fr/~charlot/>



l'institut
d'électronique



Blood circulation in microfluidics



Blood

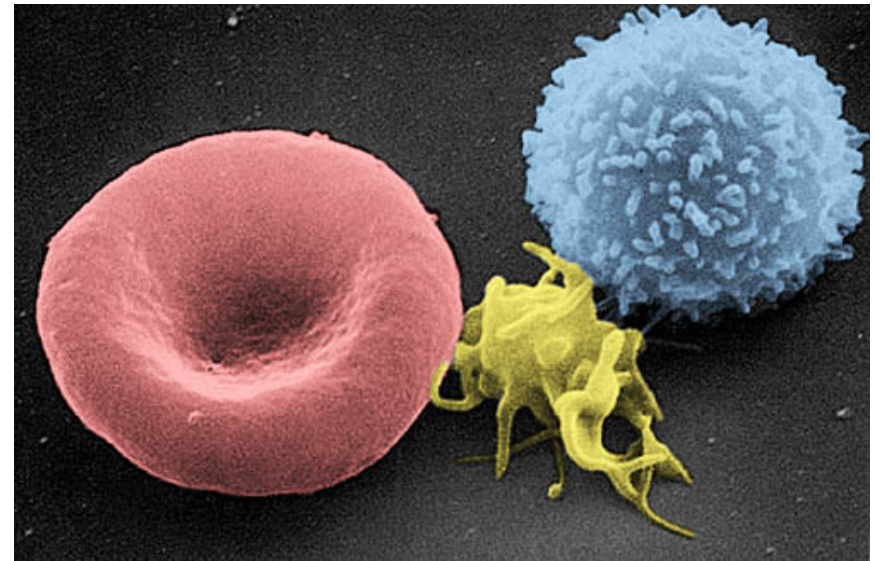
Blood is a body fluid in humans and other animals that delivers necessary substances such as nutrients and oxygen to the cells and transports metabolic waste products away.

Plasma (extracellular matrix) : water 95%
+proteins (Albumin, globulin, Fibrinogen,..), Ions,
(Na^+ , Ca^{2+} , Mg^{2+} , HCO_3^- , Cl^-) and O_2 , CO_2

Red blood cells (Erythrocytes)

White blood cells (Leukocytes)

Platelets (Thrombocytes)



The hematocrit, Ht is the volume percentage (vol%)
of red blood cells in blood : **45%**

Blood = **7-8%** body weight

RBCs

Cells that contain hemoglobin and that transport O_2 to the tissues

flexible and oval biconcave disks.

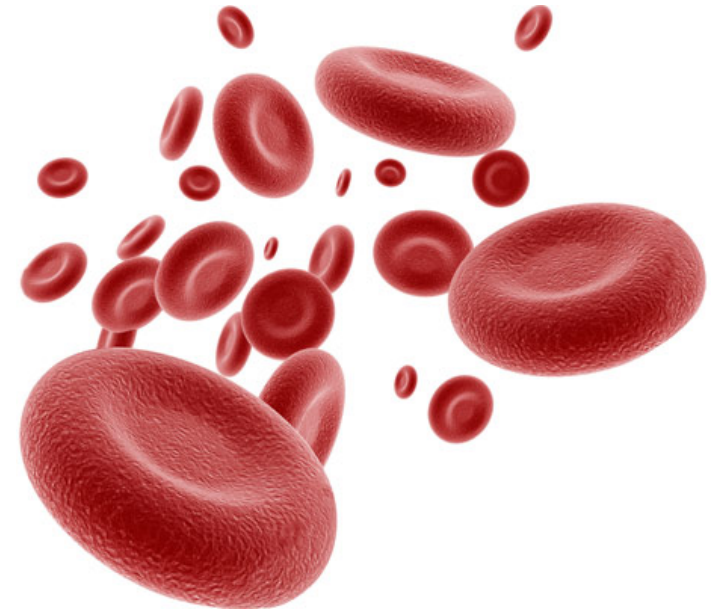
Diameter : 6.2–8.2 μm

thickness at the thickest point 2–2.5 μm

minimum thickness in the centre of 0.8–1 μm

20–30 10^{12} red blood cells

70% cells in the body



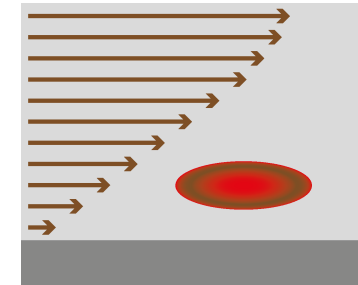
Blood Circulation

Arteries, carry the blood away from the heart

capillaries, enable exchange between the blood and tissues

Veins, carry blood from the capillaries back toward the heart.

	Diamètre	Vélocité	Taux de cisaillement
Aorte	16-32 mm	600 mm/s	150 - 300 s ⁻¹
Veines	5-10 mm	150 mm/s	100-300 s ⁻¹
Arterioles	40µm	5mm/s	1000 s ⁻¹
Capillaires	5-10µm	1mm/s	400- 1600 s ⁻¹



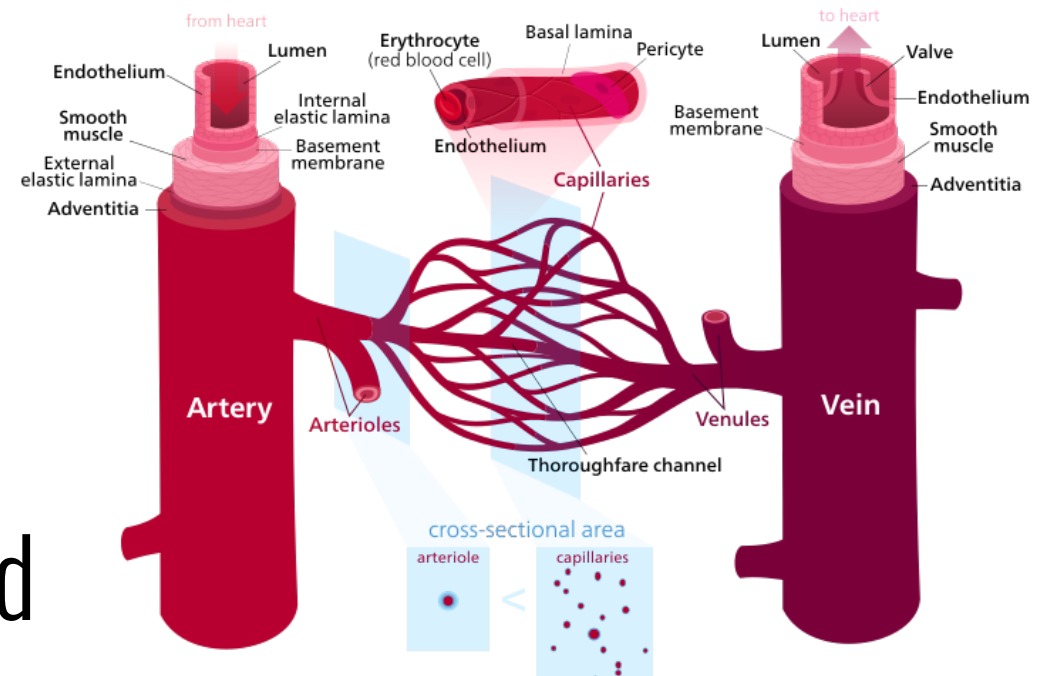
$$\lambda = \mu \frac{\partial u}{\partial z} [Pa]$$

Shear stress

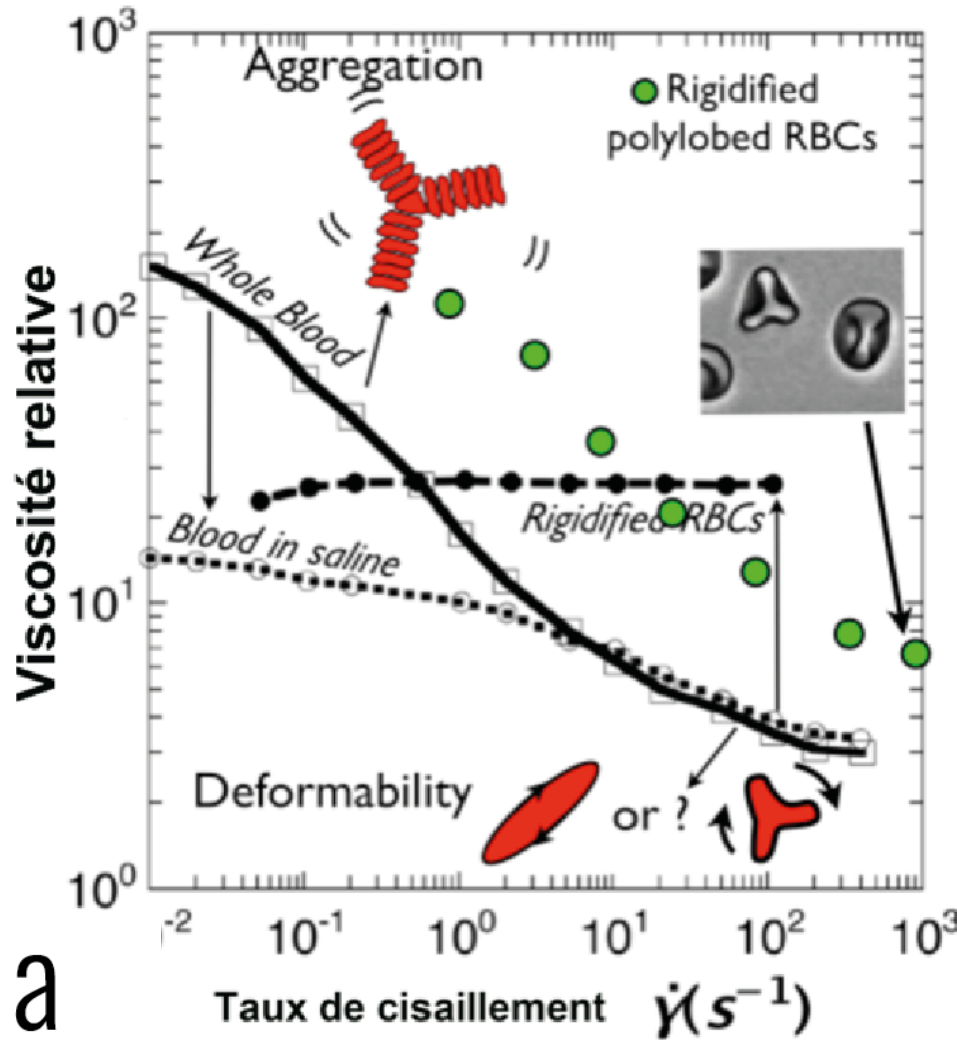
$$\dot{\gamma} = \frac{u_{max}}{h} [s^{-1}]$$

Shear Rate

Blood is a Shear thinning fluid



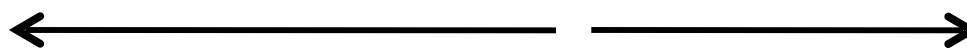
Rhéofluidification (shear thinning)



Chien et al. Science, 1967

High viscosity **a**

Low viscosity



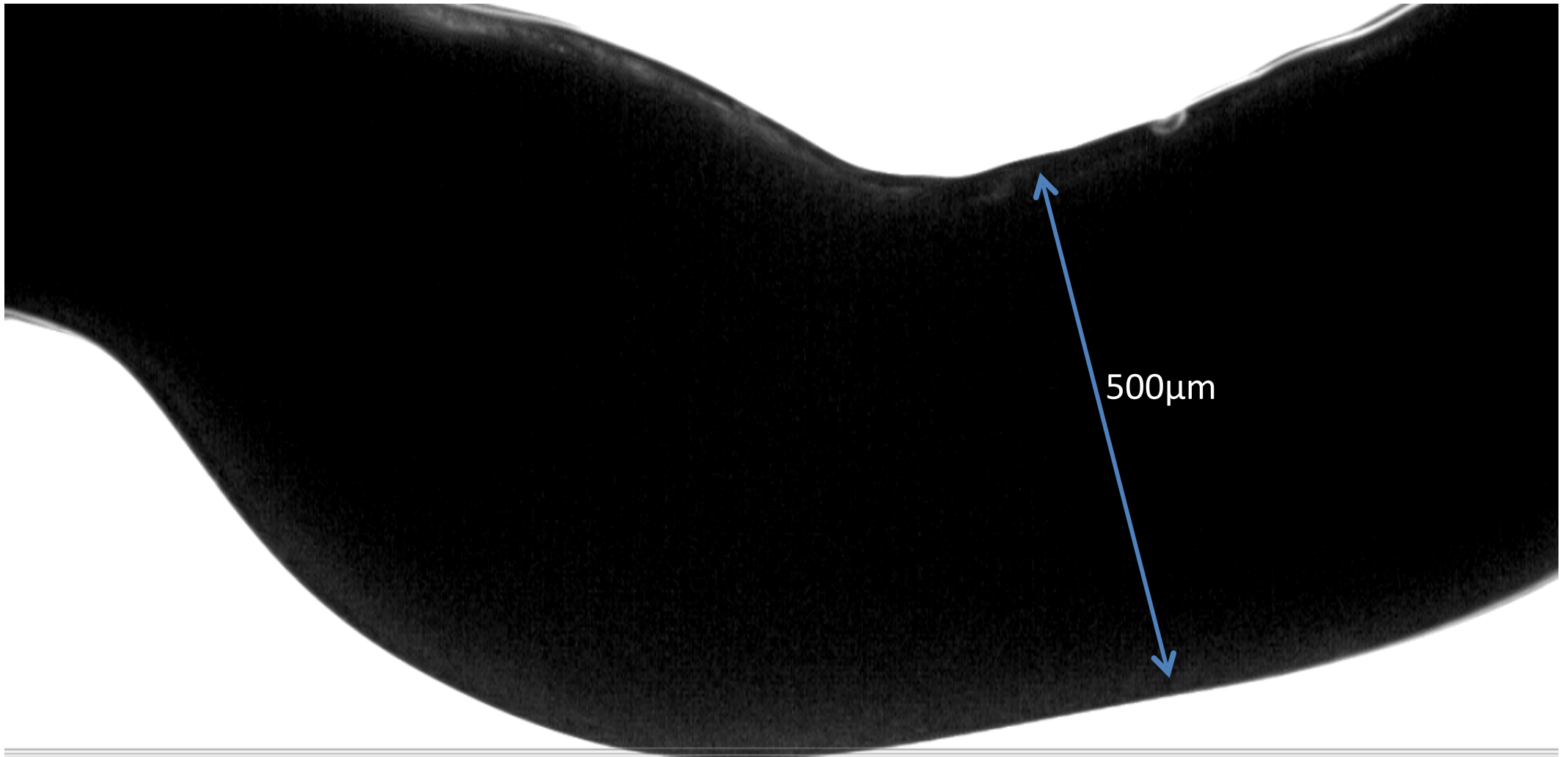
Agregation, Gelification

Thrombose, implants

RBS deformability

Drepanocytose, Sickle cell, spherocytose, malaria,

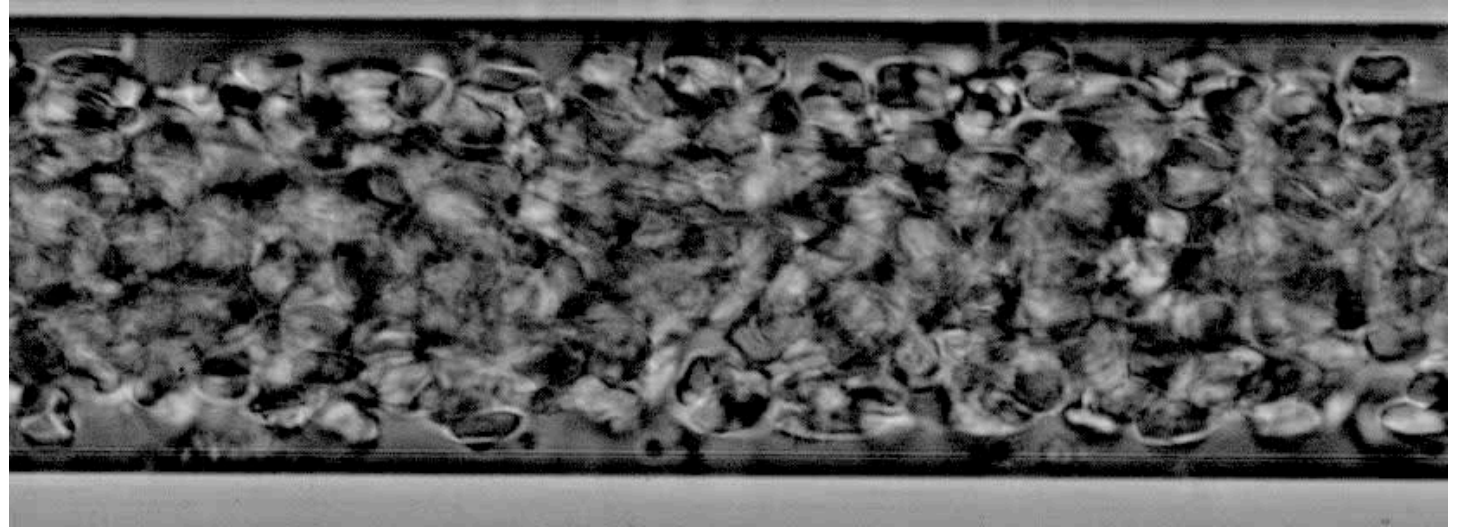
Observation of blood flows



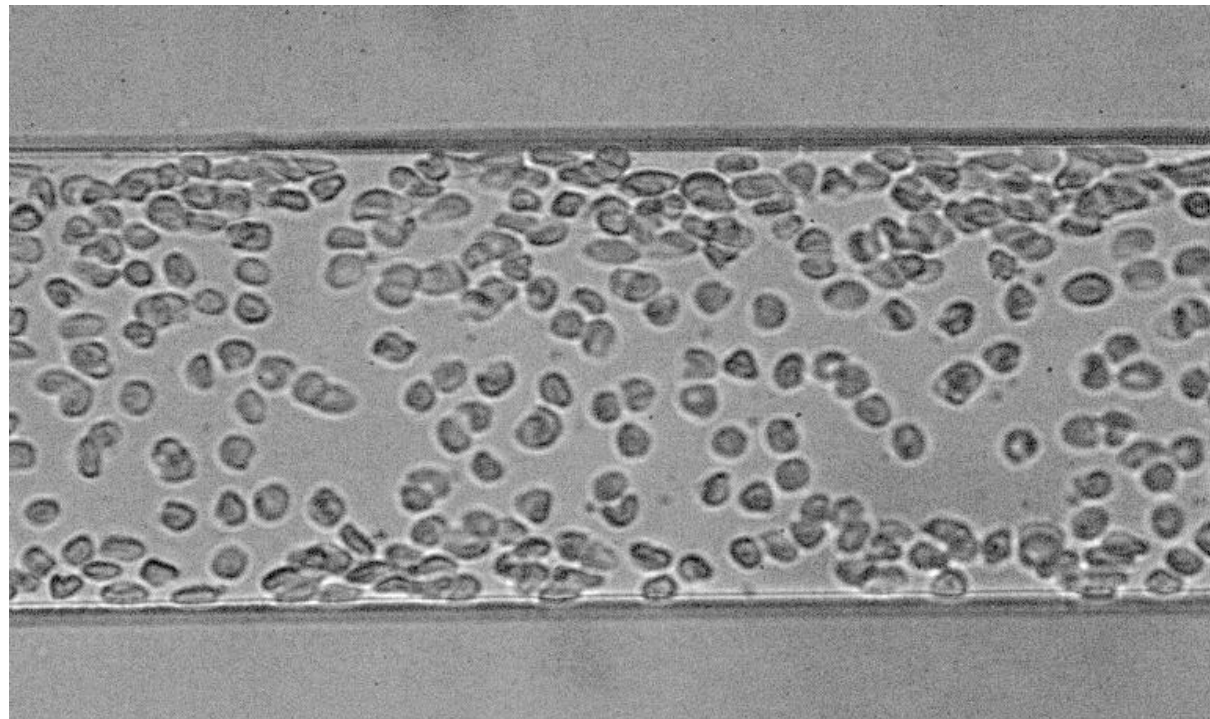
Over 200μm, too much light absorption

Blood flow in microfluidics

Glass capillary

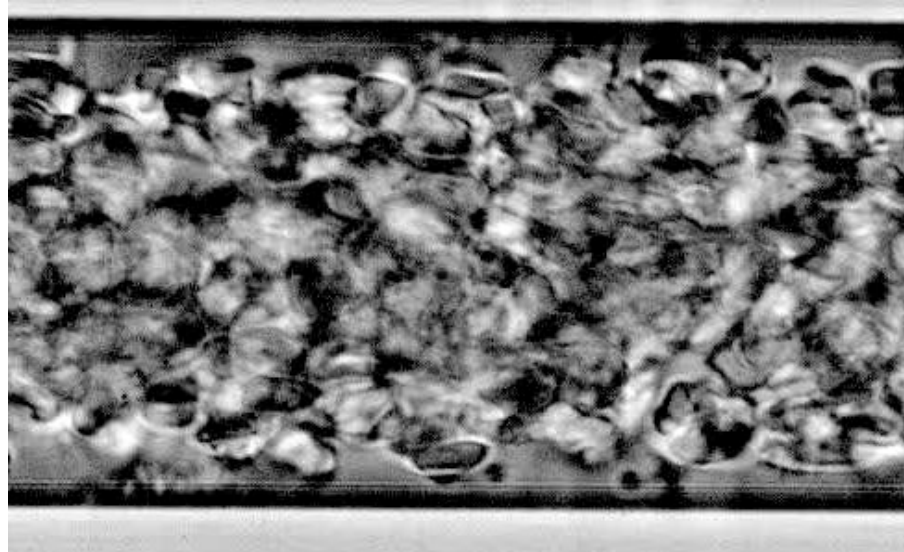


Microfluidic

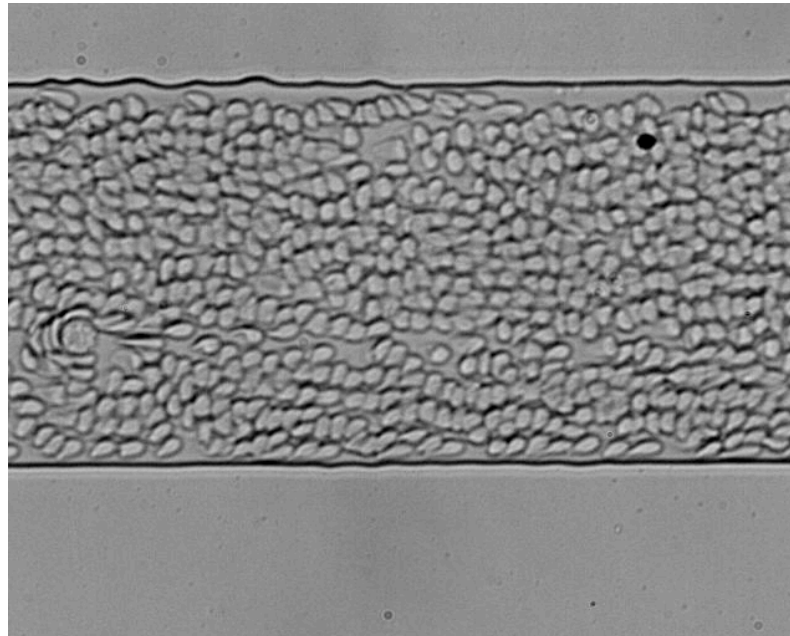


Blood flow in microfluidics

Glass capillary



Microfluidics

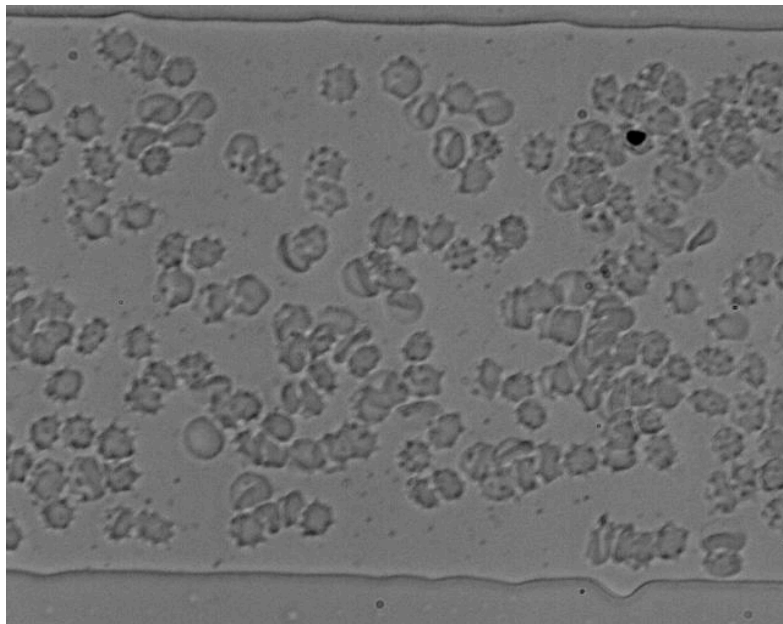


RBC collective behaviour

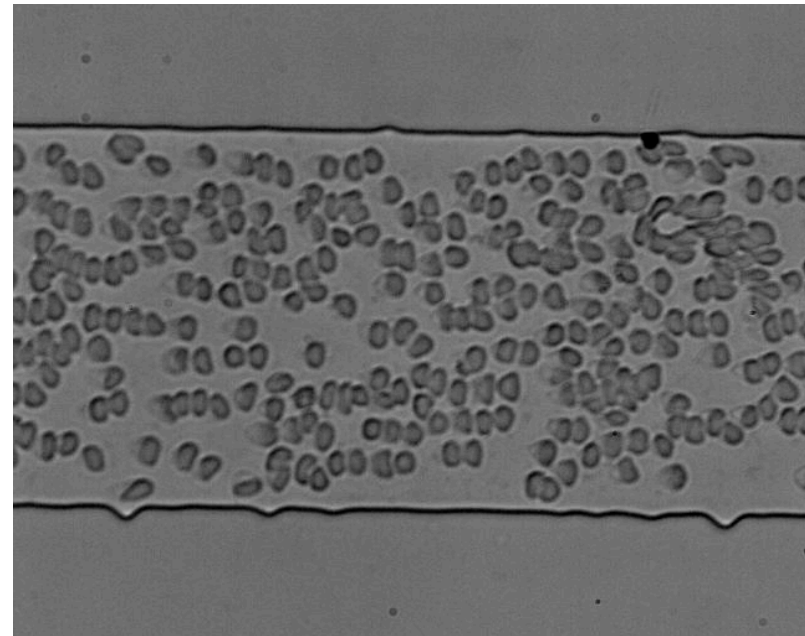
RBC individual behaviour in flows doesn't explain everything

Interaction between RBCs in flow :

- Cell free layer
- anti Weissenberg effect (Normal shear stress difference)
- Surface tension

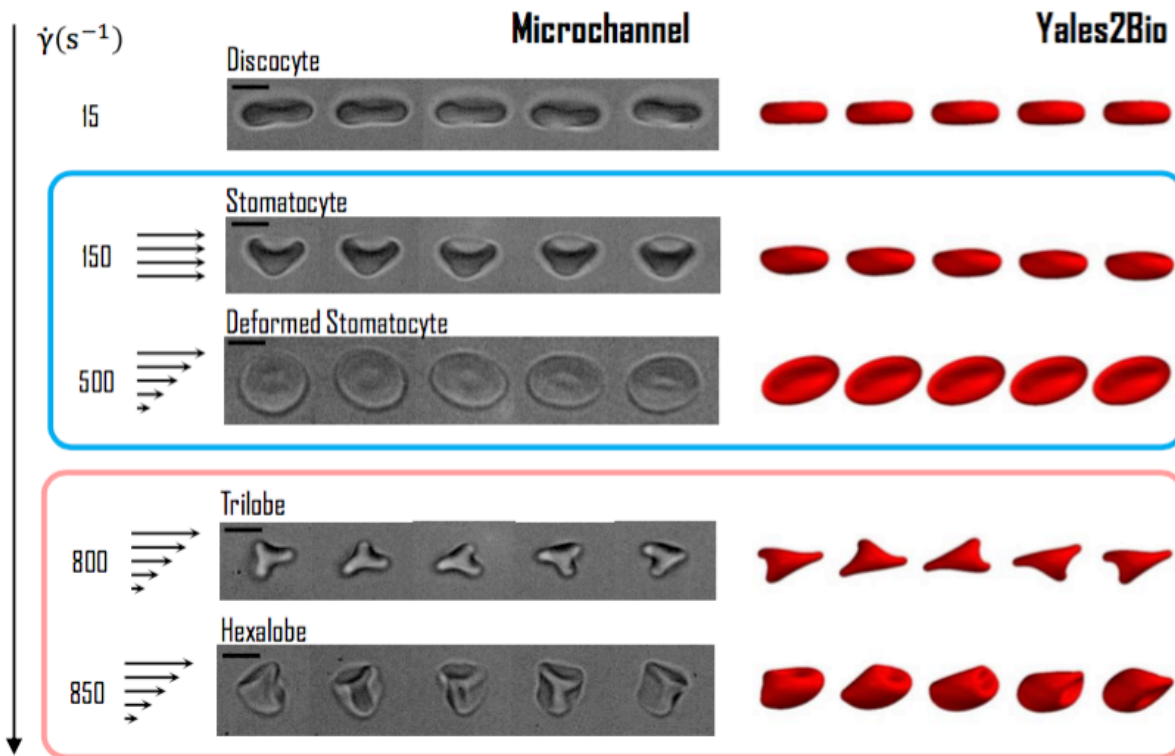


Mouvement du plasma / cellules
Nanoparticules de diamant

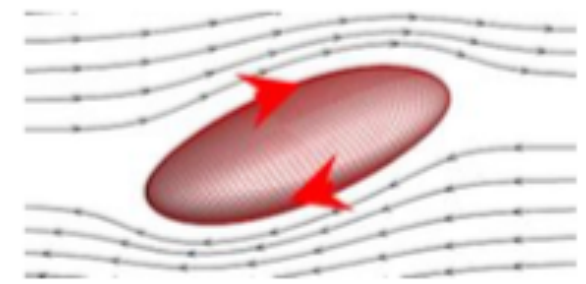


Rouleaux dynamiques

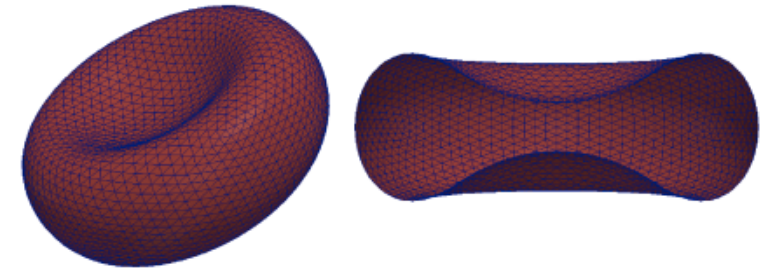
GRs under shear



L. Lanotte, J. Mauer, S. Mendez, D. Fedosov, J.-M. Fromental, V. Claveria, F. Nicoud, G. Gompper, M. Abkarian, *A new look on blood shear thinning*, **PNAS** (2016).



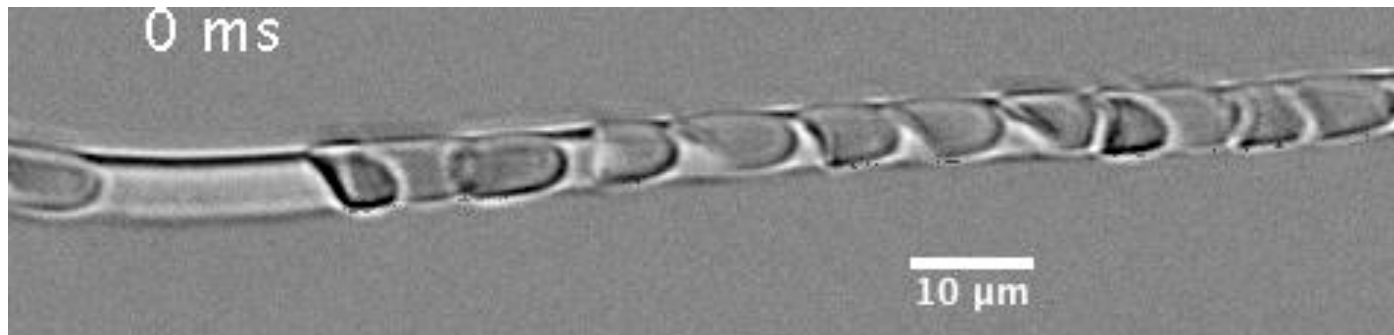
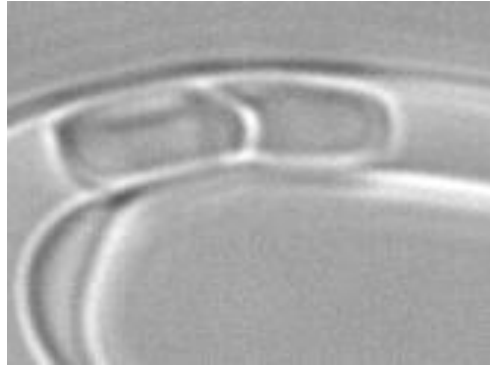
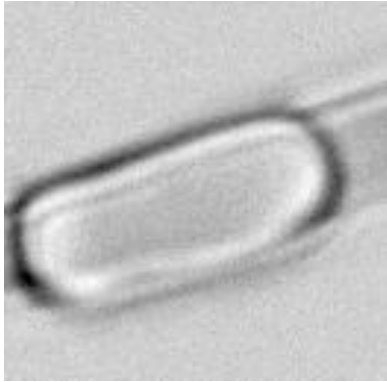
Tank-treading



Simulation Yales2bio
S.MENDEZ



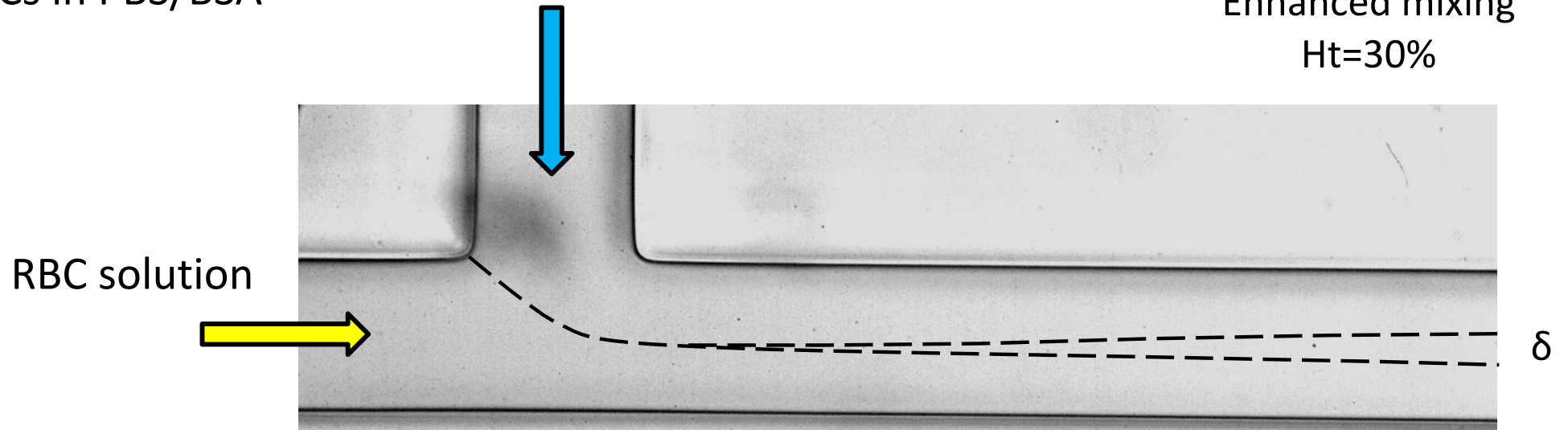
GRs under shear



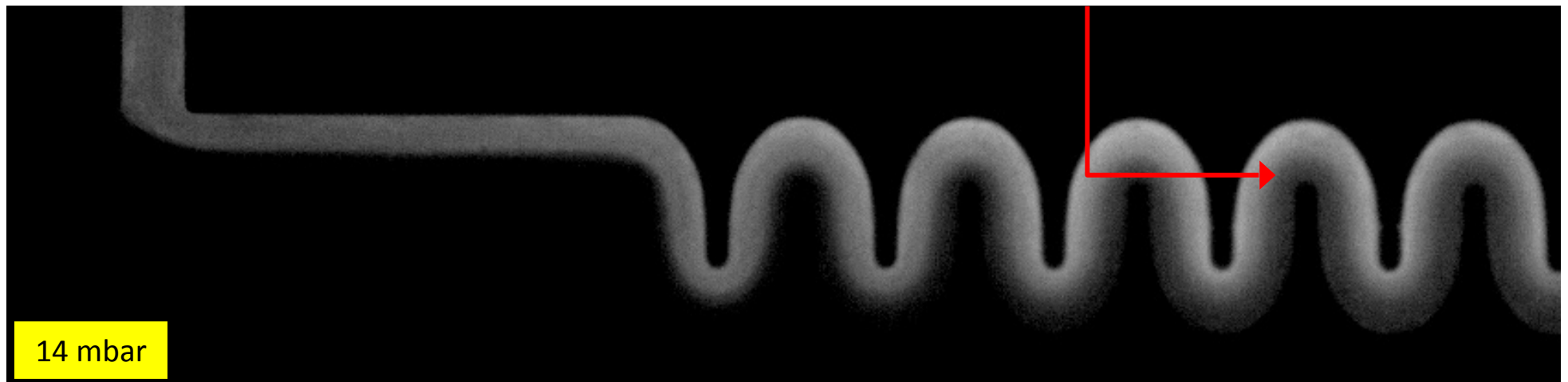
Diffusion in blood

RBCs in PBS/BSA

Enhanced mixing
Ht=30%



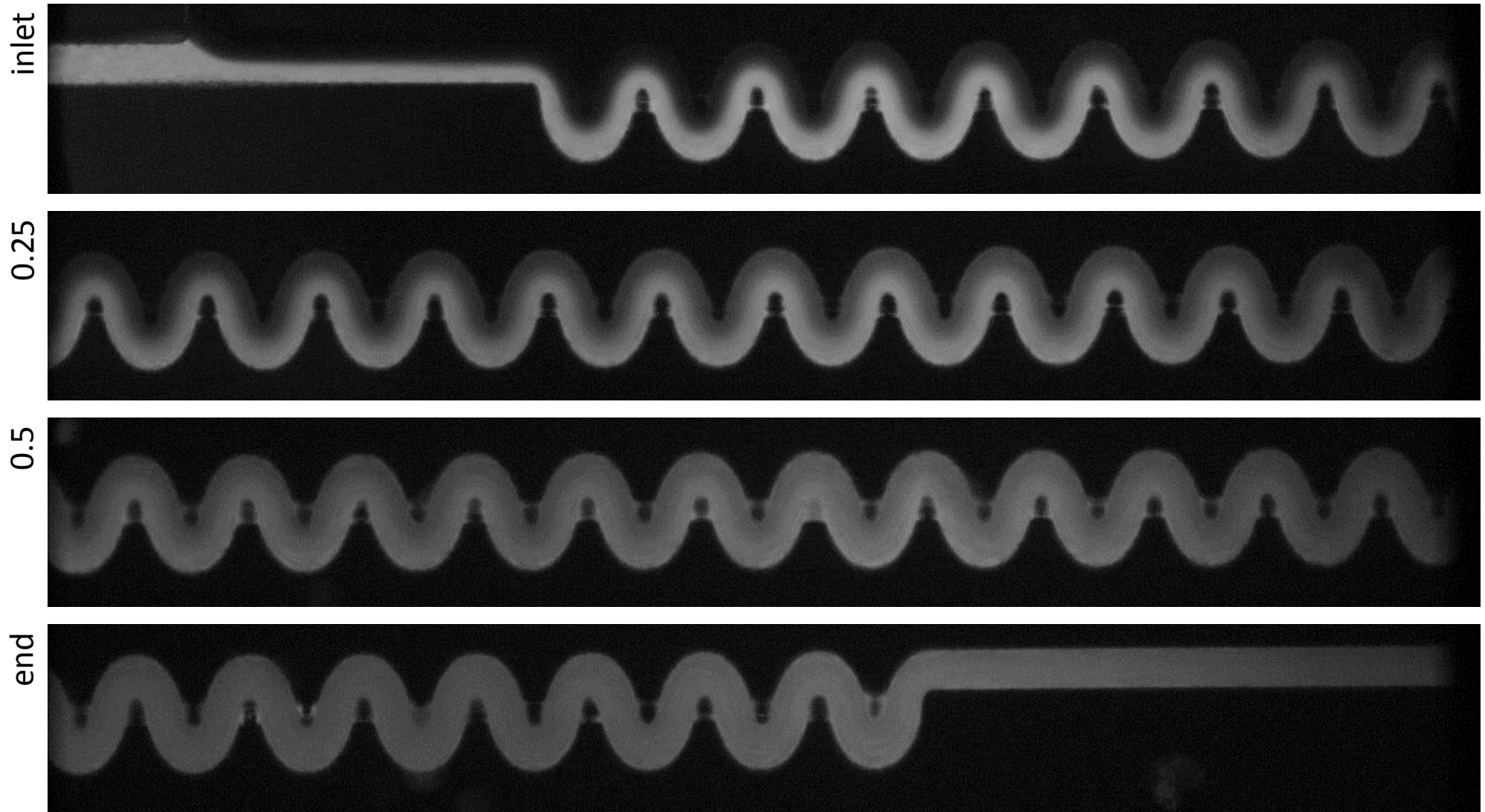
Evident mixing effects
after few curves



Diffusion in blood

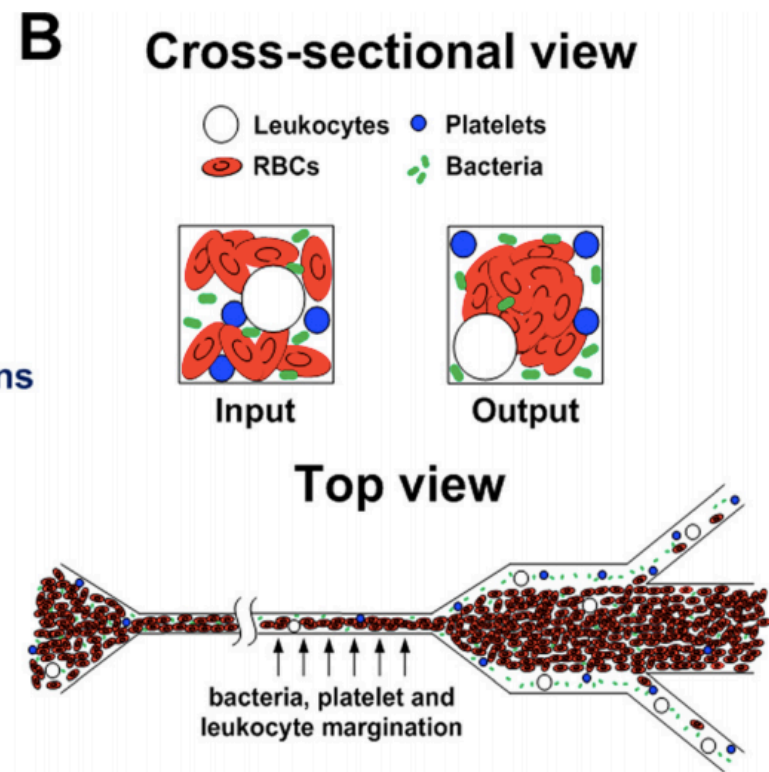
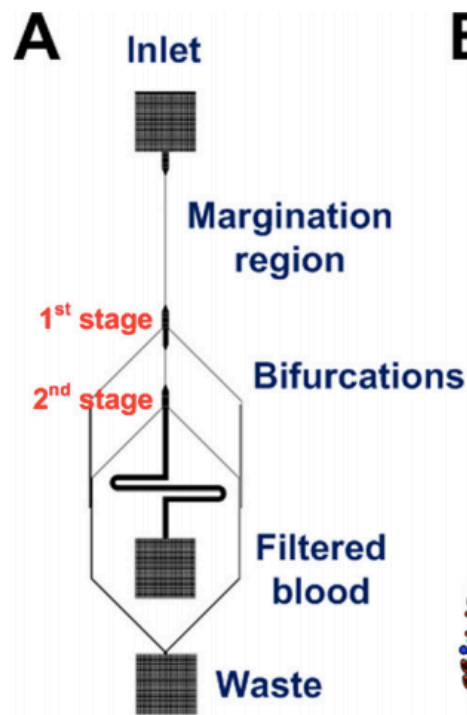
RBCs in PBS/BSA

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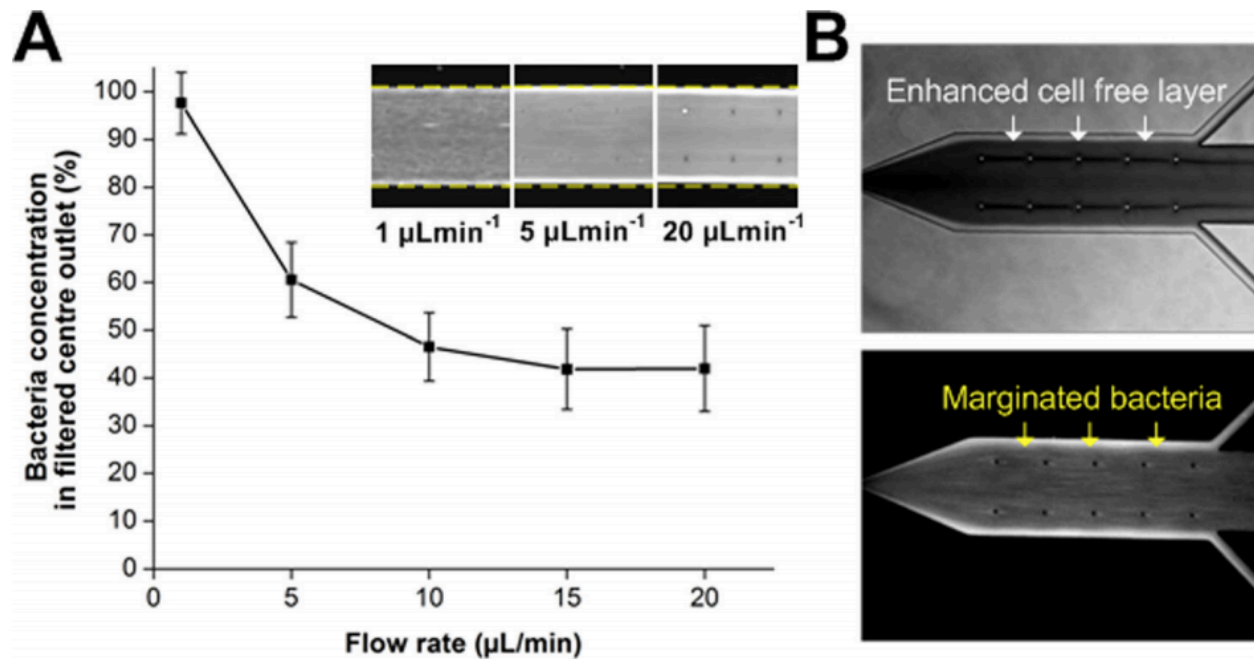


Almost doubled coefficient diffusion!!

Margination

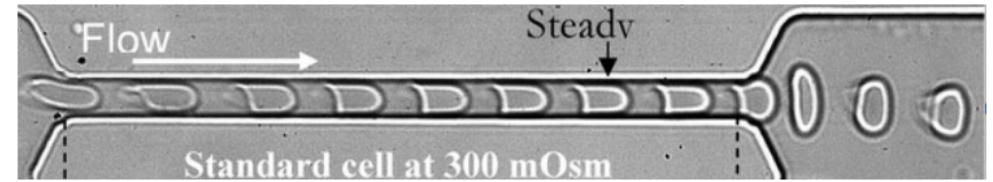
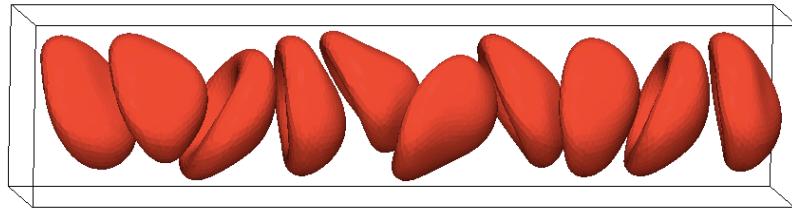


BIOMICROFLUIDICS 6, 024115 (2012)

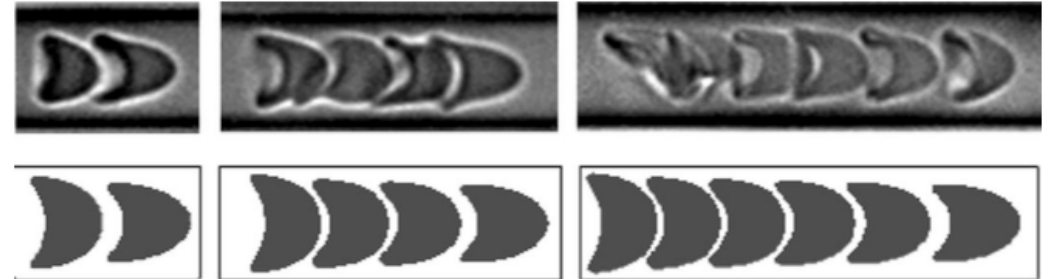


Confined circulation

Passage des GR dans des capillaires très fins
Forme parachute
Dynamique du retour à l'équilibre

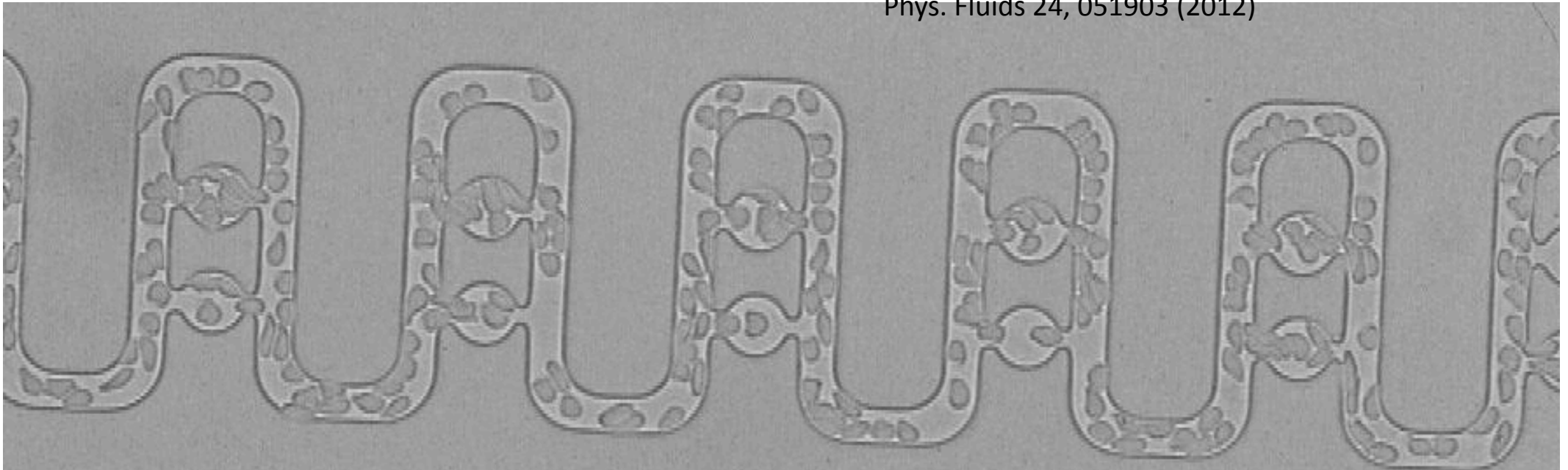


M. Abkarian

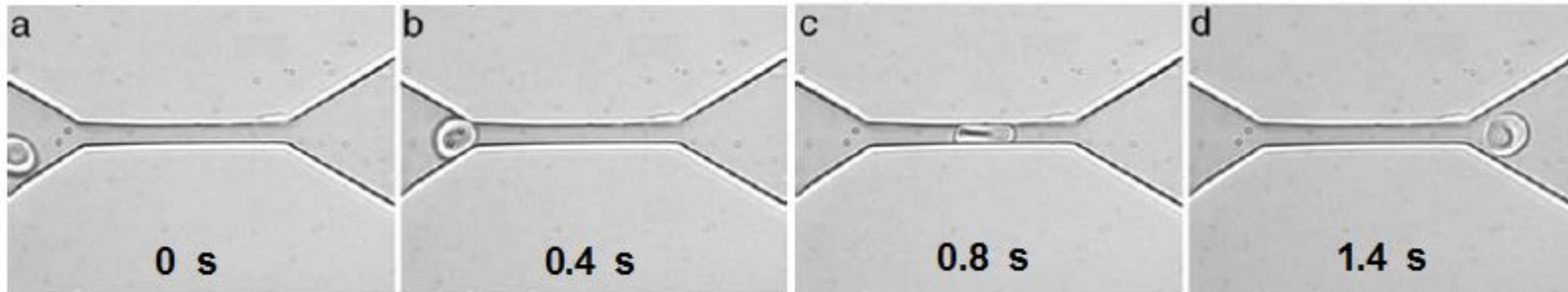


G. Tomaiuolo et al.

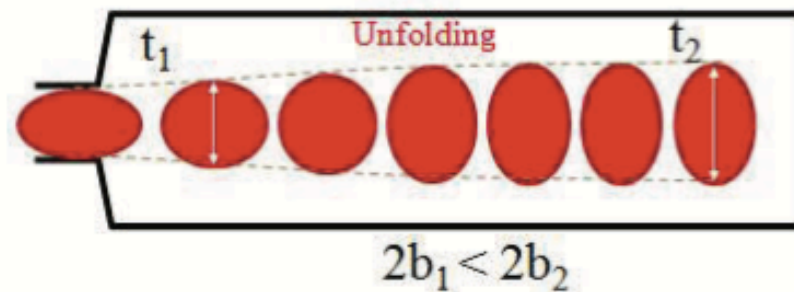
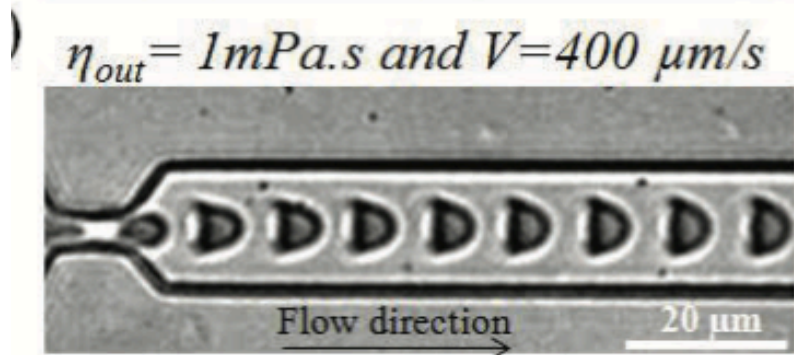
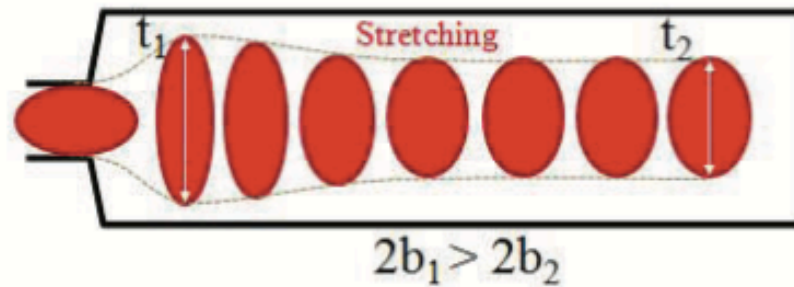
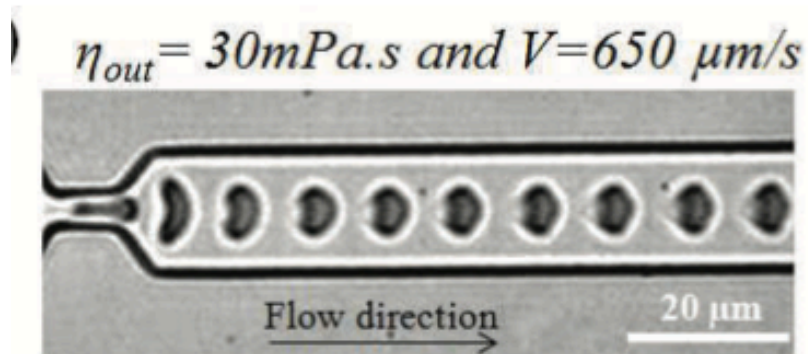
Red blood cell clustering in Poiseuille microcapillary flow
Phys. Fluids 24, 051903 (2012)



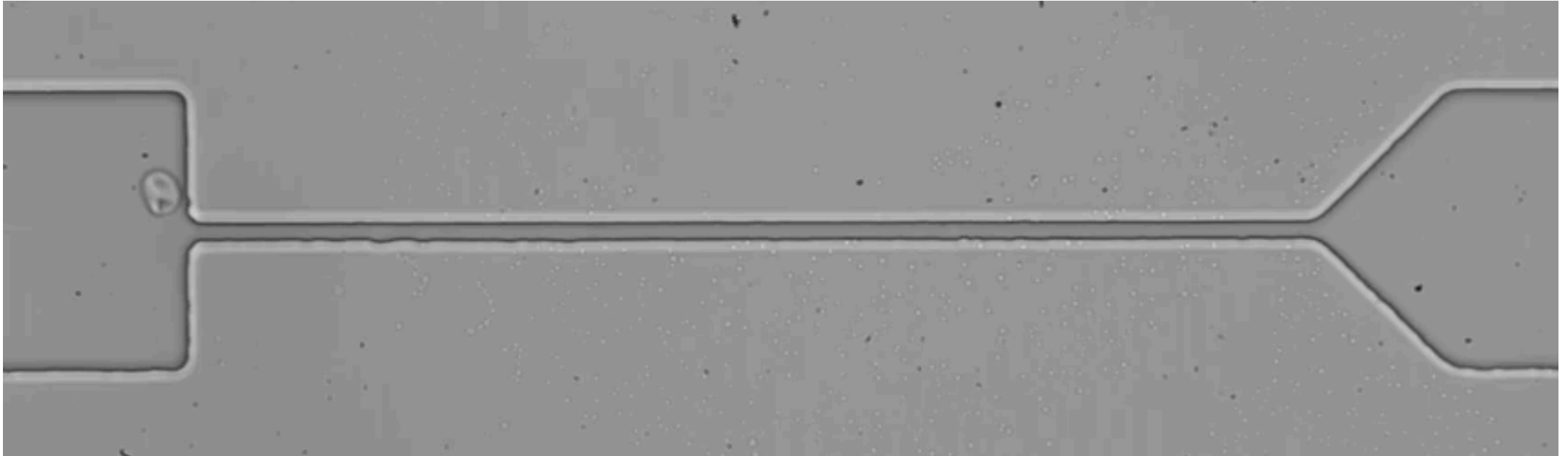
Confined circulation



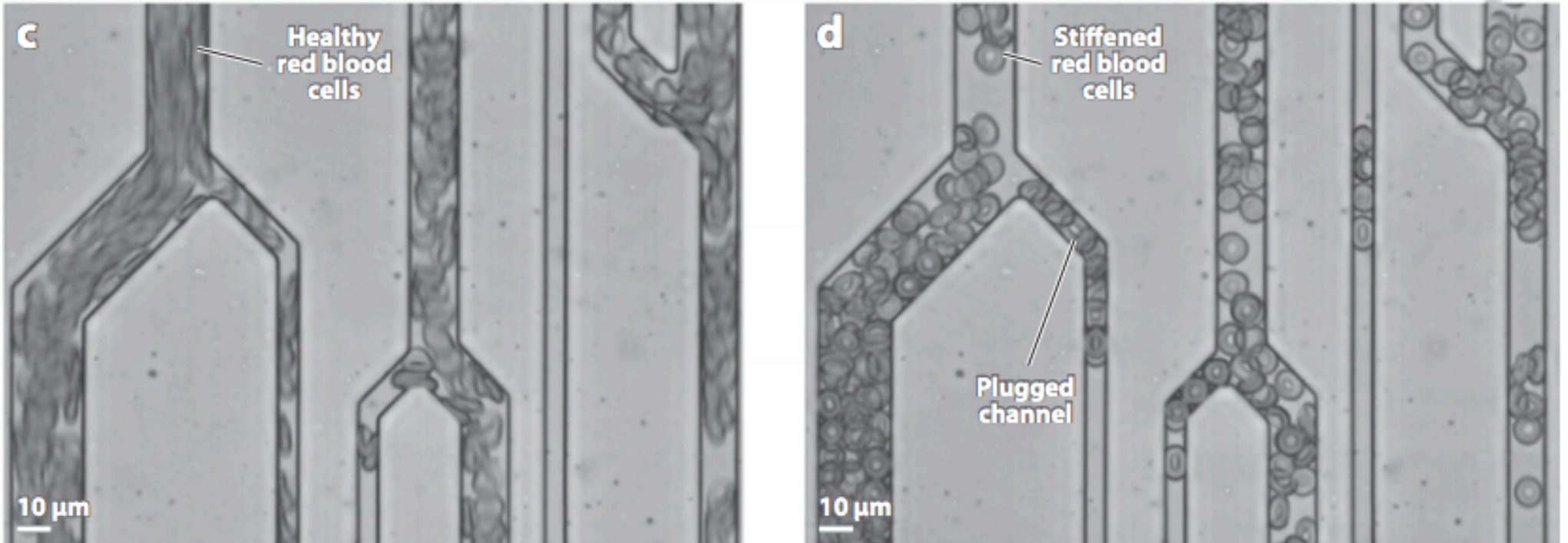
Li, Lykotrafitis et al., 2007).



Confined circulation

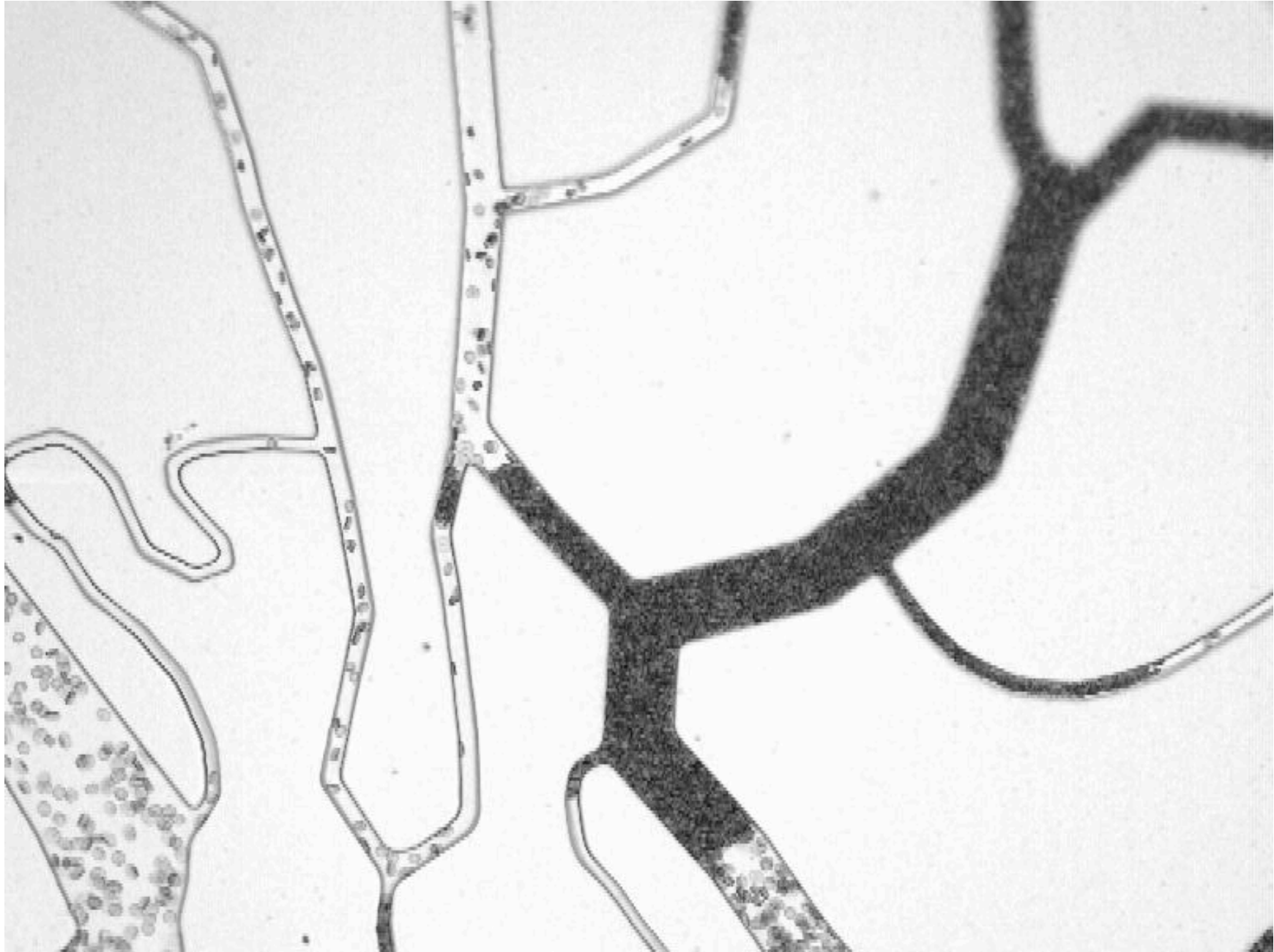


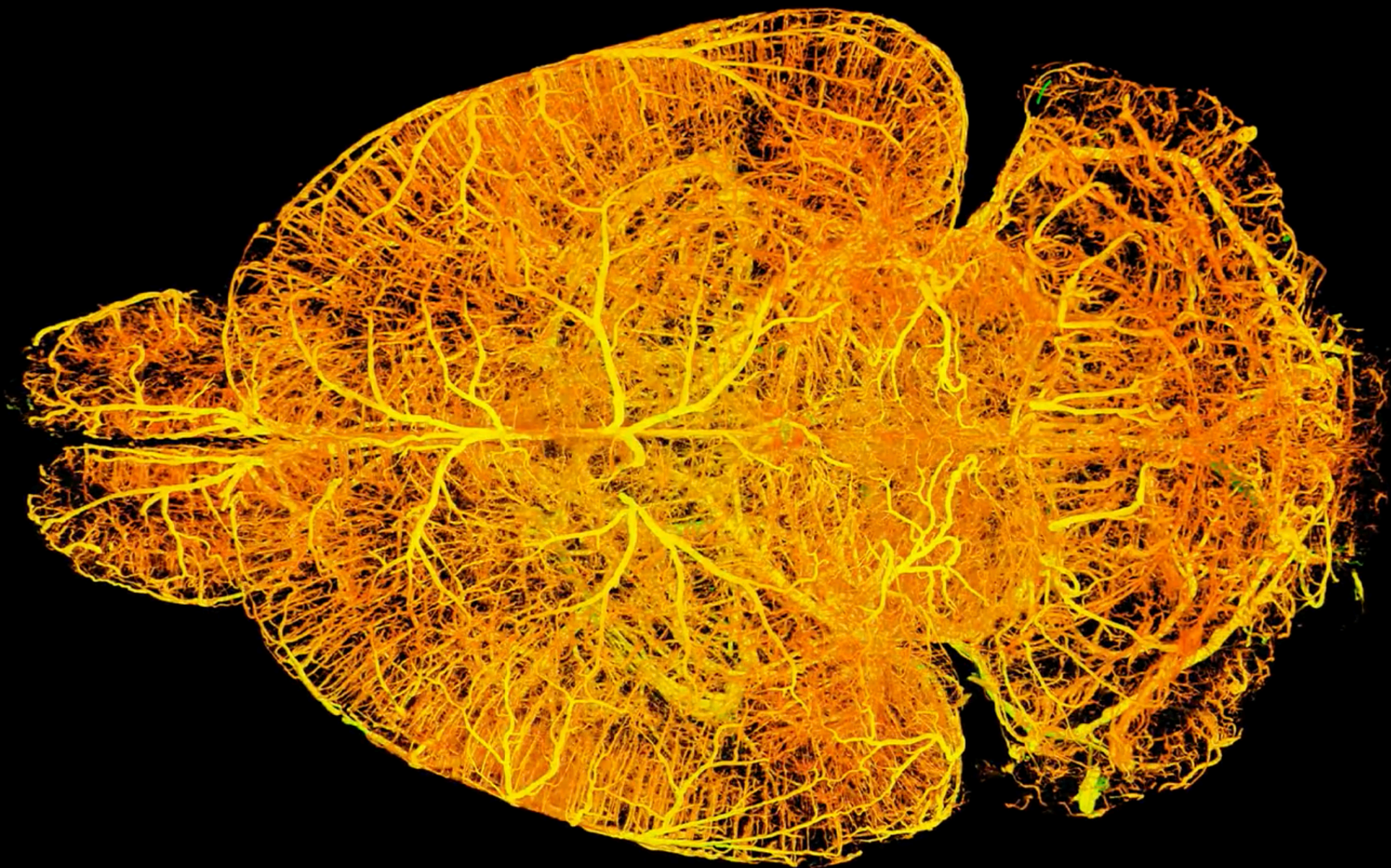
Cell deformability / clogging



S.Shevkoplias

Cell deformability / clogging

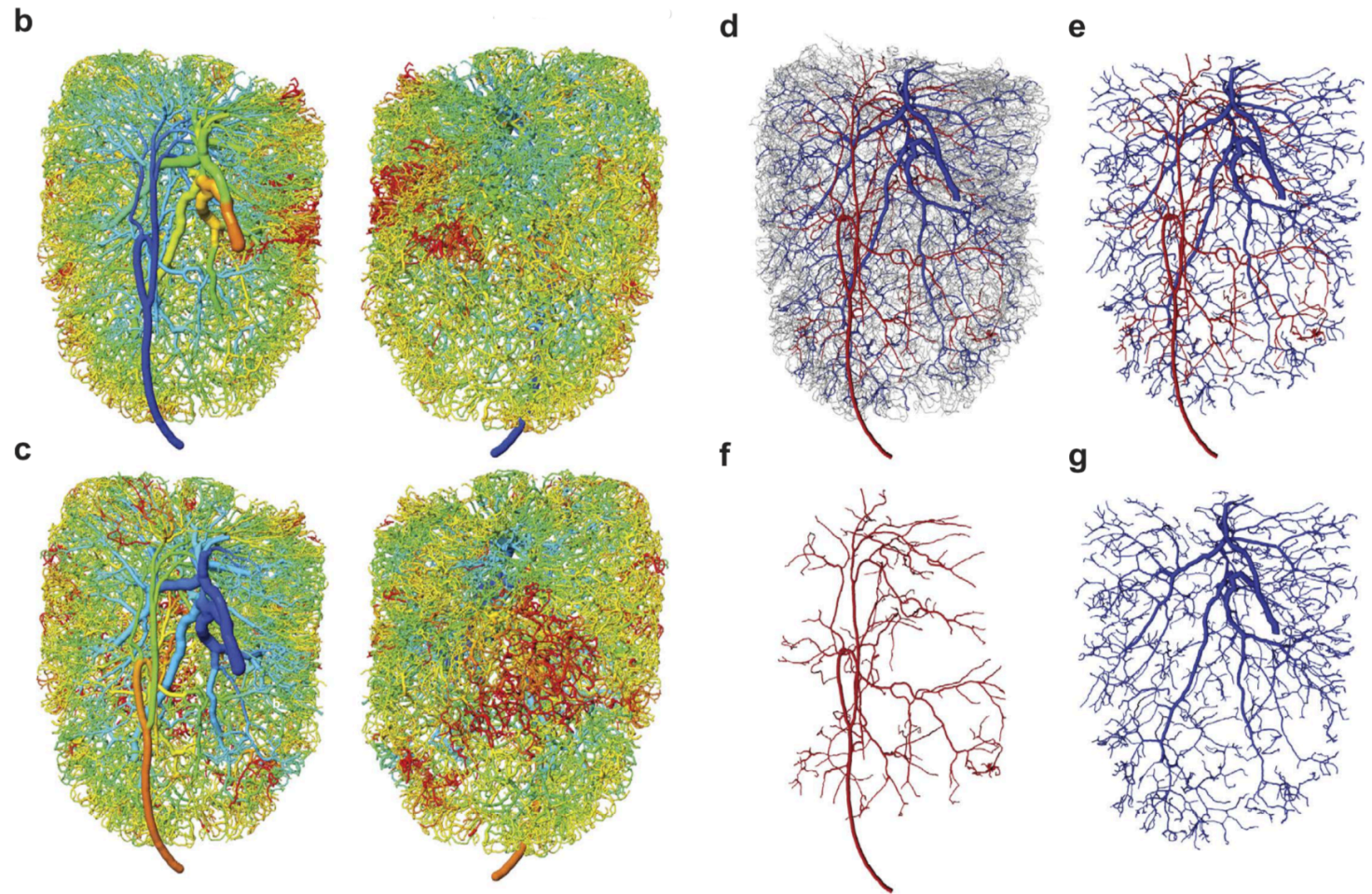




Network

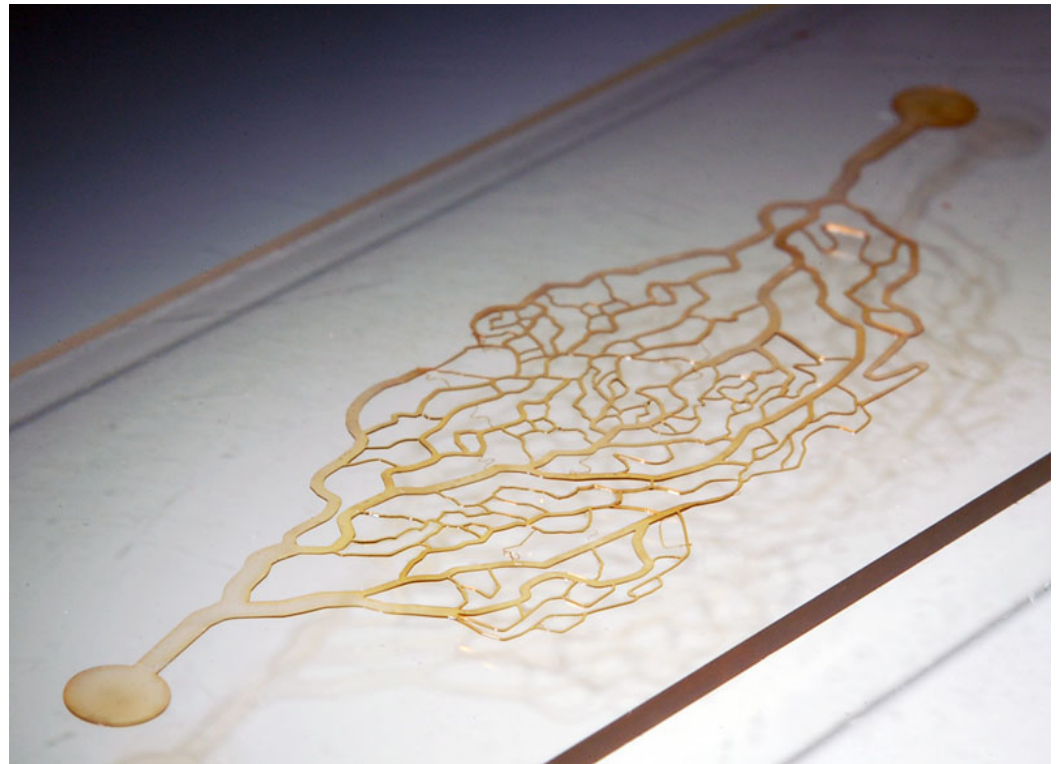
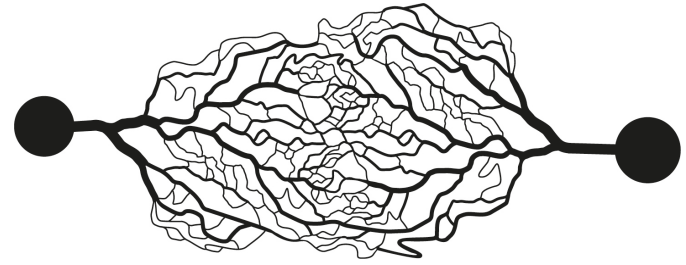
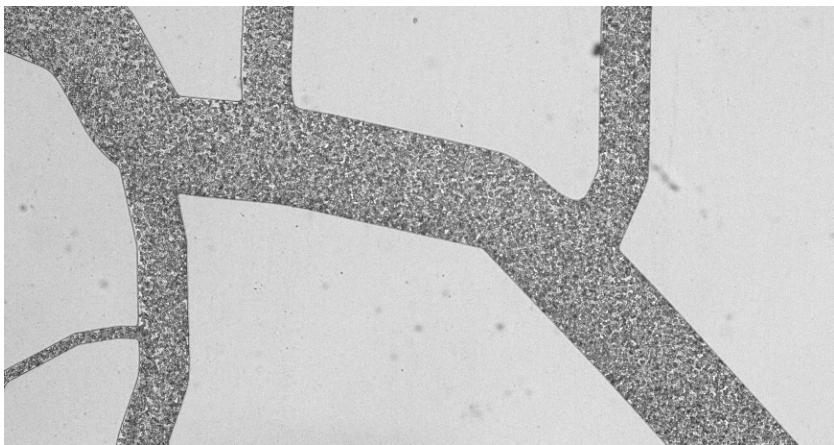
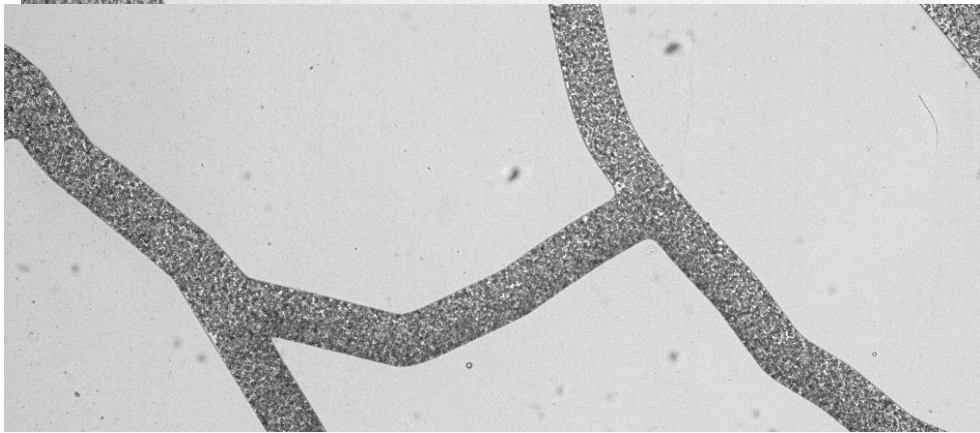
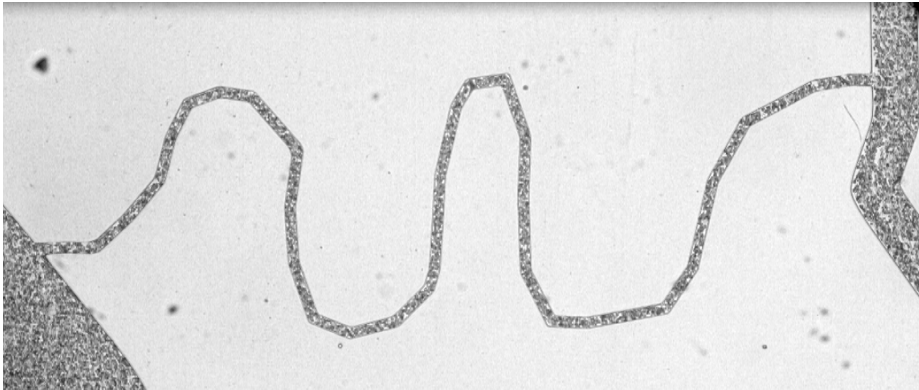
1mm long
0,2 mm³
16 000 vessels
12 000 Nodes
90cm long network

One input
One output

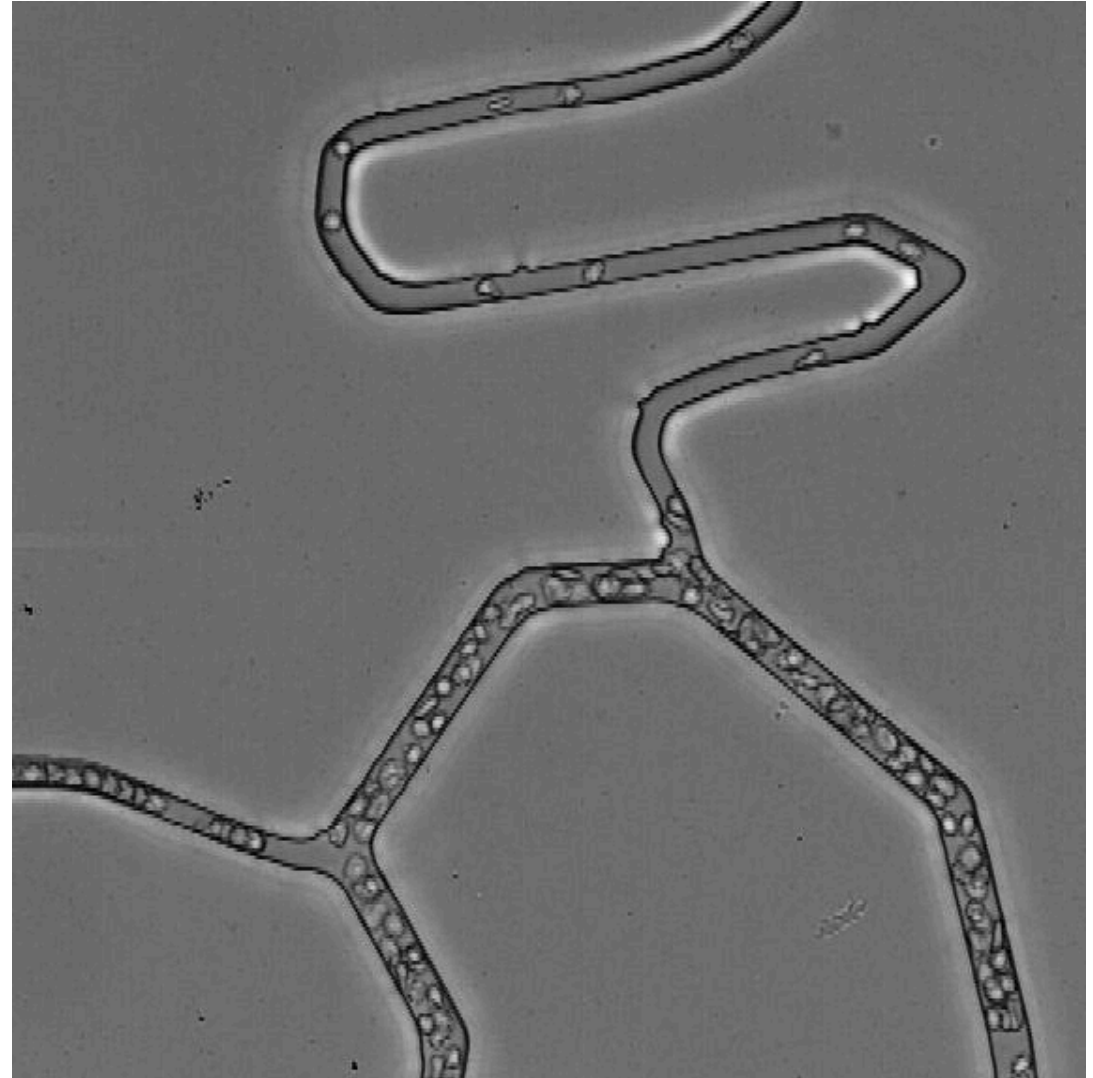
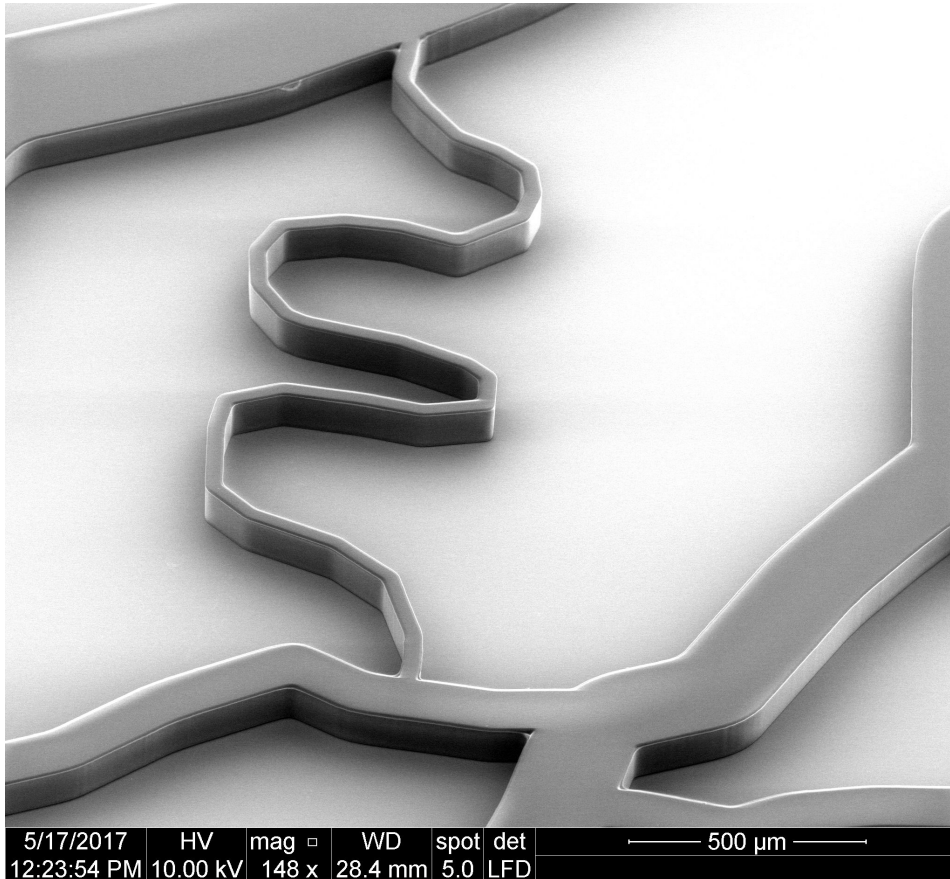
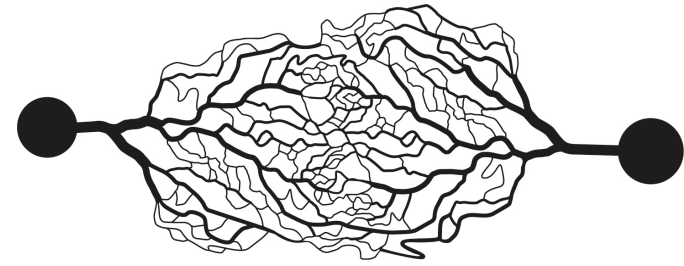


Organ-wide 3D-imaging and topological analysis of the continuous microvascular network in a murine lymph node

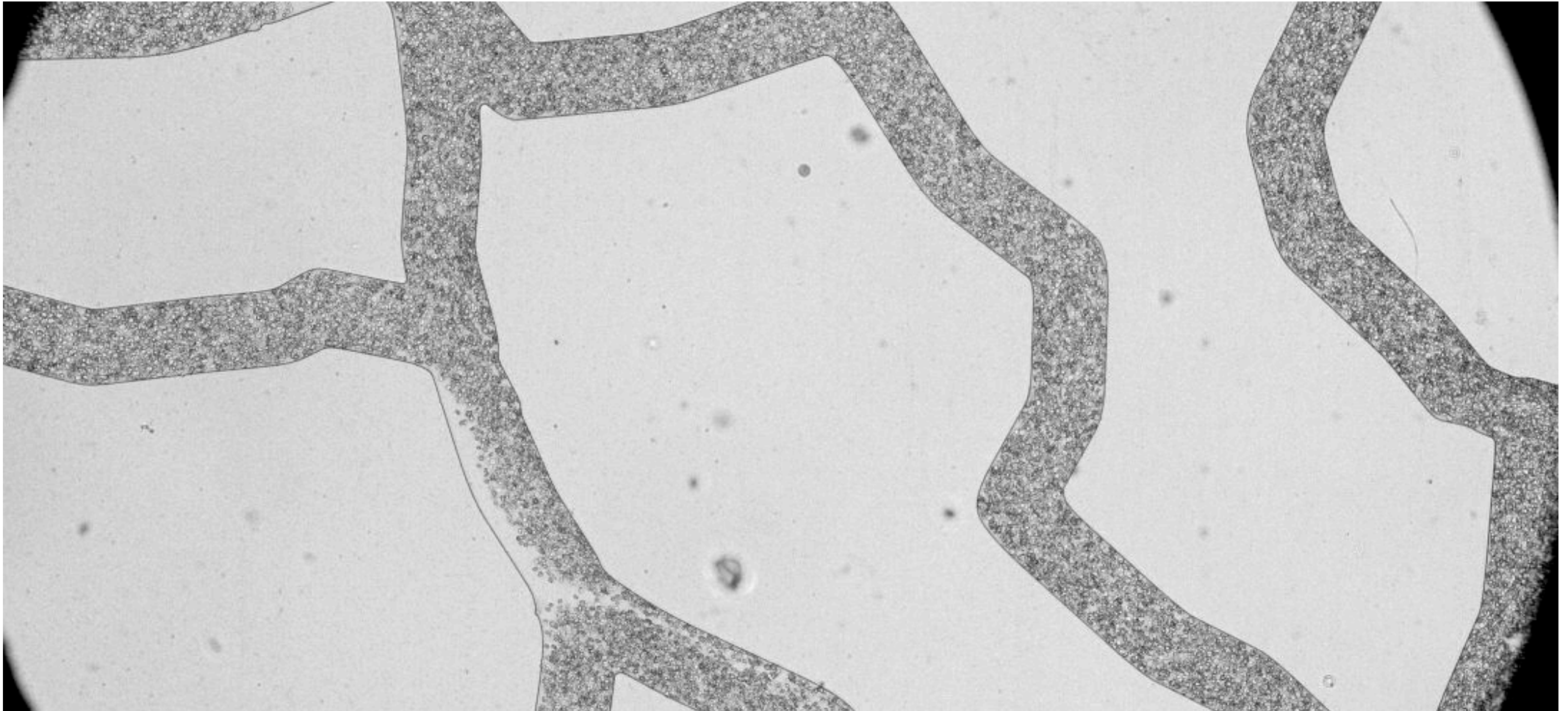
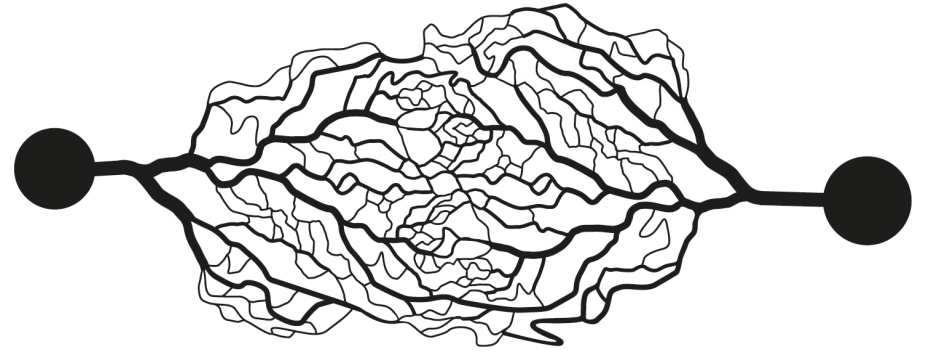
Network

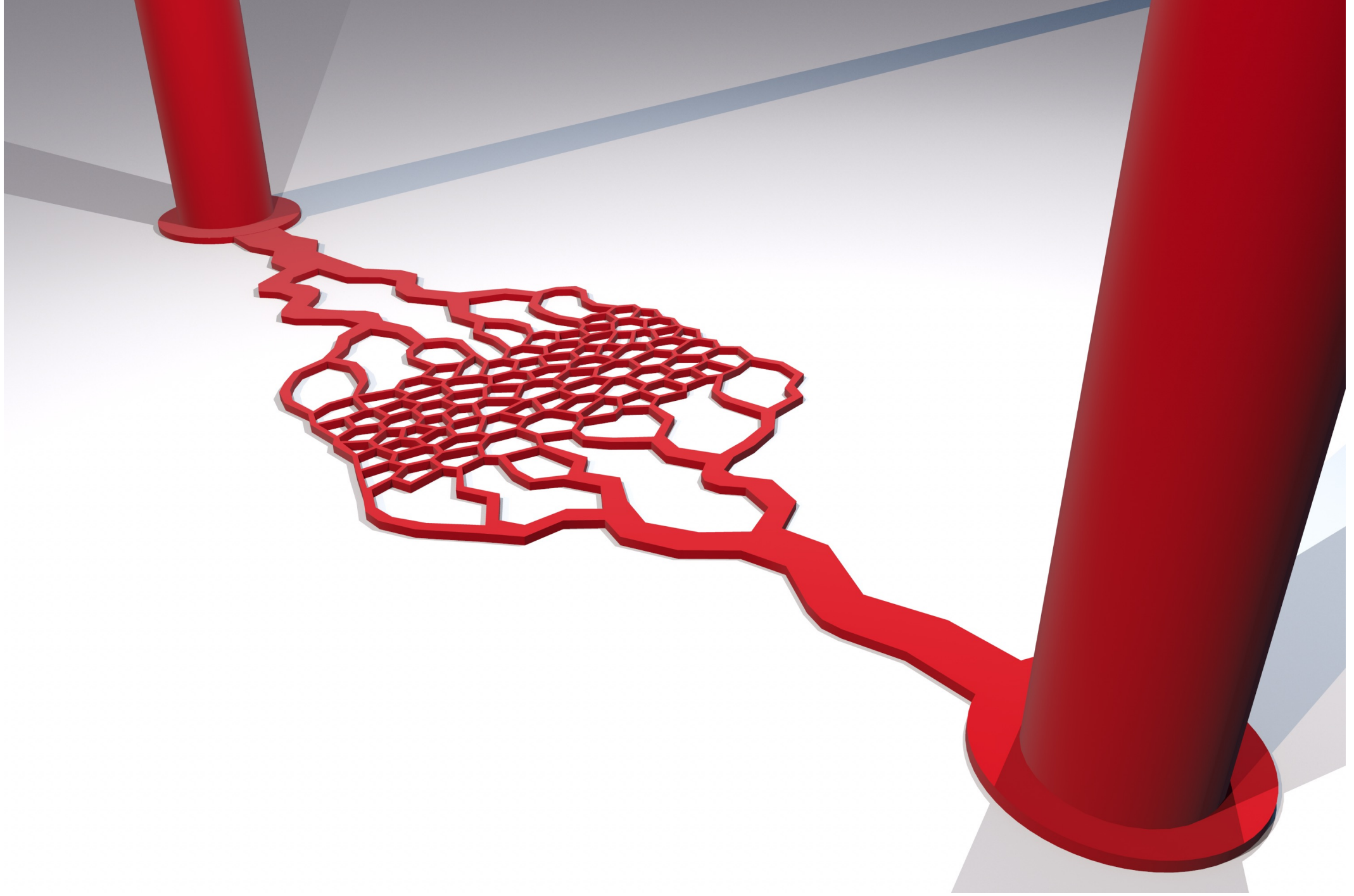


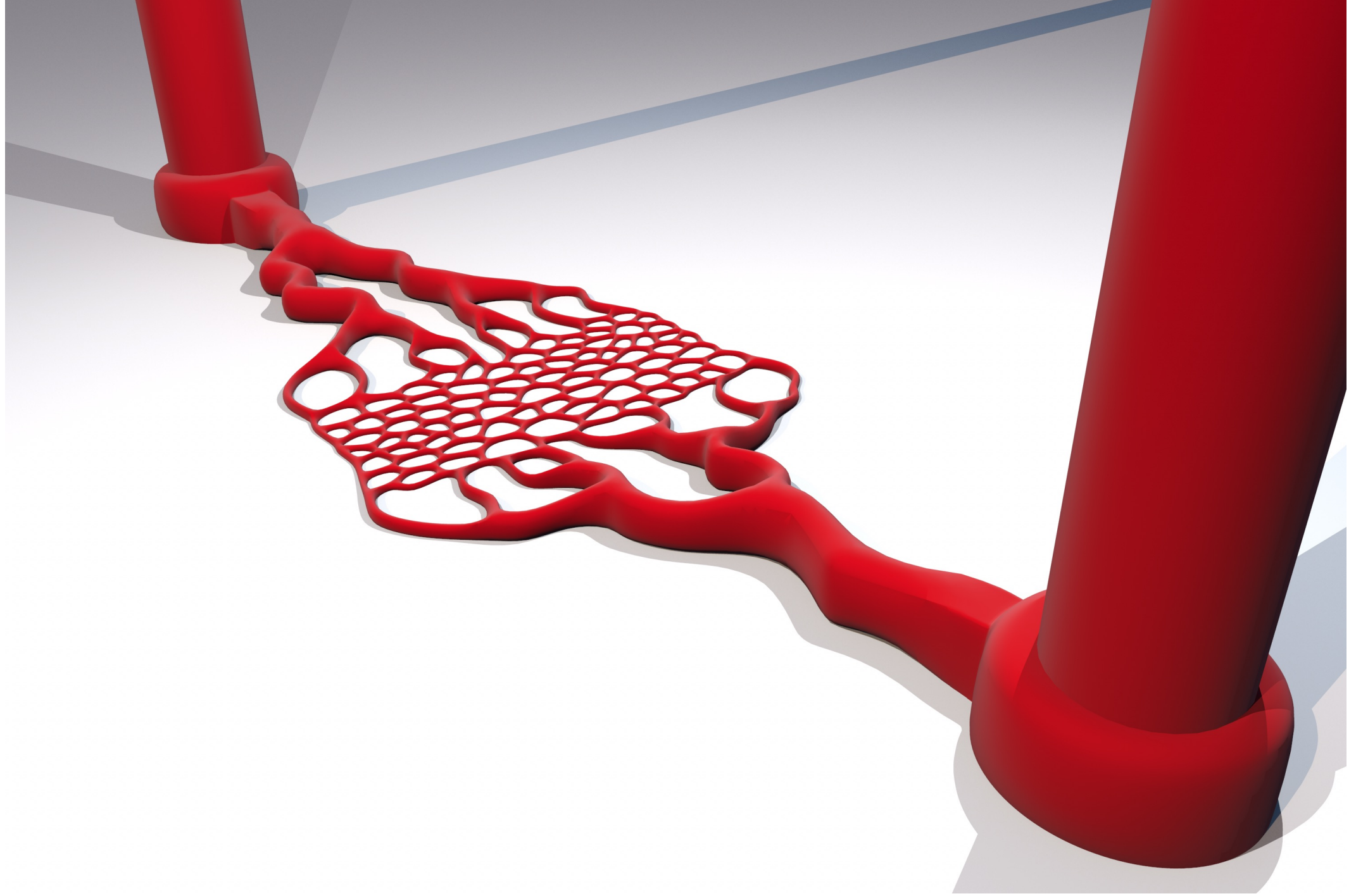
Network



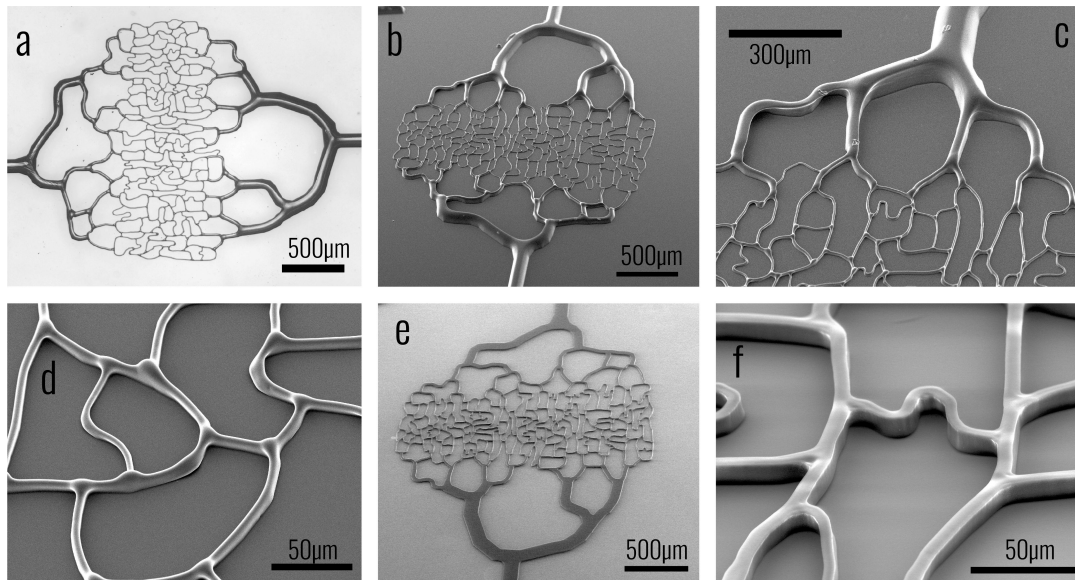
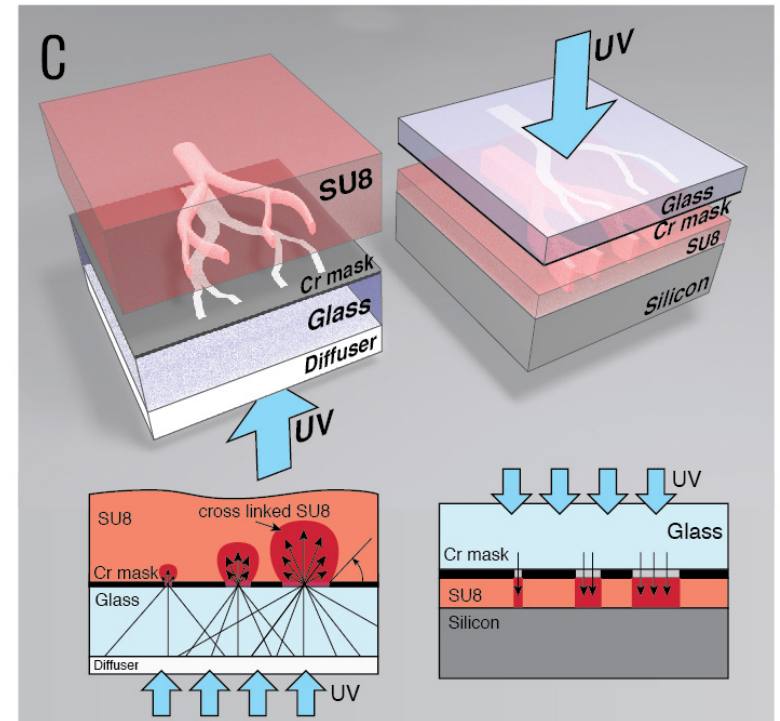
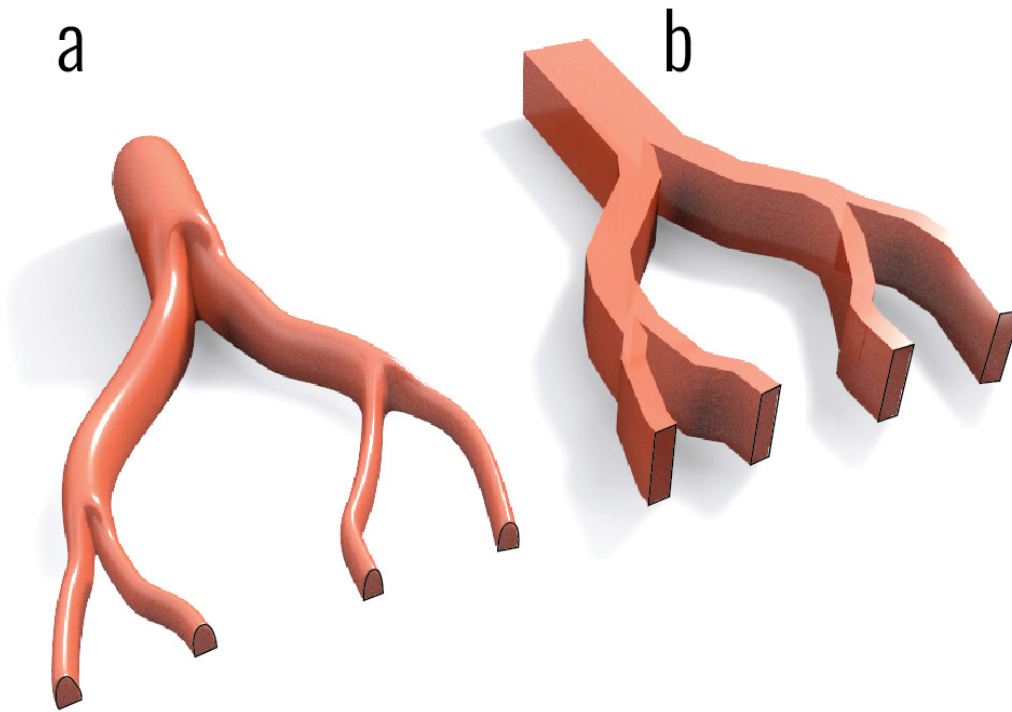
Network



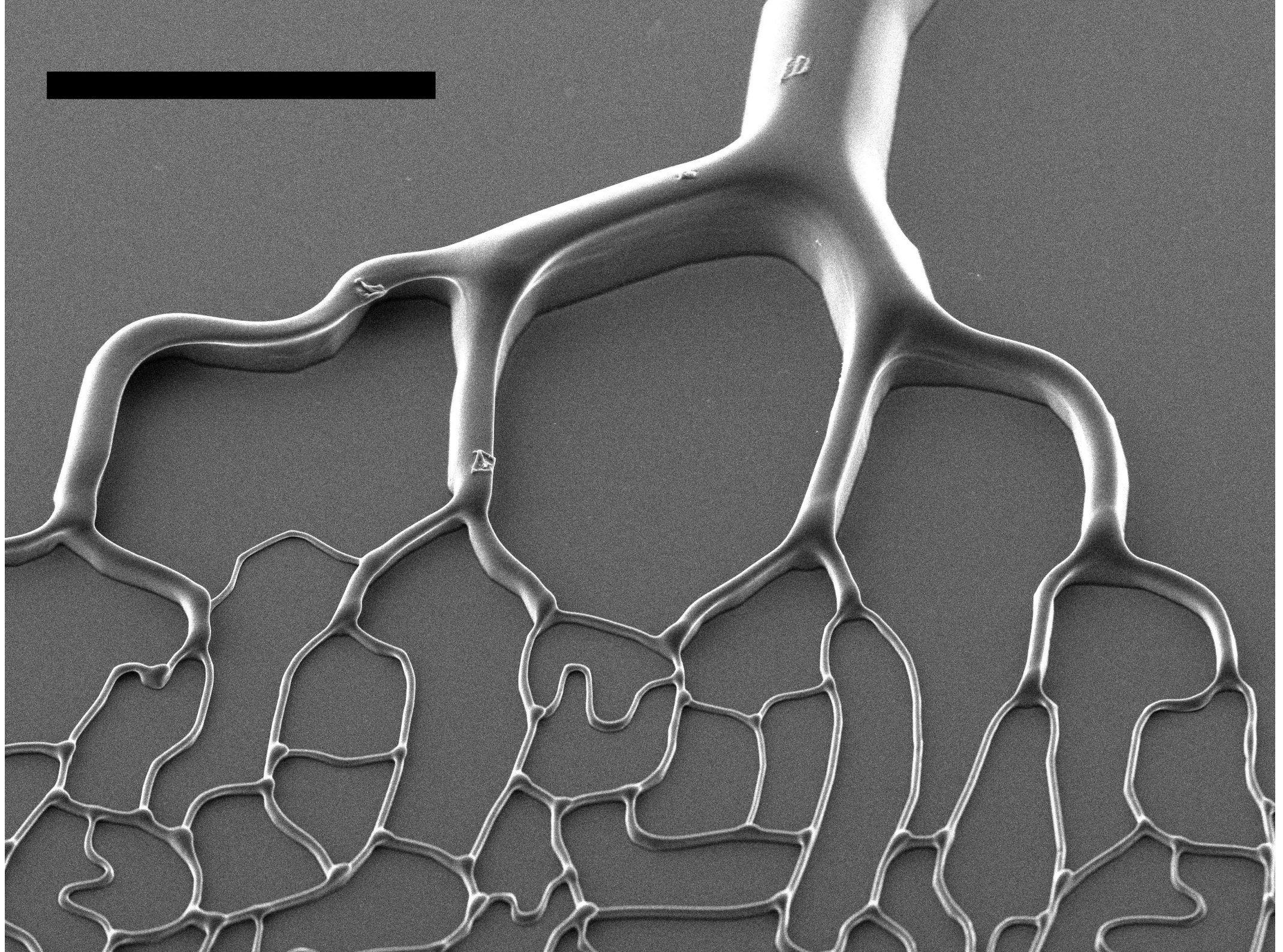




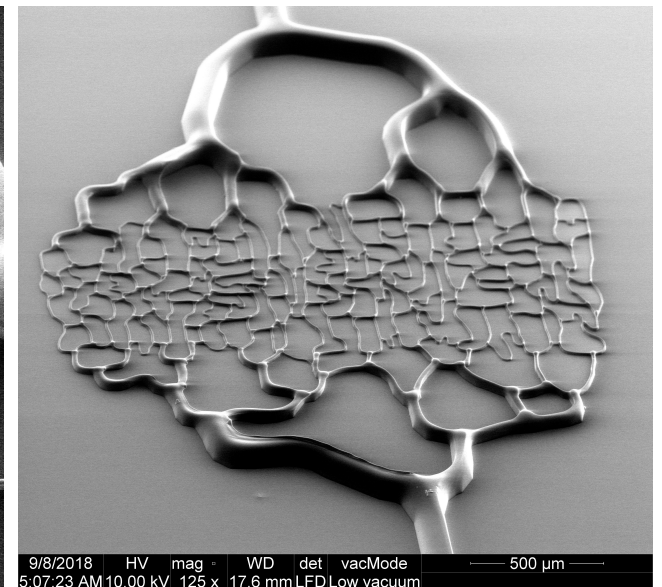
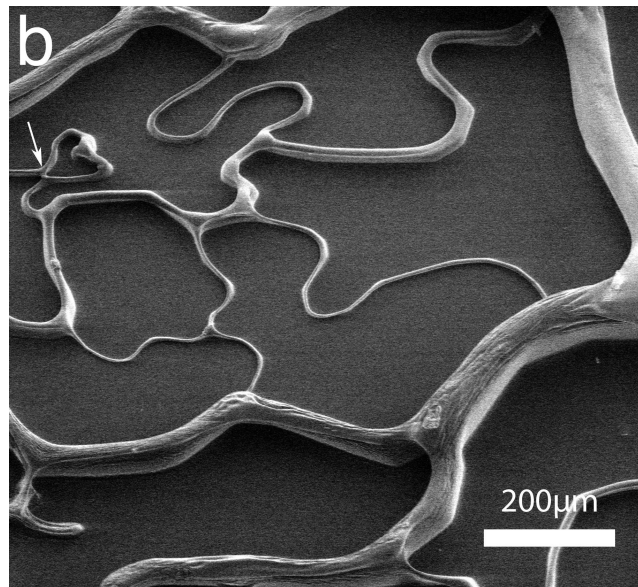
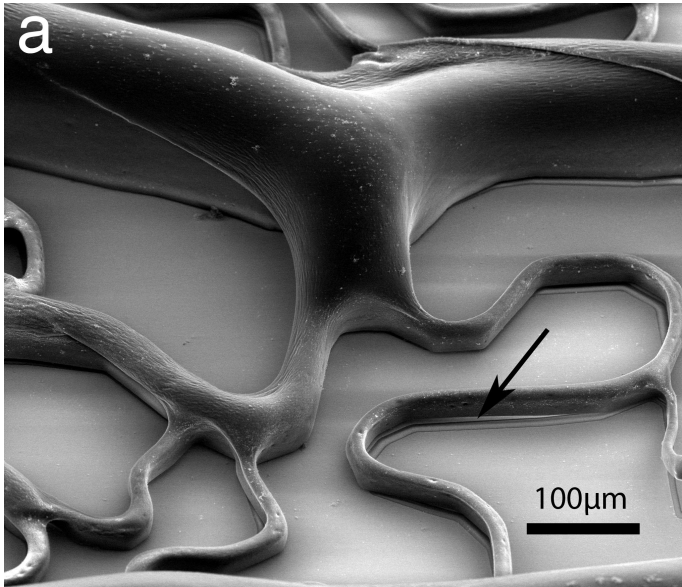
Microfabrication



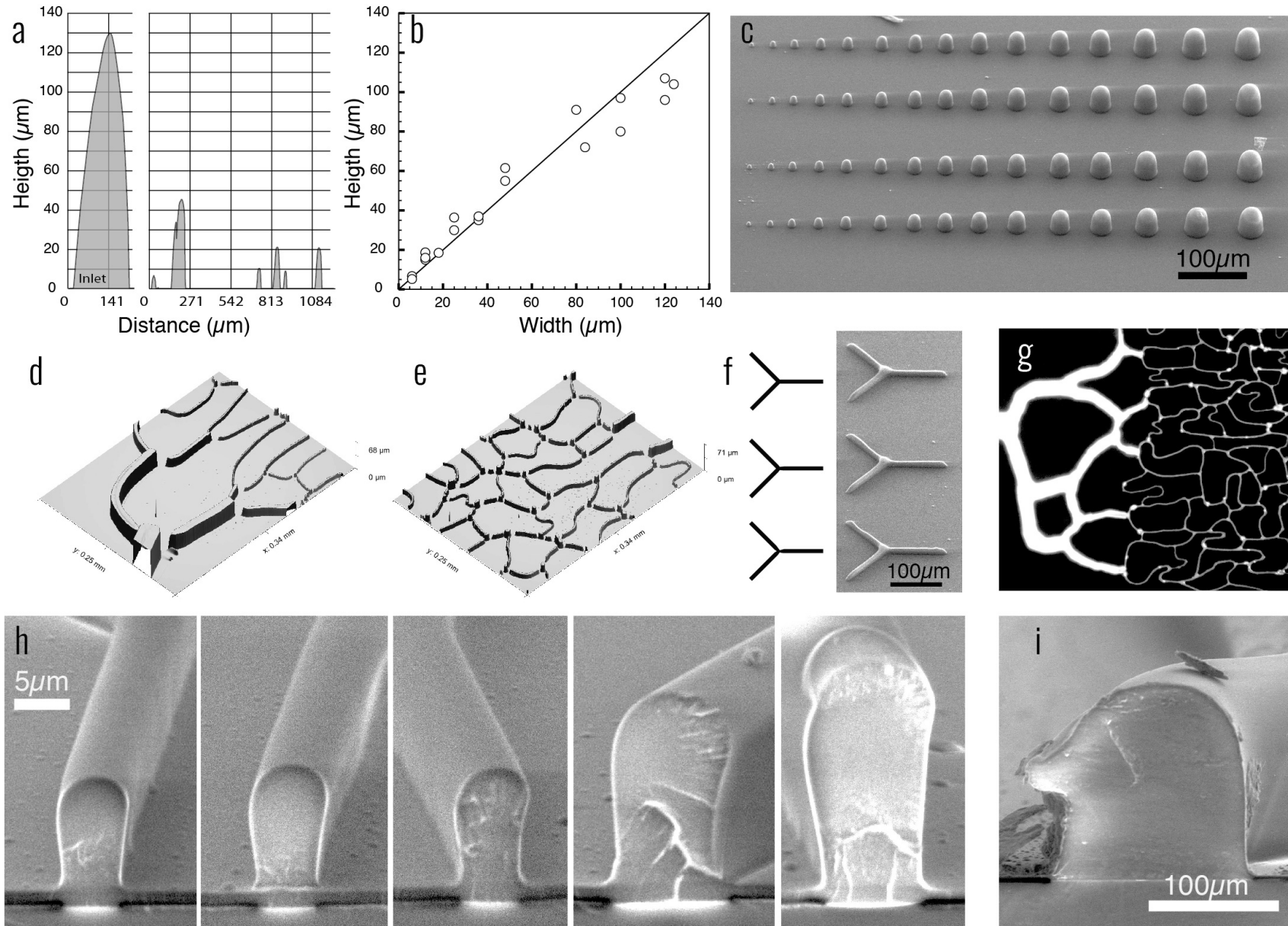
One mask
 SU8 process
 Round shapes
 Height \propto Width



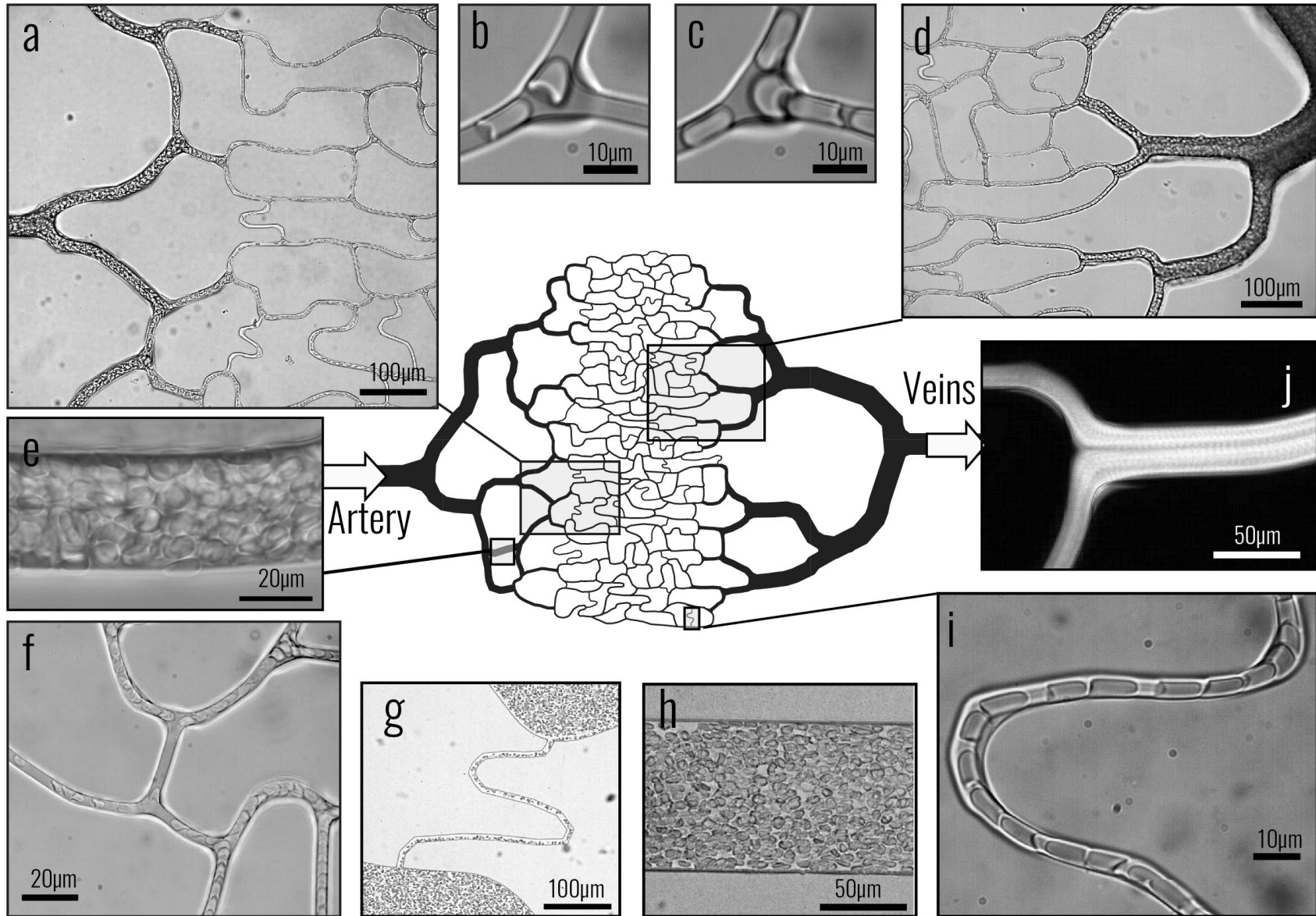
Artificial vasculature



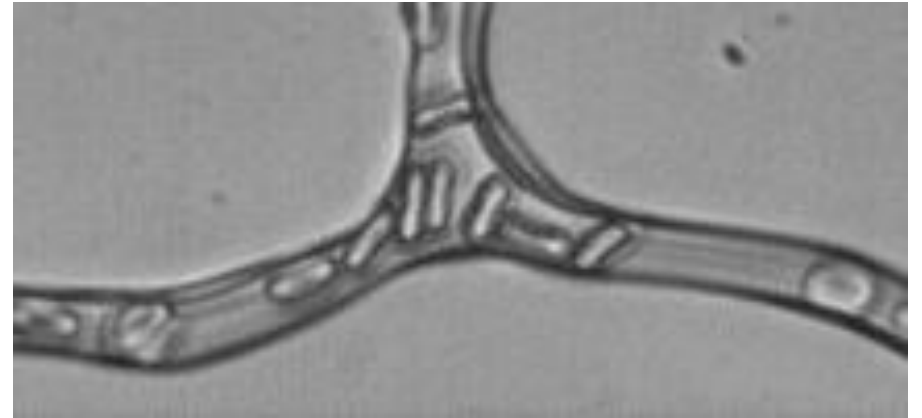
Microfabrication



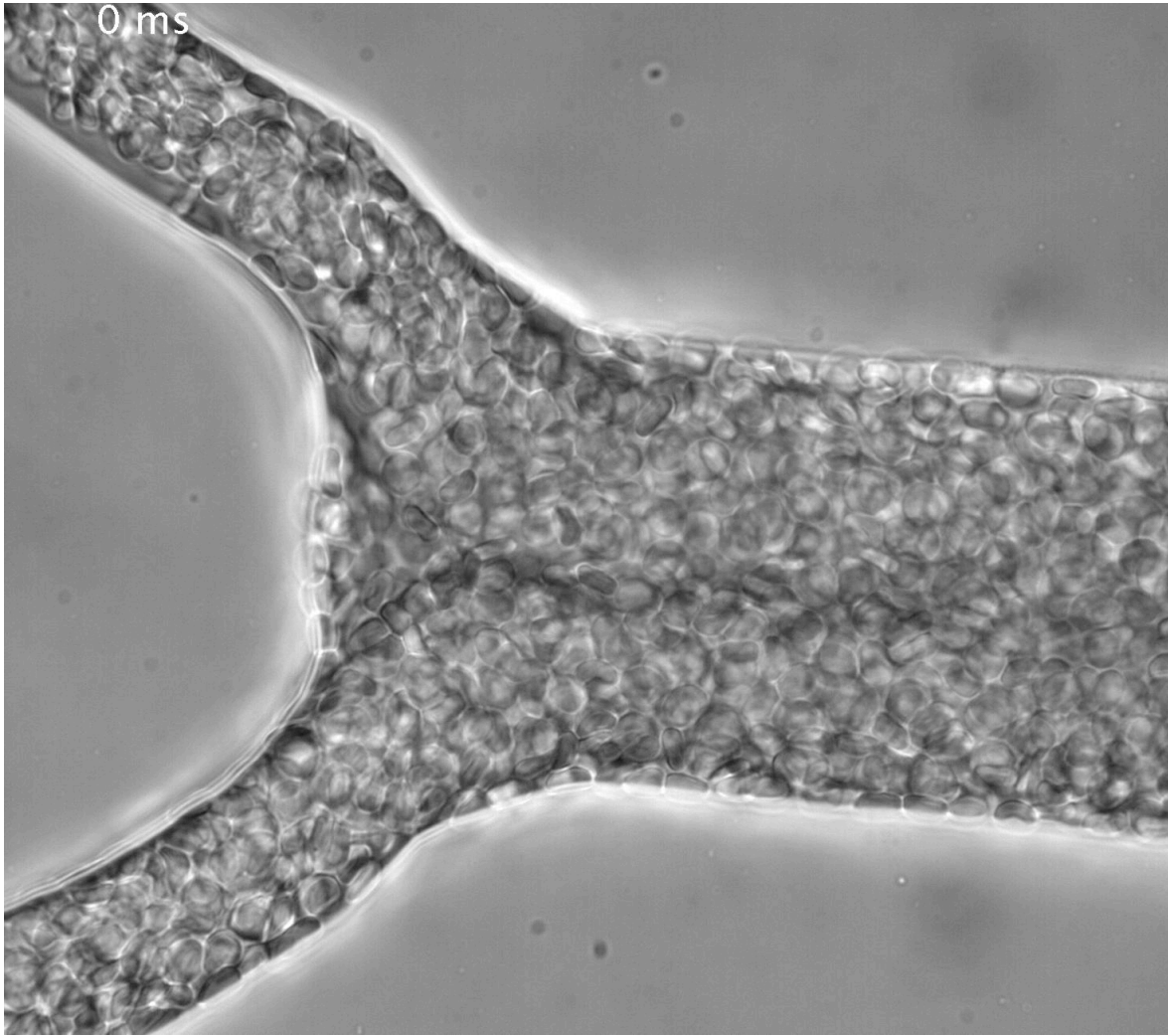
Microfabrication



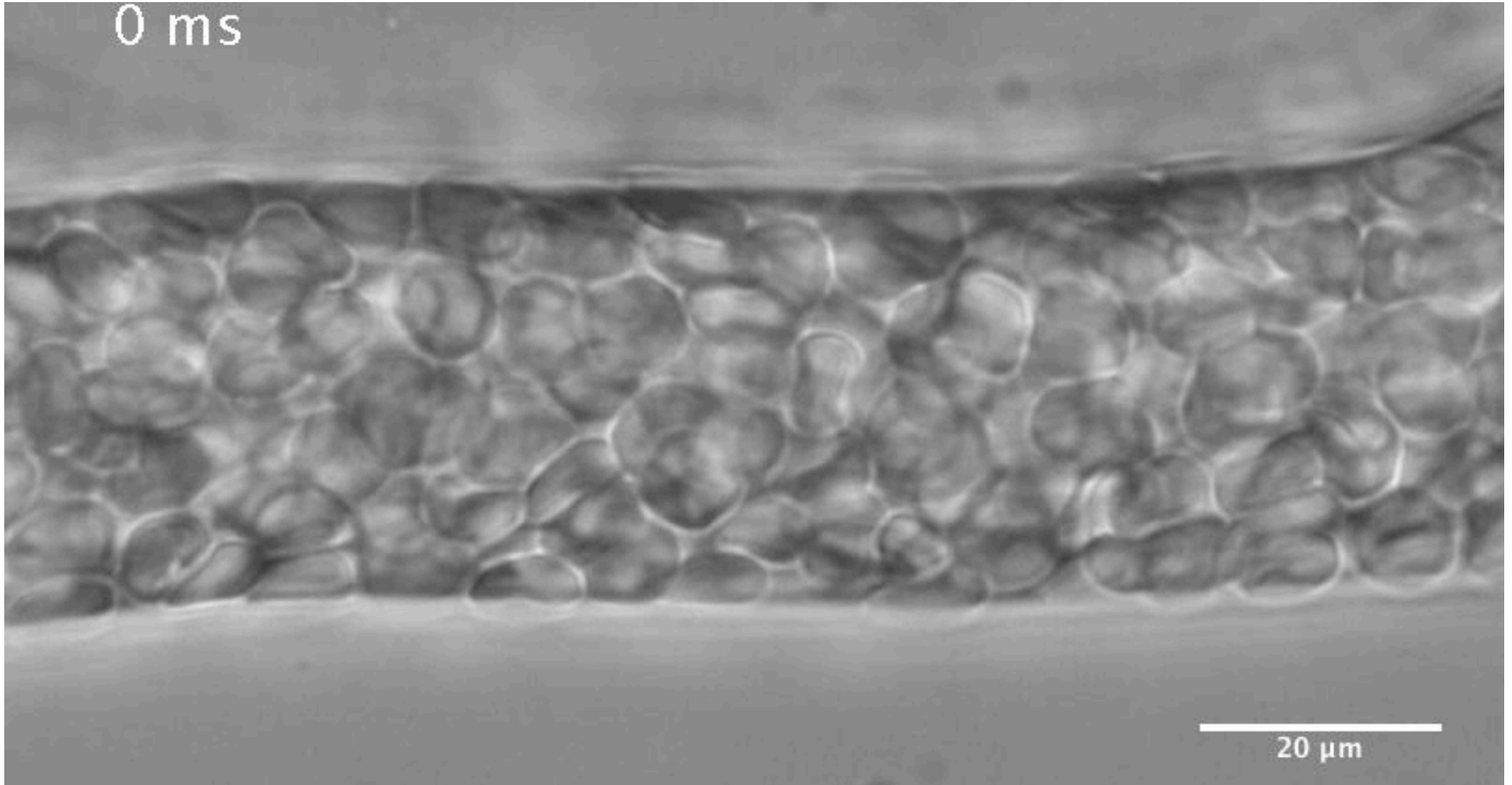
Artificial vasculature



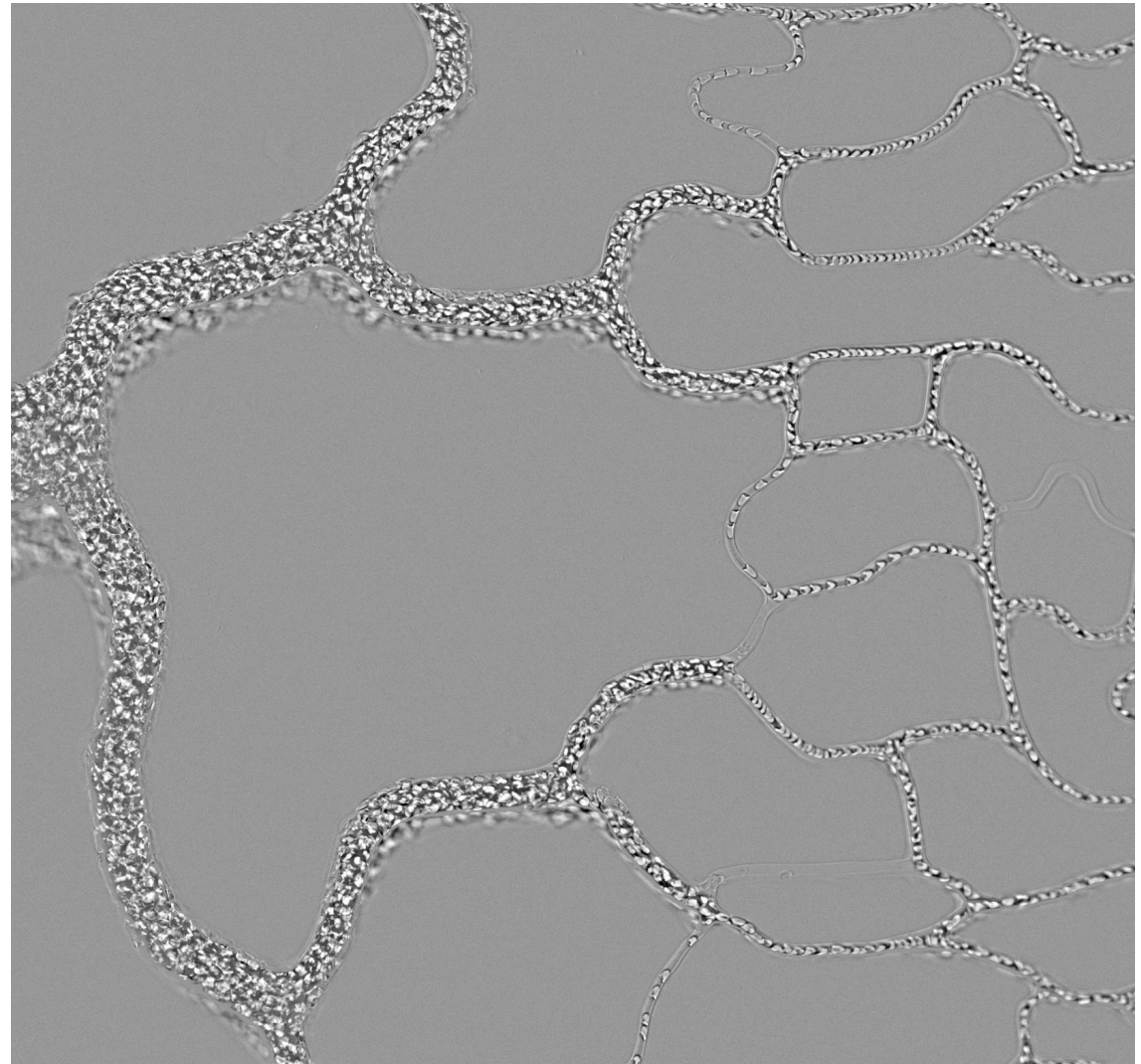
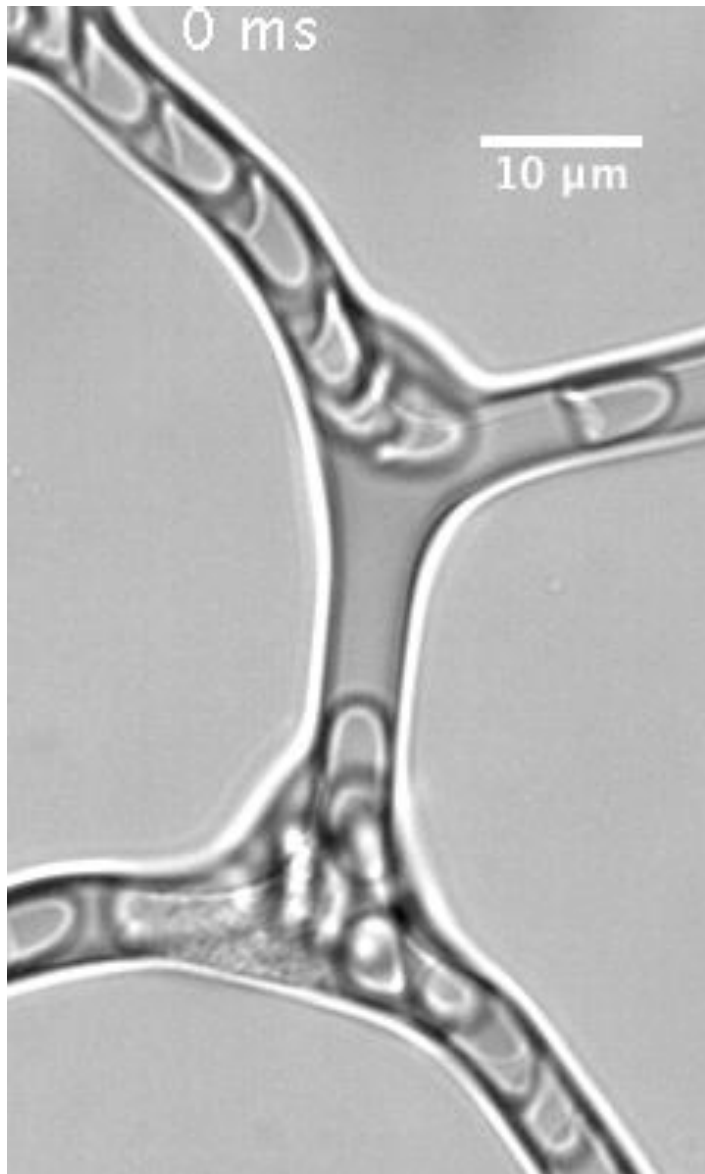
Artificial vasculature



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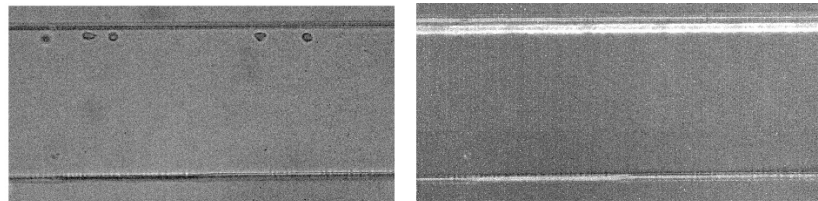
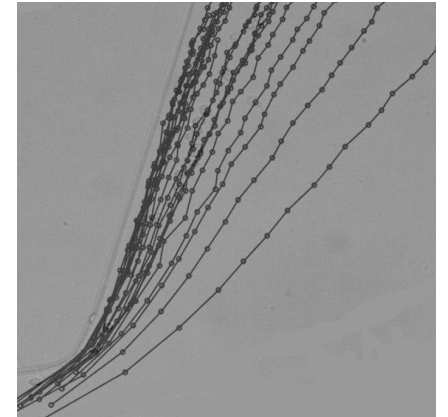
Artificial vasculature



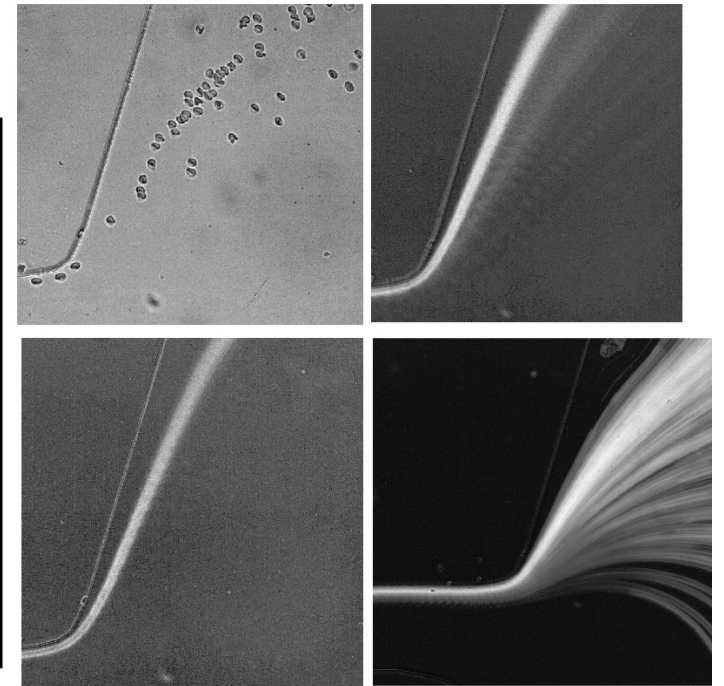
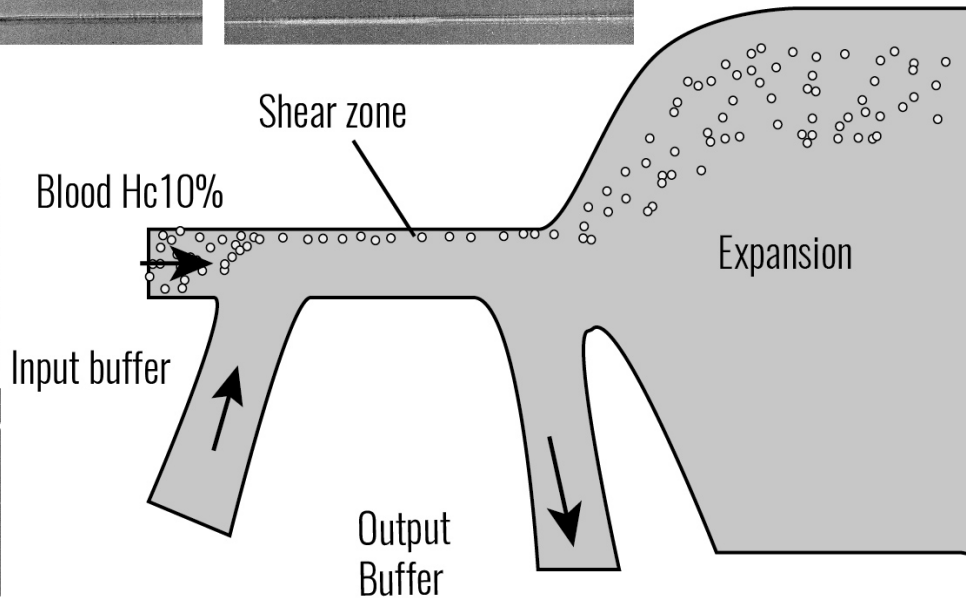
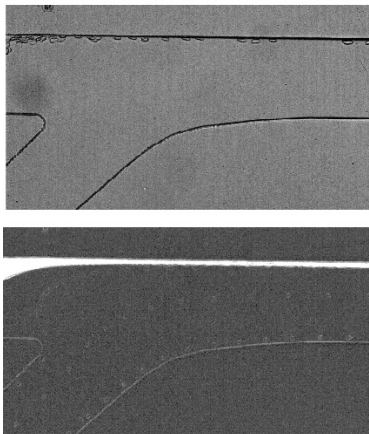
Separative techniques

Pinched flow fractionation,

Blood under shear stress : detection of RBCs having deformability diseases.

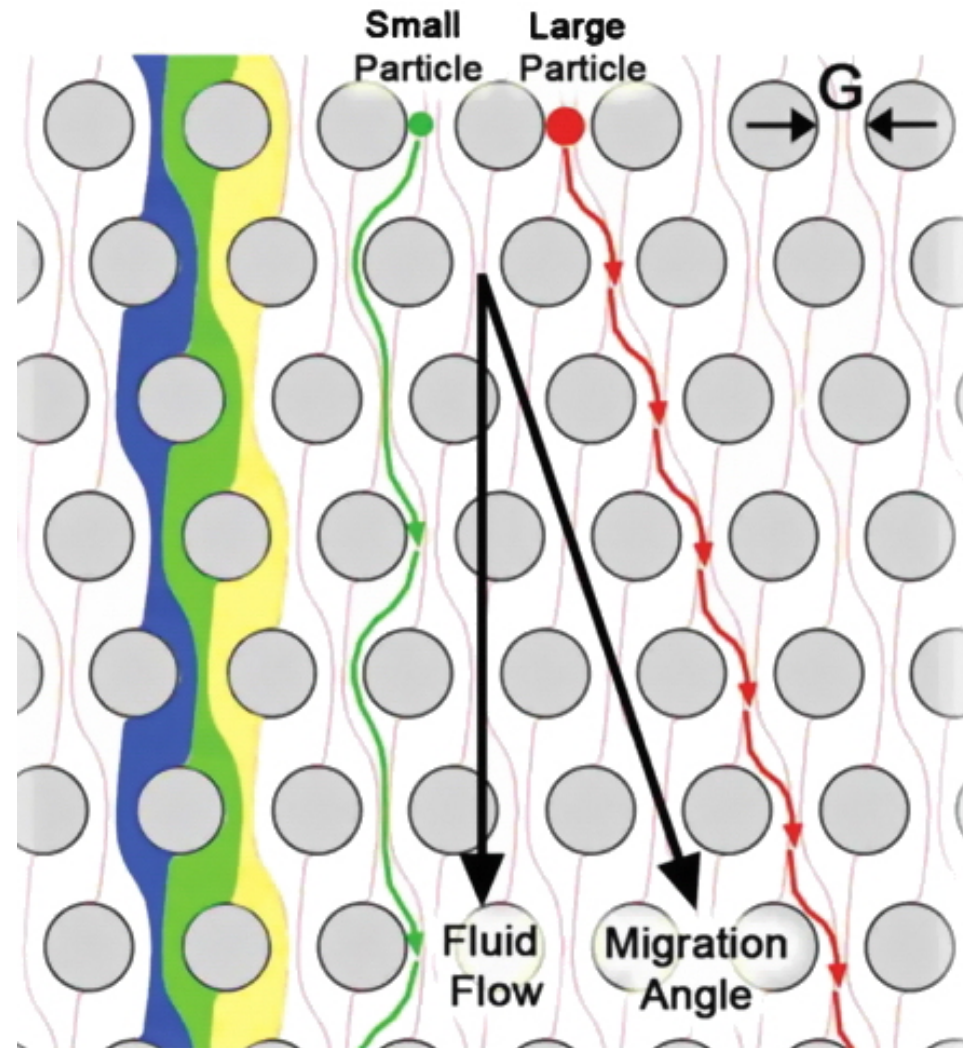


Pinching



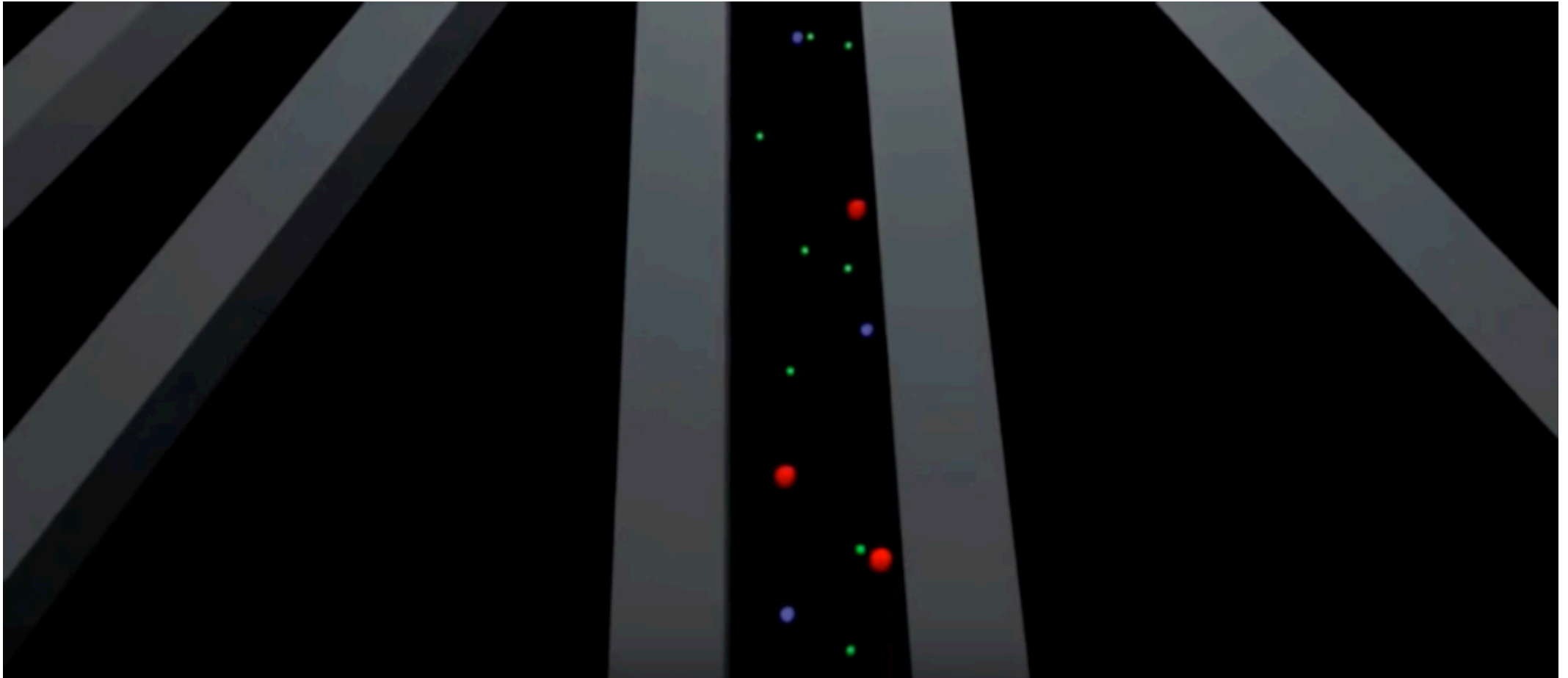
Separative techniques

Deterministic Lateral displacement



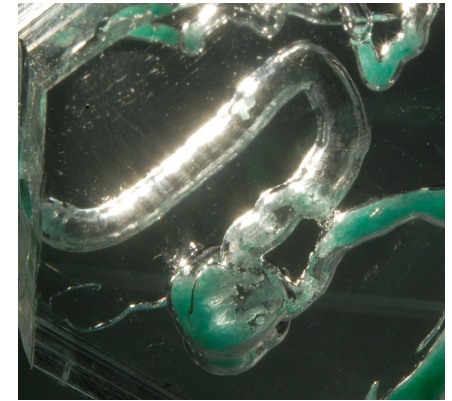
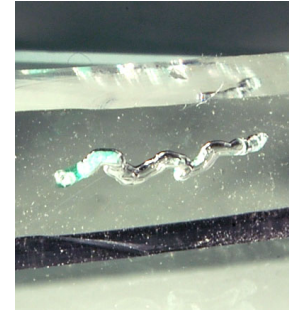
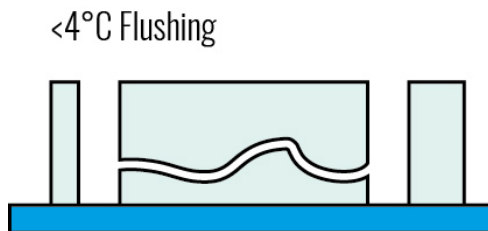
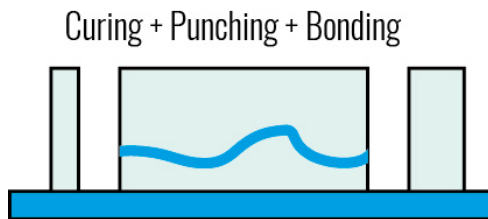
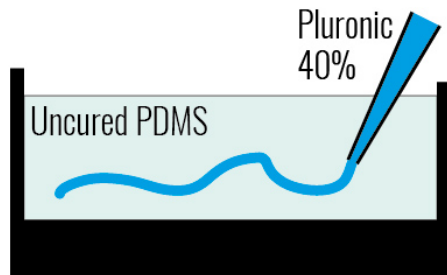
Separative techniques

Deterministic Lateral displacement



Microcirculation phantoms

Building of microcirculation models in PDMS



Fugitive inks

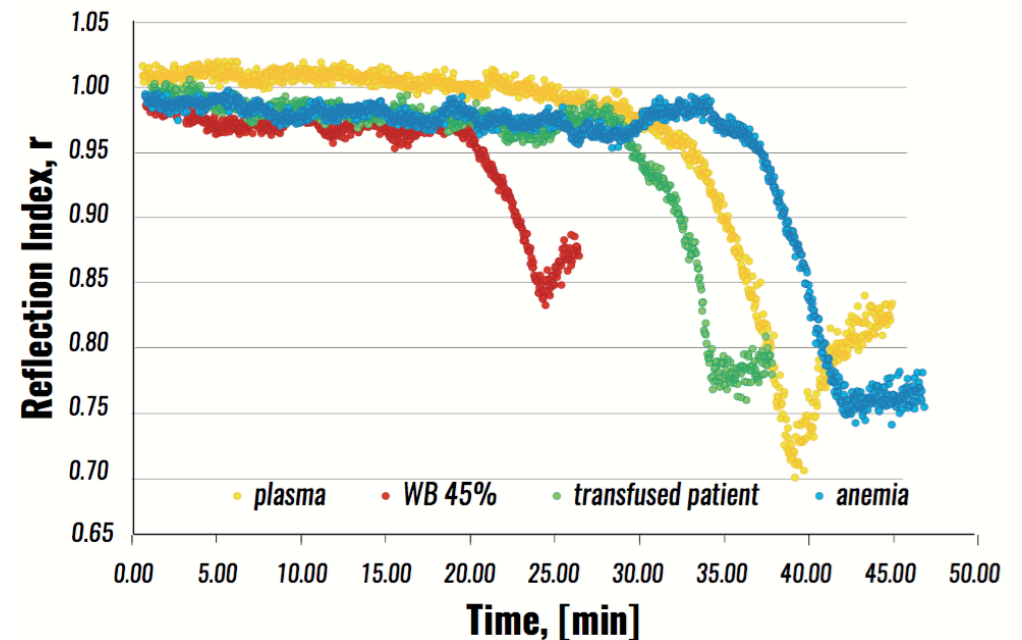
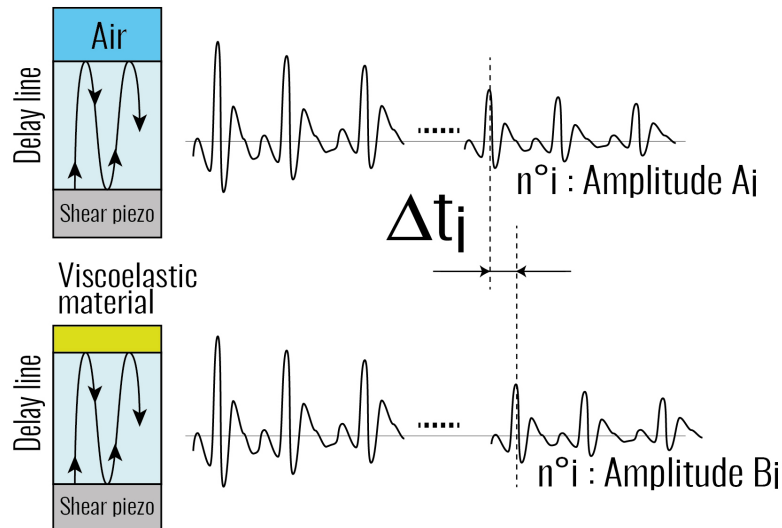
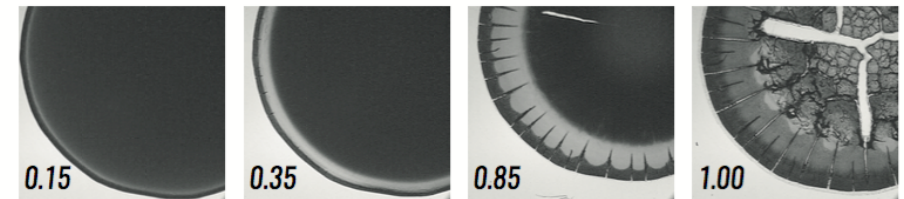
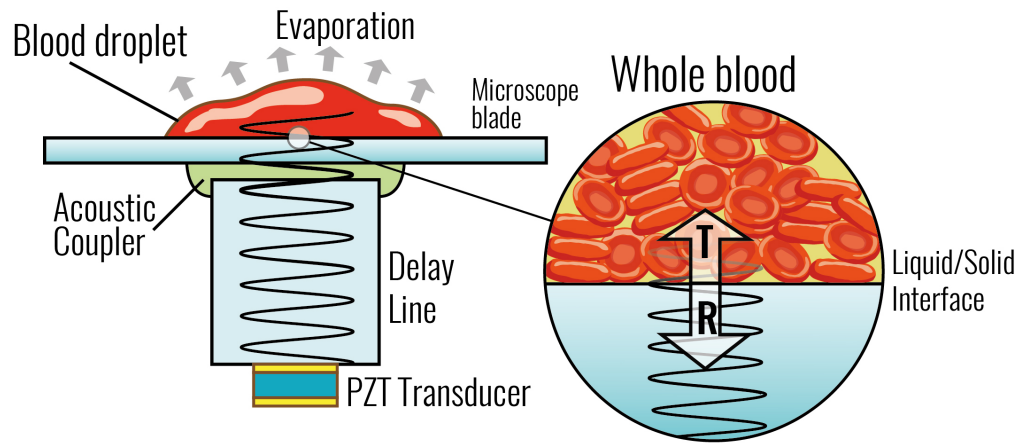
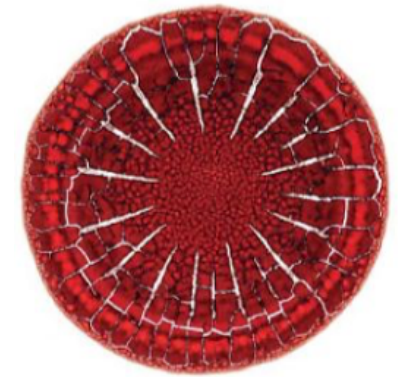
Technique described by Pr. Jennifer A. Lewis, Harvard



Acoustics and blood

Interaction blood/ acoustique wave (pulse echo)

transition liquid / gel / solid of a drying blood droplet



Artificial vascular networks

Arterioles

Capillary bed

Veinules

1mm

M.Fenech et al.
Lab on Chip, 2019