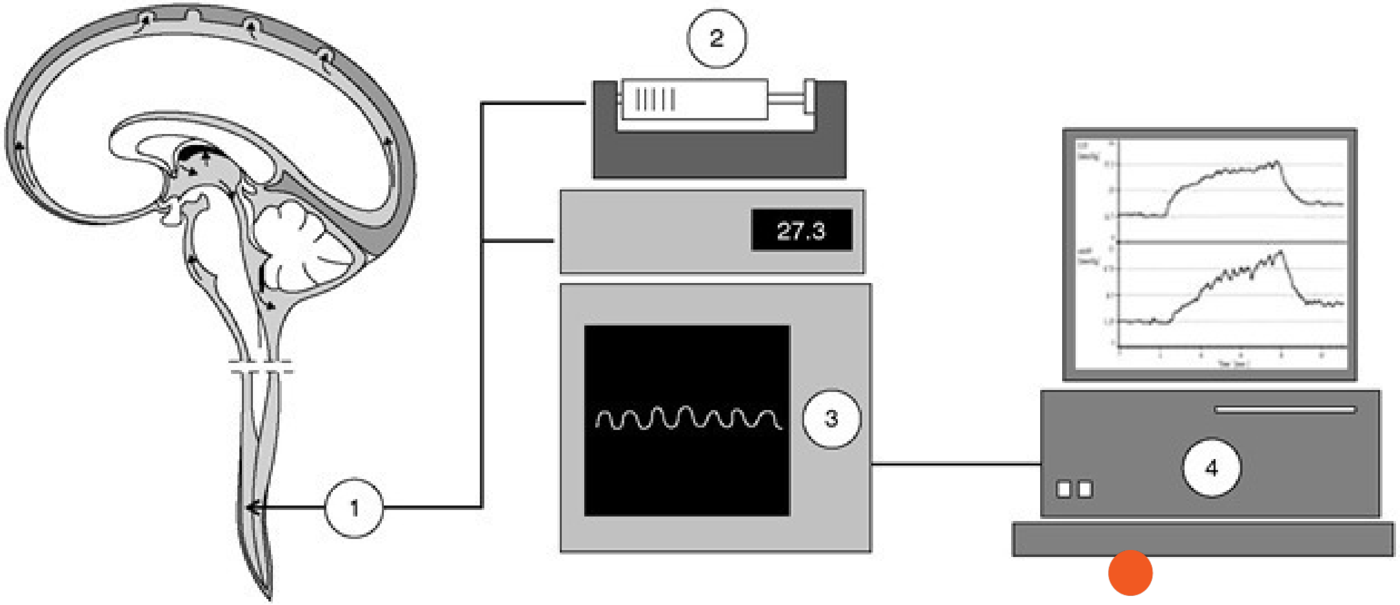
# Modeling intracranial pressure (ICP) during infusion test




**Vegard Vinje, PhD-fellow**
**Simula Research Laboratory**

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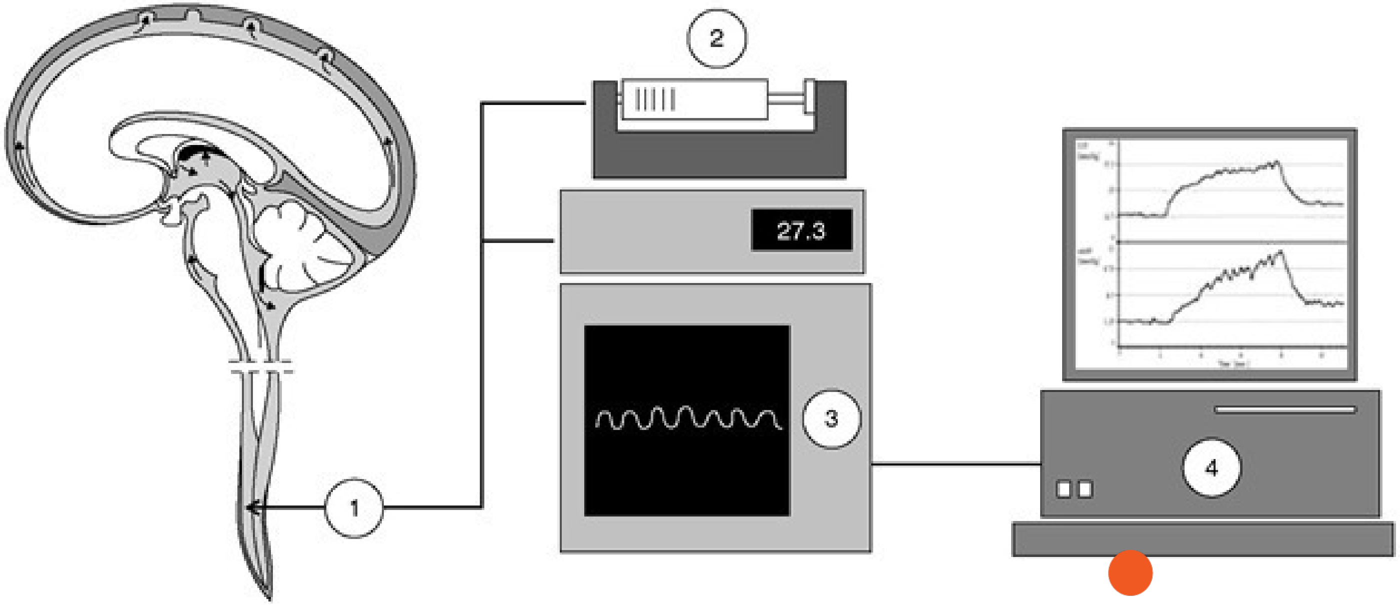
# Modeling intracranial pressure (ICP) during infusion test

…and what we can learn from back-of-the-envelope calculations

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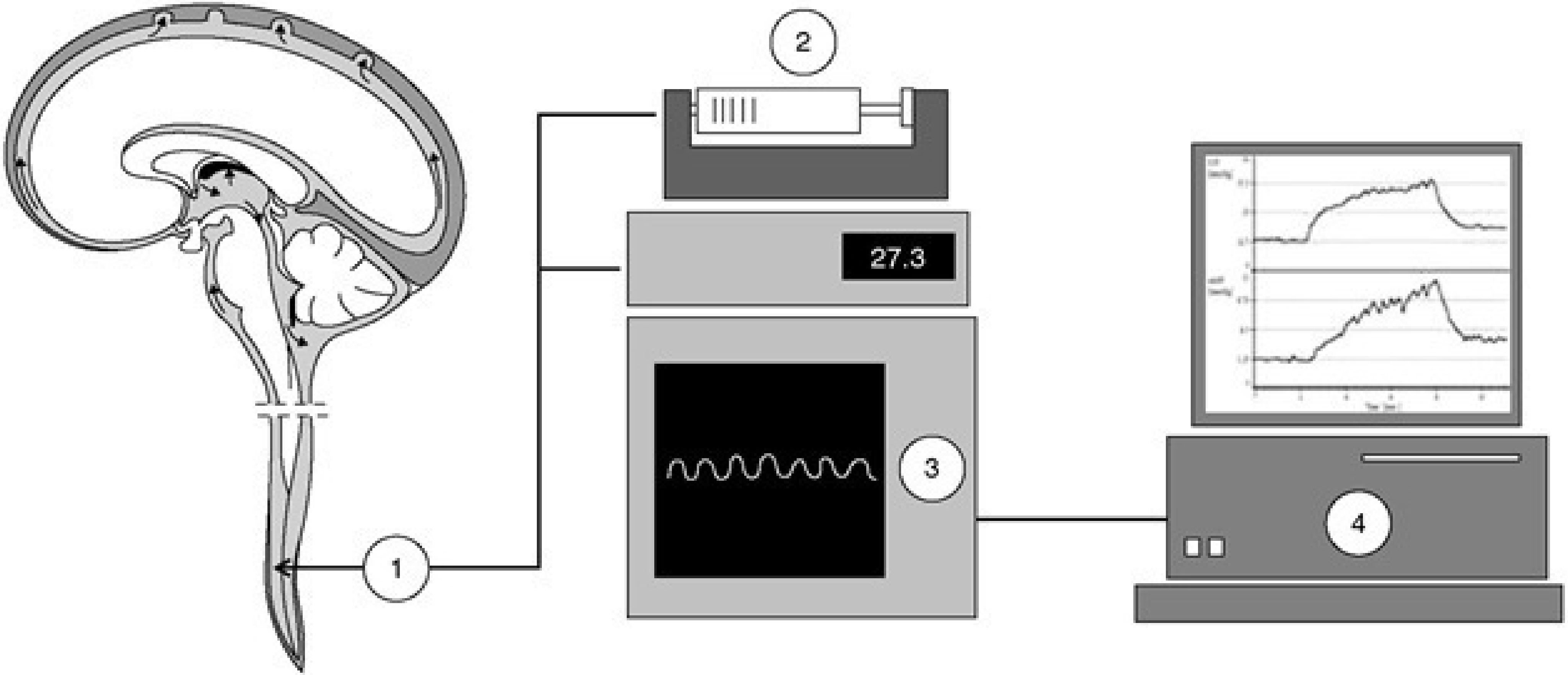
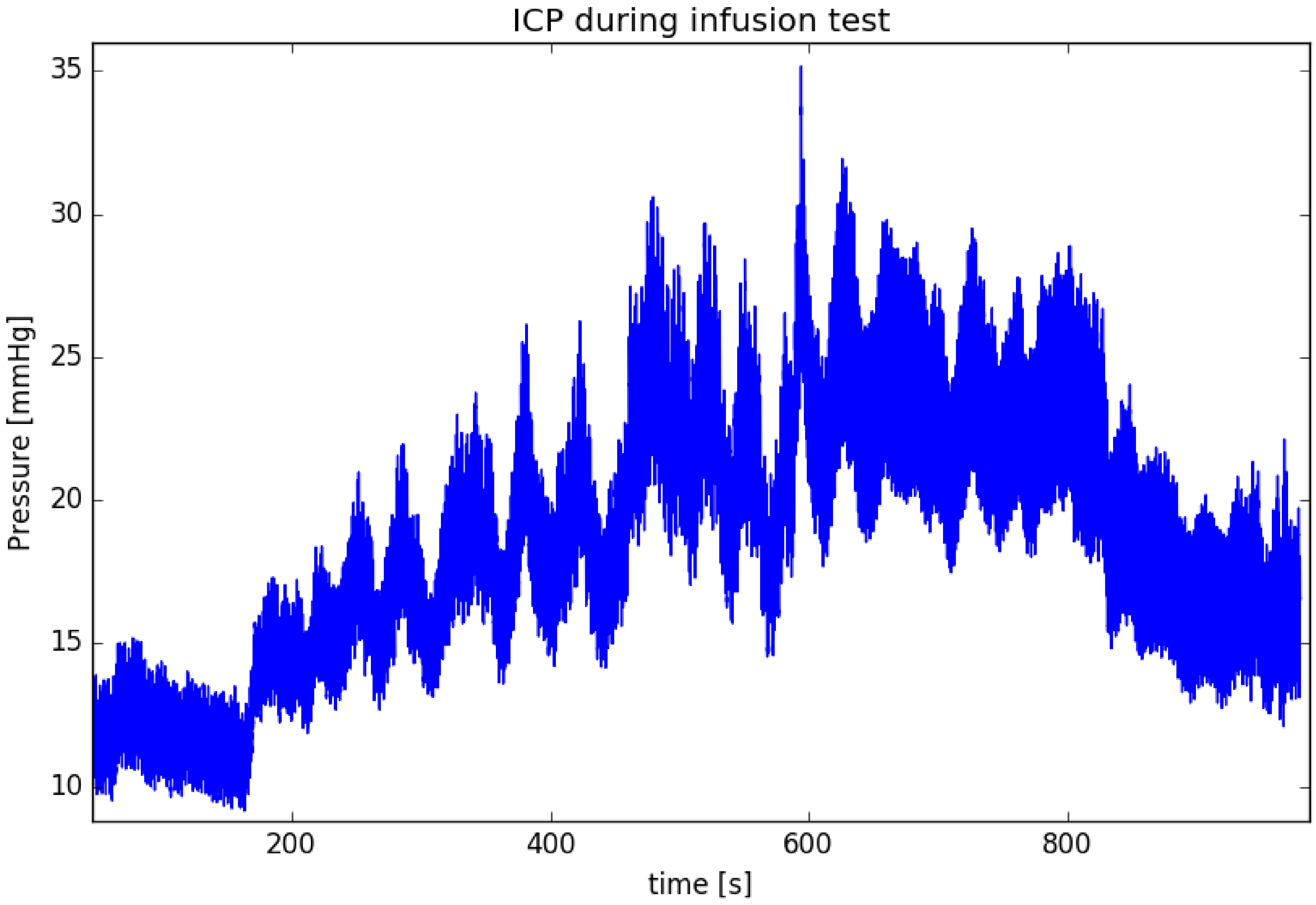
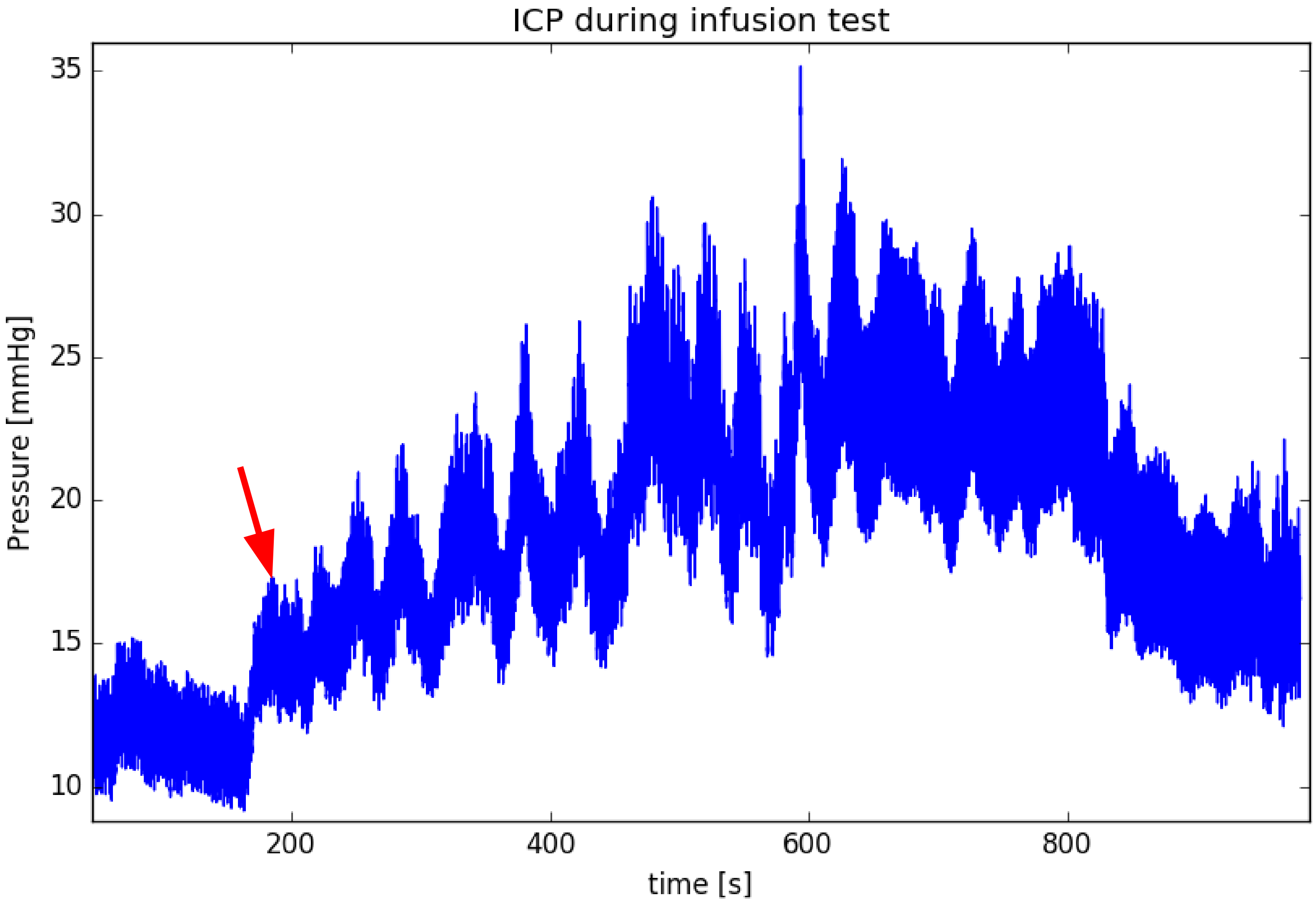
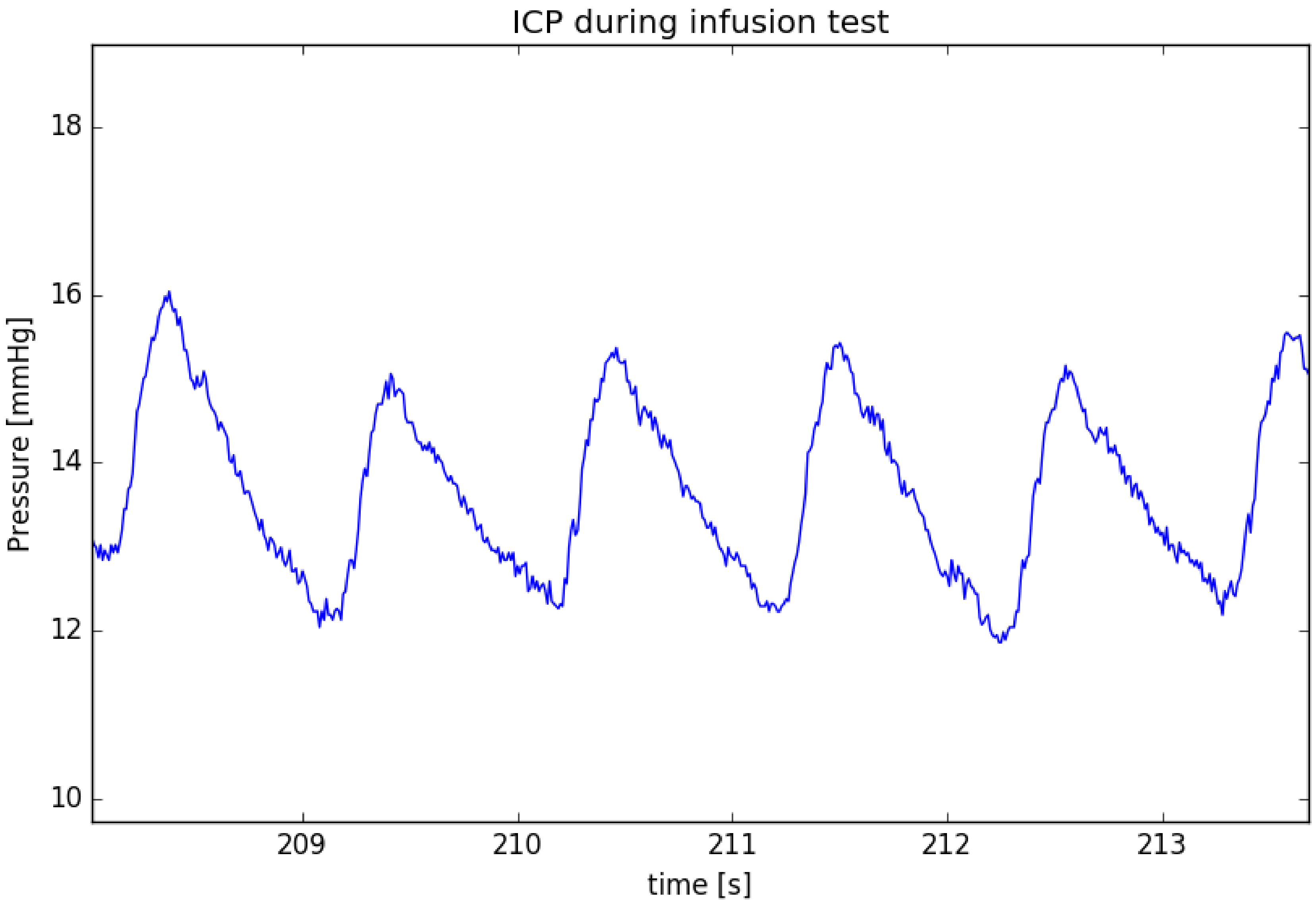
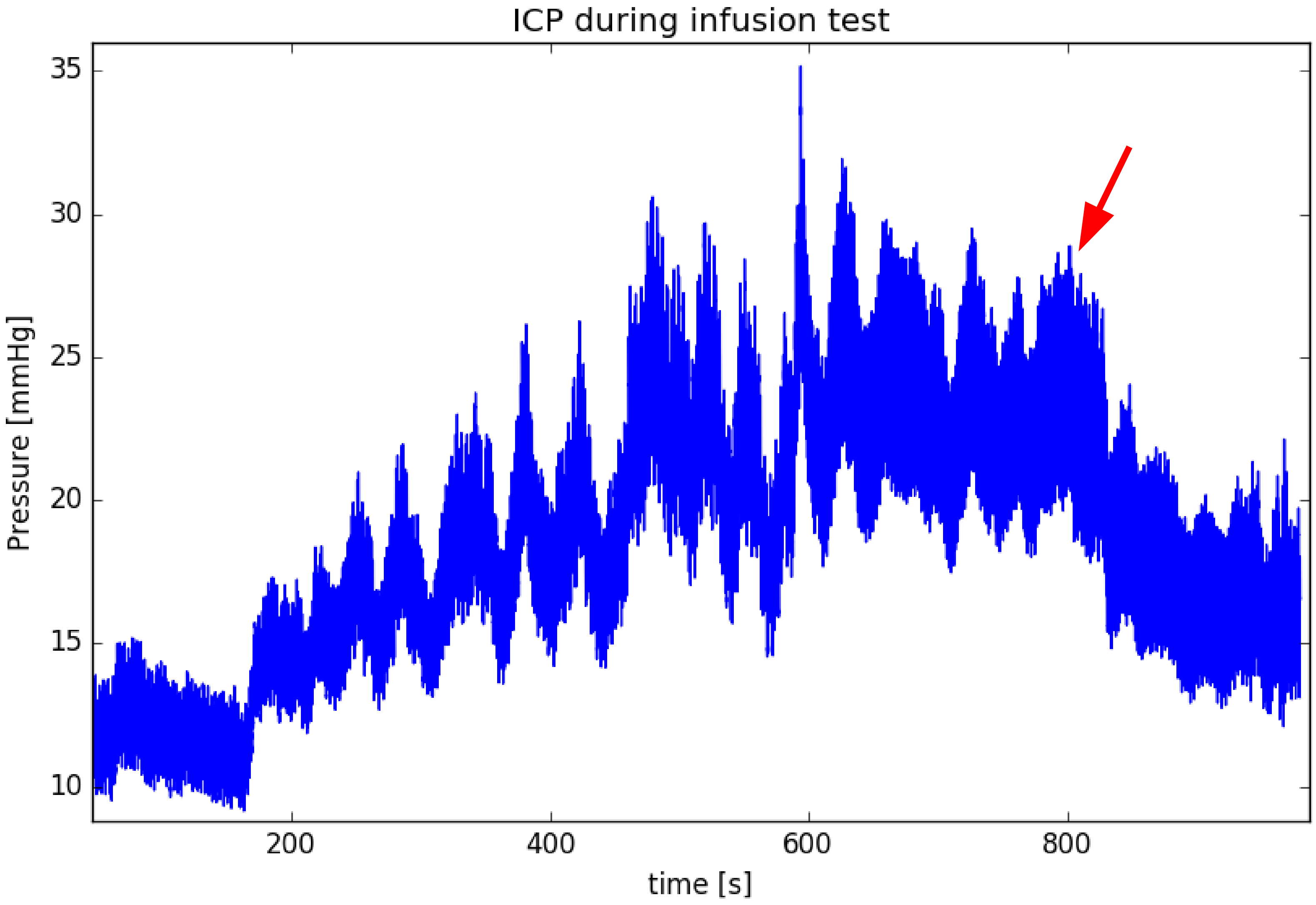
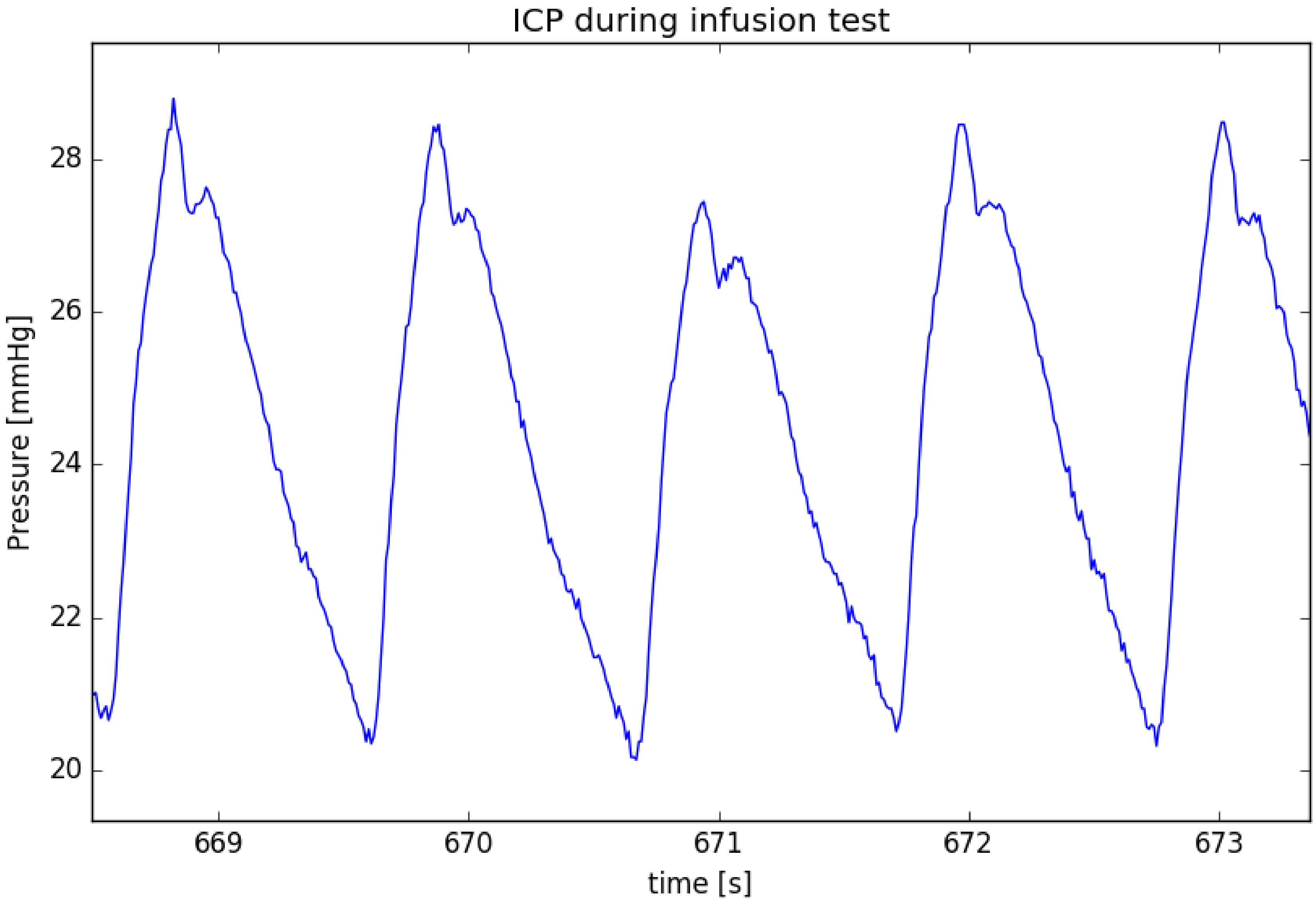

2
27.3
3
1
4

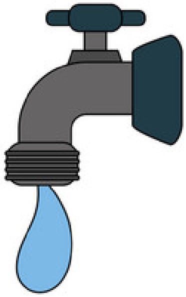

ICP during infusion test
Pressure [mmHg]
time [s]
10
15
20
25
30
35
200
400
600
800

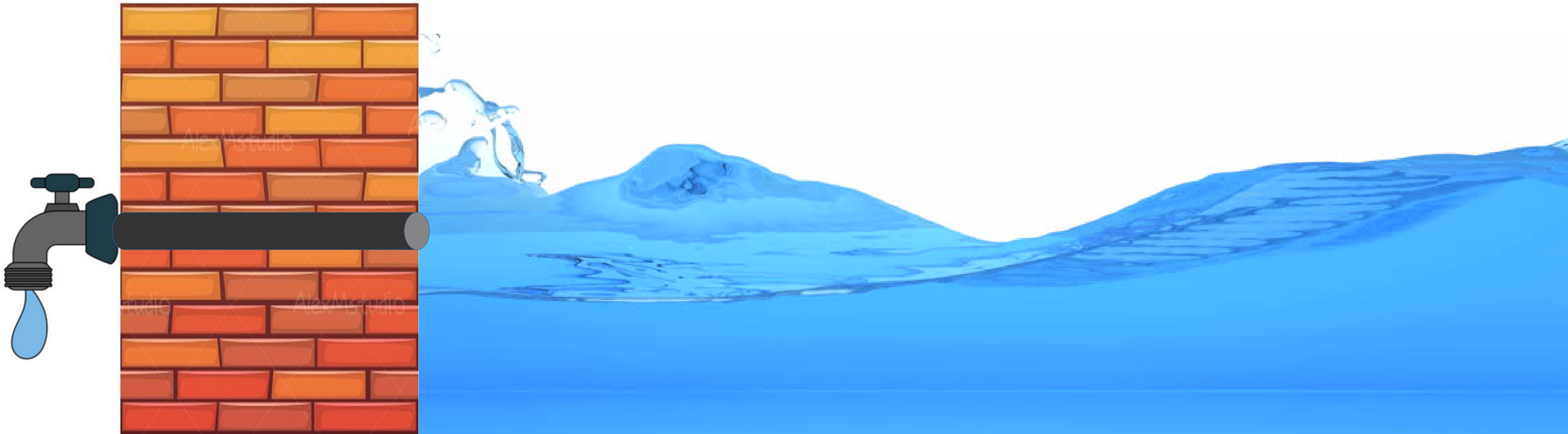

ICP during infusion test
Pressure [mmHg]
time [s]
10
15
20
25
30
35
200
400
600
800

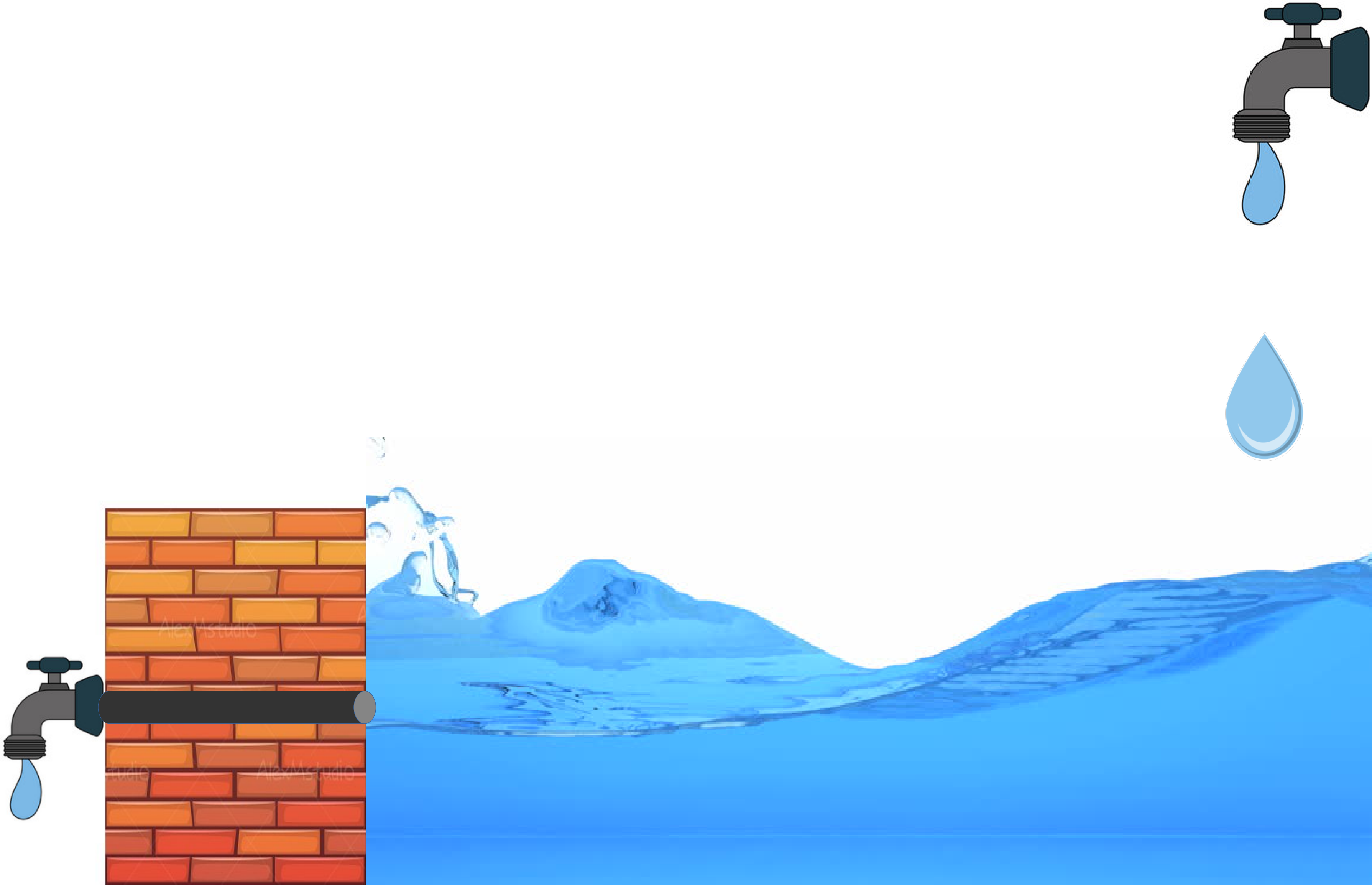

ICP during infusion test
Pressure [mmHg]
18
16
14
12
10
209
210
211
212
213
time [s]

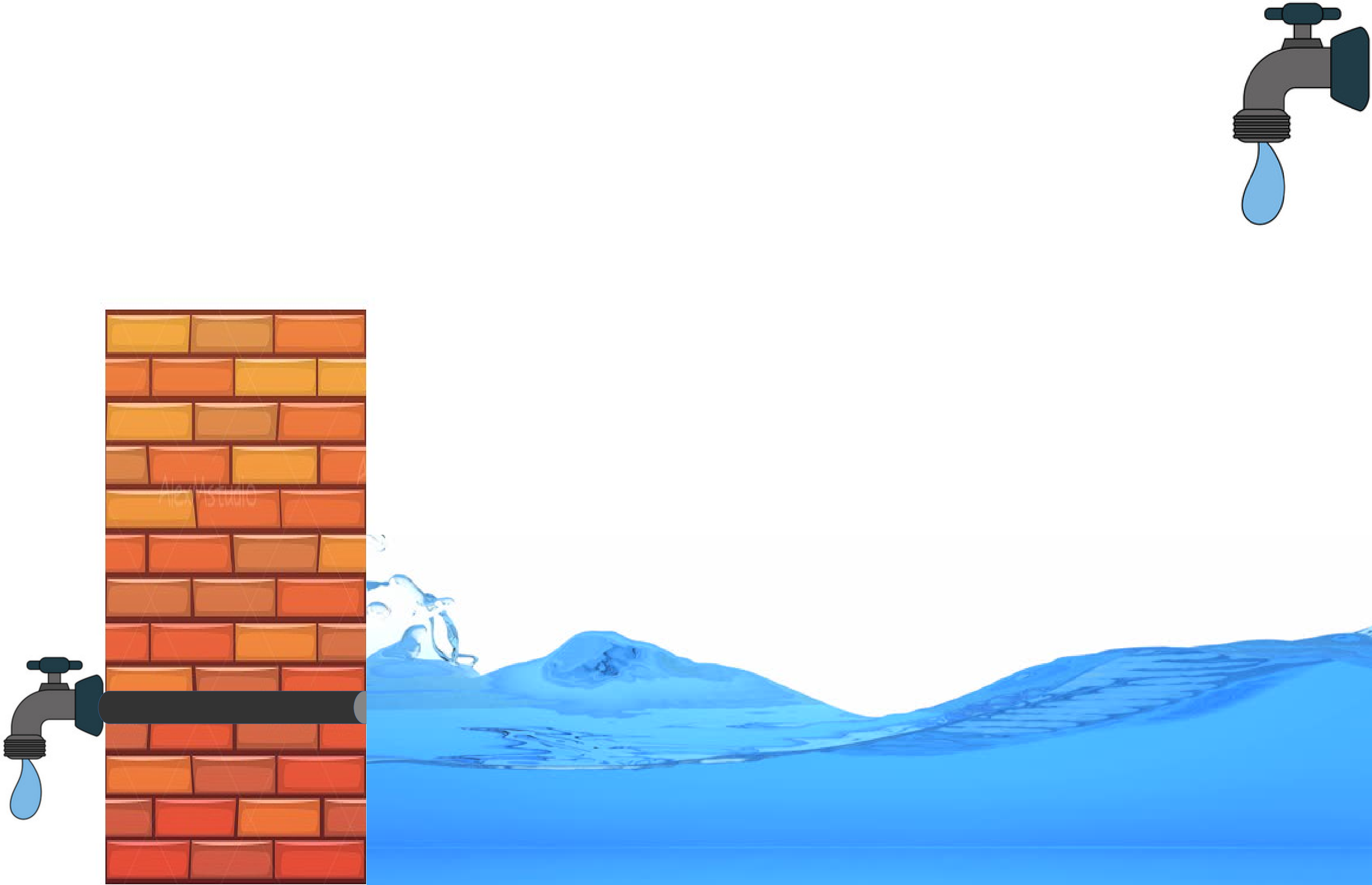

ICP during infusion test
Pressure [mmHg]
time [s]
10
15
20
25
30
35
200
400
600
800

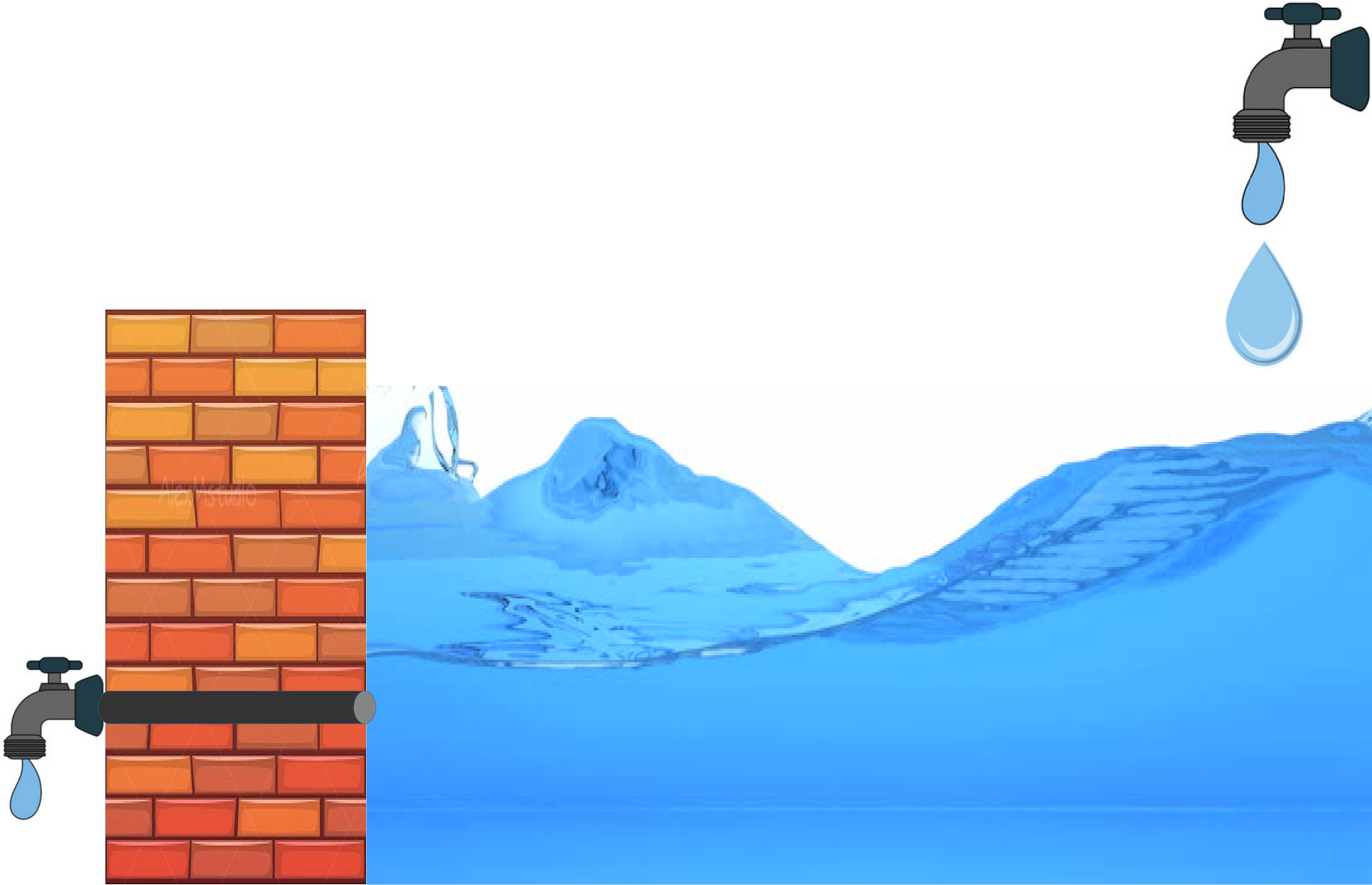

ICP during infusion test
Pressure [mmHg]
20
22
24
26
28
time [s]
669
670
671
672
673

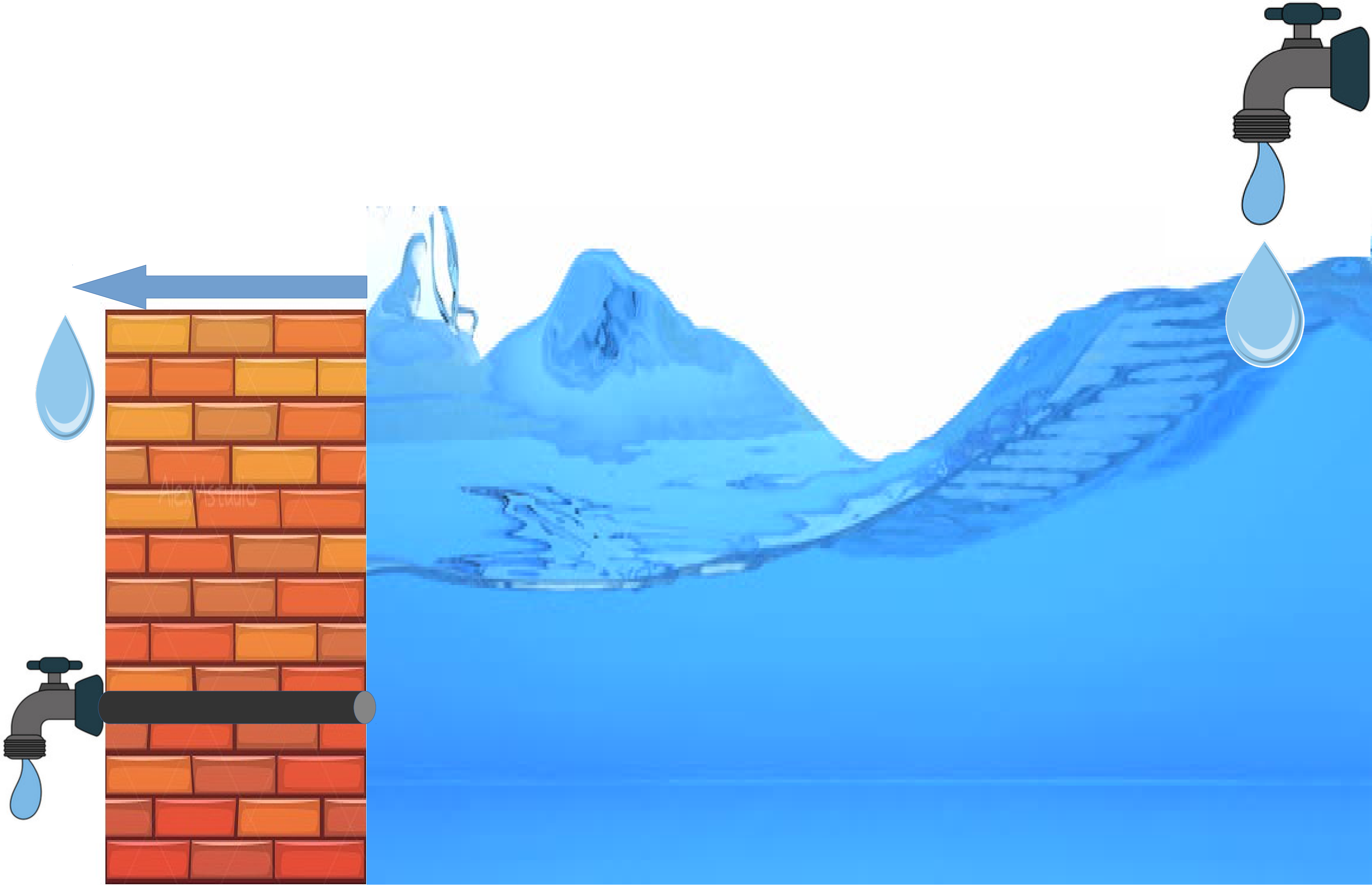


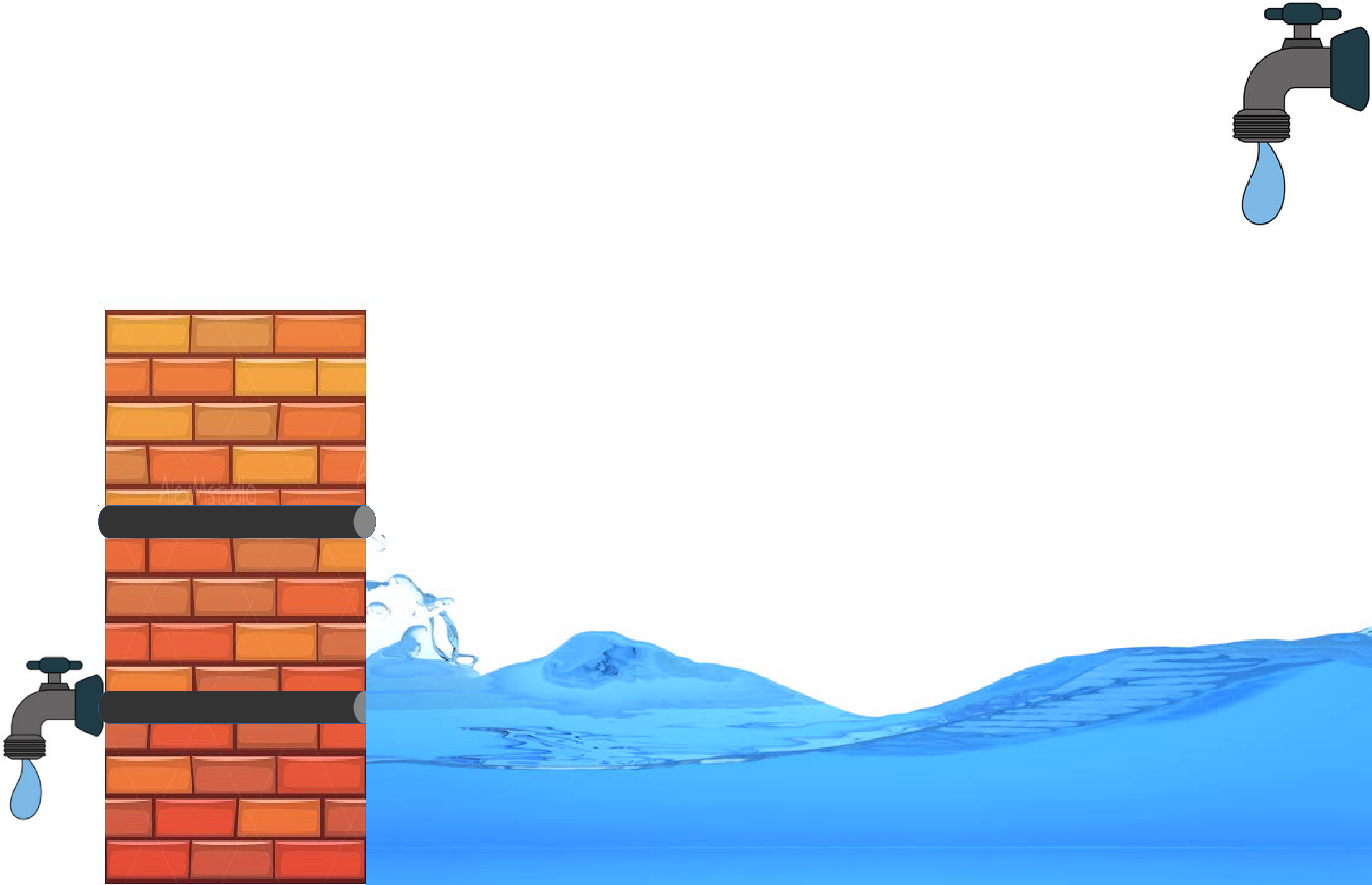


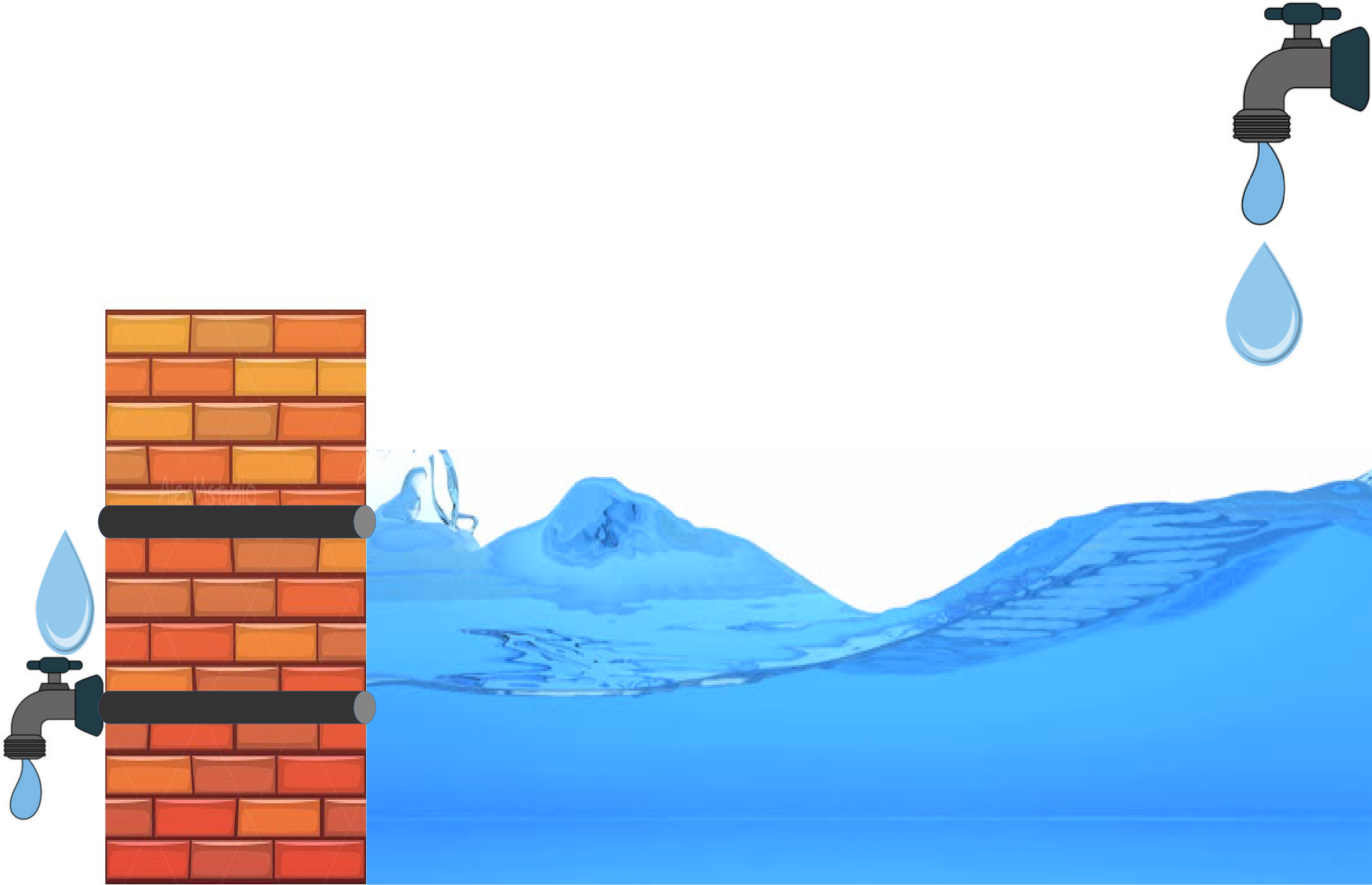




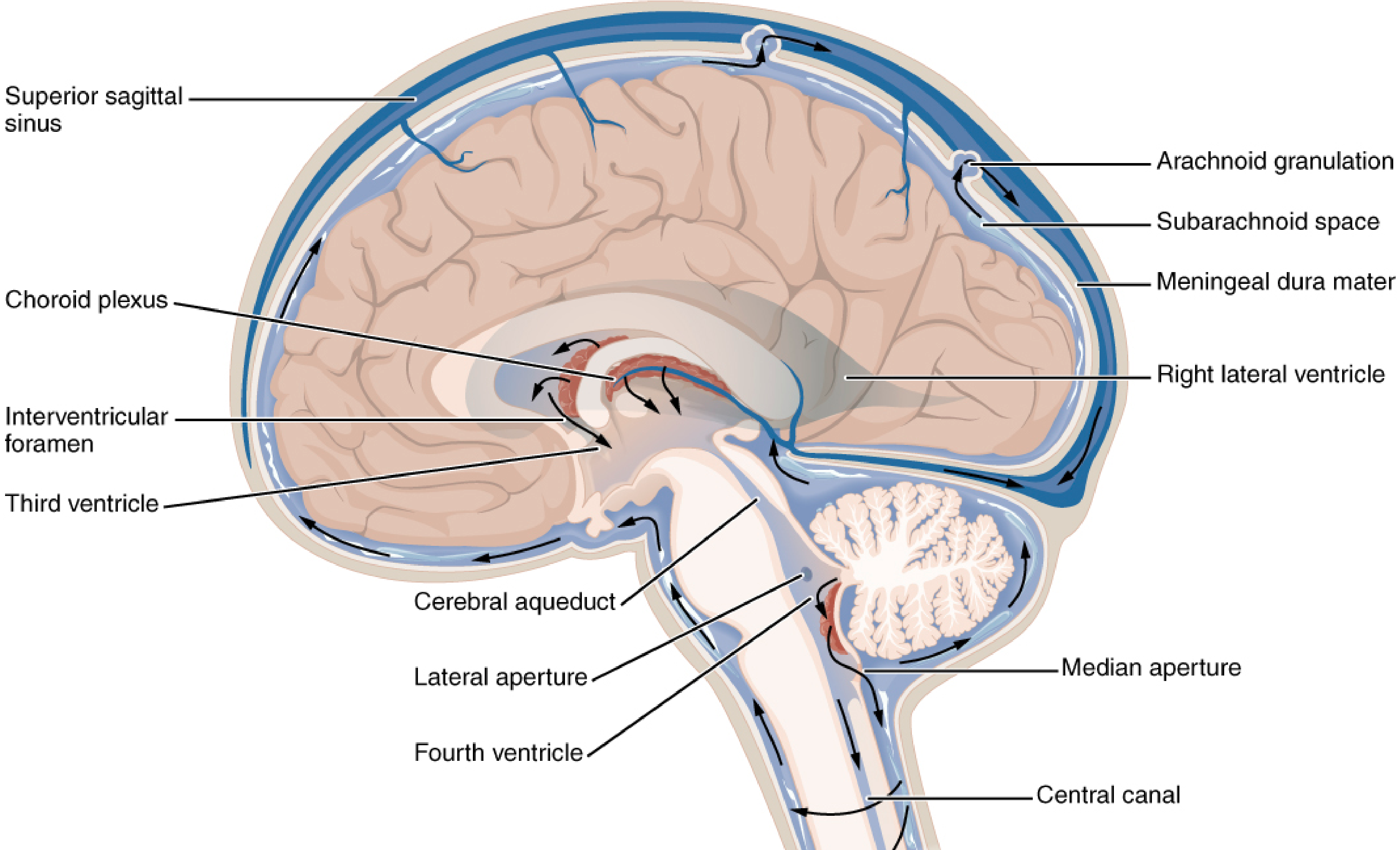




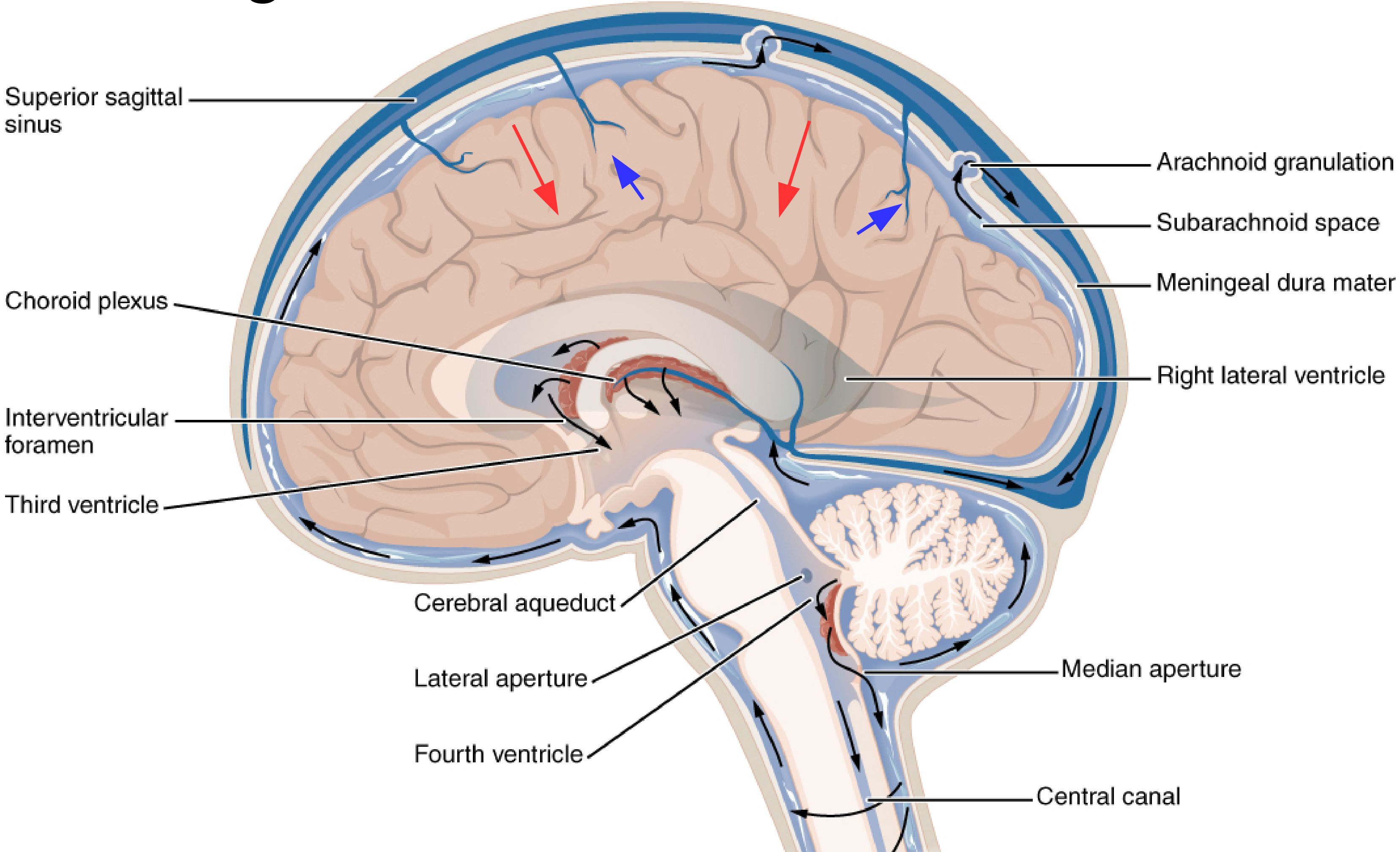




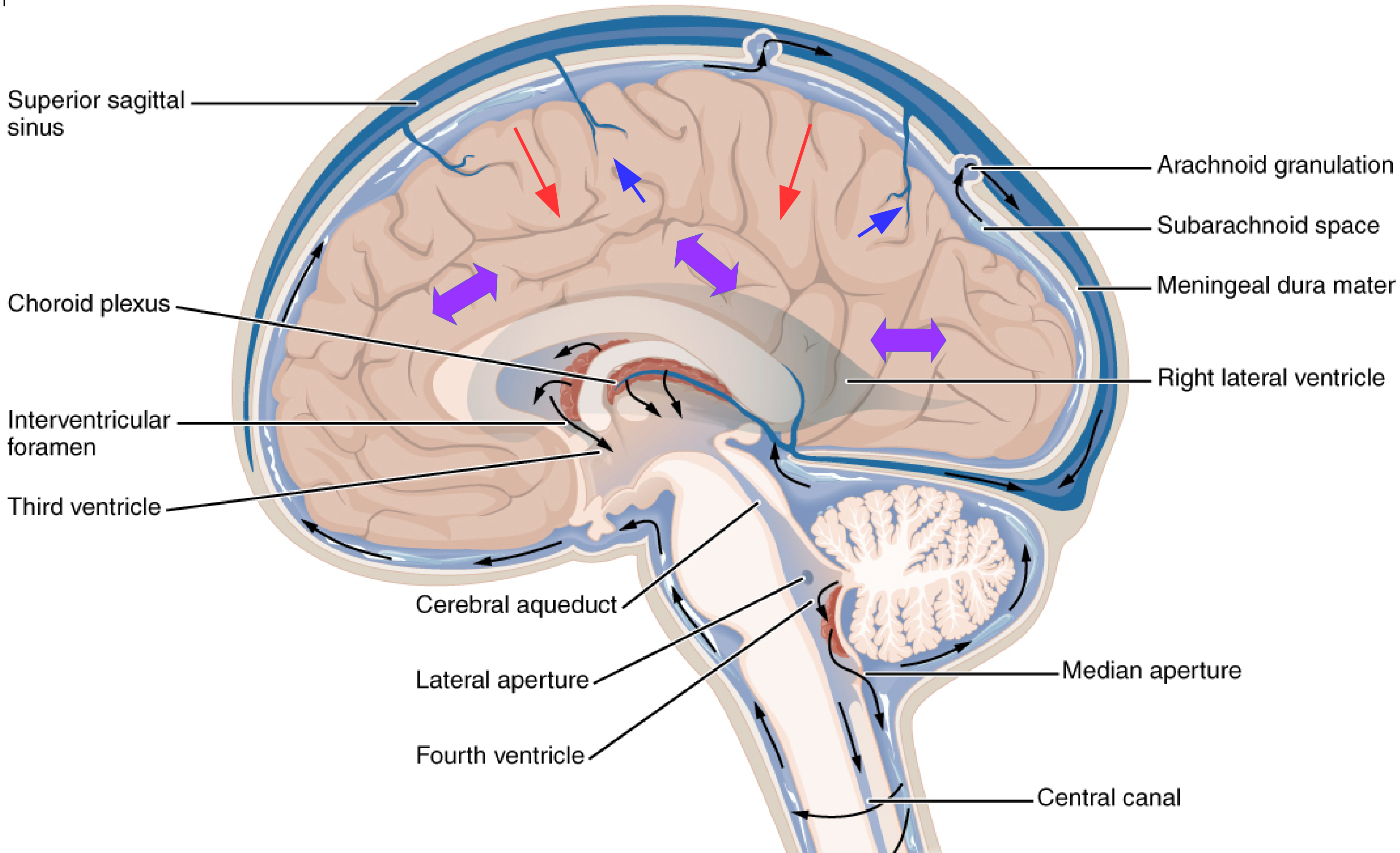
# In the **classical** hypothesis, CSF flows from the choroid plexus to the arachnoid granulations



# In the **glymphatic** theory, CSF enters the brain along penetrating arteries



# In the **microvessel** theory, ISF/CSF is filtrated through capillaries



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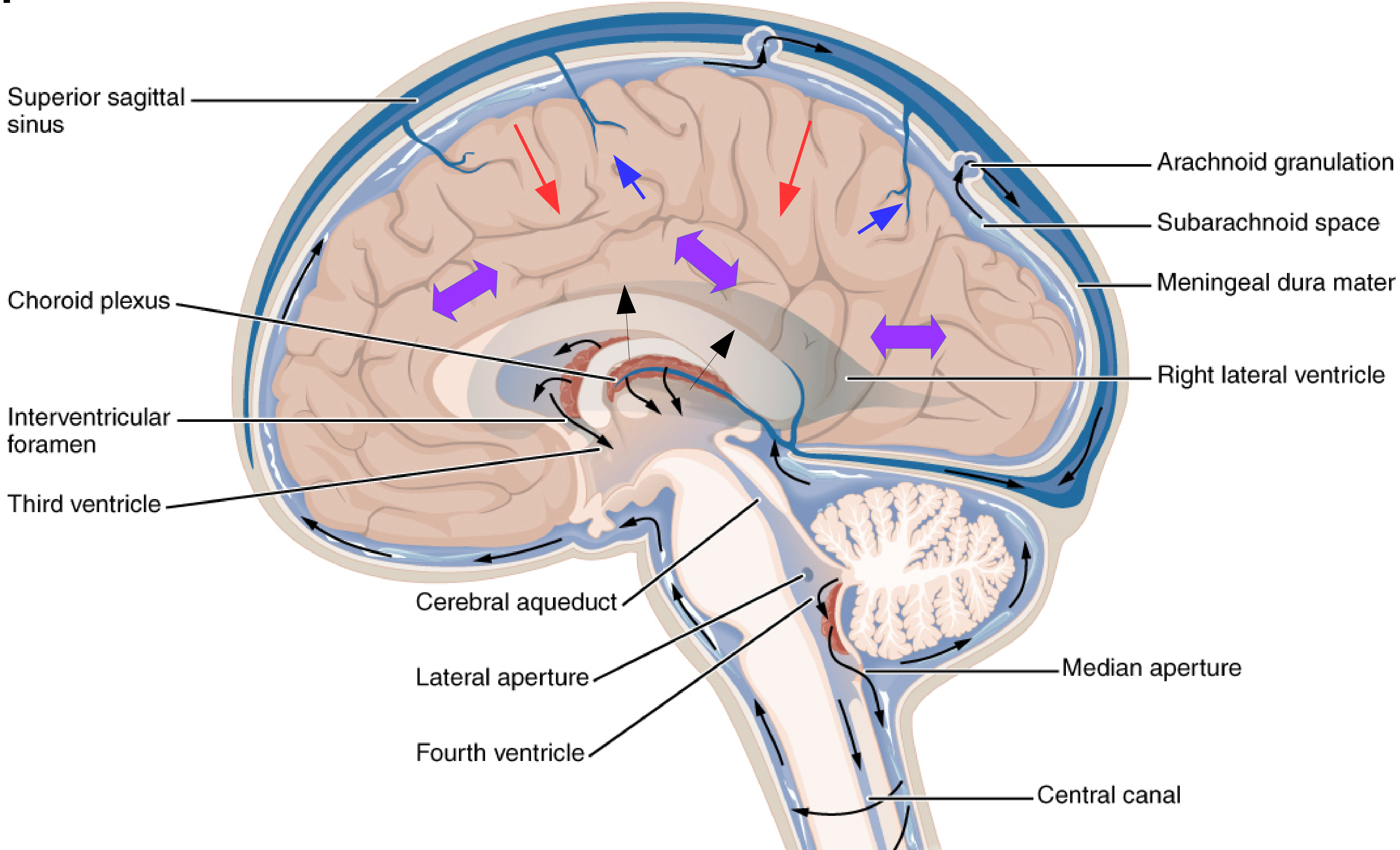
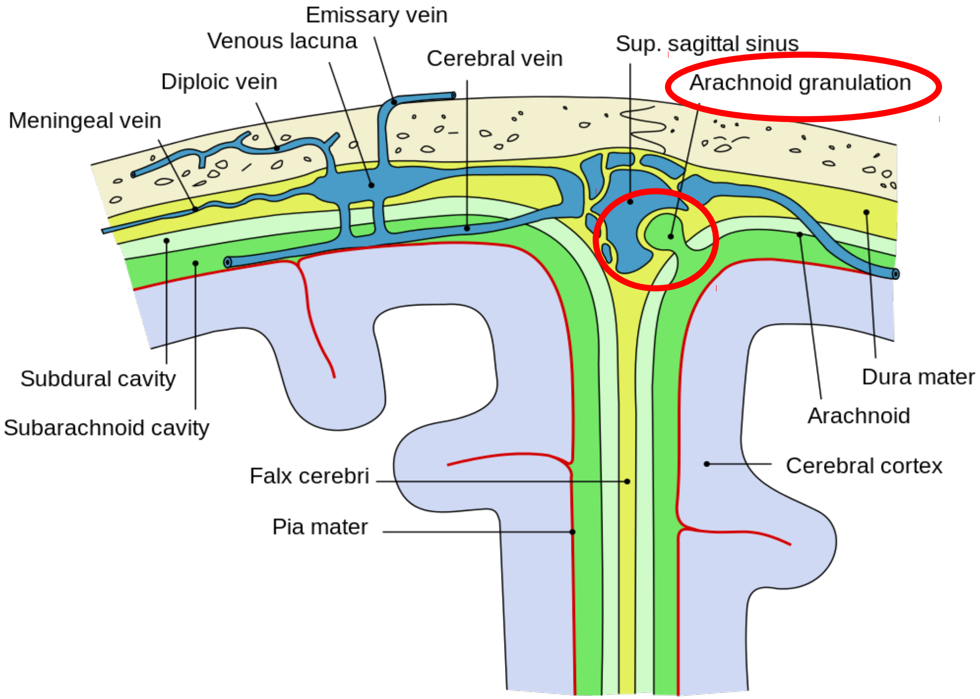
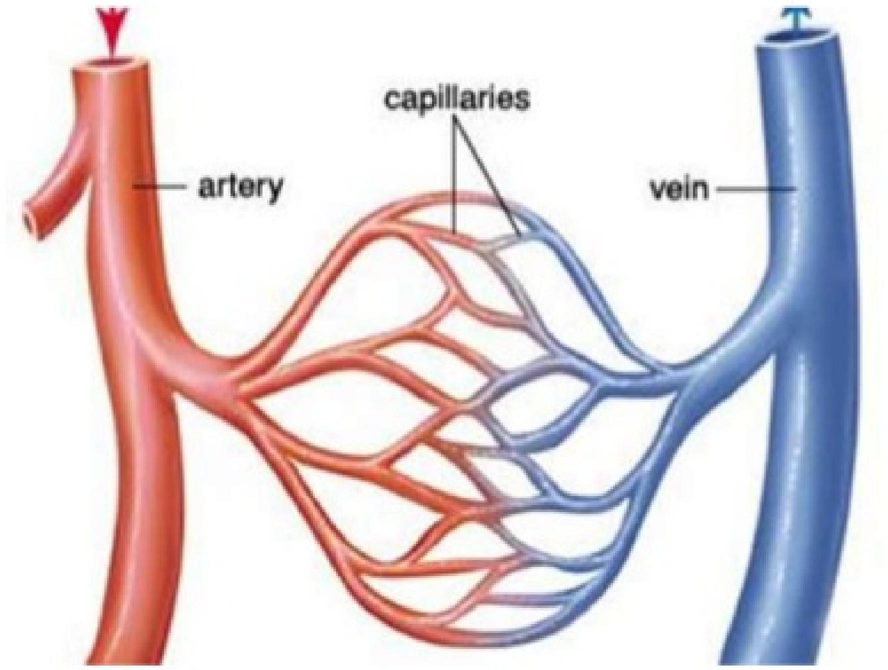


# The wall permeability of the BBB may be low, but CNS capillaries make up a massive surface area

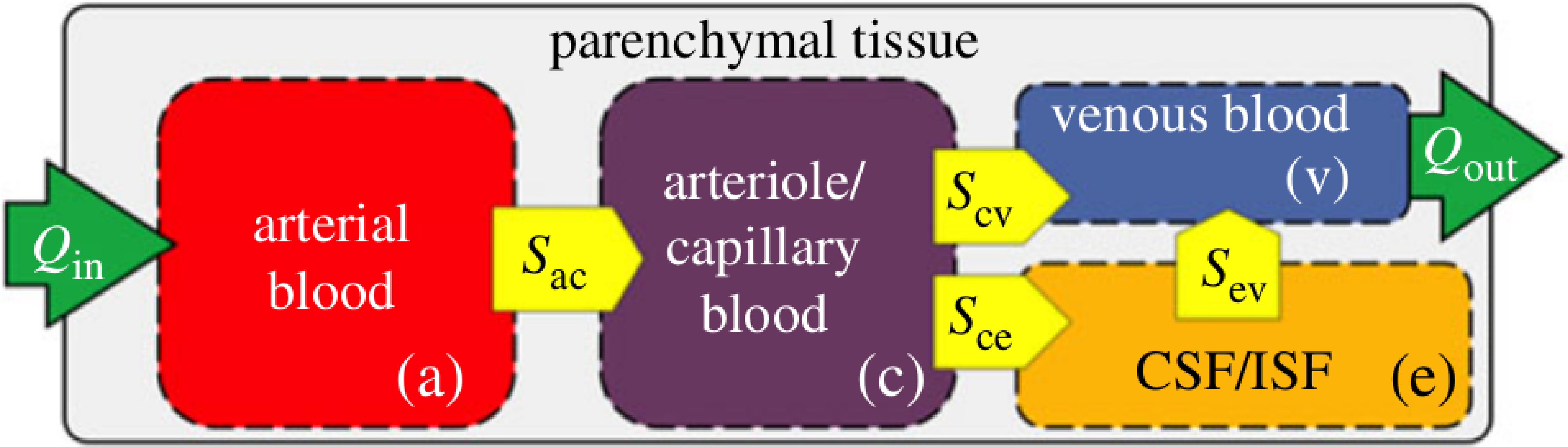



$A_{AG} \approx 10^{-4}\ m^2$
(Grzybowski et al. 2006)

$A_{cap} \approx 10\ m^2$
(Uhlirova et al. 2006)

# Our model is based on Multiple Poro-Elastic Theory (MPET) and Darcy's law




$$\mathbf{v} = -K\nabla p$$

Guo et al. 2017

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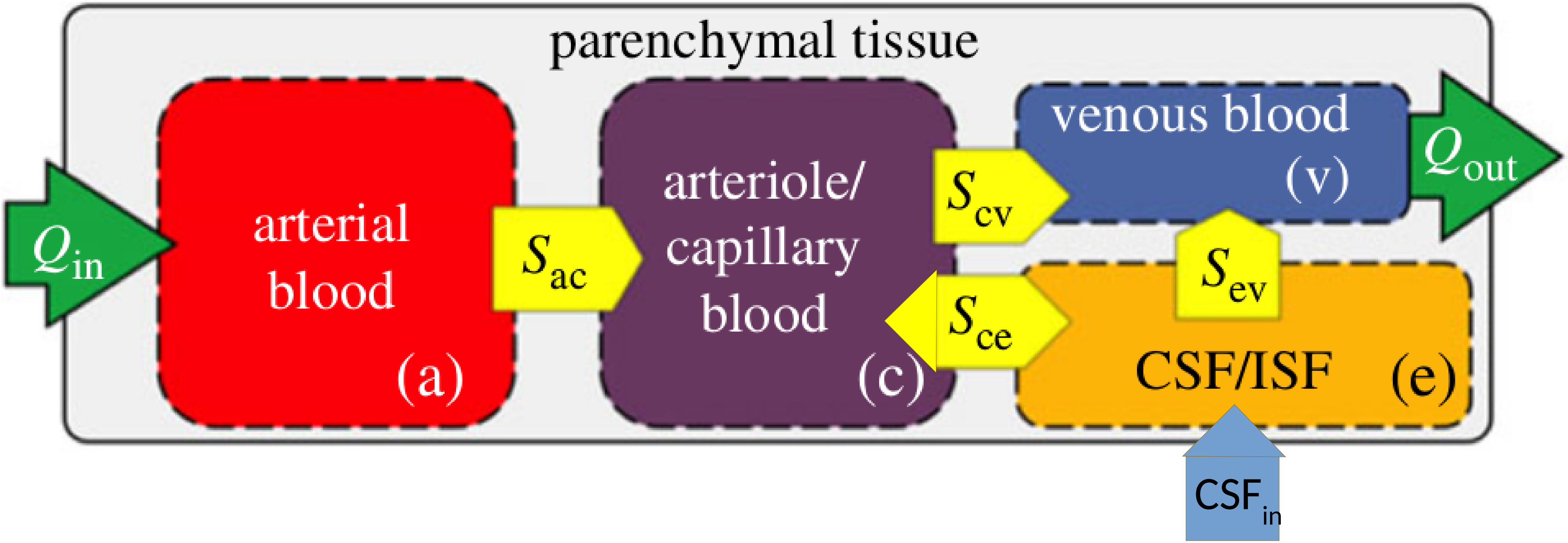


$$\mathbf{v} = -K\nabla p$$

Guo et al. 2017

# The steady-state pressure equations are independent of tissue displacement

$$-K_a \nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0 \tag{1}$$

$$-K_c \nabla^2 p_c + \gamma_{ac}(p_c - p_a) + \gamma_{ic}(p_c - p_i) = 0 \tag{2}$$

$$-K_v \nabla^2 p_v + \gamma_{vc}(p_v - p_c) = 0 \tag{3}$$

$$-K_i \nabla^2 p_i + \gamma_{ic}(p_i - p_c) = 0 \tag{4}$$

$$\nabla \cdot \sigma(u) - \sum \alpha_x \nabla p_x = 0 \tag{5}$$

$$-K_a \nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0 \quad (1)$$

$$-K_c \nabla^2 p_c + \gamma_{ac}(p_c - p_a) + \gamma_{ic}(p_c - p_i) = 0 \quad (2)$$

$$-K_v \nabla^2 p_v + \gamma_{vc}(p_v - p_c) = 0 \quad (3)$$

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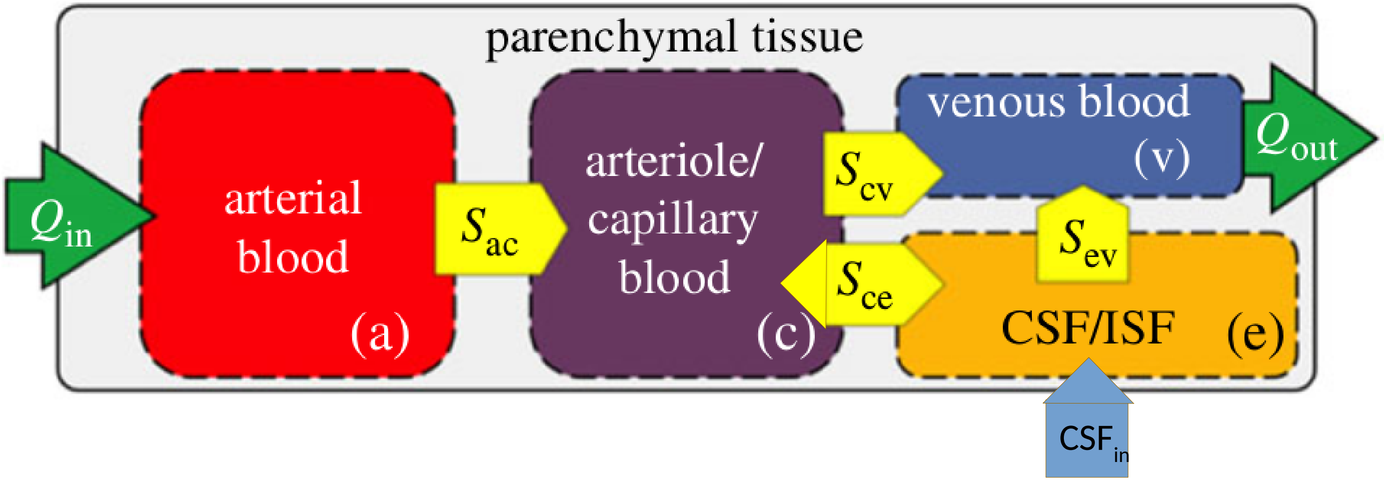


$$\mathbf{v} = -K \nabla p$$

$$-K_a \nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0 \quad (1)$$

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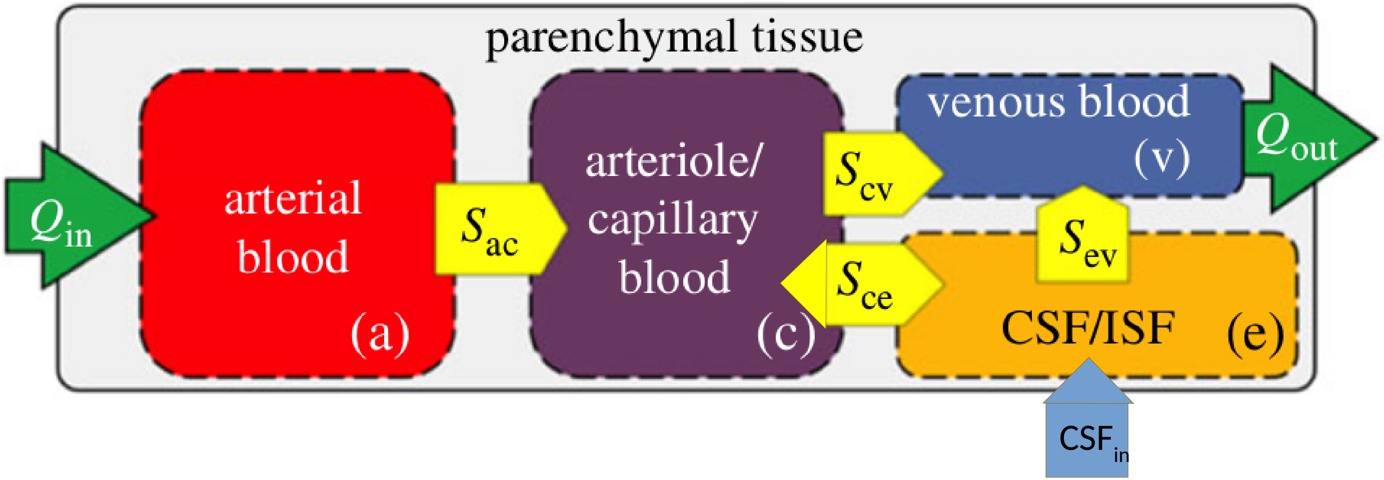
$$-K_i \nabla^2 p_i + \gamma_{ic}(p_i - p_c) = 0 \quad (4)$$

~ 750 mL/min




$$\mathbf{v} = -K \nabla p$$

~ 1 mL/min

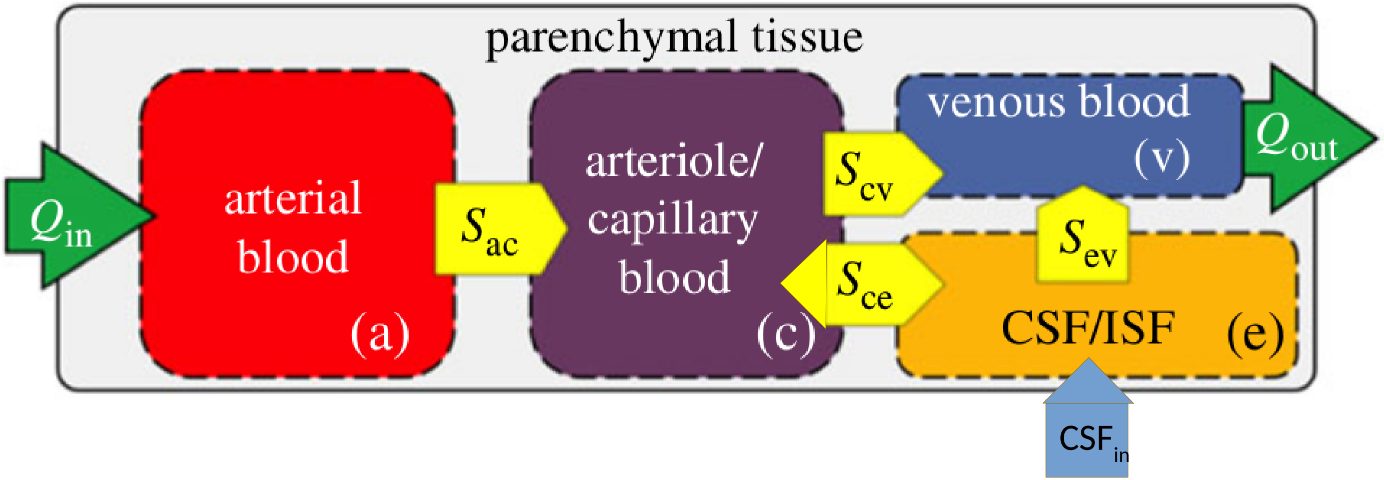
$$-K_a\nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0 \quad (1)$$

$$-K_c\nabla^2 p_c + \gamma_{ac}(p_c - p_a) + \gamma_{ic}(p_c - p_i) = 0 \quad (2)$$

$$-K_v\nabla^2 p_v + \gamma_{vc}(p_v - p_c) = 0 \quad (3)$$

$$-K_i\nabla^2 p_i + \gamma_{ic}(p_i - p_c) = 0 \quad (4)$$

~ 750 mL/min




$$\mathbf{v} = -K\nabla p$$

~ 1.0 mL/min + (1.5 mL/min)

# Time dependence is added for the infusion test

$$s_0 \frac{\partial p_a}{\partial t} - K_a \nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0$$

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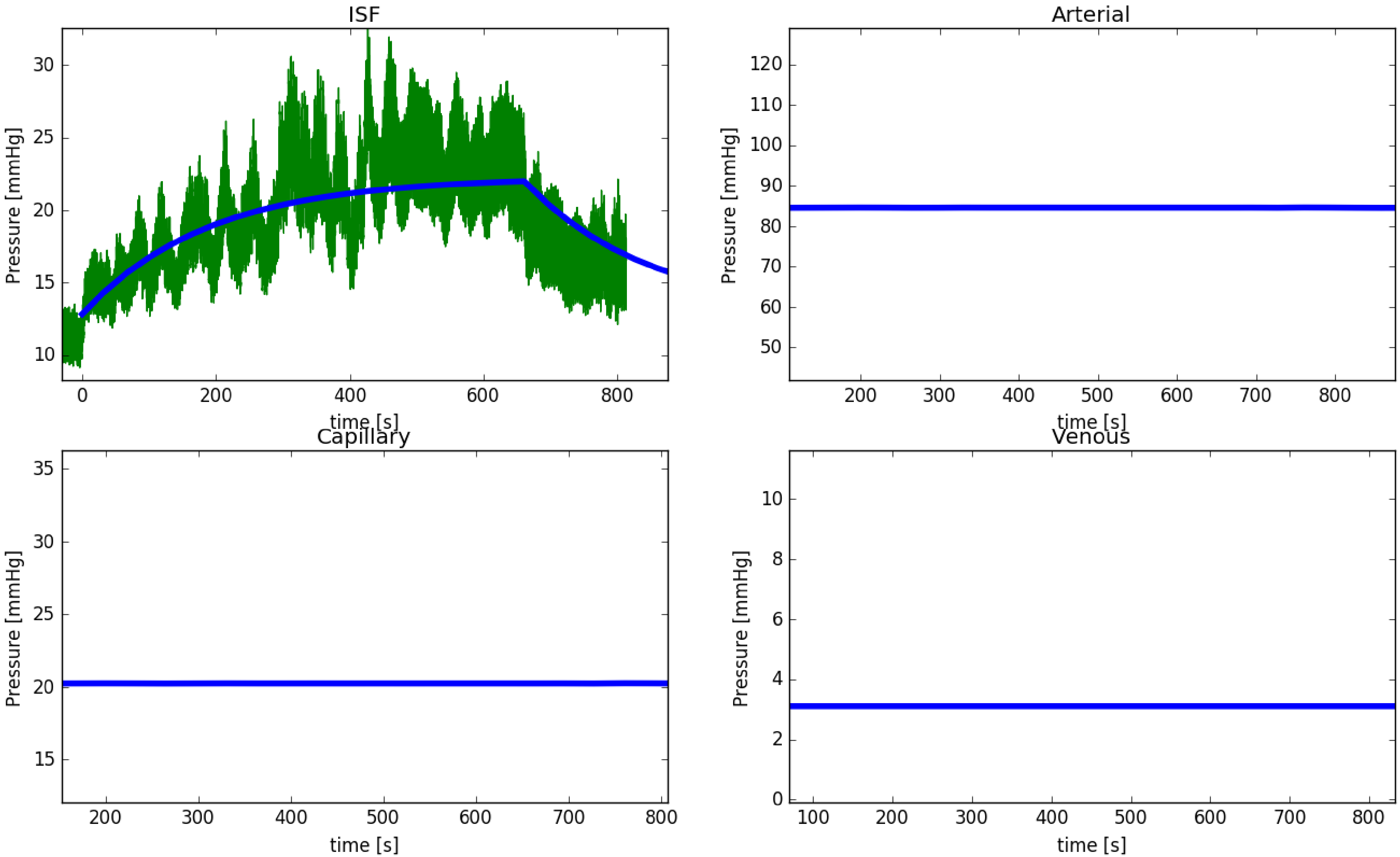
$$s_0 \frac{\partial p_a}{\partial t} - K_a \nabla^2 p_a + \gamma_{ac}(p_a - p_c) = 0$$

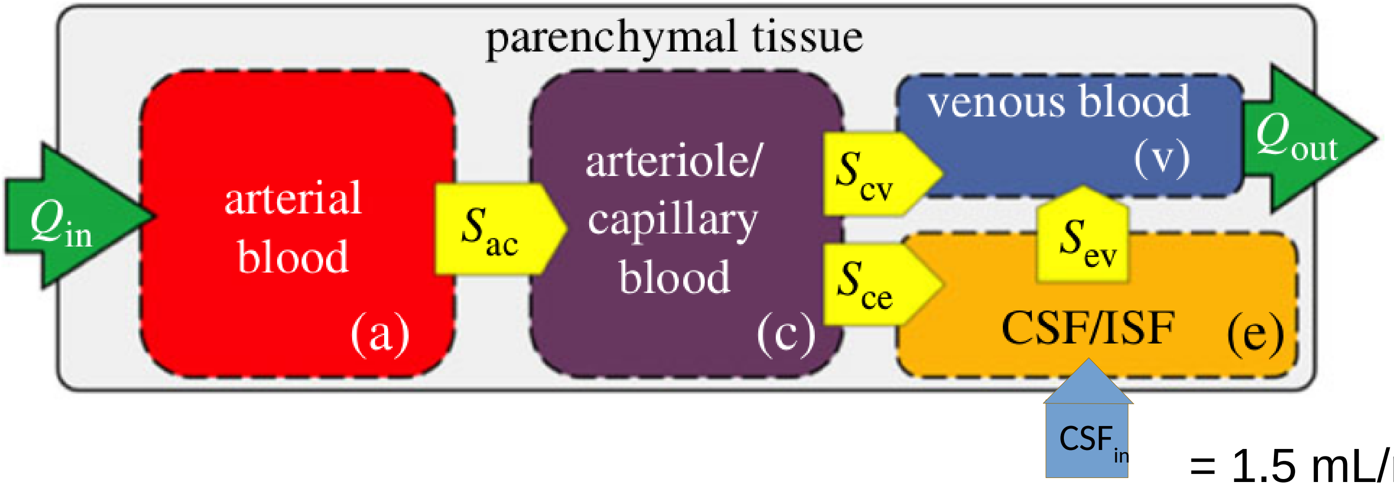


ISF
Arterial
Capillary
Venous
Pressure [mmHg]
time [s]

# Fluid transfer between compartments can be assessed during the infusion test

Baseline values, before infusion

= 750 mL/min




= 1.5 mL/min

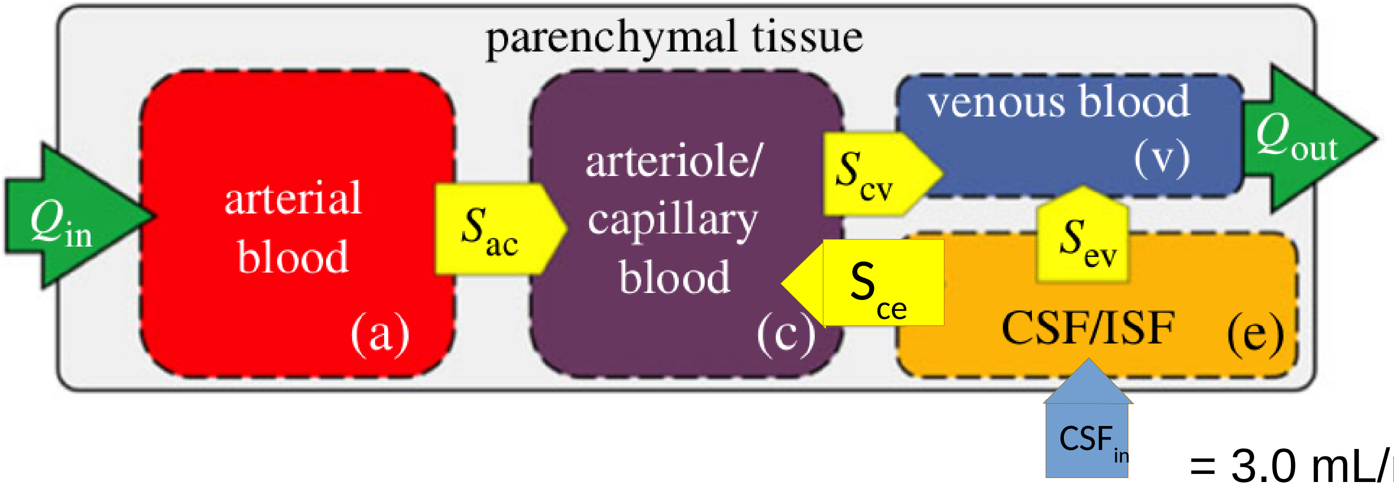
$S_{ce}$ = 0.02 mL/min

$S_{ev}$ = 1.52 mL/min

# Fluid transfer between compartments can be assessed during the infusion test

## Plateau-level during infusion test

= 750 mL/min

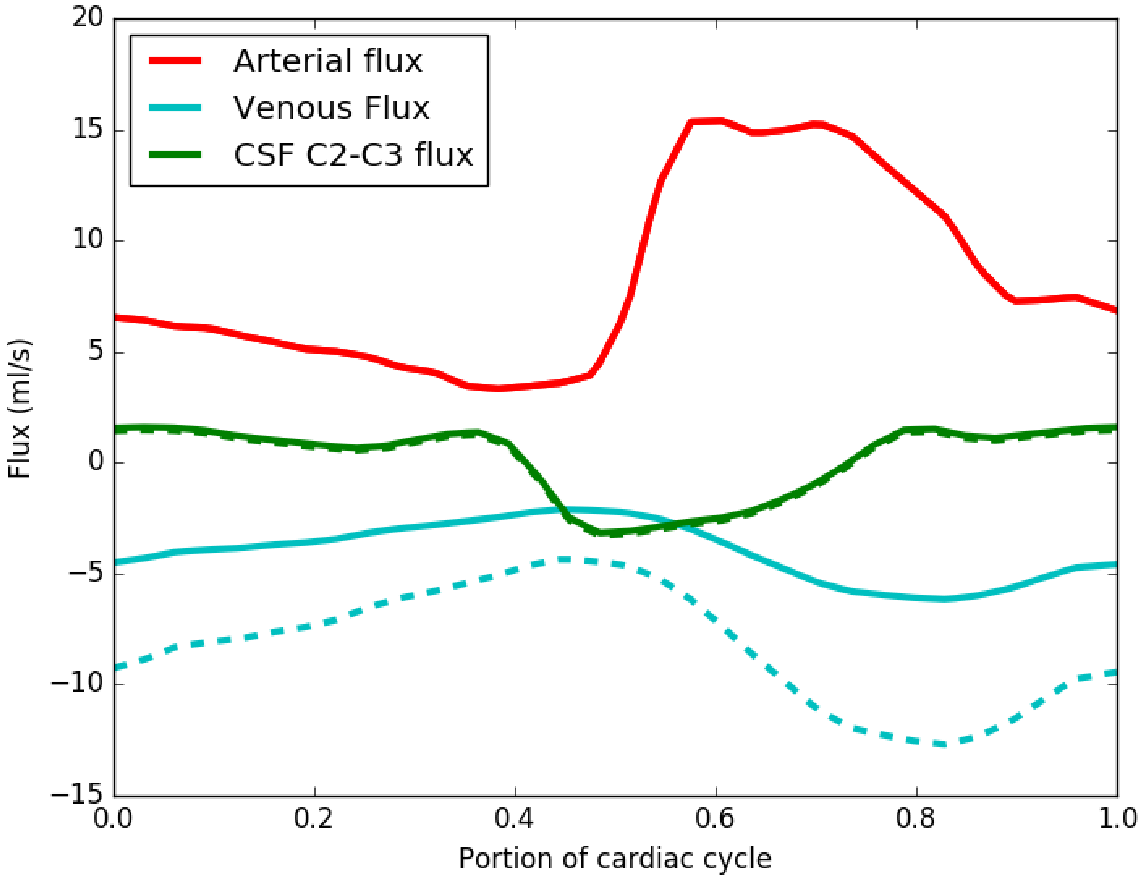


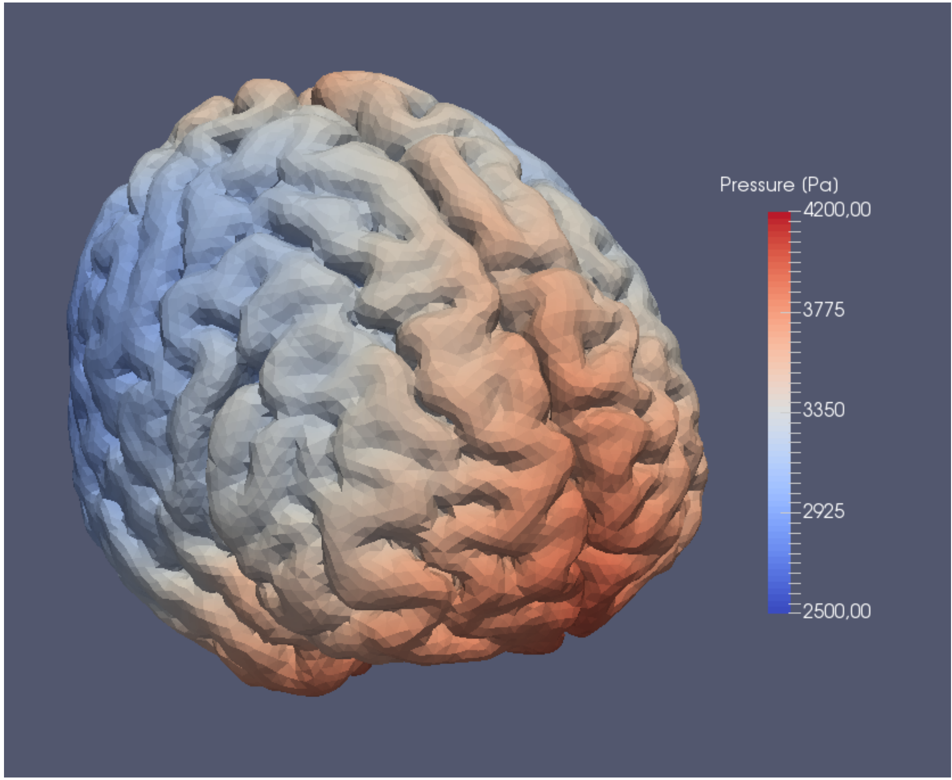

= 3.0 mL/min

$S_{ce}$ = 0.01 mL/min

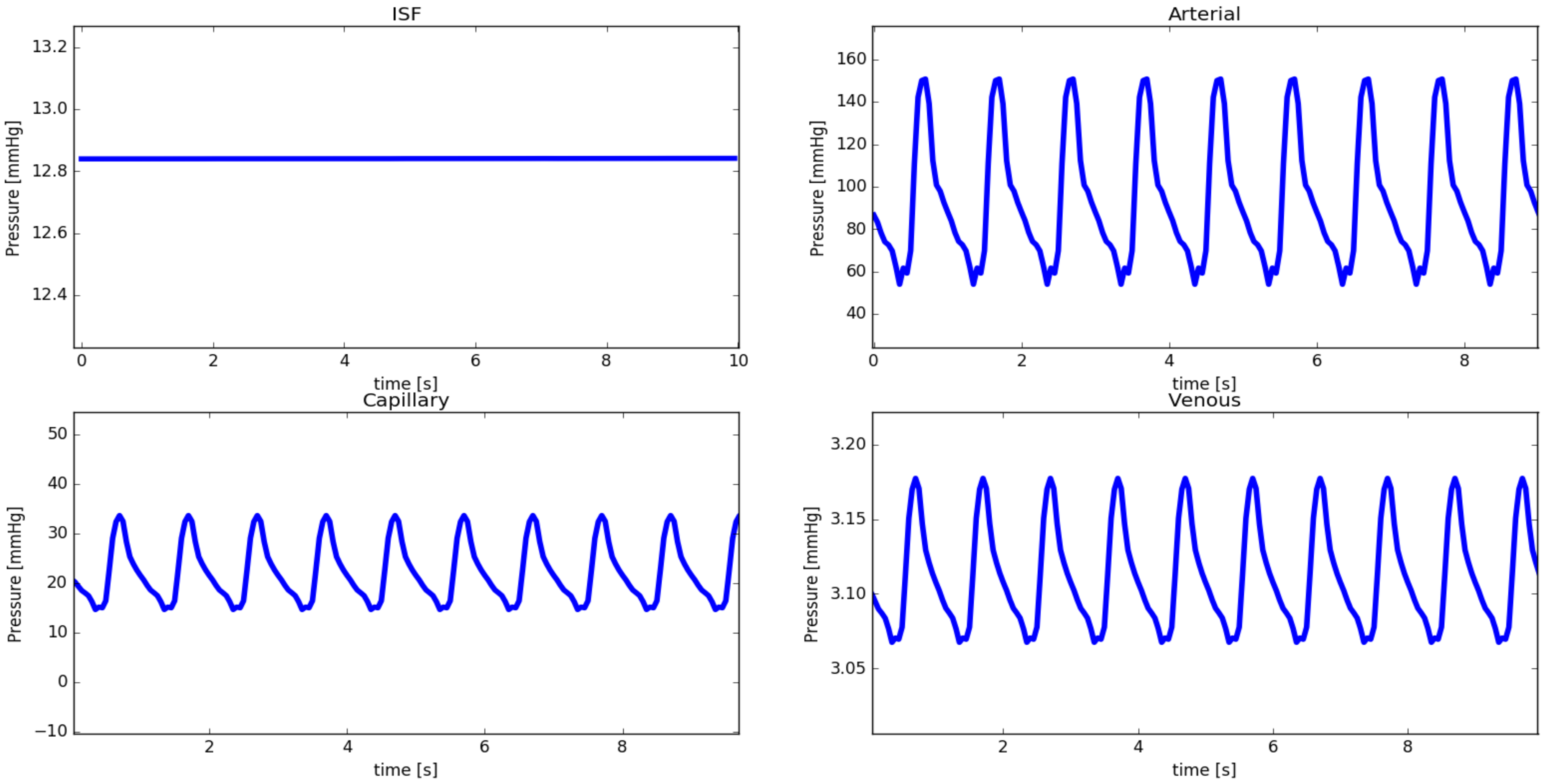
$S_{ev}$ = 2.99 mL/min

# We have access to more than 100 patient-specific meshes and boundary conditions

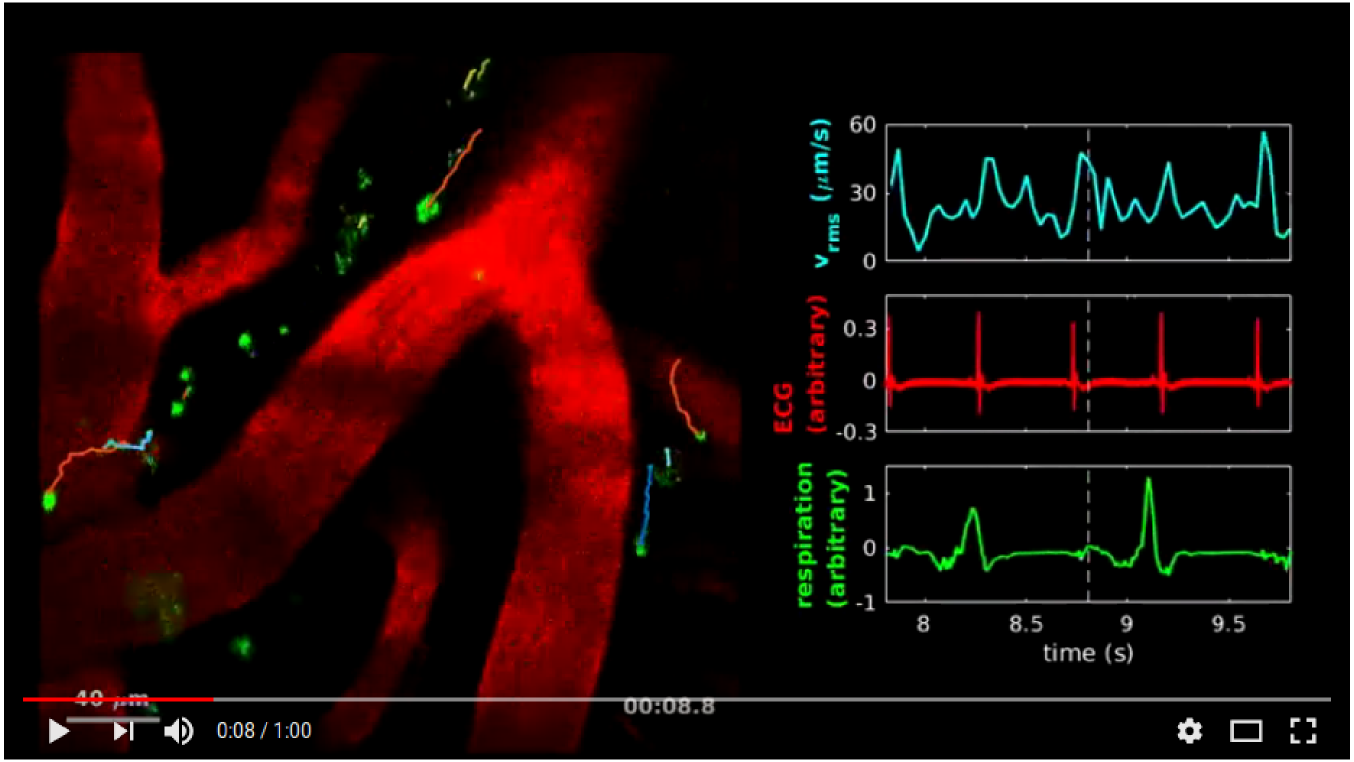


# Pulsatility is not transmitted to the ISF compartment



# Velocities up to 50 µm/sec observed in paravascular spaces



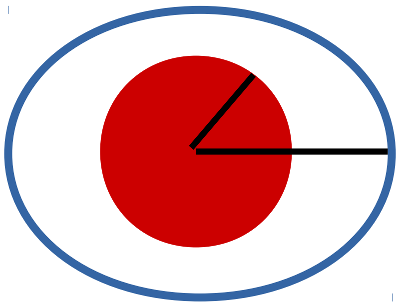

Brain waste removal by fluid flow in the glymphatic system

22 views

0 0 SHARE

By Jack Thomas and Douglas Kelley, University of Rochester

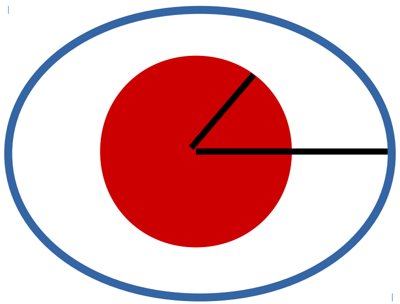
# Assume average net flow of 20 μm/sec in all PVS of a mouse




$$A_{PVS} = \pi\,(R_2^{\,2} - R_1^{\,2}) = 10^{-4}\ \text{cm}^2$$

# Assume average net flow of 20 µm/sec in all PVS of a mouse

$R_1$ = 20 µm

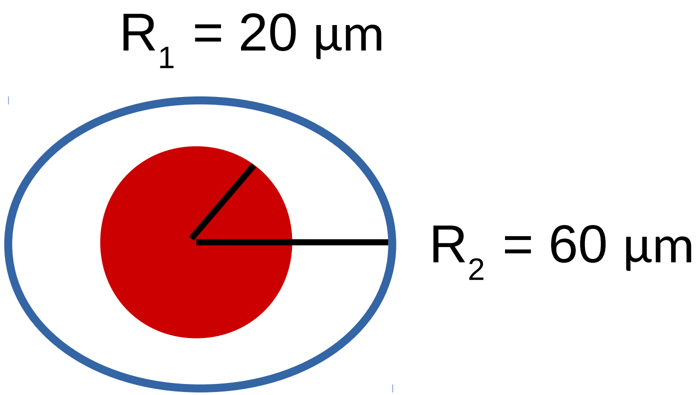


$R_2$ = 60 µm

$$A_{PVS} = \pi\,(R_2^{\,2} - R_1^{\,2}) = 10^{-4}\ \text{cm}^2$$

$$V_{PVS} = 0.002\ \text{cm/sec}$$

# Assume average net flow of 20 μm/sec in all PVS of a mouse

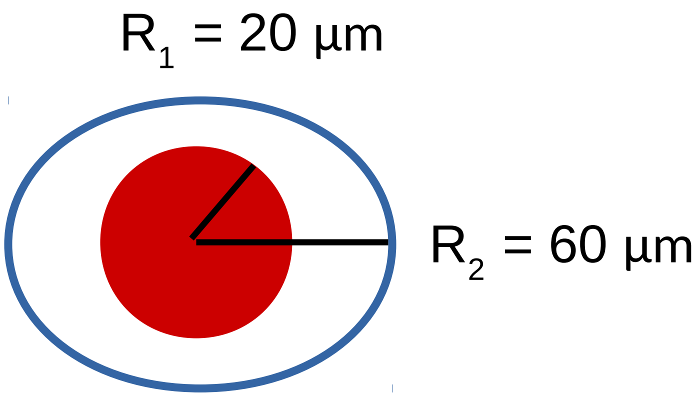



$A_{PVS} = \pi\,(R_2^2 - R_1^2) = 10^{-4}\ cm^2$

$V_{PVS} = 0.002\ cm/sec$

$Q_{PVS} = A_{PVS}V_{PVS} = 2*10^{-7}\ cm^3/sec \approx 10^{-5}\ mL/min = 0.01\ \mu L/min$

# Assume average net flow of 20 µm/sec in all PVS of a mouse

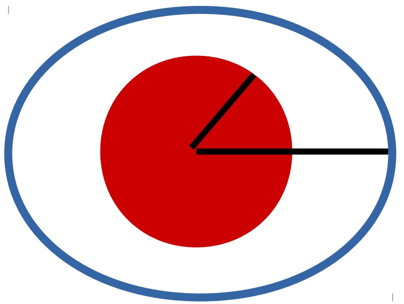



$Q_{PVS}$ = 0.01 µL/min

$CSF_{prod} \approx$ 0.5 µL/min

Oshio et al. (2004)

# Assume average net flow of 20 µm/sec in all PVS of a mouse



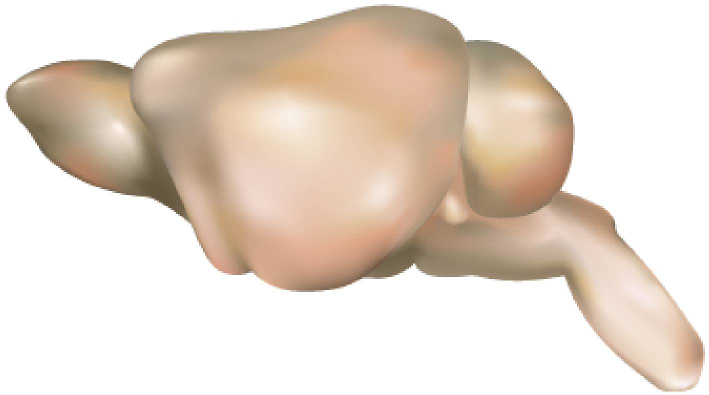

50 PVS drain all produced CSF!

$Q_{PVS}$ = 0.01 µL/min

$CSF_{prod}$ ≈ 0.5 µL/min

# Reported PVS velocities would result in “convective” flow through brain parenchyma

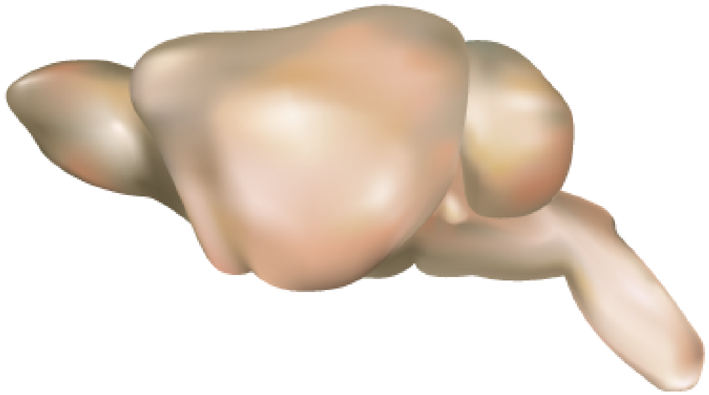
$A_{cross\text{-}seciton} \approx 0.5\ cm^2$



# Reported PVS velocities would result in “convective” flow through brain parenchyma

$A_{cross\text{-}seciton} \approx 0.5\ cm^2$

$Q = 0.5\ \mu L/min \approx 8*10^{-6}\ cm^3/sec$



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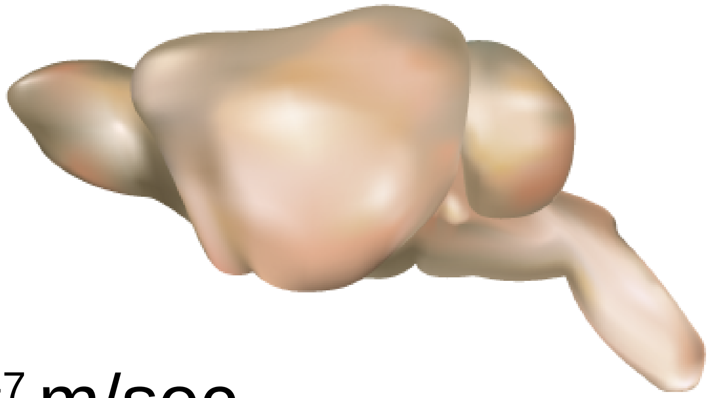
$v = Q/A = 1.6*10^{-5}\ cm/sec = 1.6*10^{-7}\ m/sec$



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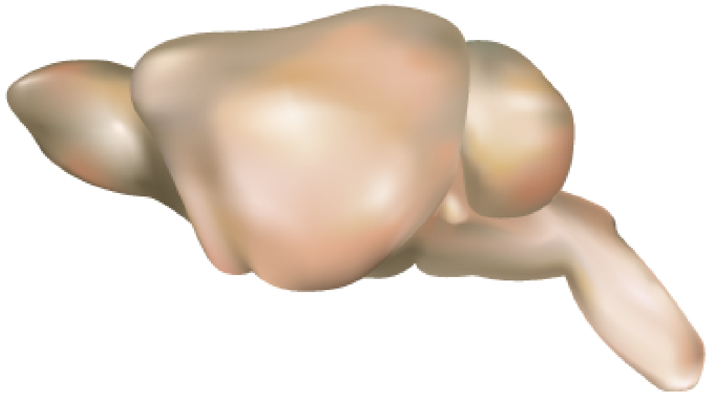
$v \approx 100\ nm/sec$



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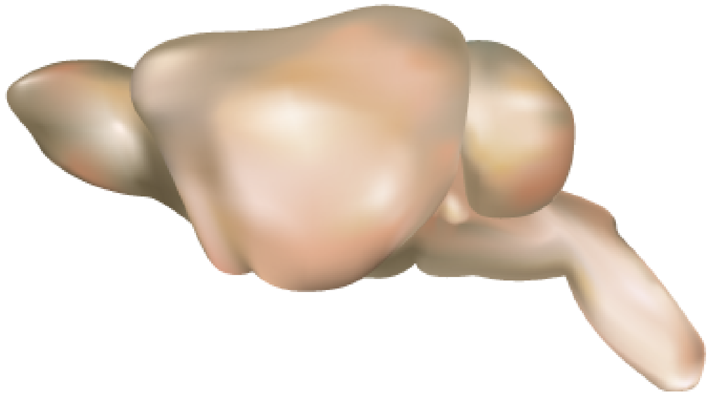
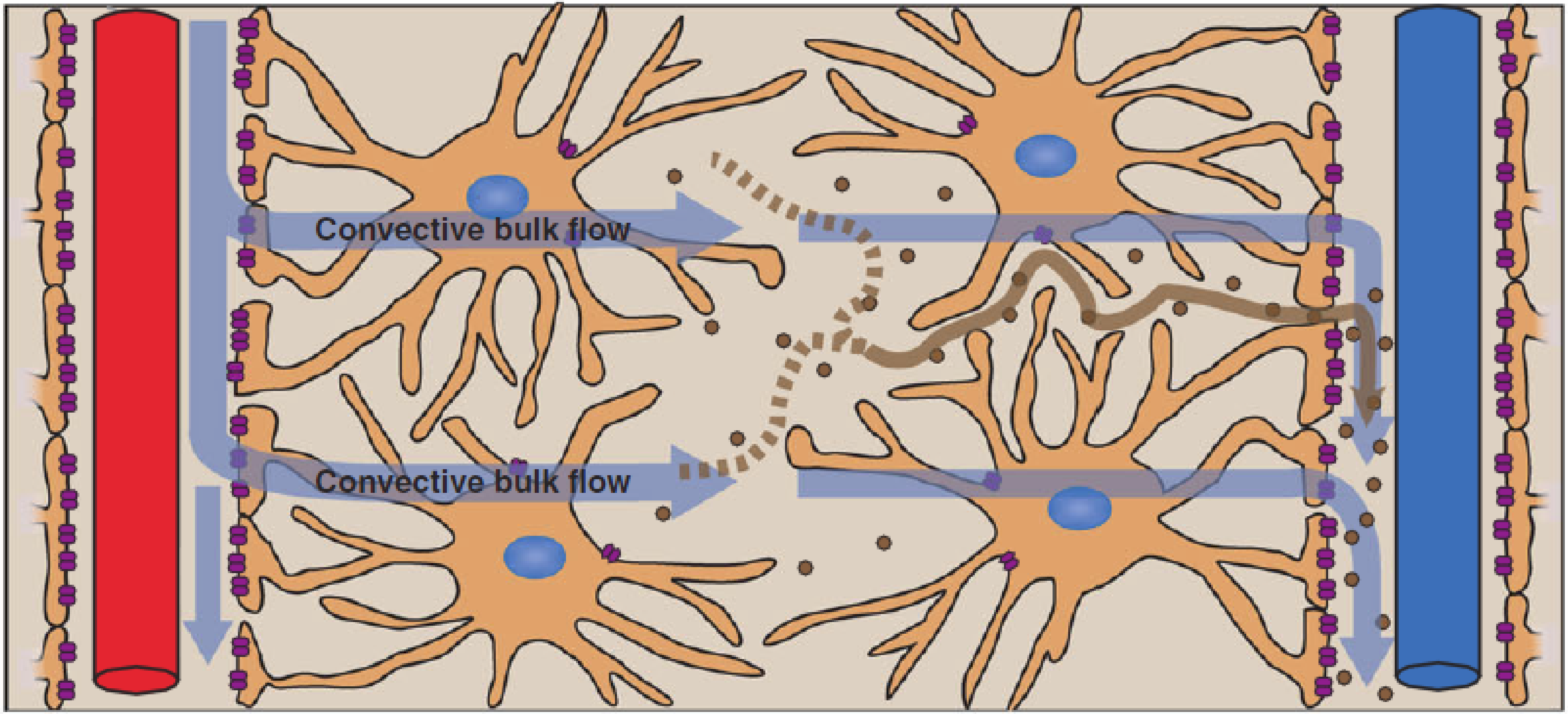
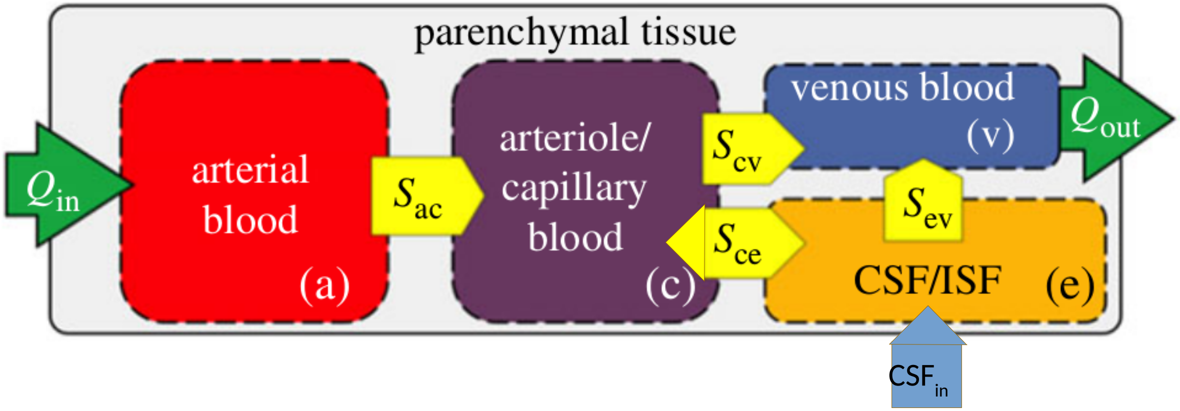


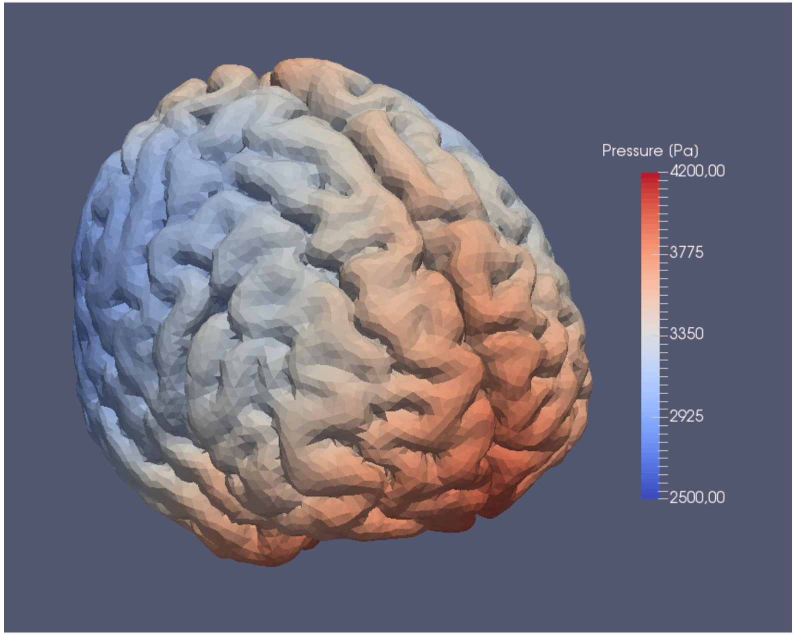
Holter et al. 2017: $v \approx 10\ nm/sec$

# There is still a discrepancy between findings regarding convective flow in the parenchyma



# Modeling infusion tests allows for investigation of theories regarding CSF production and absorption



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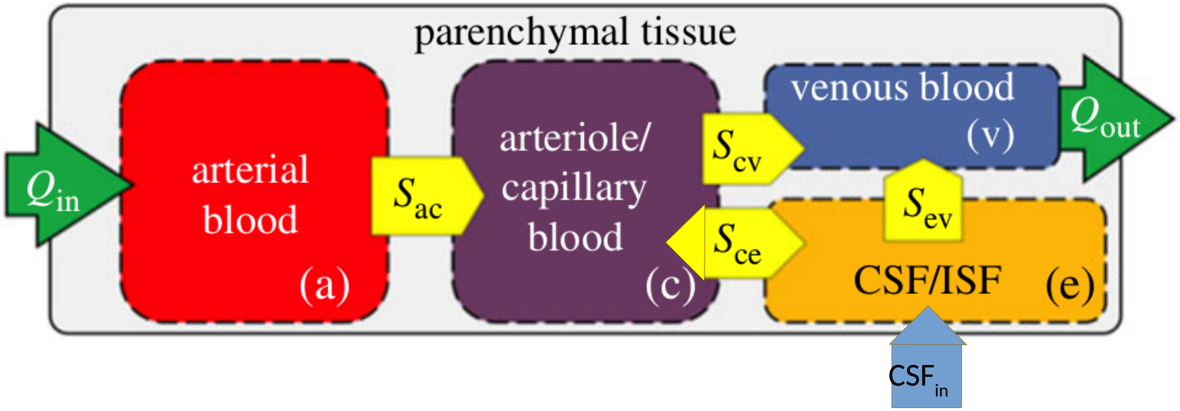


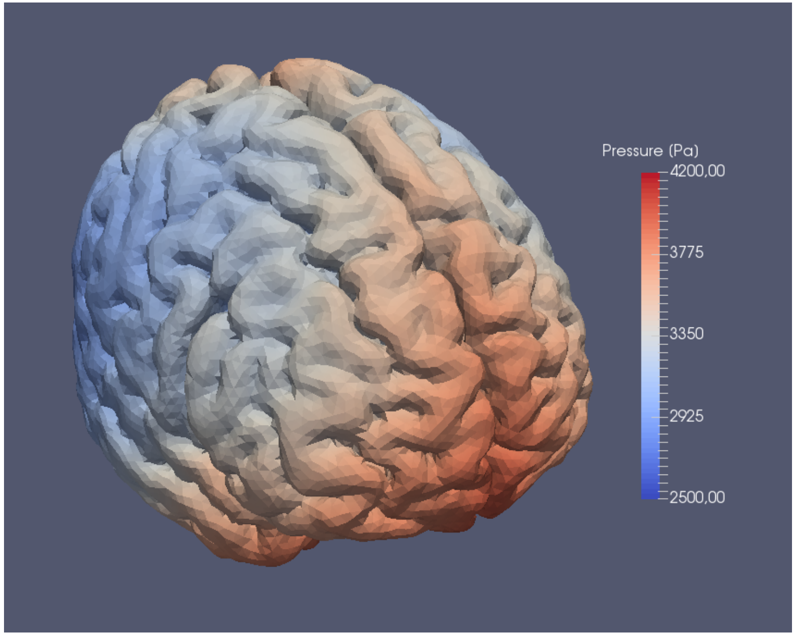


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thank you!