The role of separation of scales in the description of

FLOW AND TRANSPORT IN THE SPINAL CANAL

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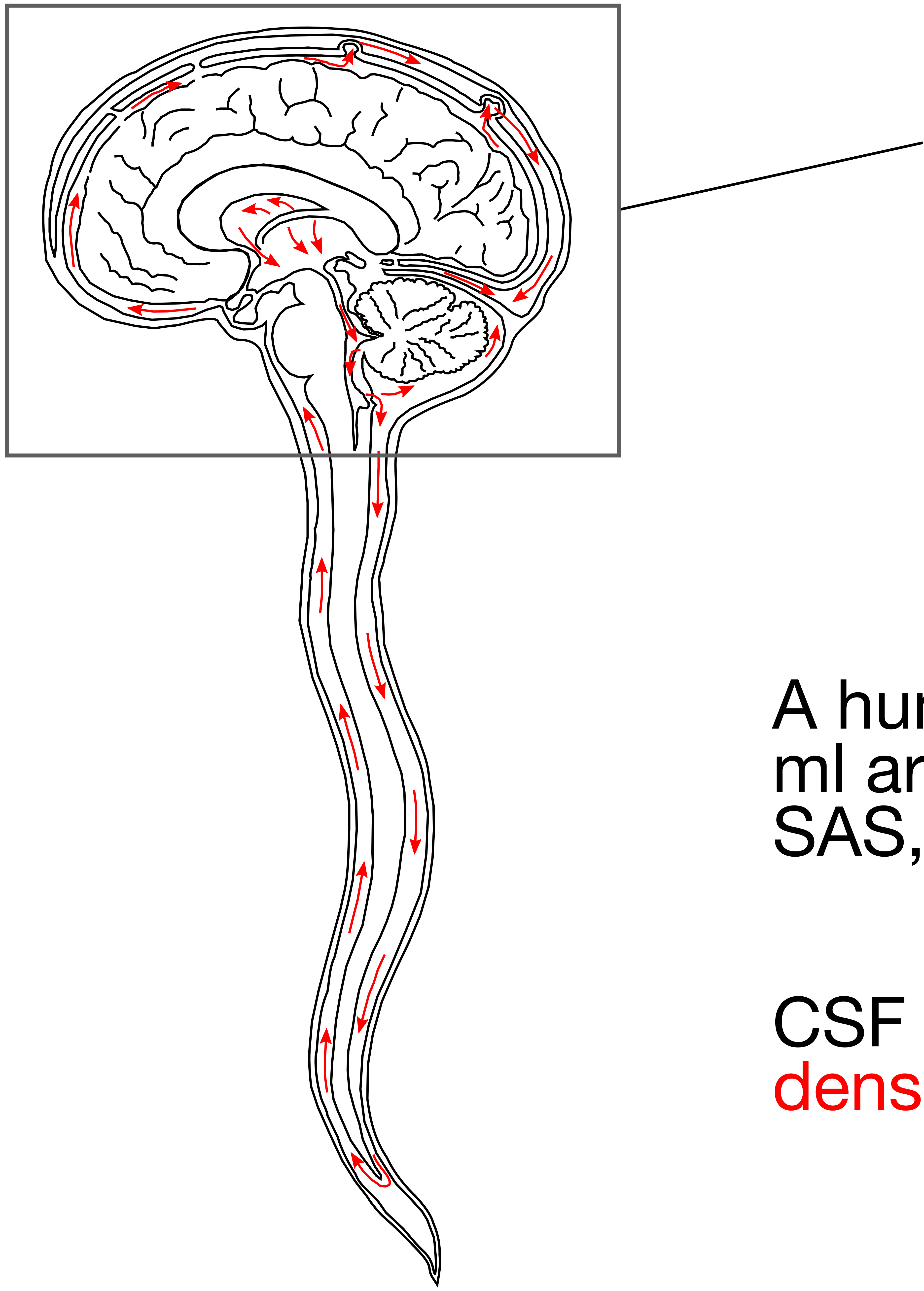
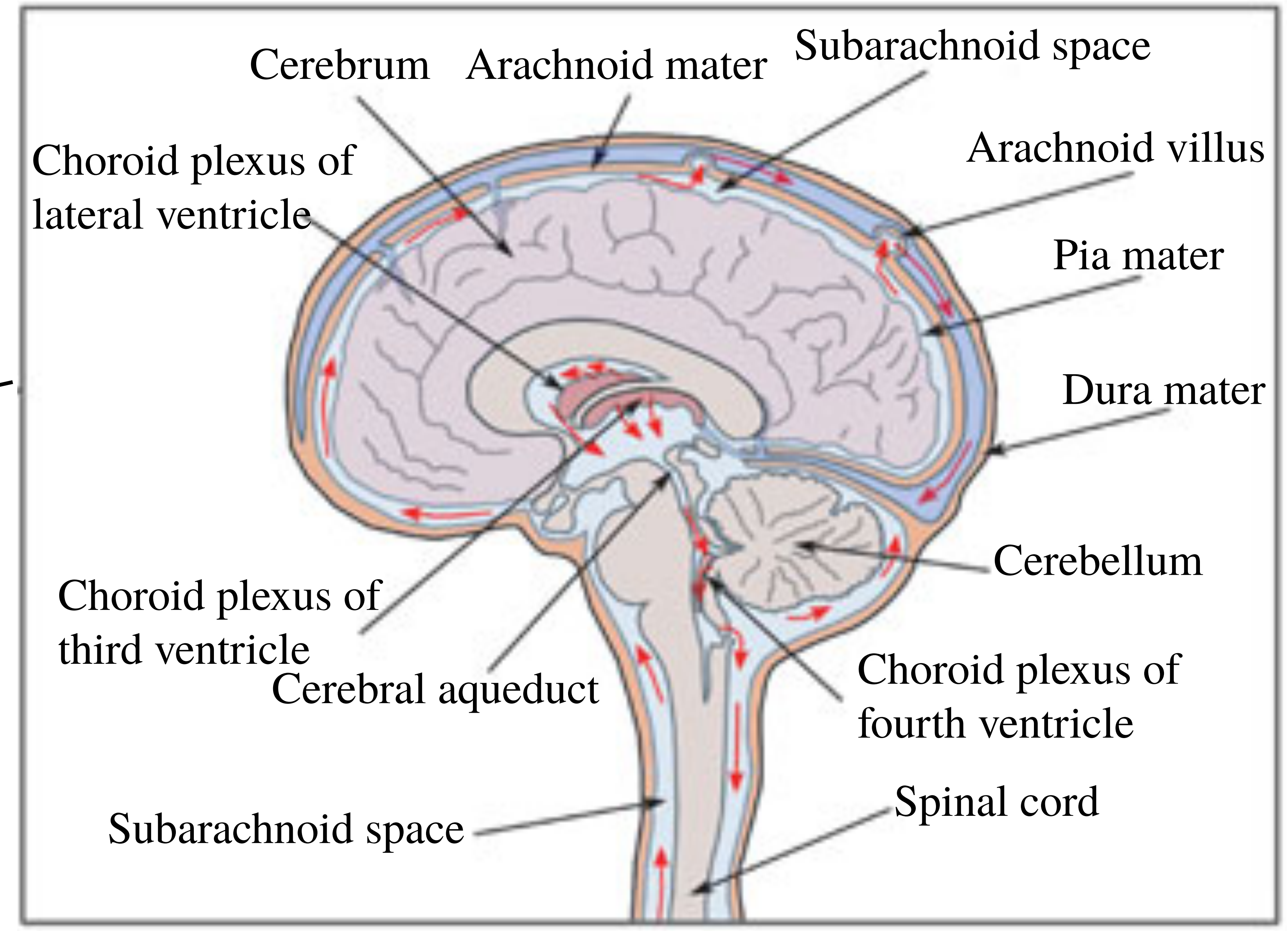
The cerebrospinal fluid (CSF)



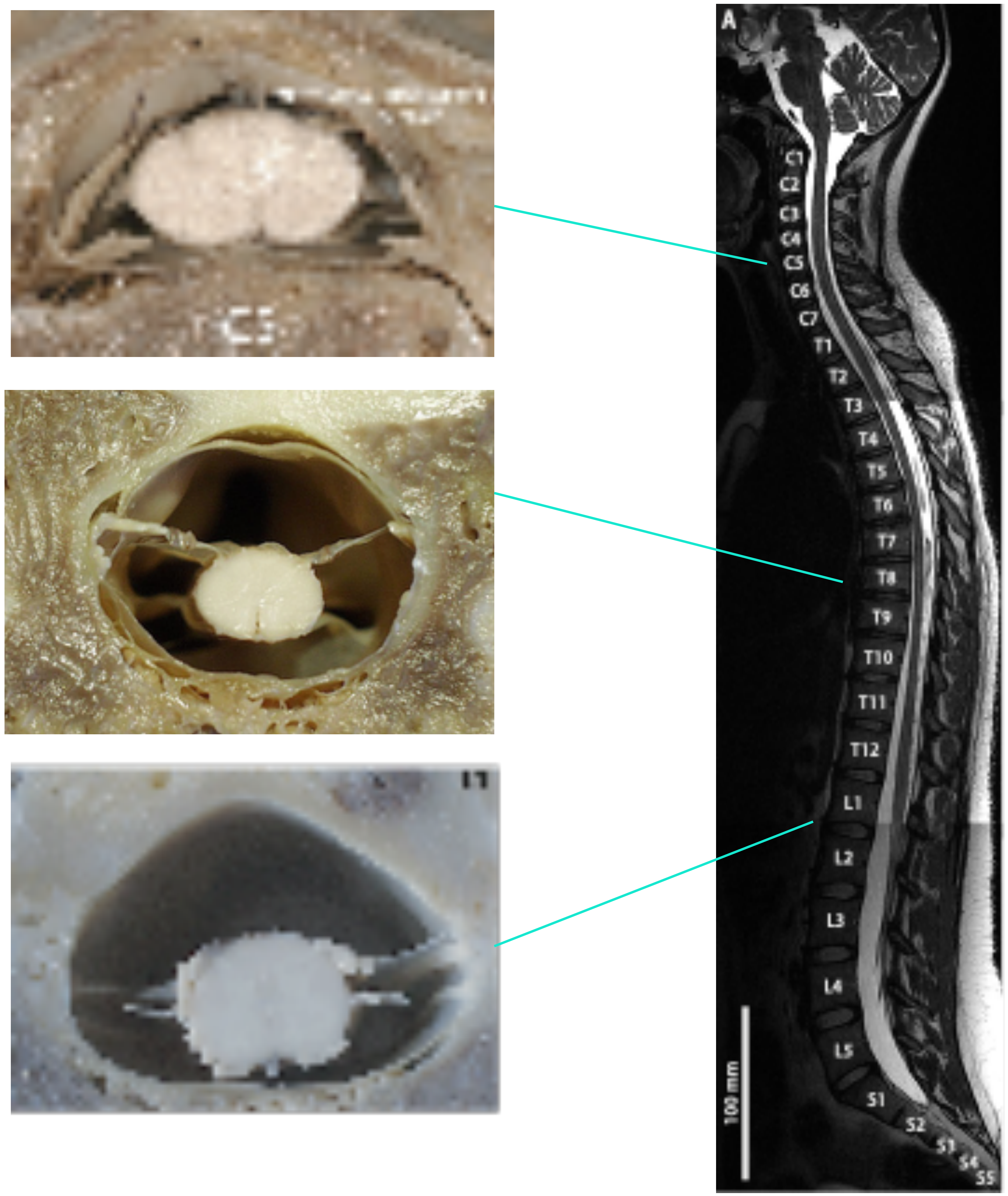


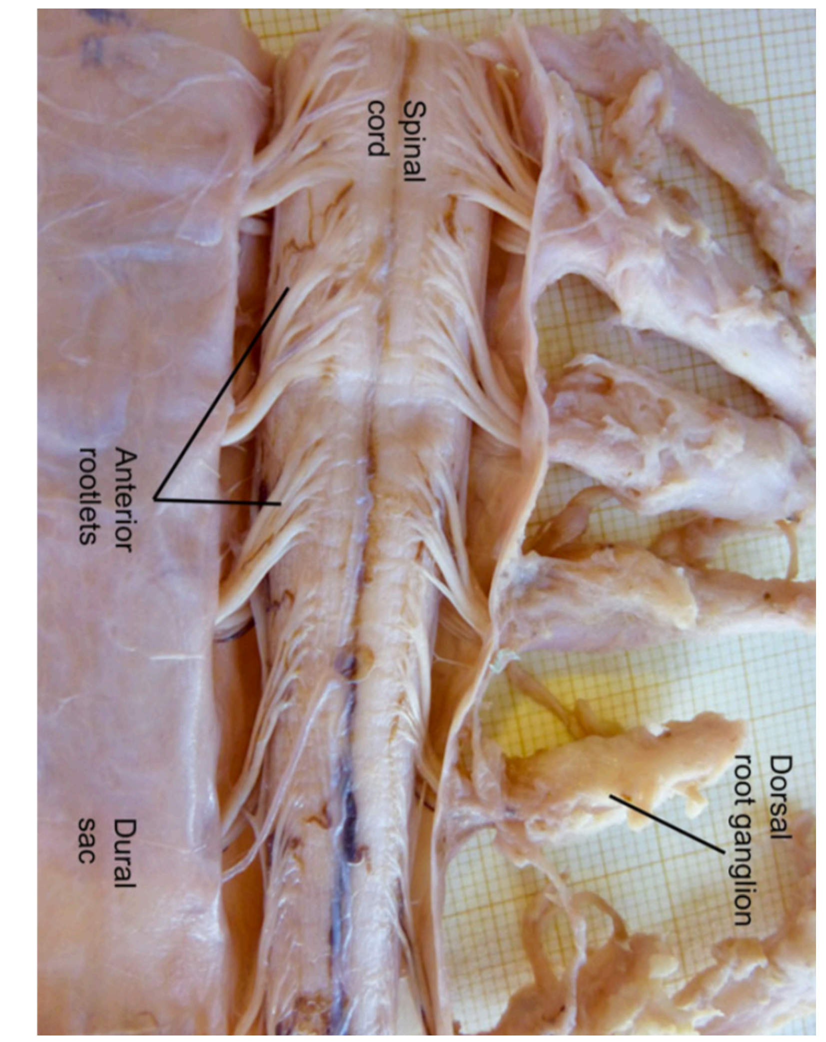
A human adult has about 140-170 ml of CSF (30 ml are in the ventricles, 70-80 ml in the cerebral SAS, and about 50 ml in the spinal SAS).

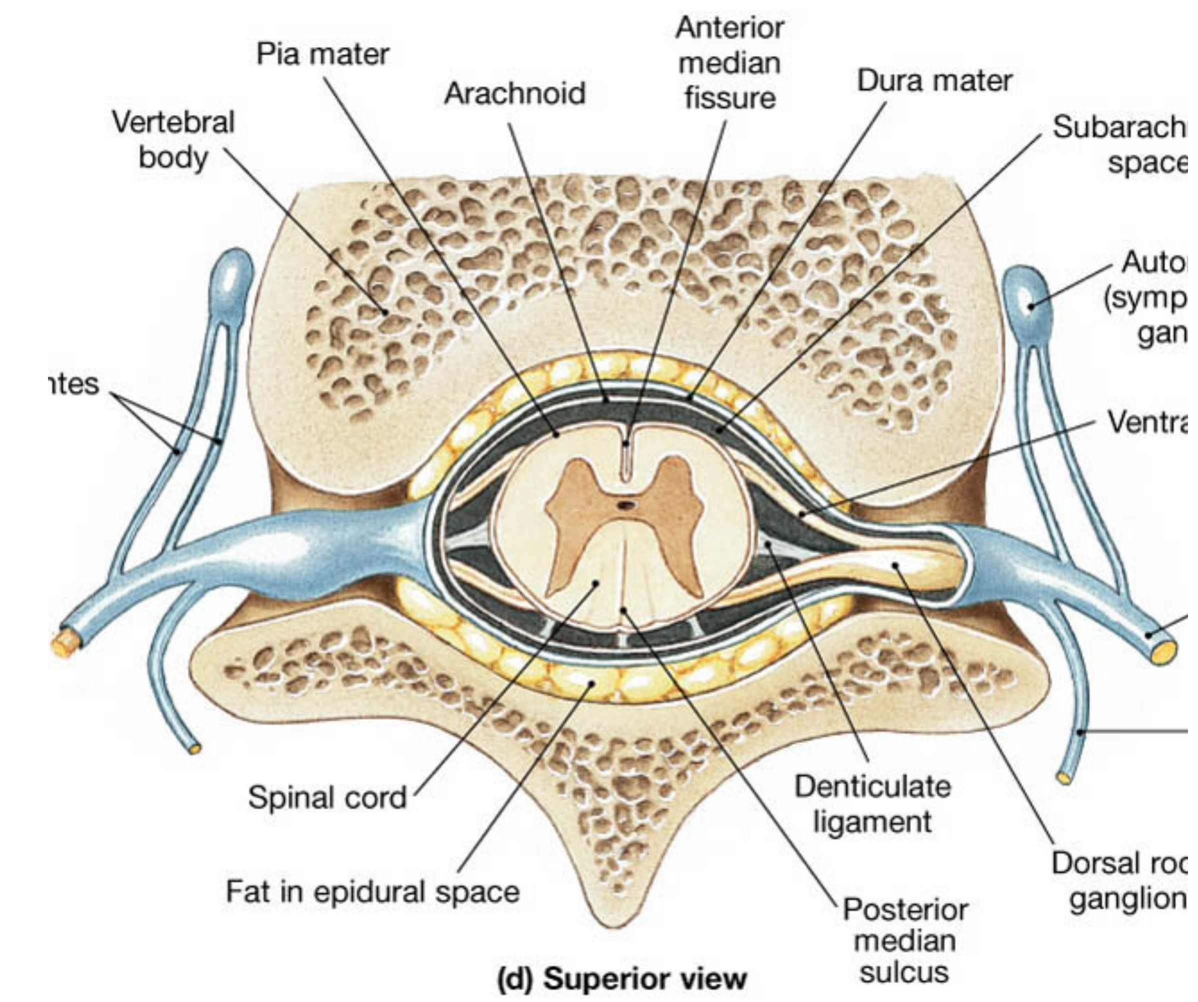
CSF is a newtonian fluid, and its viscosity and density are very similar to those of water.

The spinal canal

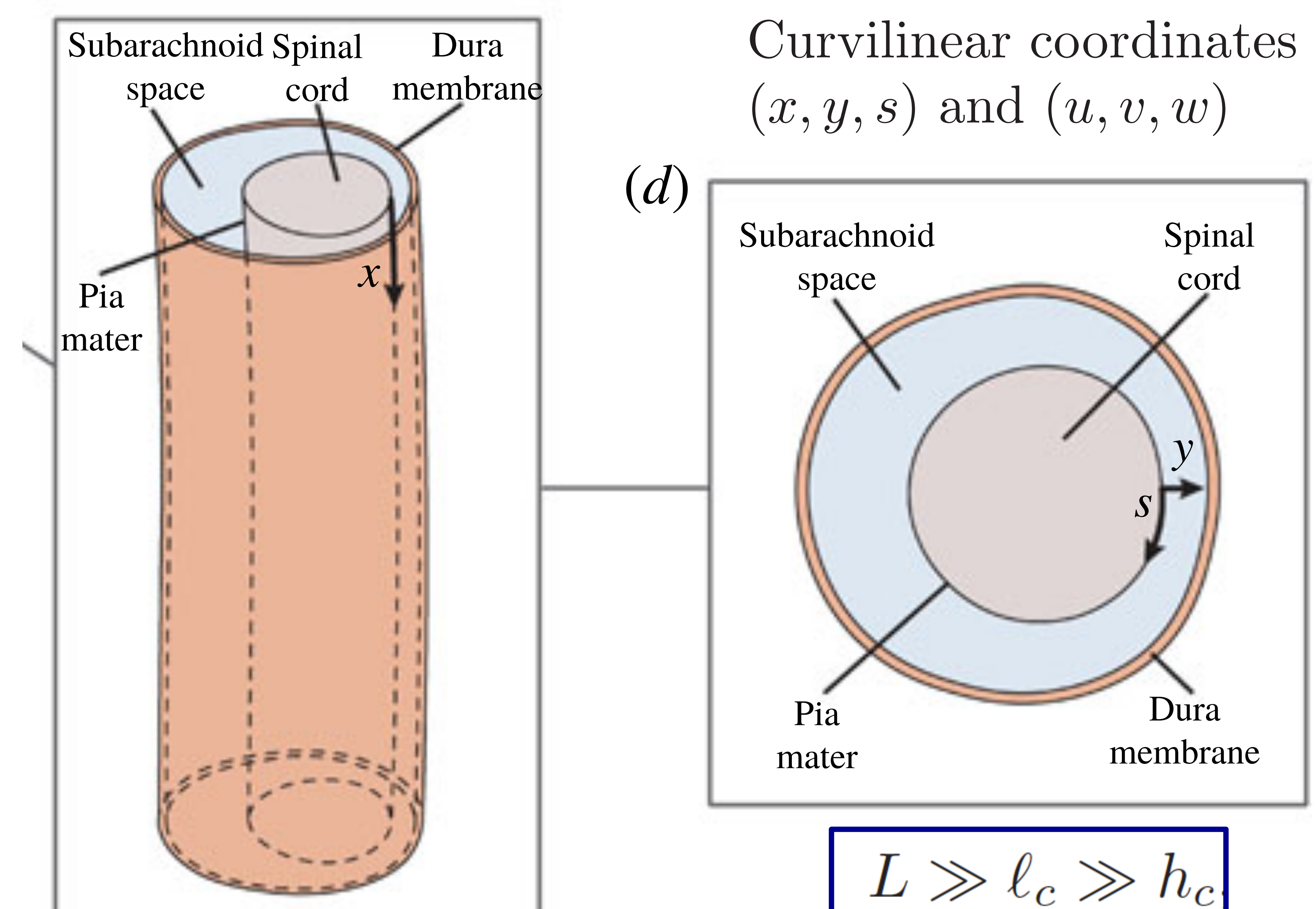
The spinal SAS, filled with CSF, is a thin annular canal of thickness $h(x,s,t)$, perimeter $\ell(x)$, and length L.







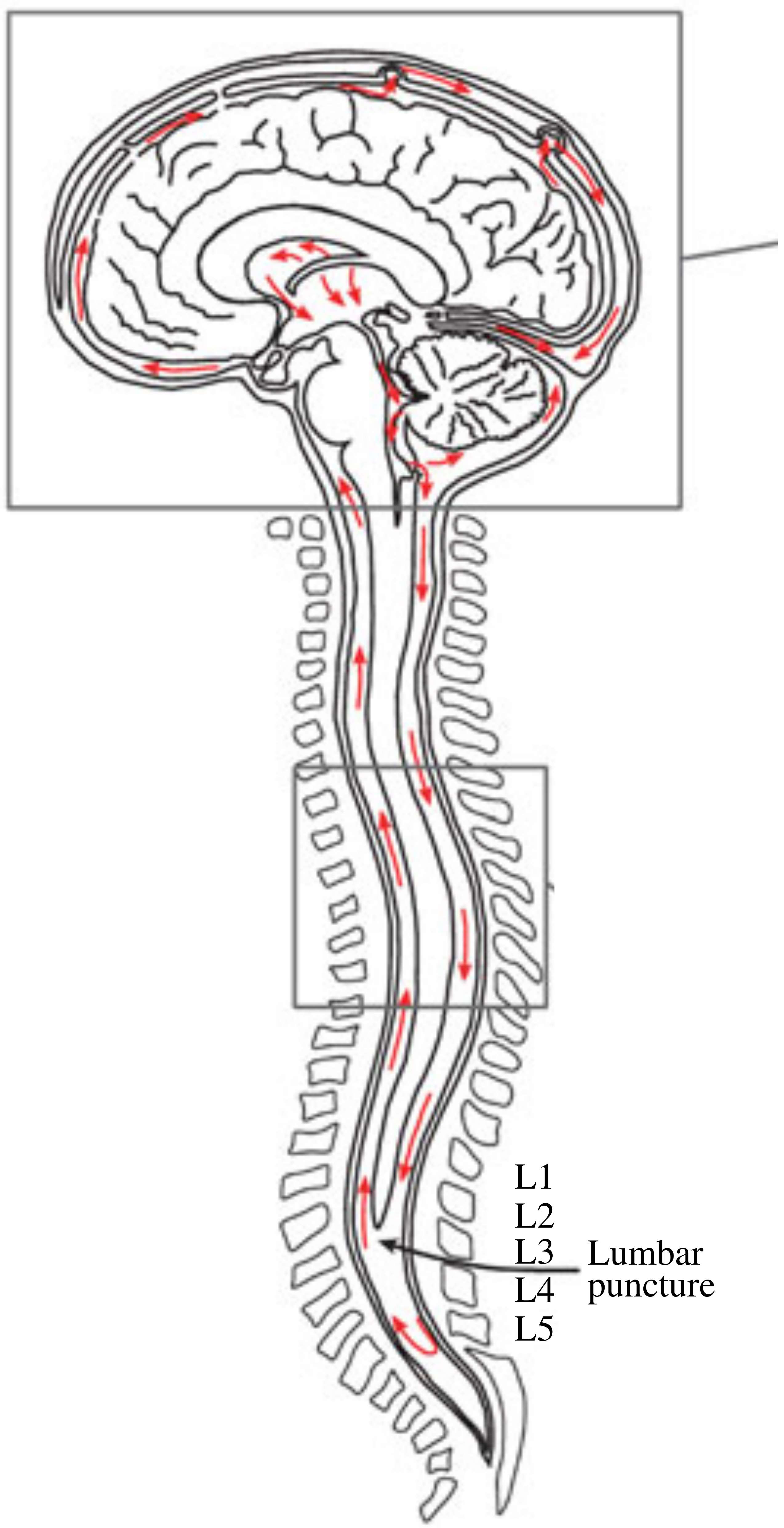
Curvilinear coordinates (x, y, s) and (u, v, w)

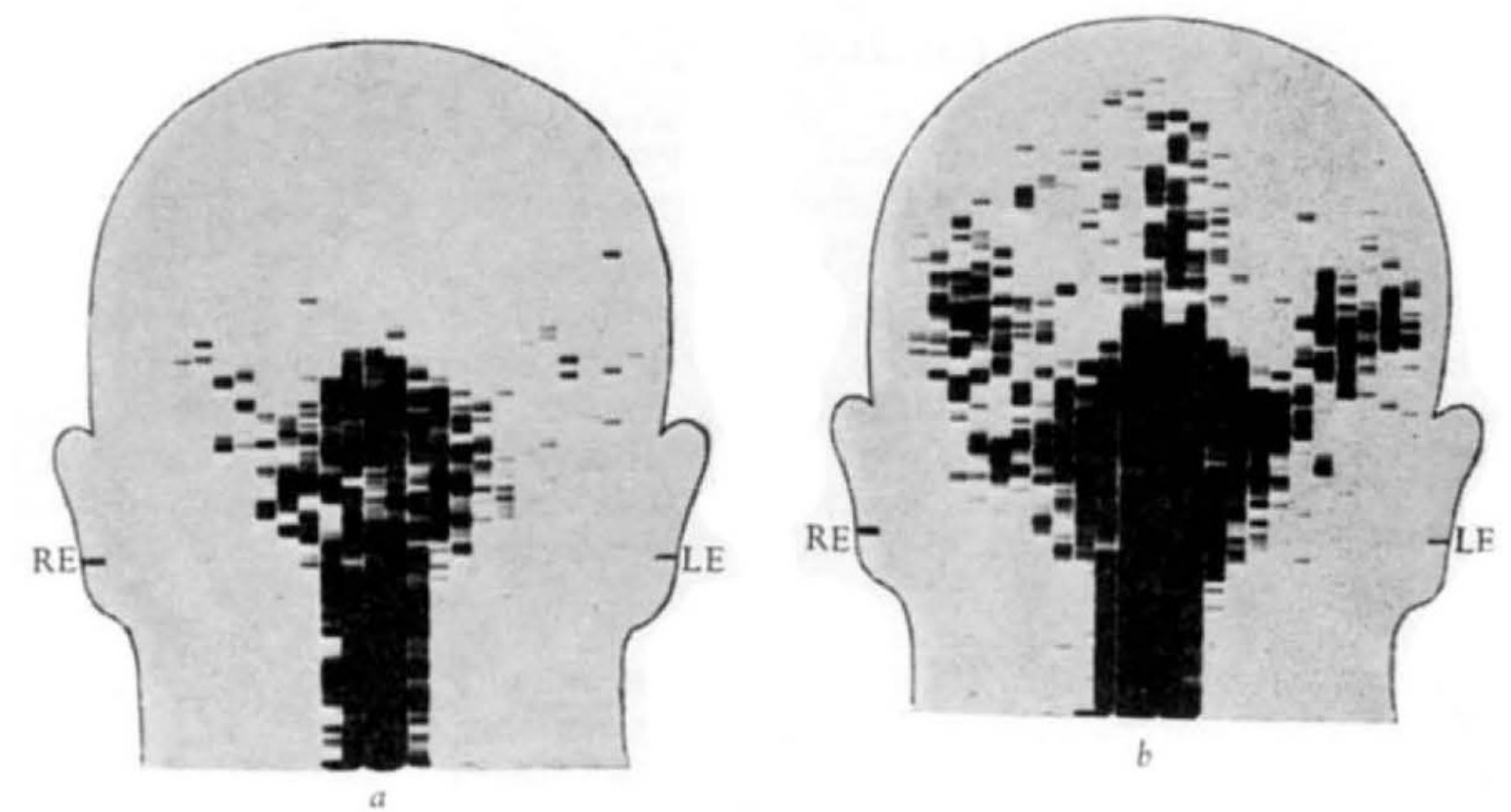


$$L \gg \ell_c \gg h_c$$

70 cm $\gg$ 2 cm $\gg$ 0.2 cm

Bulk flow in the spinal canal (DiChiro, Nature, 1964)





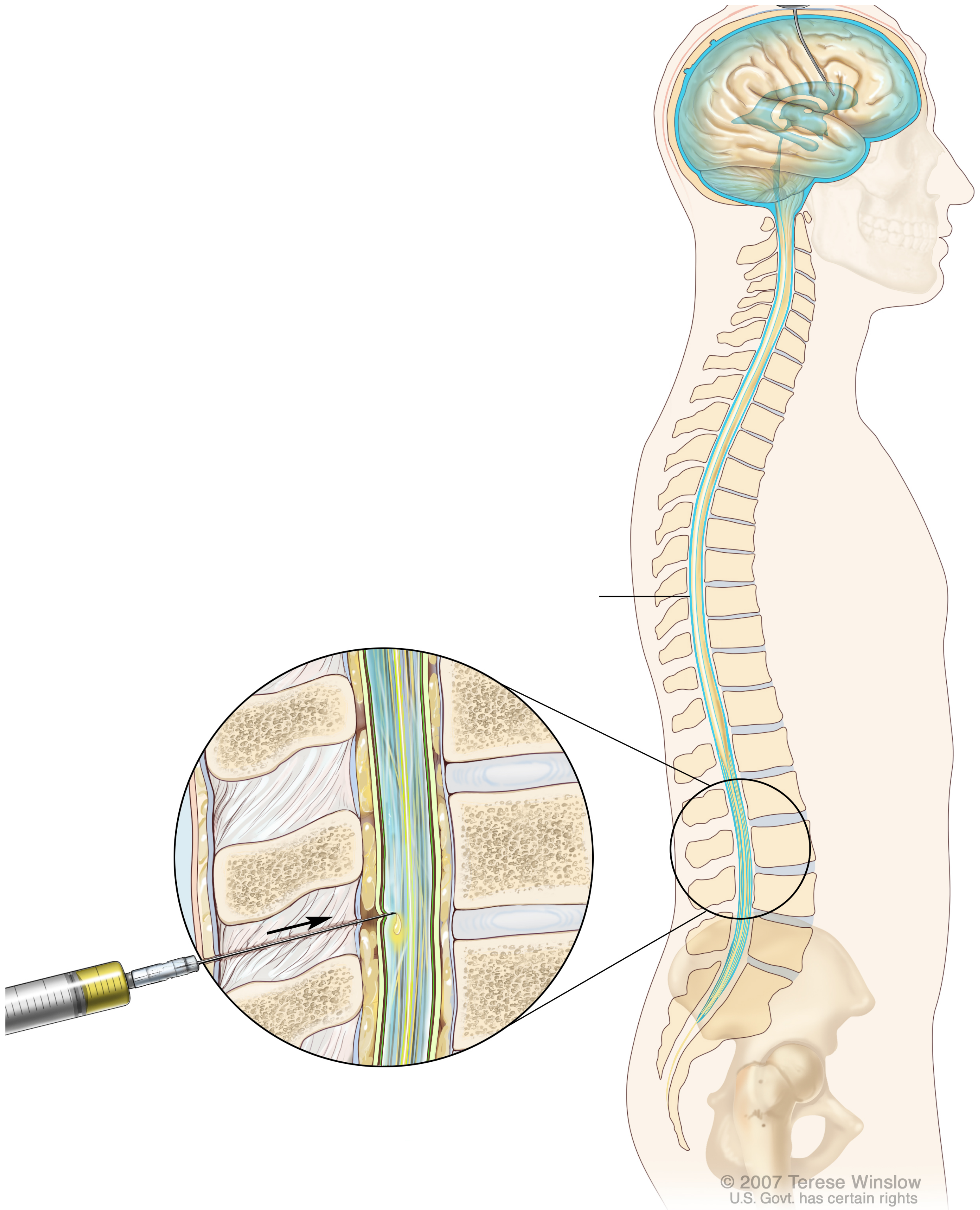
After 1 hour   After 3 hours

Characteristic bulk-flow velocity: cm/min

Why is CSF bulk flow important?

- It is key to the normal functioning of the CNS (it is responsible for the supply of nutrients to neuronal and glial cells, the removal of the waste products of cellular metabolism, and the transport of hormones,neurotransmitters, and other neuropeptides throughout the CNS.)
- It plays a fundamental role in the distribution of drugs, anesthetics and chemotherapeutic agents delivered intrathecally in the SSAS.

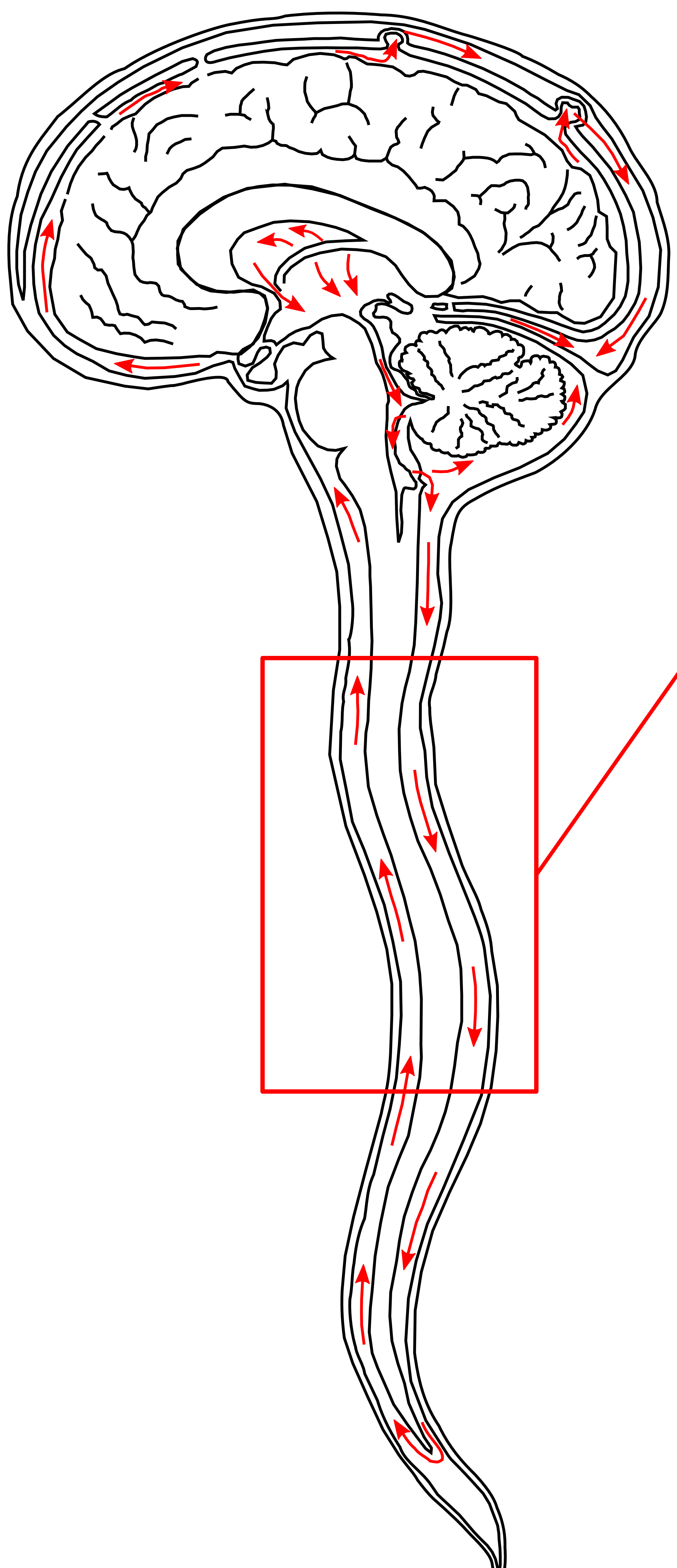
Intrathecal Drug Delivery (ITDD)

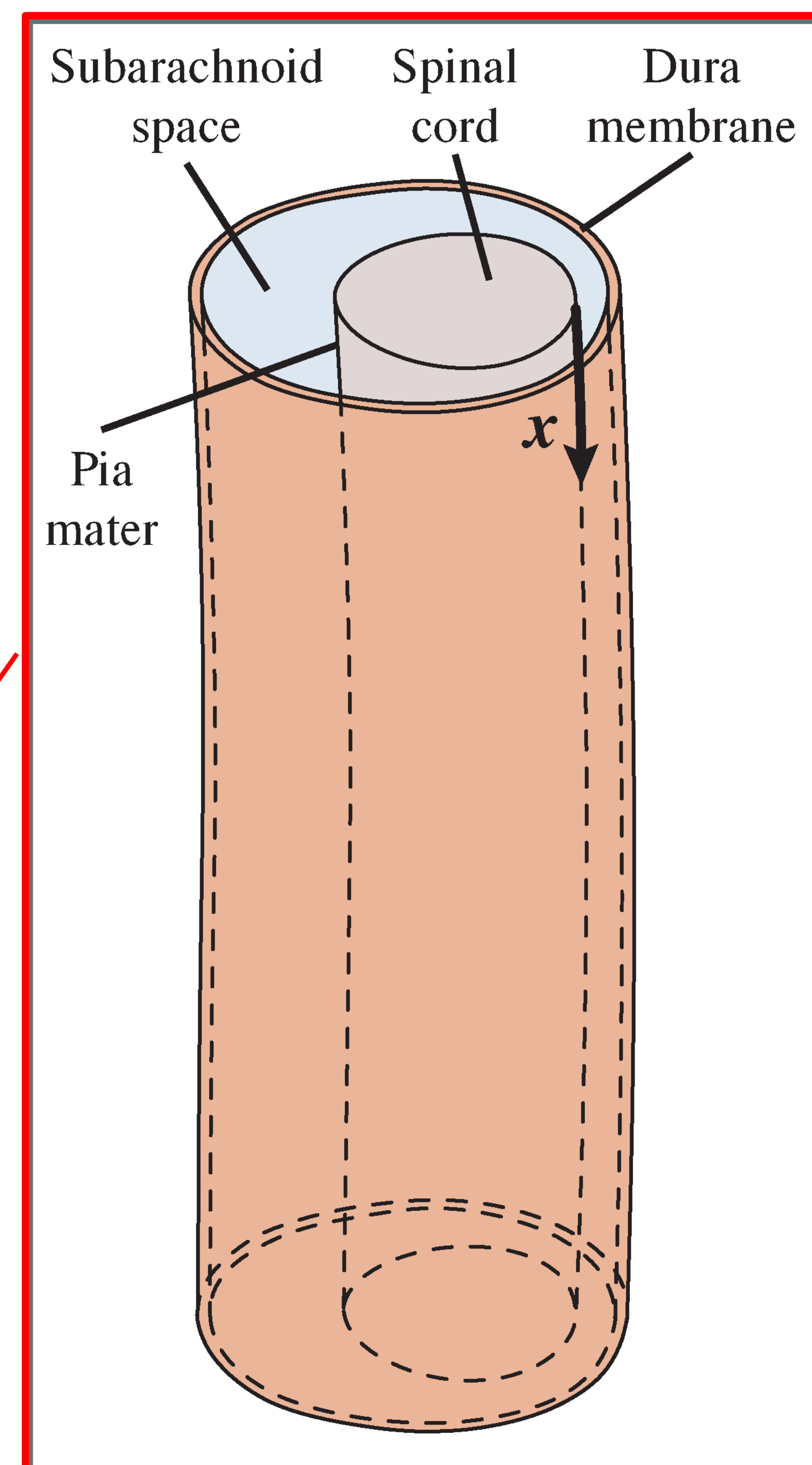


Disparity of time scales: pulsation time (~1 sec) vs residence time (~30 min)

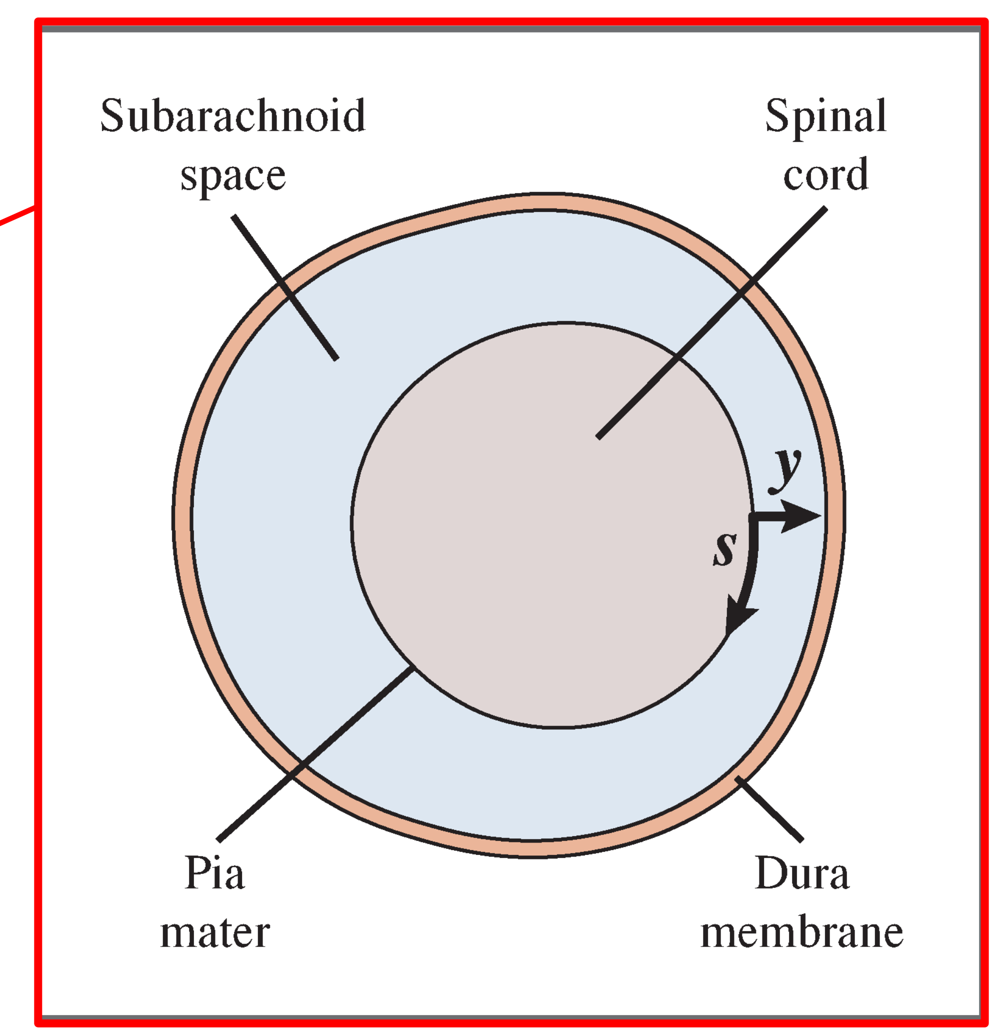
Characteristics of the flow

The spinal SAS, filled with CSF, is a thin annular canal of thickness $h(x, s, t)$, perimeter $\ell(x)$, and length L.





Curvilinear coordinates (x, y, s) and (u, v, w)



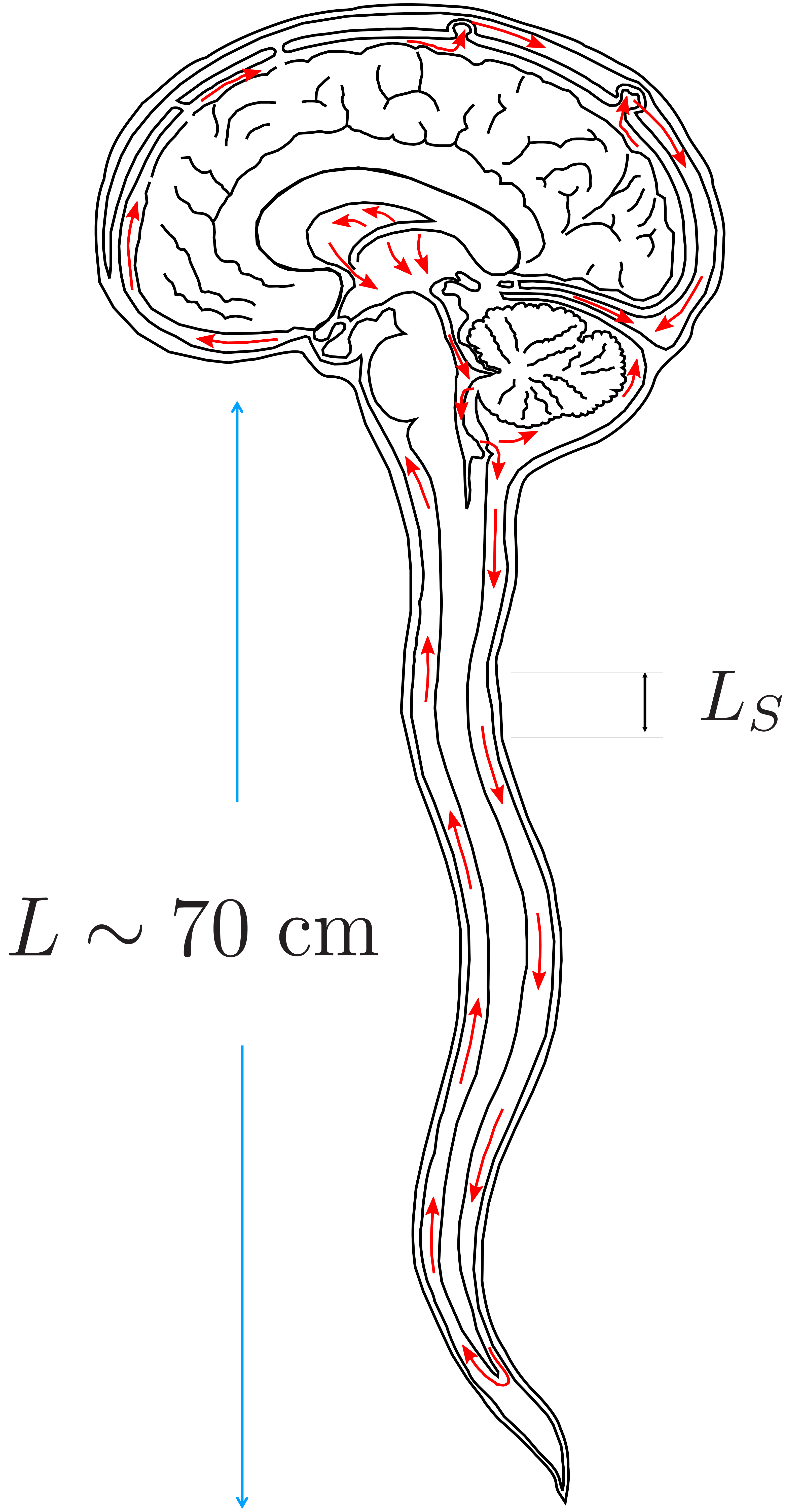
$$L \gg \ell_c \gg h_c$$

70 cm $\gg$ 2 cm $\gg$ 0.2 cm

$$\frac{1}{\ell}\frac{\partial}{\partial x}(\ell u) + \frac{\partial v}{\partial y} + \frac{1}{\ell}\frac{\partial w}{\partial s} = 0$$

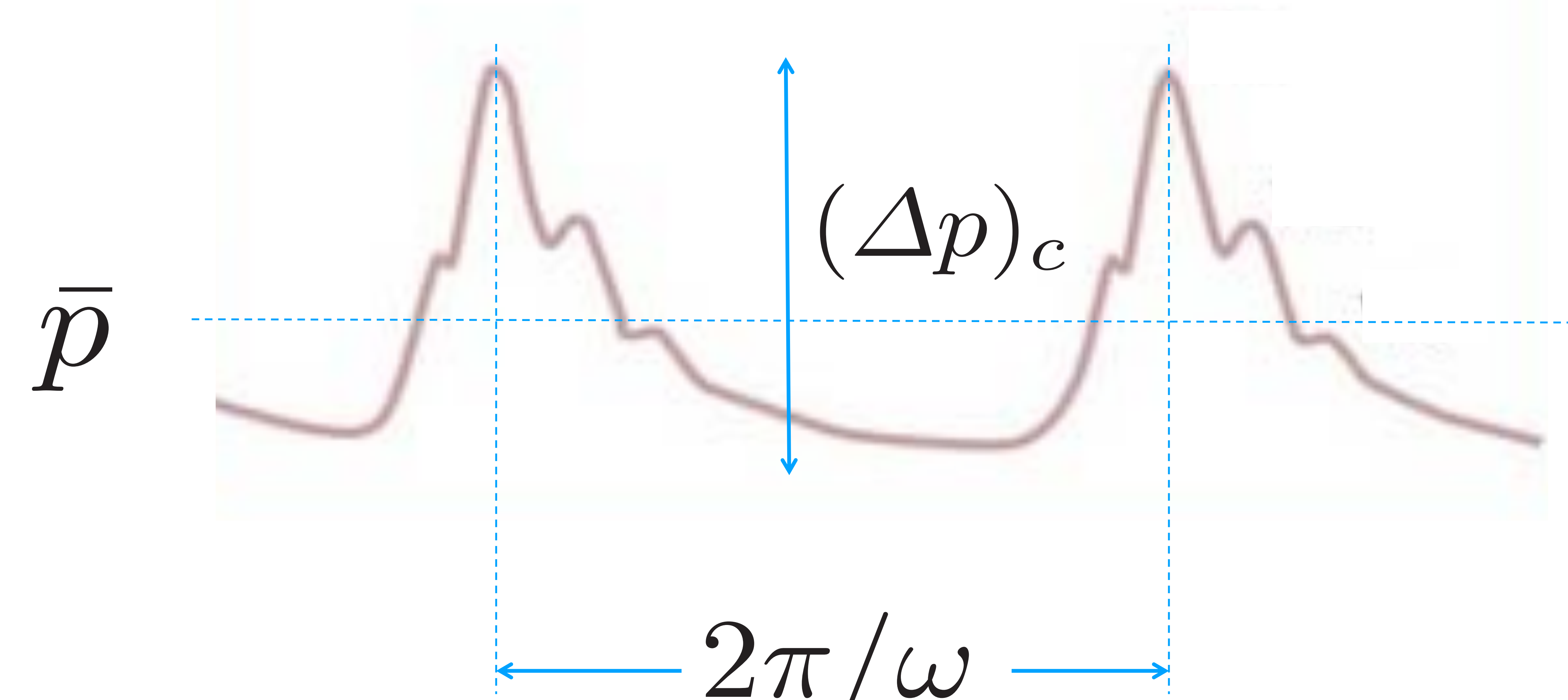
$$u_c \gg w_c \gg v_c$$

$$\frac{u_c}{L} \sim \frac{v_c}{h_c} \sim \frac{w_c}{\ell_c}$$



Characteristics of the flow

$$p_c(t) = \bar{p} + (\Delta p)_c \Pi(\omega t)$$



Linear elastic equation

$$h(x,s,t) - \bar{h}(x,s) = \gamma(x,s)p'(x,t)$$

$$(\Delta h)_c = \gamma_c(\Delta p)_c \rightarrow \varepsilon = \frac{(\Delta h)_c}{h_c} \sim \frac{\Delta V}{V} \sim \frac{1}{50} \ll 1$$

Characteristics of the flow

Stroke length

$$\varepsilon = \frac{(\Delta h)_c}{h_c} \sim \frac{\Delta V}{V} \sim \frac{L_S}{L} \sim \frac{1}{50} \ll 1 \quad \Rightarrow \quad u_c \sim \frac{L_S}{\omega^{-1}} = \varepsilon \omega L$$

Momentum balance

$$\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \cdot \nabla \mathbf{v} = -\nabla \left(\frac{p}{\rho} \right) + \nu \nabla^2 \mathbf{v}$$

$$\frac{\mathcal{O}(\partial \mathbf{v}/\partial t)}{\mathcal{O}(\mathbf{v} \cdot \nabla \mathbf{v})} \sim \varepsilon^{-1} \gg 1$$

$$\frac{\mathcal{O}(\partial \mathbf{v}/\partial t)}{\mathcal{O}(\nu \nabla^2 \mathbf{v})} \sim \alpha^2 = \left(\frac{h_c}{(\nu/\omega} \right)^2$$

Womersley number

$$\alpha = \frac{h_c}{(\nu/\omega)^{1/2}} \sim \mathcal{O}(1)$$

Dimensionless wave number:

$$k = \frac{L\omega}{[(h_c/\gamma_c')/\rho]^{1/2}}$$

Elastic wave speed

Eulerian velocity field: dimensionless formulation

Unknowns: $u(x,y,s,t), \quad v(x,y,s,t), \quad w(x,y,s,t), \quad h'(x,s,t) = h - \bar{h}(x,s), \quad p - \Pi(t) = k^2 p'(x,t), \quad \hat{p}(x,s,t)$

Continuity Eq: $$\frac{1}{\ell}\frac{\partial}{\partial x}(\ell u) + \frac{\partial v}{\partial y} + \frac{1}{\ell}\frac{\partial w}{\partial s} = 0$$

Constitutive Eq: $$h' = \gamma[\Pi(t) + k^2 p']$$

Momentum Eq:
$$\frac{\partial u}{\partial t} + \varepsilon\left[\frac{1}{\ell}\frac{\partial}{\partial x}(\ell u^2) + \frac{\partial}{\partial y}(uv) + \frac{1}{\ell}\frac{\partial}{\partial s}(uw)\right] = -\frac{\partial p'}{\partial x} + \frac{1}{\alpha^2}\frac{\partial^2 u}{\partial y^2}$$
$$\frac{\partial w}{\partial t} + \varepsilon\left[\frac{\partial}{\partial x}(uw) + 2\frac{uw}{\ell}\frac{\partial \ell}{\partial x} + \frac{\partial}{\partial y}(vw) + \frac{1}{\ell}\frac{\partial}{\partial s}(w^2)\right] = -\frac{1}{\ell}\frac{\partial \hat{p}}{\partial s} + \frac{1}{\alpha^2}\frac{\partial^2 w}{\partial y^2}$$

Boundary Conditions: $$y = 0, h : u = w = v - \frac{\partial h'}{\partial t} = 0; \quad x = 0 : p' = 0; \quad x = 1 : \int_0^1 \left(\int_0^h u\right) \mathrm{d}s = 0$$

Dimensionless spinal-canal functions: $\bar{h}(x,s), \quad \ell(x), \quad \gamma(x,s), \quad \Pi(t)$

We seek solutions for $\varepsilon \ll 1$
with $\alpha \sim 1, \quad k \sim 1$

$$u = u_0 + \varepsilon u_1 + \cdots, \; v = v_0 + \varepsilon v_1 + \cdots, \; w = w_0 + \varepsilon w_1 + \cdots$$
$$p' = p'_0 + \varepsilon p'_1 + \cdots, \; \hat{p} = \hat{p}_0 + \varepsilon \hat{p}_1 + \cdots, \; h' = h'_0 + \varepsilon h'_1 + \cdots$$

Eulerian velocity field: solution for $\Pi(t) = \cos t$

$$u = u_0 + \varepsilon u_1 + \cdots, \; v = v_0 + \varepsilon v_1 + \cdots, \; w = w_0 + \varepsilon w_1 + \cdots$$
$$p' = p'_0 + \varepsilon p'_1 + \cdots, \; \hat{p} = \hat{p}_0 + \varepsilon \hat{p}_1 + \cdots, \; h' = h'_0 + \varepsilon h'_1 + \cdots$$

Leading-order oscillatory motion

The linear unsteady lubrication problem that appears at $\mathcal{O}(1)$ can be solved to give

$$u_0 = \mathrm{Re}\left(\mathrm{i}\mathrm{e}^{\mathrm{i}t} U\right), v_0 = \mathrm{Re}\left(\mathrm{i}\mathrm{e}^{\mathrm{i}t} V\right), w_0 = \mathrm{Re}\left(\mathrm{i}\mathrm{e}^{\mathrm{i}t} W\right),$$
$$p'_0 = \mathrm{Re}\left(\mathrm{e}^{\mathrm{i}t} P'\right), \hat{p}_0 = \mathrm{Re}\left(\mathrm{e}^{\mathrm{i}t} \hat{P}\right), h'_0 = \mathrm{Re}\left(\mathrm{e}^{\mathrm{i}t} H'\right),$$

involving the complex functions $U(x, \eta, s)$, $V(x, \eta, s)$, $W(x, \eta, s)$, $P'(x)$, $\hat{P}(x, s)$, and $H'(x, s)$, with $\eta = y/h$

The time average vanishes $\langle u_0 \rangle = \langle v_0 \rangle = \langle w_0 \rangle = \langle h'_0 \rangle = \langle p'_0 \rangle = \langle \hat{p}_0 \rangle = 0$ with $\langle \cdot \rangle = \frac{1}{2\pi} \int_0^{2\pi} \cdot \, \mathrm{d}t$

This harmonic oscillatory motion correspond to axial velocities $u_c \sim \varepsilon \omega L \sim 1 \text{ cm/s}$

Eulerian velocity field: solution for $\Pi(t) = \cos t$

$$u = u_0 + \varepsilon u_1 + \cdots, \; v = v_0 + \varepsilon v_1 + \cdots, \; w = w_0 + \varepsilon w_1 + \cdots$$
$$p' = p'_0 + \varepsilon p'_1 + \cdots, \; \hat{p} = \hat{p}_0 + \varepsilon \hat{p}_1 + \cdots, \; h' = h'_0 + \varepsilon h'_1 + \cdots$$

First-order corrections: steady streaming

Collecting terms of order ε and taking the time average $\langle \cdot \rangle = \frac{1}{2\pi}\int_0^{2\pi} \cdot \,\mathrm{d}t$ yields

$$\mathcal{F}_x = -\frac{\partial \langle p'_1 \rangle}{\partial x} + \frac{1}{\bar{h}^2\alpha^2}\frac{\partial^2 \langle u_1 \rangle}{\partial \eta^2}$$
$$\mathcal{F}_s = -\frac{1}{\ell}\frac{\partial \langle \tilde{p}_1 \rangle}{\partial s} + \frac{1}{\bar{h}^2\alpha^2}\frac{\partial^2 \langle w_1 \rangle}{\partial \eta^2},$$
$$\langle u_1 \rangle = \langle w_1 \rangle = 0 \text{ at } \eta = 0, 1$$

$$\frac{\langle u_1 \rangle}{\bar{h}^2\alpha^2} = -\frac{\mathrm{d}\langle p'_1 \rangle}{\mathrm{d}x}\frac{(1-\eta)\eta}{2} + \eta\int_0^{\eta}\mathcal{F}_x \mathrm{d}\bar{\eta} - \int_0^{\eta}\mathcal{F}_x\bar{\eta}\mathrm{d}\bar{\eta} - \eta\int_0^1 \mathcal{F}_x(1-\eta)\mathrm{d}\eta$$

$$\frac{\langle w_1 \rangle}{\bar{h}^2\alpha^2} = -\frac{1}{\ell}\frac{\partial\langle \tilde{p}_1 \rangle}{\partial s}\frac{(1-\eta)\eta}{2} + \eta\int_0^{\eta}\mathcal{F}_s \mathrm{d}\bar{\eta} - \int_0^{\eta}\mathcal{F}_s\bar{\eta}\mathrm{d}\bar{\eta} - \eta\int_0^1 \mathcal{F}_s(1-\eta)\mathrm{d}\eta$$

where $\mathcal{F}_x(x,\eta,s)$ and $\mathcal{F}_s(x,\eta,s)$ are nonlinear terms arising from convective acceleration that can be evaluated in terms of the leading-order solution.

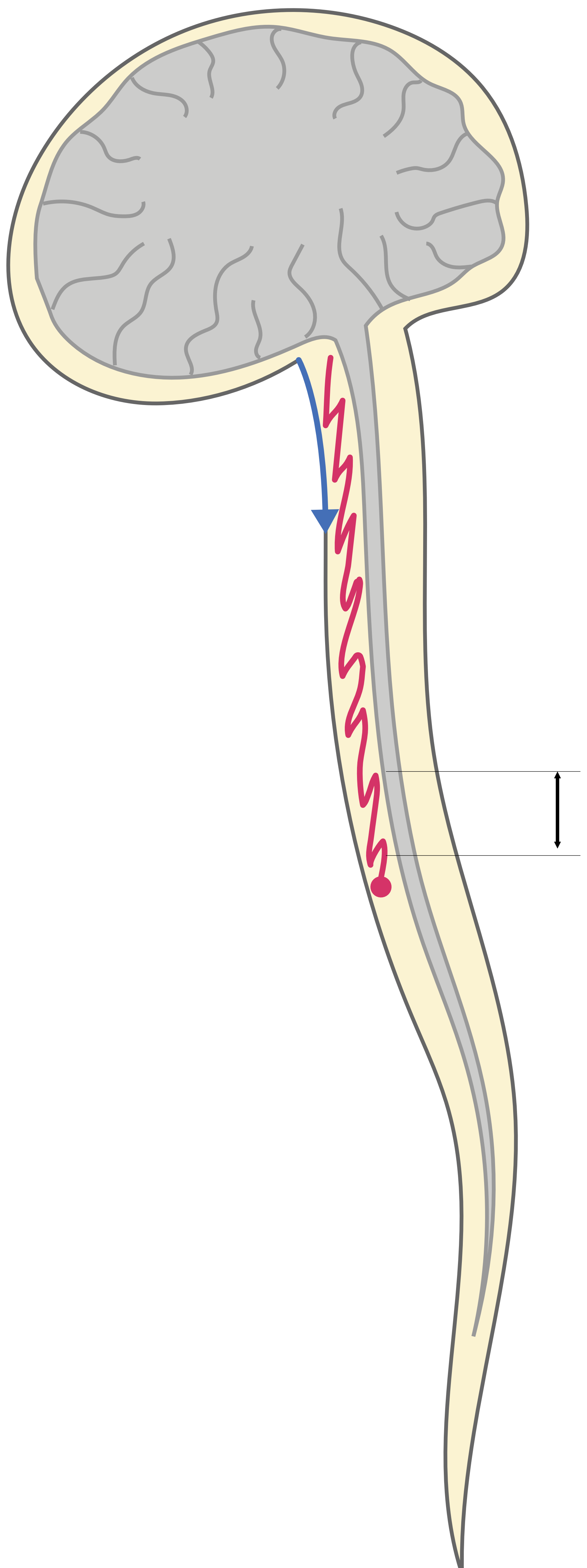
Eulerian velocity field: $\mathbf{v}(\mathbf{x},t) = (u,v,w) = \mathbf{v}_0(\mathbf{x},t) + \varepsilon \mathbf{v}_1(\mathbf{x},t) + \cdots$

$$u_c = \varepsilon \omega L \sim 1 \text{ cm/s}$$

$$\langle \mathbf{v}_0 \rangle = \frac{1}{2\pi}\int_0^{2\pi} \mathbf{v}_0 \, \mathrm{d}t = 0$$

$$\varepsilon u_c = \varepsilon^2 \omega L \sim 1 \text{ cm/min}$$

$\langle \mathbf{v}_1 \rangle \neq 0$ **Steady streaming**



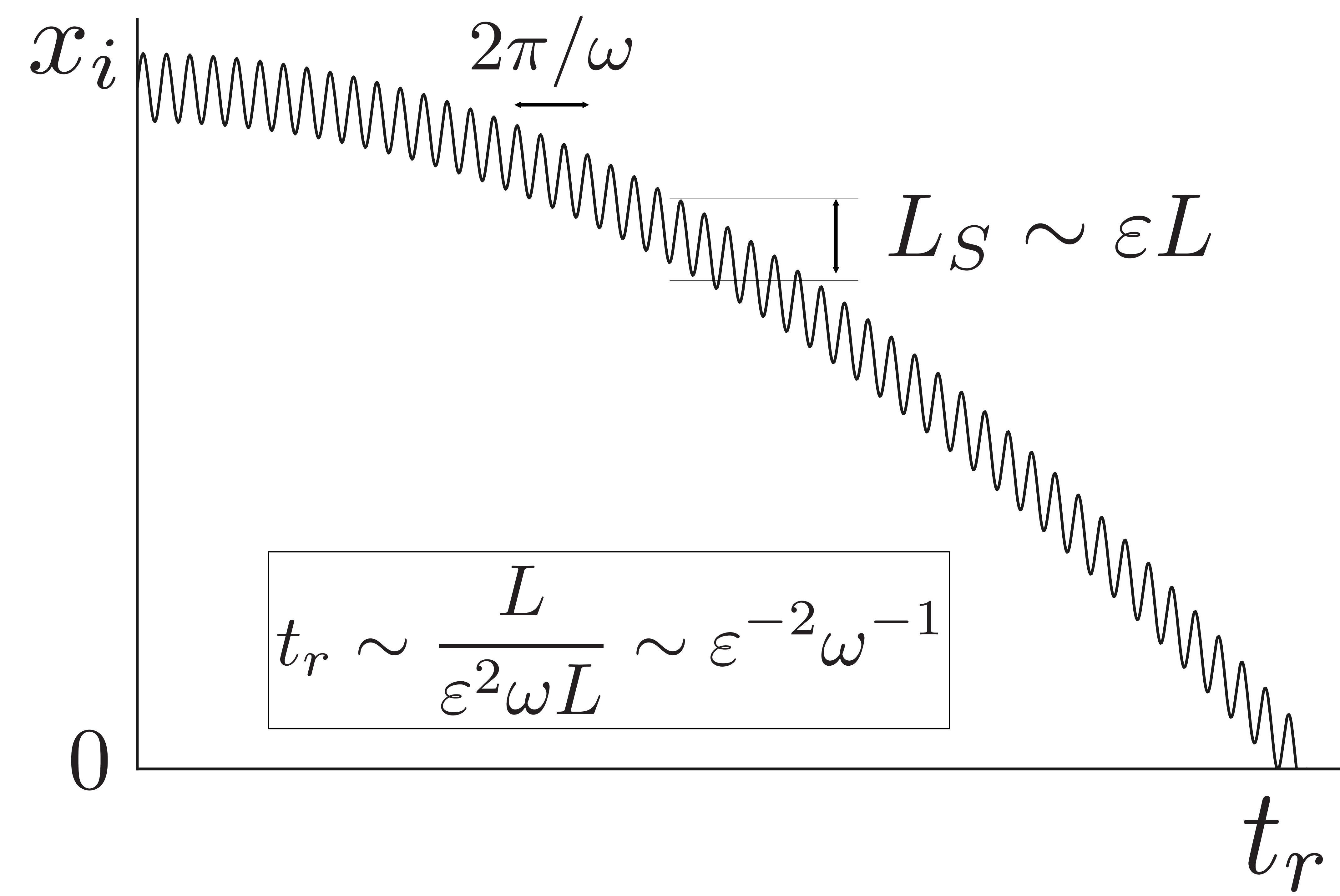
$L_S \sim \varepsilon L$

$$\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \mathbf{v}(\mathbf{x},t); \quad \mathbf{x} = \mathbf{x}_i \text{ at } t = 0$$

$$\delta \mathbf{v} \sim L_S |\nabla \mathbf{v}_0| \sim L_S \frac{u_c}{L} \sim \varepsilon u_c$$

$$\delta x \sim \delta \mathbf{v}\, \omega^{-1} \sim \varepsilon^2 L$$

$u_d \sim \varepsilon^2 \omega L \sim \langle u_1 \rangle$ **Stokes drift**



Fluid-particle trajectories

$$\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \varepsilon \mathbf{v}(\mathbf{x},t); \quad \mathbf{v}(\mathbf{x},t) = \mathbf{v}_0(\mathbf{x},t) + \varepsilon \mathbf{v}_1(\mathbf{x},t) + \cdots$$

Relevant time scales $\boxed{\omega^{-1} \sim 1 \text{ sec and } t_r \sim \varepsilon^{-2}\omega^{-1} \sim 30 \text{ min}}$ ➡ $\boxed{t, \tau = \varepsilon^2 t}$

$$\mathbf{x} = \mathbf{x}_0(t,\tau) + \varepsilon \mathbf{x}_1(t,\tau) + \varepsilon^2 \mathbf{x}_2(t,\tau) + \cdots \quad \left\{ \begin{array}{l} \dfrac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \dfrac{\partial \mathbf{x}_0}{\partial t} + \varepsilon \dfrac{\partial \mathbf{x}_1}{\partial t} + \varepsilon^2 \left(\dfrac{\partial \mathbf{x}_0}{\partial \tau} + \dfrac{\partial \mathbf{x}_2}{\partial t} \right) + \cdots \\ \mathbf{v}(\mathbf{x},t) = \mathbf{v}_0(\mathbf{x}_0,t) + \varepsilon \left[\mathbf{v}_1(\mathbf{x}_0,t) + \mathbf{x}_1 \cdot \nabla \mathbf{v}_0(\mathbf{x}_0,t) \right] + \cdots \end{array} \right.$$

$$O(1): \frac{\partial \mathbf{x}_0}{\partial t} = 0 \quad ➡ \quad \mathbf{x}_0 = \mathbf{x}_0(\tau)$$

$$O(\varepsilon): \frac{\partial \mathbf{x}_1}{\partial t} = \mathbf{v}_0[\mathbf{x}_0(\tau), t] \quad ➡ \quad \mathbf{x}_1 = \int_0^t \mathbf{v}_0(\mathbf{x}_0, t')\mathrm{d}t' + \hat{\mathbf{x}}_1(\tau)$$

$$O(\varepsilon^2): \frac{\mathrm{d}\mathbf{x}_0}{\mathrm{d}\tau} + \frac{\partial \mathbf{x}_2}{\partial t} = \mathbf{v}_1(\mathbf{x}_0,t) + \int_0^t \mathbf{v}_0(\mathbf{x}_0,t')\mathrm{d}t' \cdot \nabla \mathbf{v}_0(\mathbf{x}_0,t) + \hat{\mathbf{x}}_1(\tau) \cdot \nabla \mathbf{v}_0(\mathbf{x}_0,t)$$

$$\langle \cdot \rangle = \tfrac{1}{2\pi} \int_0^{2\pi} \cdot \, \mathrm{d}t \quad ➡ \quad \boxed{\underbrace{\frac{\mathrm{d}\mathbf{x}_0}{\mathrm{d}\tau} = (u_{\mathrm{L}}, v_{\mathrm{L}}, w_{\mathrm{L}})}_{\text{Time-averaged Lagrangian velocity}} = \underbrace{\langle \mathbf{v}_1 \rangle (\mathbf{x}_0)}_{\text{Steady streaming}} + \underbrace{\left\langle \int_0^t \mathbf{v}_0(\mathbf{x}_0,t')\mathrm{d}t' \cdot \nabla \mathbf{v}_0(\mathbf{x}_0,t) \right\rangle}_{\text{Stokes drift}}}$$

Time-averaged Lagrangian velocities

$$u_{\mathrm{L}} = \frac{\mathrm{d}x_0}{\mathrm{d}\tau} = \langle u_1 \rangle + \frac{1}{\bar{h}} \left\{ \langle u_0 h_0' \rangle + \frac{1}{\ell} \frac{\partial}{\partial s} \left(\bar{h} \left\langle u_0 \int w_0 \mathrm{d}t \right\rangle \right) \right\} + \frac{1}{\bar{h}} \frac{\partial}{\partial \eta} \left\langle u_0 \left[\int v_0 \mathrm{d}t - \eta \left(h_0' + \frac{1}{\ell} \frac{\partial \bar{h}}{\partial s} \int w_0 \mathrm{d}t \right) \right] \right\rangle$$

$$v_{\mathrm{L}} = \langle v_1 \rangle + \frac{1}{\ell} \frac{\partial}{\partial x} \left(\ell \left\langle v_0 \int u_0 \mathrm{d}t \right\rangle \right) + \frac{1}{\ell} \frac{\partial}{\partial s} \left\langle v_0 \int w_0 \mathrm{d}t \right\rangle - \frac{\eta}{\bar{h}} \frac{\partial}{\partial \eta} \left\langle v_0 \left(h_0' + \frac{\partial \bar{h}}{\partial x} \int u_0 \mathrm{d}t + \frac{1}{\ell} \frac{\partial \bar{h}}{\partial s} \int w_0 \mathrm{d}t \right) \right\rangle$$

$$w_{\mathrm{L}} = \langle w_1 \rangle + \frac{1}{\bar{h}} \left[\langle w_0 h_0' \rangle + \frac{\partial}{\partial x} \left(\bar{h} \left\langle w_0 \int u_0 \mathrm{d}t \right\rangle \right) \right] + \frac{1}{\bar{h}} \frac{\partial}{\partial \eta} \left\langle w_0 \left[\int v_0 \mathrm{d}t - \eta \left(h_0' + \frac{\partial \bar{h}}{\partial x} \int u_0 \mathrm{d}t \right) \right] \right\rangle$$

Preliminary Conclusions

- The time-averaged Lagrangian velocity is found to be the result of a combination of the steady-streaming Eulerian velocity, associated with inertia, and the Stokes drift, associated with the non-uniformity of the leading-order oscillatory flow.

- The estimated magnitude of the velocity of the bulk recirculating flow of the CSF in the spinal canal is

$$\varepsilon u_c = \varepsilon^2 \omega L \sim 1 \text{ cm/min}$$

- Correspondingly, typical residence times are of order $\varepsilon^{-2}\omega^{-1} \sim 20 - 30 \text{ min}$, much larger than the characteristic time $\omega^{-1} \sim 1 \text{ sec}$ of the pulsatile flow

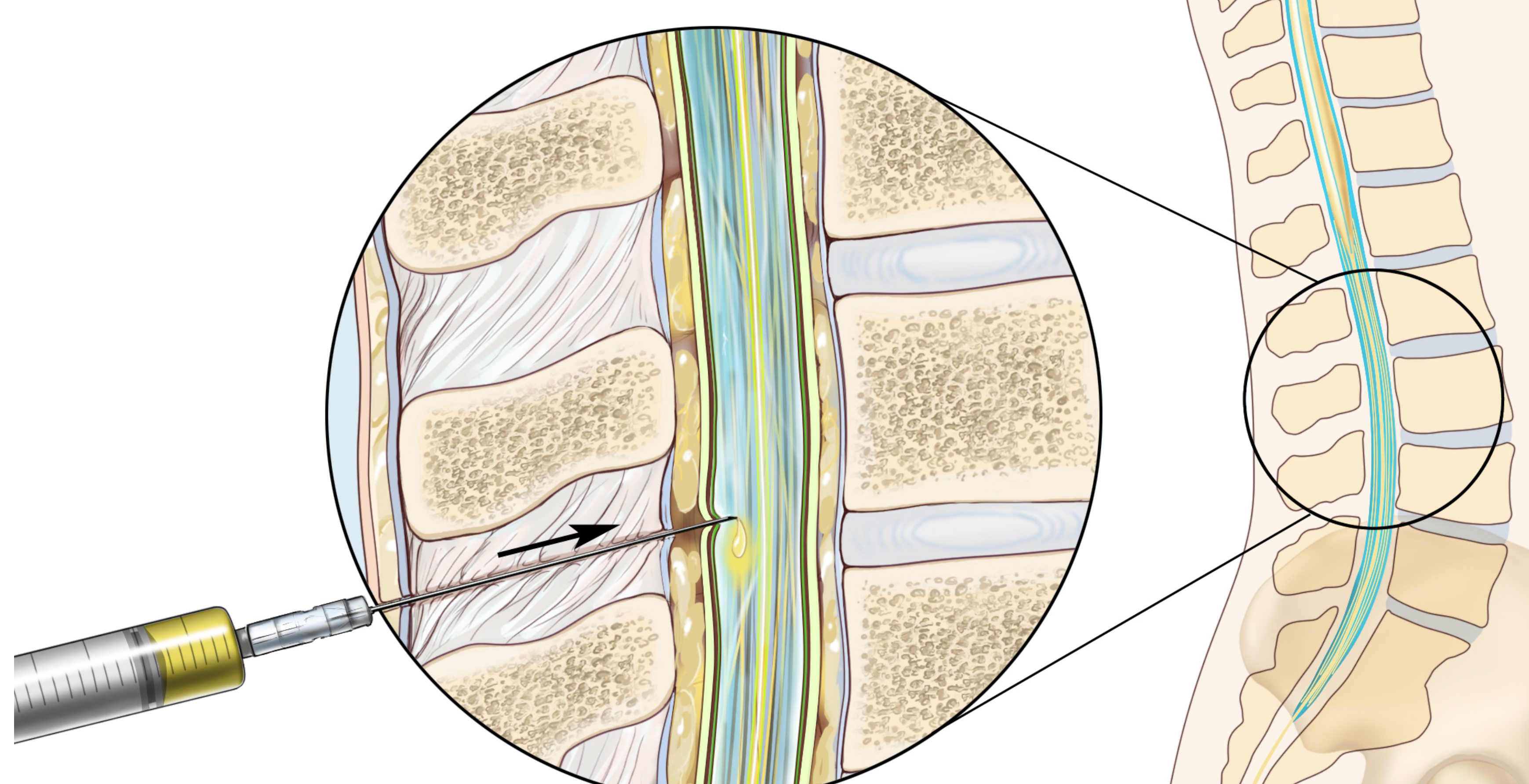
- The results are in qualitative agreement with the radioactive-tracer observations of DiChiro (tracers with negligly small diffusivity)

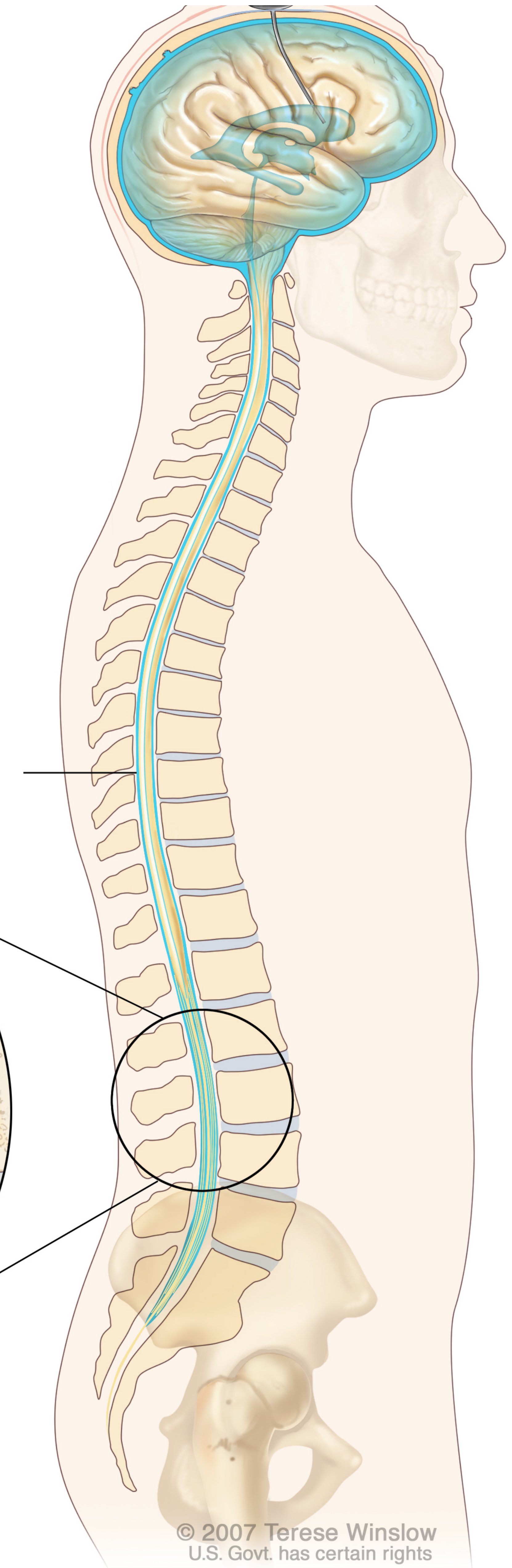
Intrathecal Drug Delivery (ITDD)

Direct injection of drugs into the subarachnoid space

$$\frac{\rho_{\mathrm{drug}} - \rho_{\mathrm{CSF}}}{\rho_{\mathrm{CSF}}} \simeq 10^{-3}$$

$$\frac{\nu_{\mathrm{CSF}}}{\kappa_{\mathrm{drug}}} = S \simeq 1000$$





Injection methods:
- Single dose
- Continuous dose

Target locations:
- Along the spinal cord
- Brain

Can Shear-Enhanced Axial Diffusion contribute significantly to solute dispersion?

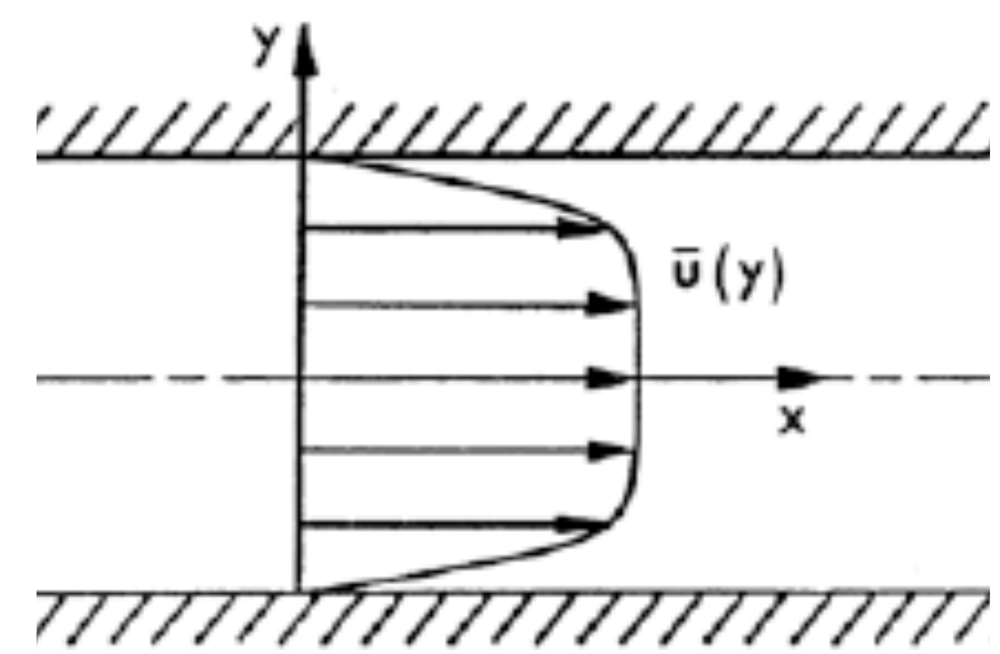
- G.I. Taylor. Dispersion of soluble matter in solvent flowing slowly through a tube. *Proceedings Of The Royal Society Of London Series A-Mathematical And Physical Sciences*, 219(1137):186–203, 1953.
- E. J. Watson. Diffusion in oscillatory pipe-flow. *Journal Of Fluid Mechanics*, 133(AUG):233–244, 1983.

molecular diffusivity

augmentation factor $10 \lesssim R \lesssim 100$

$$D_{eff} = \kappa(1+R)$$

h



$$\frac{h_c^2}{\kappa} = \underbrace{\left(\frac{h_c^2\omega}{\nu}\right)}_{\alpha^2 \sim 1} \underbrace{\left(\frac{\nu}{\kappa}\right)}_{S} \omega^{-1} = \alpha^2 S \omega^{-1}$$

The coupling between oscillatory shear and transverse diffusion is effective when $\frac{h_c^2}{\kappa} \sim \omega^{-1}$

$S \sim 1$ (gases) ➡ $\frac{h_c^2}{\kappa} \sim \omega^{-1}$ ➡ Significant Taylor dispersion (e.g. High-frequency ventilation)

$S \gg 1$ (liquids) ➡ $\frac{h_c^2}{\kappa} \gg \omega^{-1}$ ➡ Negligible Taylor dispersion (e.g. ITDD applications, $S \simeq 1000$)

Solute dispersion in the spinal canal

$$\frac{\partial c}{\partial t} + \varepsilon \mathbf{v} \cdot \nabla c = \frac{1}{\alpha^2 S} \frac{\partial^2 c}{\partial y^2}; \quad \frac{\partial c}{\partial y} = 0 \text{ at } y = 0, h \quad \begin{cases} c = c_0(\mathbf{x}, t, \tau) + \varepsilon c_1(\mathbf{x}, t, \tau) + \cdots \\ \mathbf{v} = \mathbf{v}_0(\mathbf{x}, t) + \varepsilon \mathbf{v}_1(\mathbf{x}, t) + \cdots \end{cases}$$

where

$$\tau = \varepsilon^2 t$$

$c_0(\mathbf{x}, \tau)$:

- $S \sim \varepsilon^{-2}$ ➡

$$\frac{\partial c_0}{\partial \tau} + u_L \frac{\partial c_0}{\partial x} + v_L \frac{\partial c_0}{\partial y} + \frac{w_L}{\ell} \frac{\partial c_0}{\partial s} = \frac{1}{\alpha^2 \varepsilon^2 S} \frac{\partial^2 c_0}{\partial y^2}$$

- $1 \ll S \ll \varepsilon^{-2}$ ➡

$$\frac{\partial c_0}{\partial \tau} + \left(\int_0^1 u_L \, \mathrm{d}\eta \right) \frac{\partial c_0}{\partial x} + \left(\int_0^1 w_L \, \mathrm{d}\eta \right) \frac{1}{\ell} \frac{\partial c_0}{\partial s} = 0$$

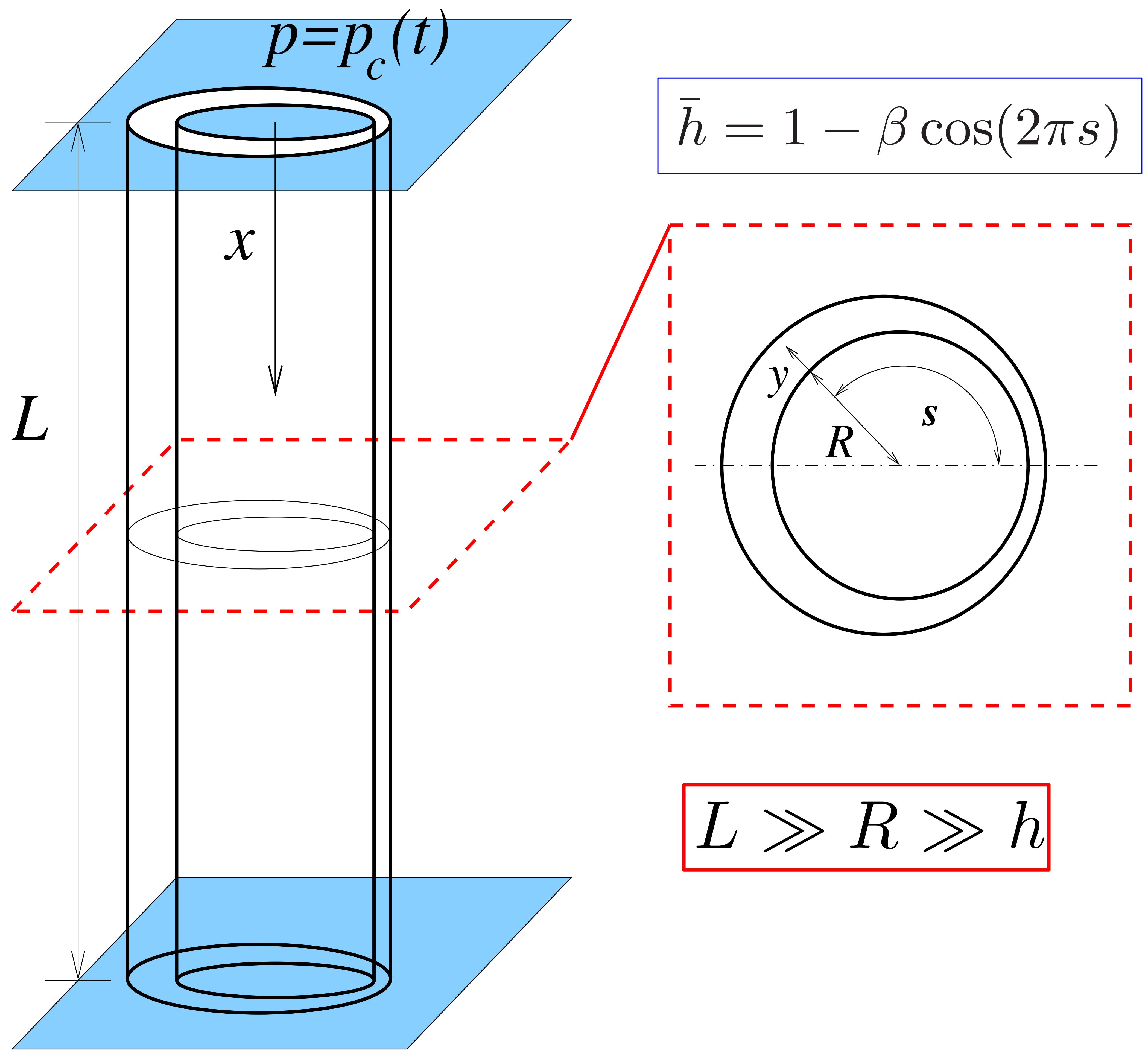
- $S \sim 1$ ➡

$$\bar{h} \frac{\partial c_0}{\partial \tau} + \bar{h} \left(\int_0^1 u_L \, \mathrm{d}\eta \right) \frac{\partial c_0}{\partial x} + \bar{h} \left(\int_0^1 w_L \, \mathrm{d}\eta \right) \frac{1}{\ell} \frac{\partial c_0}{\partial s} = \frac{1}{\ell} \frac{\partial}{\partial x} \left(\ell D_{xx} \frac{\partial c_0}{\partial x} \right) + \frac{1}{\ell} \frac{\partial}{\partial x} \left(D_{xs} \frac{\partial c_0}{\partial s} \right) + \frac{1}{\ell} \frac{\partial}{\partial s} \left(D_{sx} \frac{\partial c_0}{\partial x} \right) + \frac{1}{\ell} \frac{\partial}{\partial s} \left(D_{ss} \frac{1}{\ell} \frac{\partial c_0}{\partial s} \right),$$

- **Convective transport driven by the time-averaged Lagrangian velocity is found to be important for all values of the solute Schmidt number**
- **Taylor dispersion, which is important for solutes Schmidt numbers of order unity, is negligible for ITDD drugs.**

Application to a Simplified Canonical Problem

The spinal canal is modeled as an annular canal with uniform elastic properties bounded between two parallel circular cylinders whose radii differ by a small amount h_c and their axes are displaced by βh_c



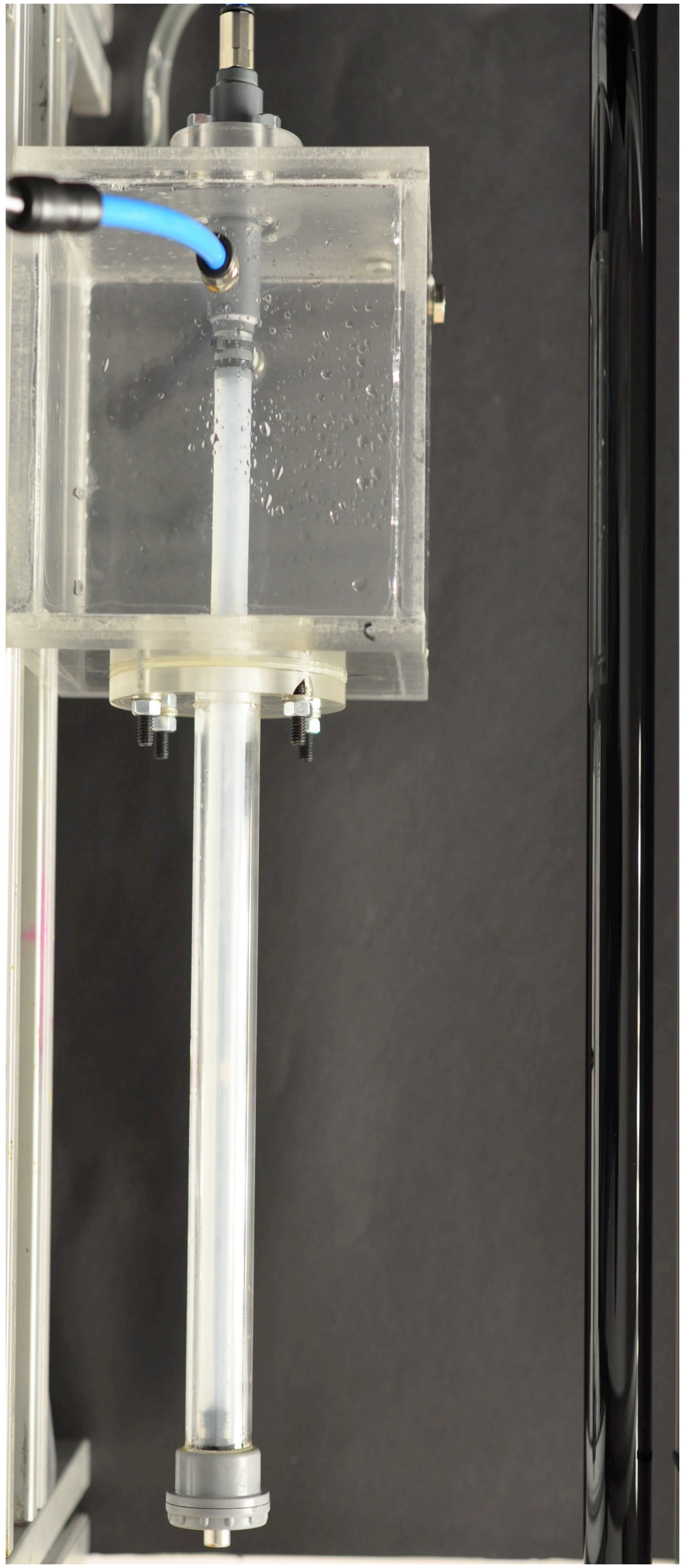
$\bar{h} = 1 - \beta \cos(2\pi s)$

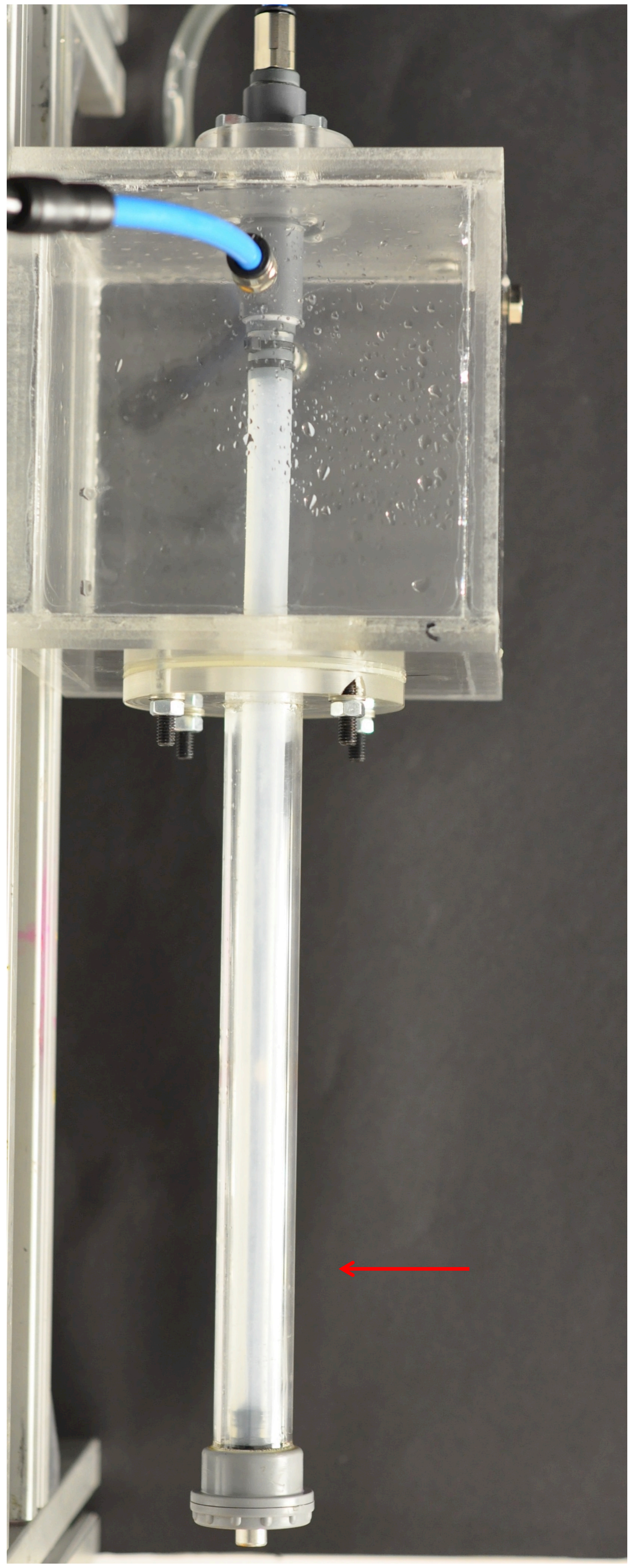
$L \gg R \gg h$

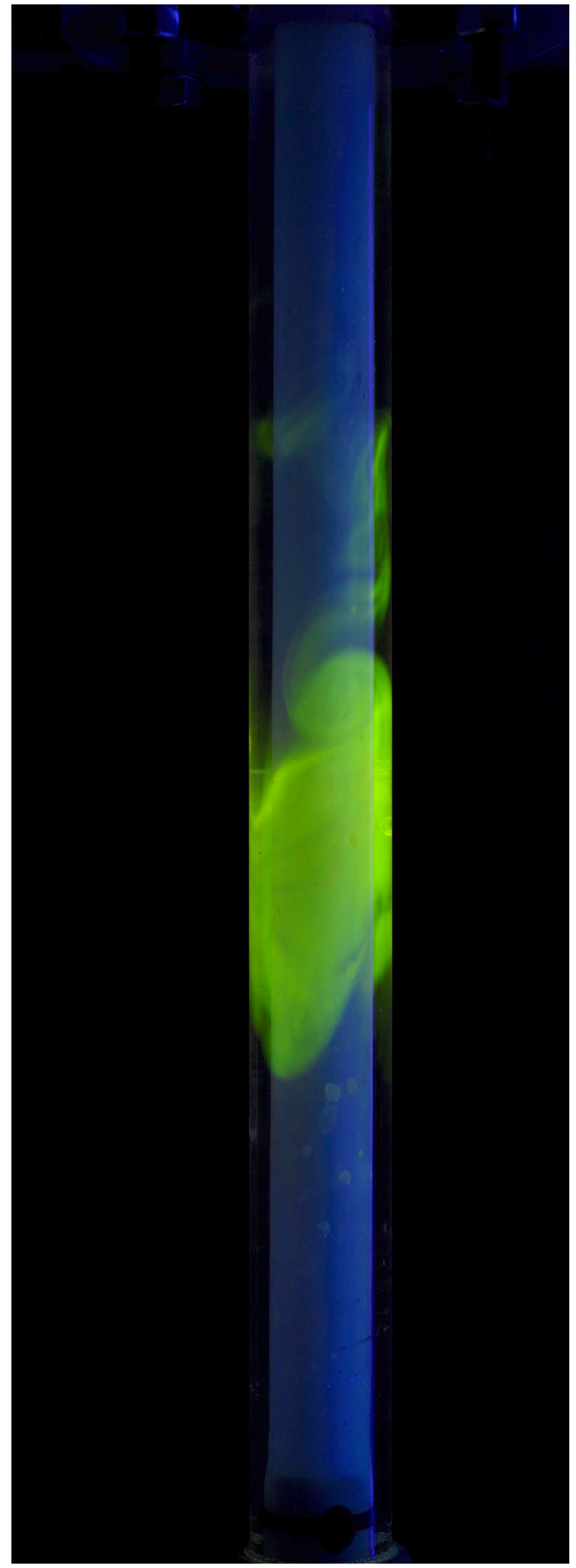
Experimental setup

- Cranial vault modeled as a tank made of rigid plexiglass in which we impose a sinusoidal pressure pulsation with a peristaltic pump with frequency of 60 cycles/minute.

- Elastic outer cylindrical tube and rigid inner rod (concentric and eccentric)

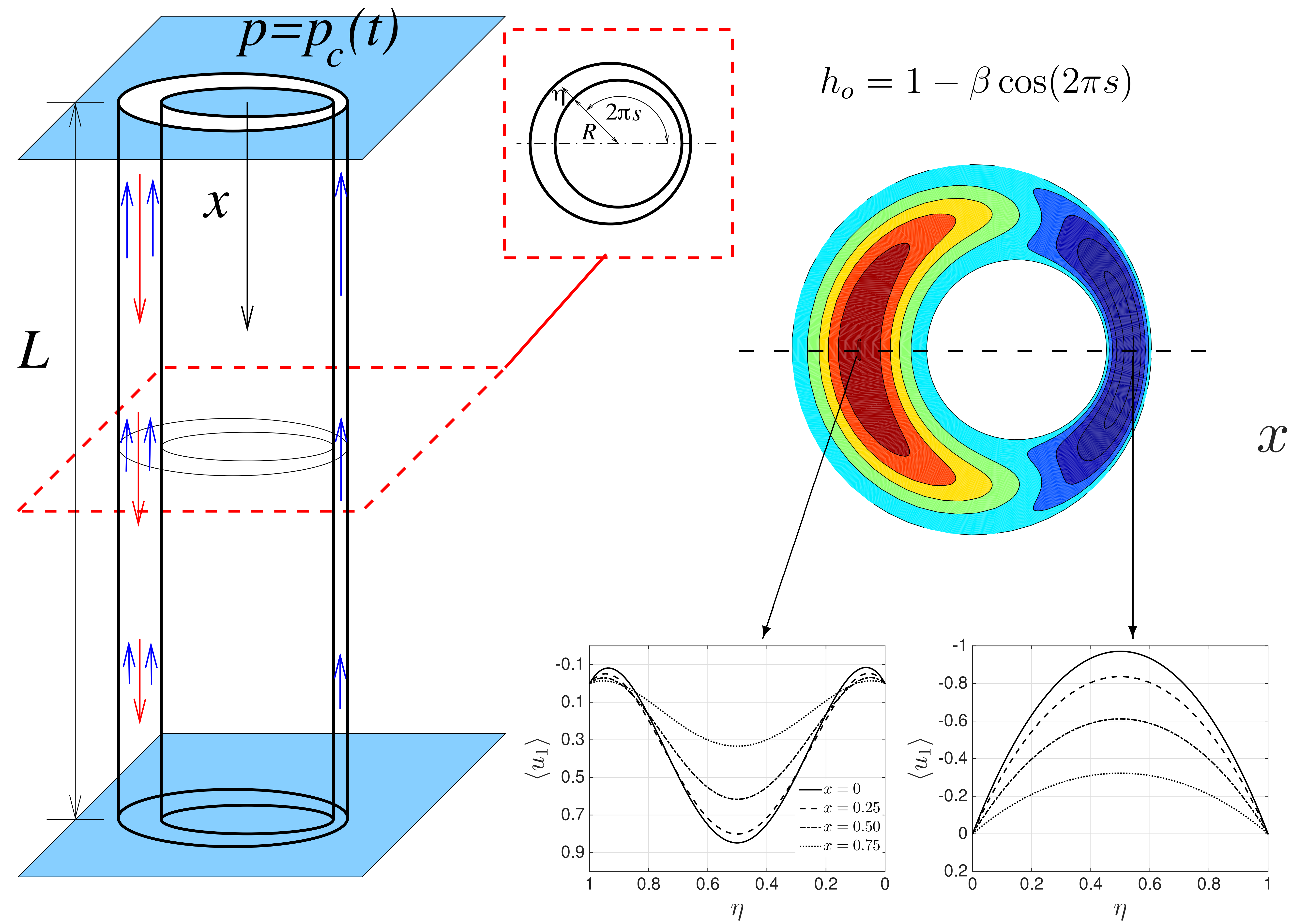






Time frame evolution of fluorescent dye during 20 minutes (compressed in 10 sec). Each frame in the movie is the florescence intensity averaged over 10 images acquired every 0.1s (3s)

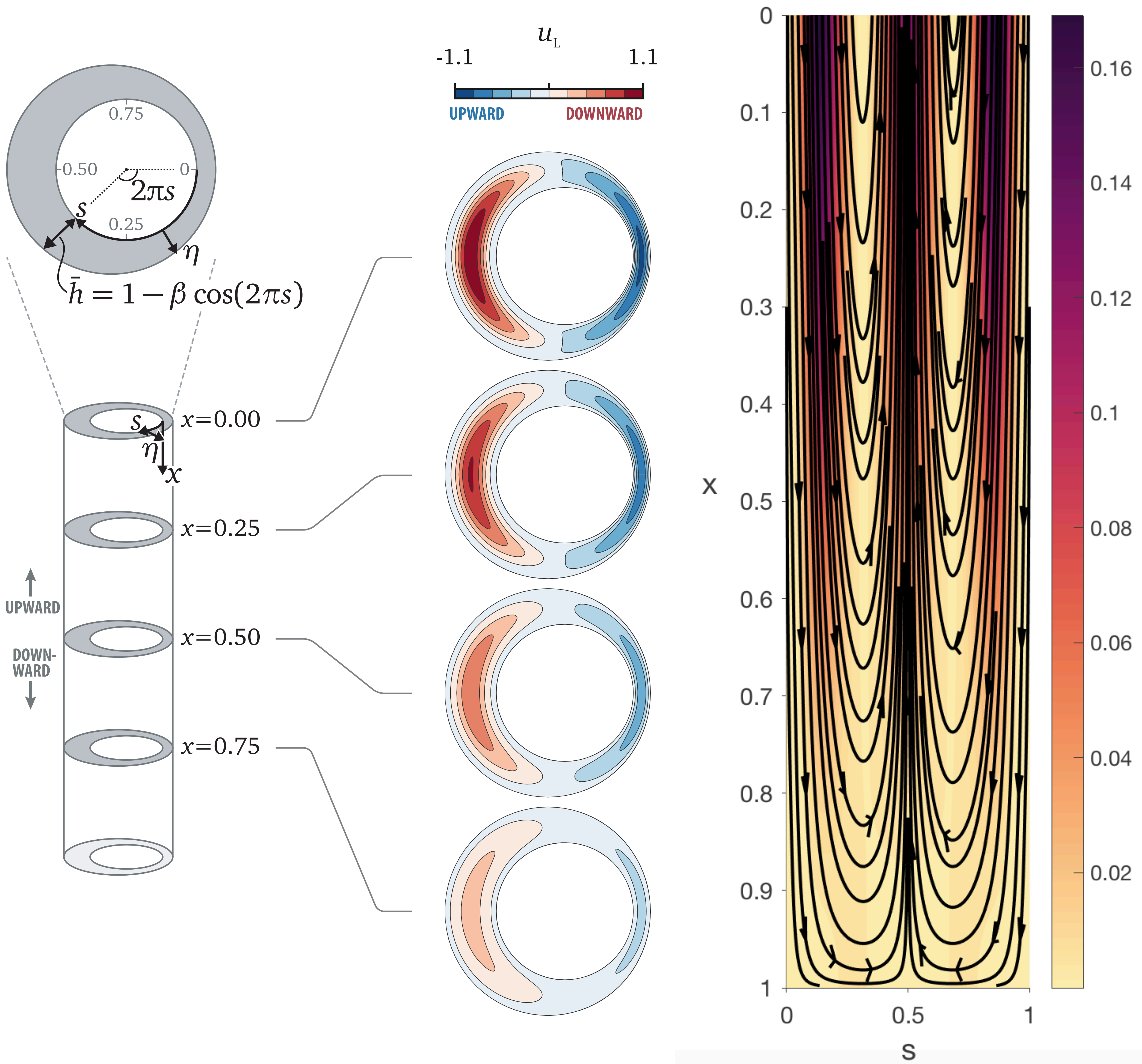
TIME-AVERAGED LAGRANGIAN VELOCITY



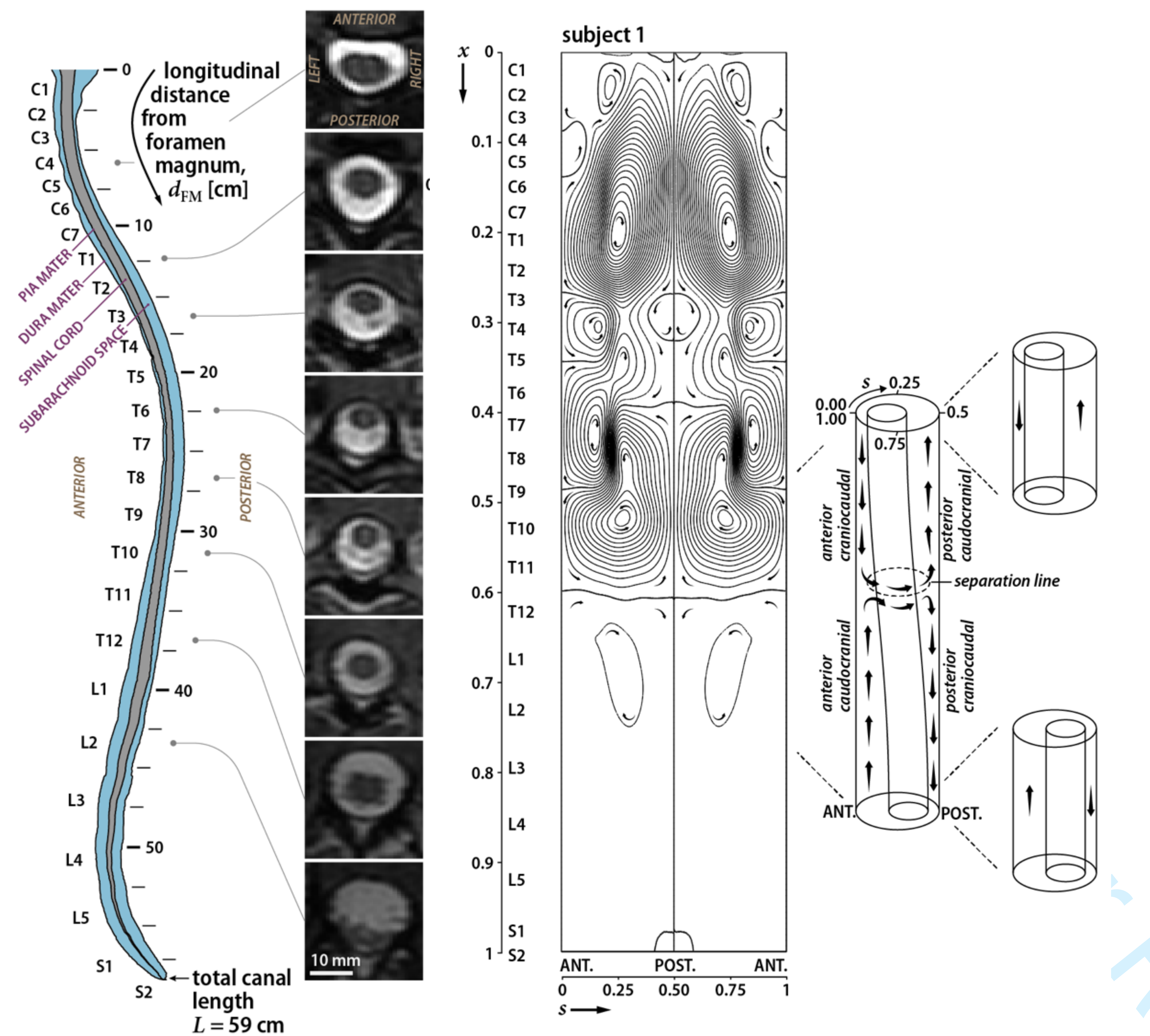
$$\varepsilon u_c = \varepsilon^2 \omega L \sim 1 \text{ cm/min}$$

Consistent with the measured magnitude of the dispersion velocity

Idealized model



Real anatomy



Conclusions & future work

Our preliminary efforts to develop a patient-specific predictive tools for ITDD dispersion have revealed that the time-averaged Lagrangian motion exhibits closed recirculating regions that depend on the subject anatomy and posture.

Connectivity between adjacent recirculating region may be a associated with enhanced diffusion by micro-anatomical features or buoyancy-driven motion resulting from small density differences between the drug and the CSF.

$$\Delta\rho = (\rho - \rho_d) \sim 10^{-3}\rho \ll \rho \quad \begin{cases} \dfrac{O(\Delta\rho\,\mathbf{g})}{O(\rho\,\partial\mathbf{v}/\partial t)} = \dfrac{(\rho-\rho_d)}{\rho}\dfrac{g}{\varepsilon\omega^2 L} \sim \varepsilon \\ Ri = \dfrac{\Delta\rho\,\mathbf{g}}{\rho\mathbf{v}\cdot\nabla\mathbf{v}} = \dfrac{g(\rho-\rho_d)/\rho}{\varepsilon^2\omega^2 L} \sim 1 \end{cases}$$

$$\frac{1}{\ell}\frac{\partial}{\partial x}(\ell u) + \frac{\partial v}{\partial y} + \frac{1}{\ell}\frac{\partial w}{\partial s} = 0,$$

$$\frac{\partial u}{\partial t} + \varepsilon\left[\frac{1}{\ell}\frac{\partial}{\partial x}(\ell u^2) + \frac{\partial}{\partial y}(uv) + \frac{1}{\ell}\frac{\partial}{\partial s}(uw)\right] = -\frac{\partial p'}{\partial x} + \frac{1}{\alpha^2}\frac{\partial^2 u}{\partial y^2} - \varepsilon Ri\; c,$$

$$\frac{\partial w}{\partial t} + \varepsilon\left[\frac{\partial}{\partial x}(uw) + 2\frac{uw}{\ell}\frac{\partial \ell}{\partial x} + \frac{\partial}{\partial y}(vw) + \frac{1}{\ell}\frac{\partial}{\partial s}(w^2)\right] = -\frac{1}{\ell}\frac{\partial \hat{p}}{\partial s} + \frac{1}{\alpha^2}\frac{\partial^2 w}{\partial y^2},$$

$$\frac{\partial c}{\partial t} + \varepsilon\left(u\frac{\partial c}{\partial x} + v\frac{\partial c}{\partial y} + \frac{w}{\ell}\frac{\partial c}{\partial s}\right) = \frac{\varepsilon^2}{\alpha^2\sigma}\frac{\partial^2 c}{\partial y^2},$$