

# MODELLING OF THE ROLE OF GLIAL CELLS IN CEREBRAL INTERSTITIAL FLUID MOVEMENT

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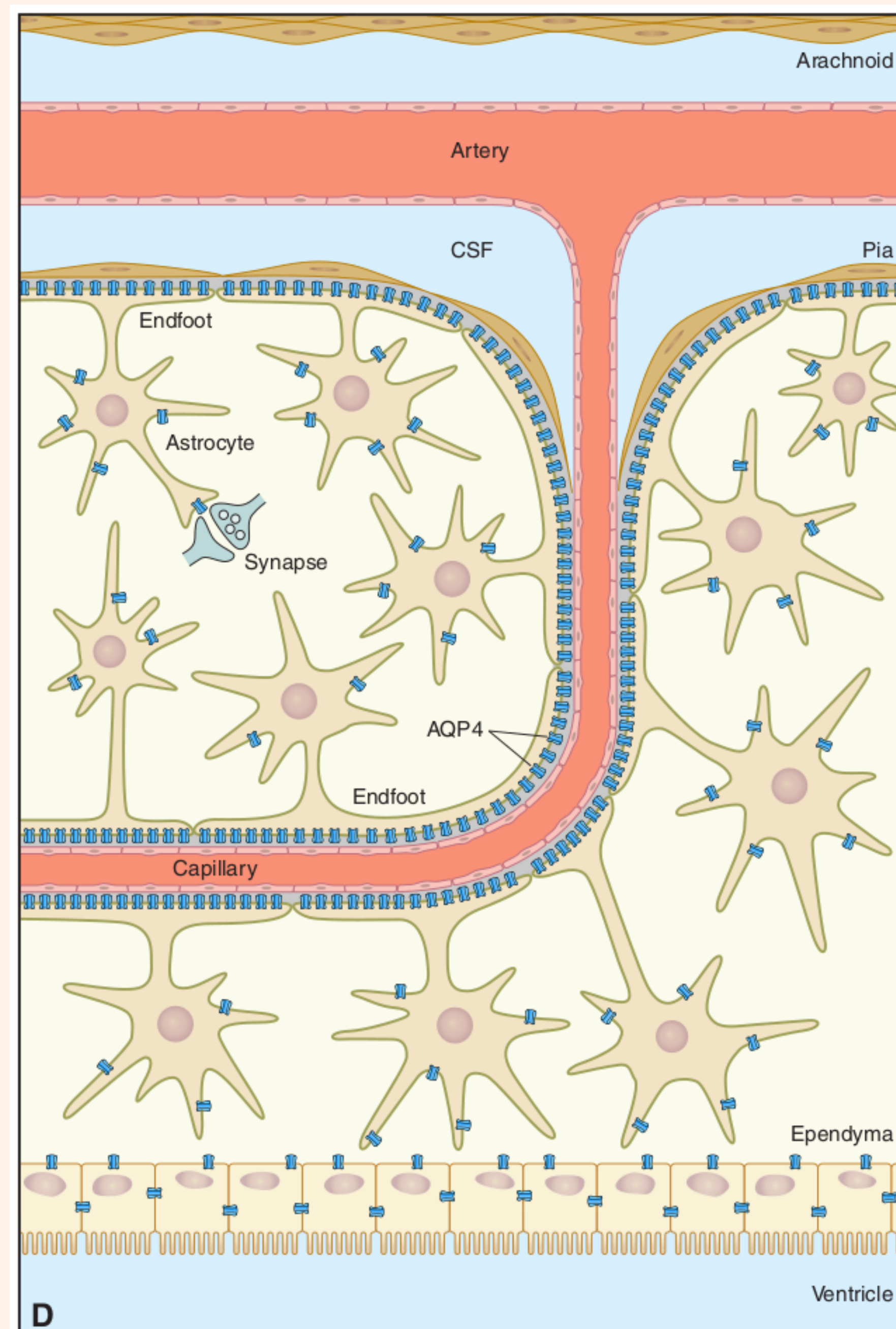
## PHYSIOLOGY

### CEREBRAL WATER HOMEOSTASIS

**There are still open questions related to how astrocyte water dynamics affect the overall water flow in the brain and removal of metabolic waste and solutes.**

Within the endfoot barrier of astrocytes near the perivascular spaces surrounding the blood vessels, there is a high concentration of the water channel membrane protein aquaporin-4 (AQP4). The water transport through AQP4 is driven by osmotic pressure gradients, primarily regulated by movement of ions in the brain tissue.

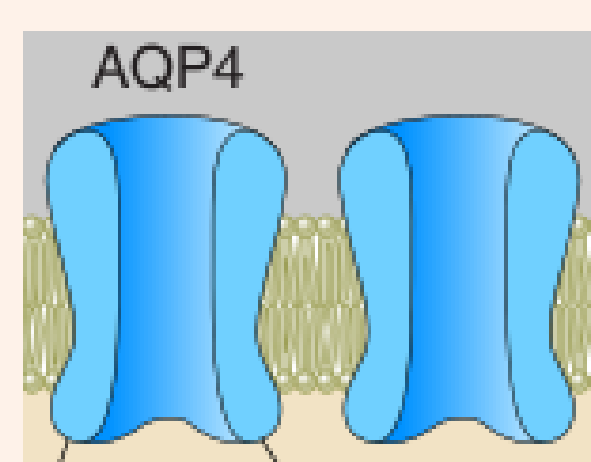
Traditional techniques, such as digital imaging, struggle to give insight due to both technical and ethical challenges. Mathematical and numerical modelling could give new insight.



[E. A. Nagelhus et al, 2013]

### AQP4

Aquaporin-4 (AQP4) is a channel membrane protein and is the most prevalent aquaporin channel in the central nervous system. The AQP4 proteins form structures in the cell membranes allowing for highly efficient water transport.



## MODELLING

### MATHEMATICAL MODELS

Models for astrocyte dynamics at cellular level commonly take the form of systems of ODEs and/or PDEs on the general form:

Find the ion concentration  $[k]_r$  for each ion specie  $k \in K$ , the electrical potential  $\phi_r$  and the volume fraction  $\alpha_r$  for each compartment  $r = I, E$  such that:

$$\begin{aligned} \frac{\partial \alpha_r}{\partial t} &= \pm \gamma_m w_m, \quad \alpha_E + \alpha_I = 1 \\ \frac{\partial (\alpha_r [k]_r)}{\partial t} + \nabla \cdot \mathbf{J}_r^k &= \pm \gamma_m J_m^k \\ \sum_k z_k (\nabla \cdot \mathbf{J}_r^k \pm \gamma_m J_m^k) &= 0 \end{aligned}$$

where

$$\mathbf{J}_r^k = -D_r^k (\nabla [k]_r + \frac{z_k F}{RT} [k]_r \nabla \phi_r).$$

Models that additionally address mechanical variables such as [fluid velocity](#) and [hydrostatic pressure](#), e.g. [\[Y. Mori, 2015\]](#), are not well explored numerically.

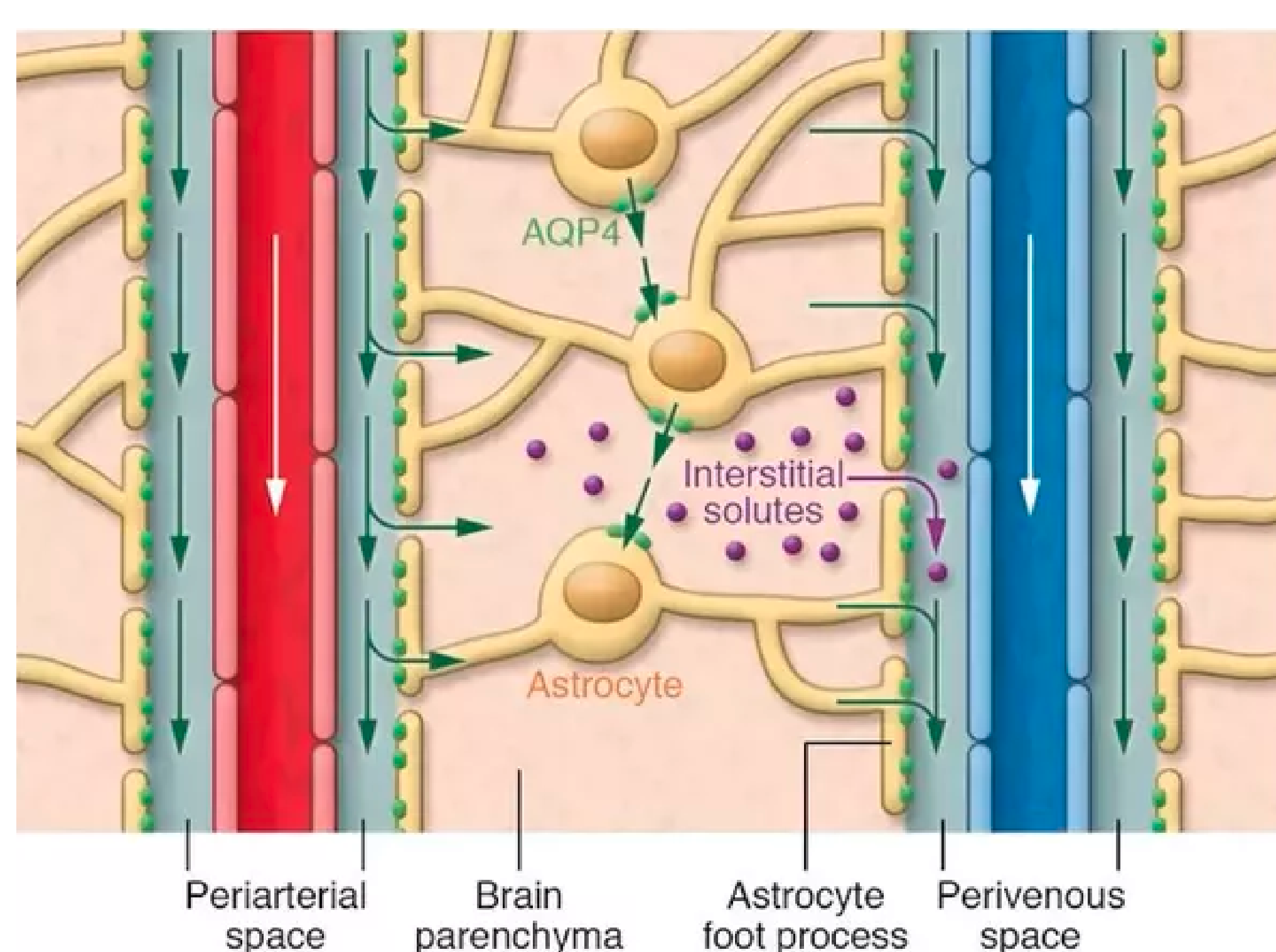
### NUMERICAL METHODS

**We aim to develop new mathematical and numerical models across scales to study the effects of osmotic pressure and microscopic fluid flow in brain water homeostasis.**

- Design and analyze numerical schemes for existing mathematical models connecting mechanical and electrochemical variables at cellular level
- Extend model to couple glial dynamics at cellular level with fluid flow at perivascular level and develop corresponding numerical schemes
- The finite element method (FEM) in space and an implicit scheme in time. The new schemes should ideally be robust, efficient and property preserving

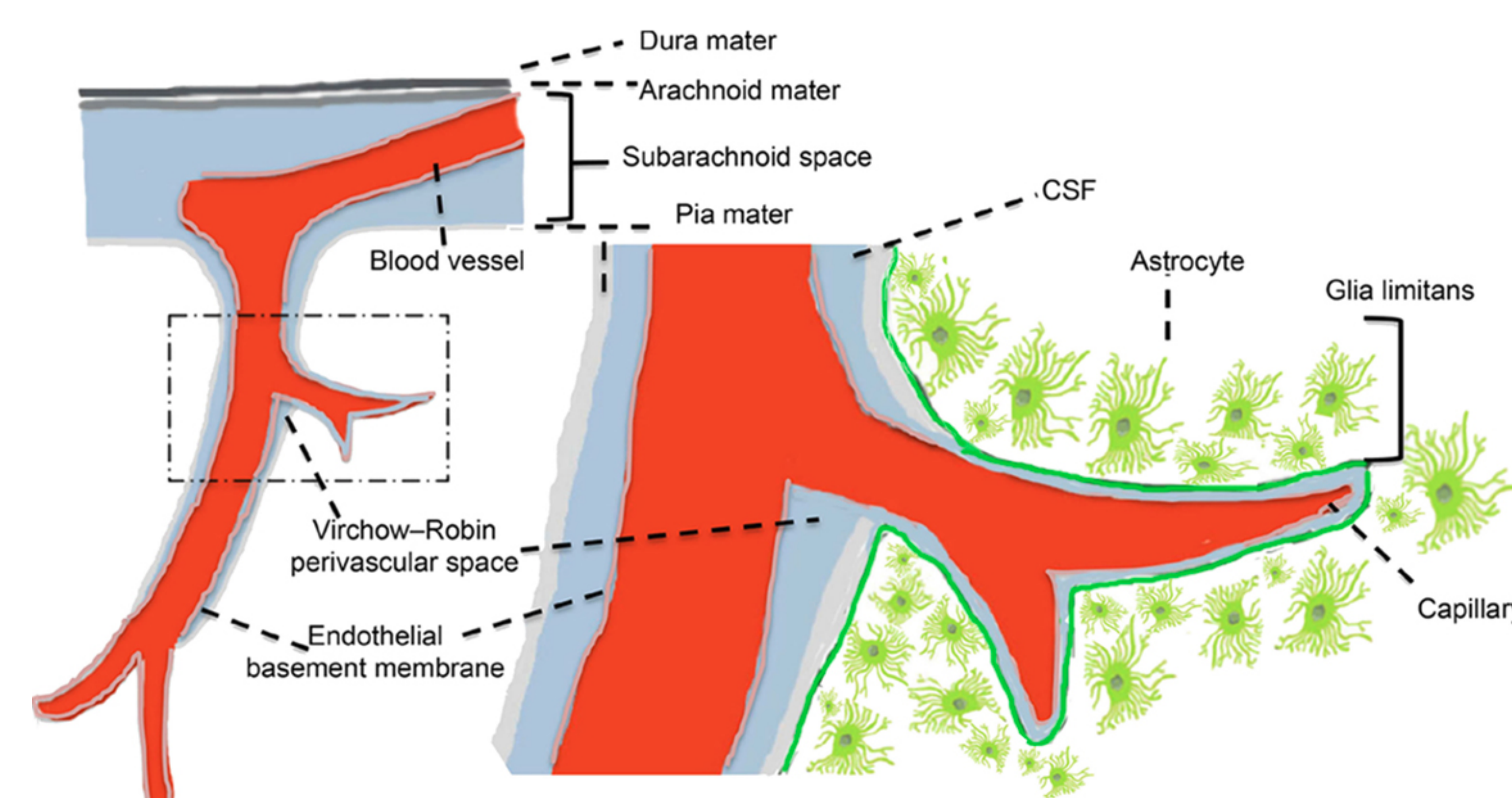


**How does astrocytic water dynamics affect the flow and transport of metabolic waste and solutes within the extracellular space?**



[Quora, 2017]

**Could the osmotic pressure generated by ion concentration gradients be a driving force for flow in perivascular spaces?**



[R. Khoroshchi et al, 2015]



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This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under grant agreement 714892.