

A Preliminary Study On Estimating Amyloid-beta Clearance Efficiency in the Perivascular Space With Electro-osmotic Effects

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INTRODUCTION

- The glymphatic system clears **amyloid-beta (A β)** through CSF-ISF exchange along perivascular spaces (PVS)[1], and its impairment drives A β accumulation in Alzheimer's disease. While computational fluid dynamics (CFD) studies of CSF flow have proliferated[2], the critical **electro-osmotic and surface-charge effects** remain neglected in current models.
- A β is an anionic polyelectrolyte**, and the brain extracellular matrix (ECM) carries a strong fixed negative charge(heparan-sulfate & chondroitin-sulfate proteoglycans) that forms an electrical double layer (EDL)[3]. **We postulate** that streaming potentials and surface-charge interactions act as auxiliary forces for A β clearance, and **we aim to quantify their contribution** with respect to physiological tissue charge[4].

METHODS

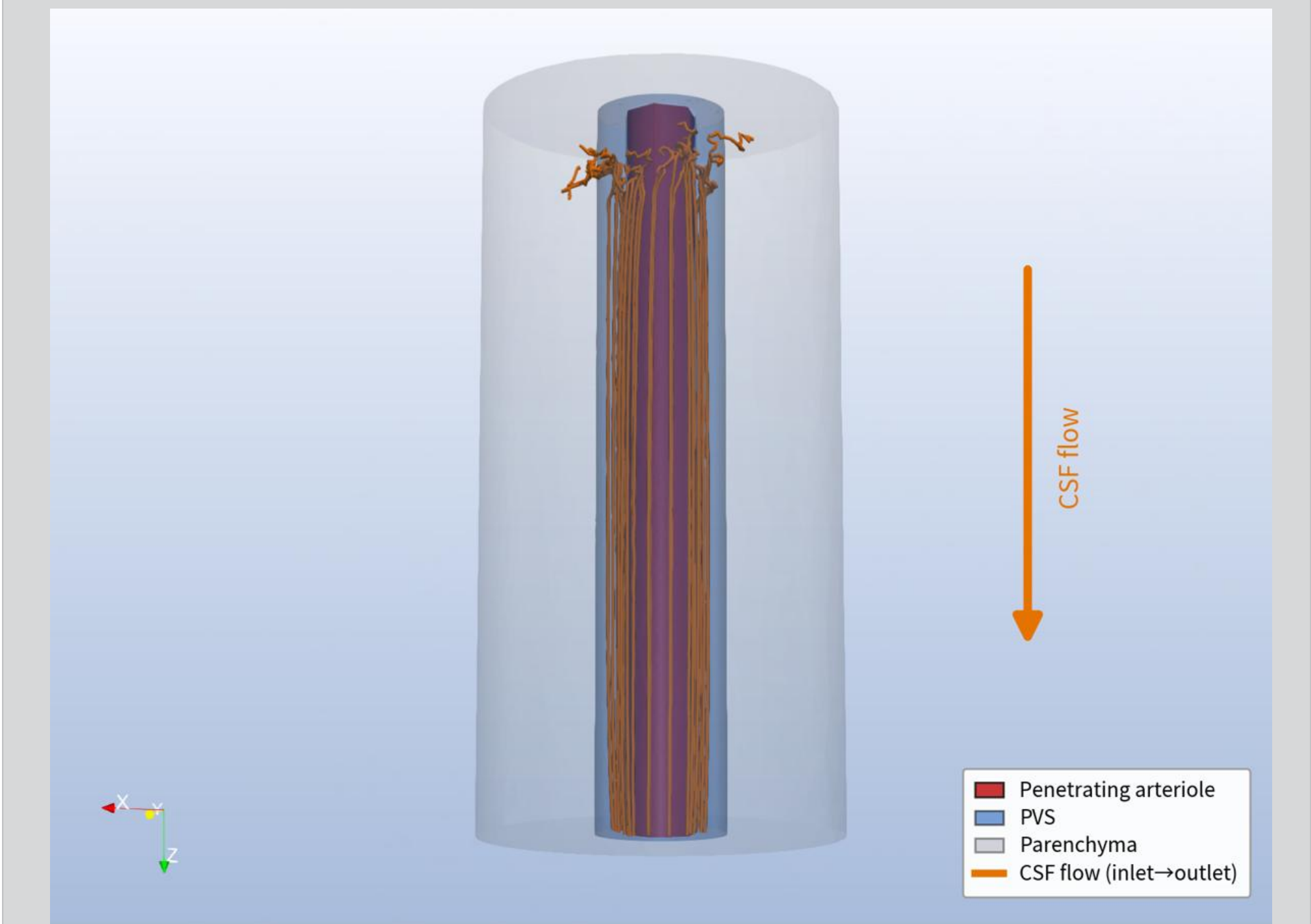


Fig 1. 3-D single-vessel model — a cortical penetrating arteriole sheathed by an annular PVS (8 μ m) within brain parenchyma. Streamlines show CSF flow along the PVS.

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RESULTS & CONCLUSIONS

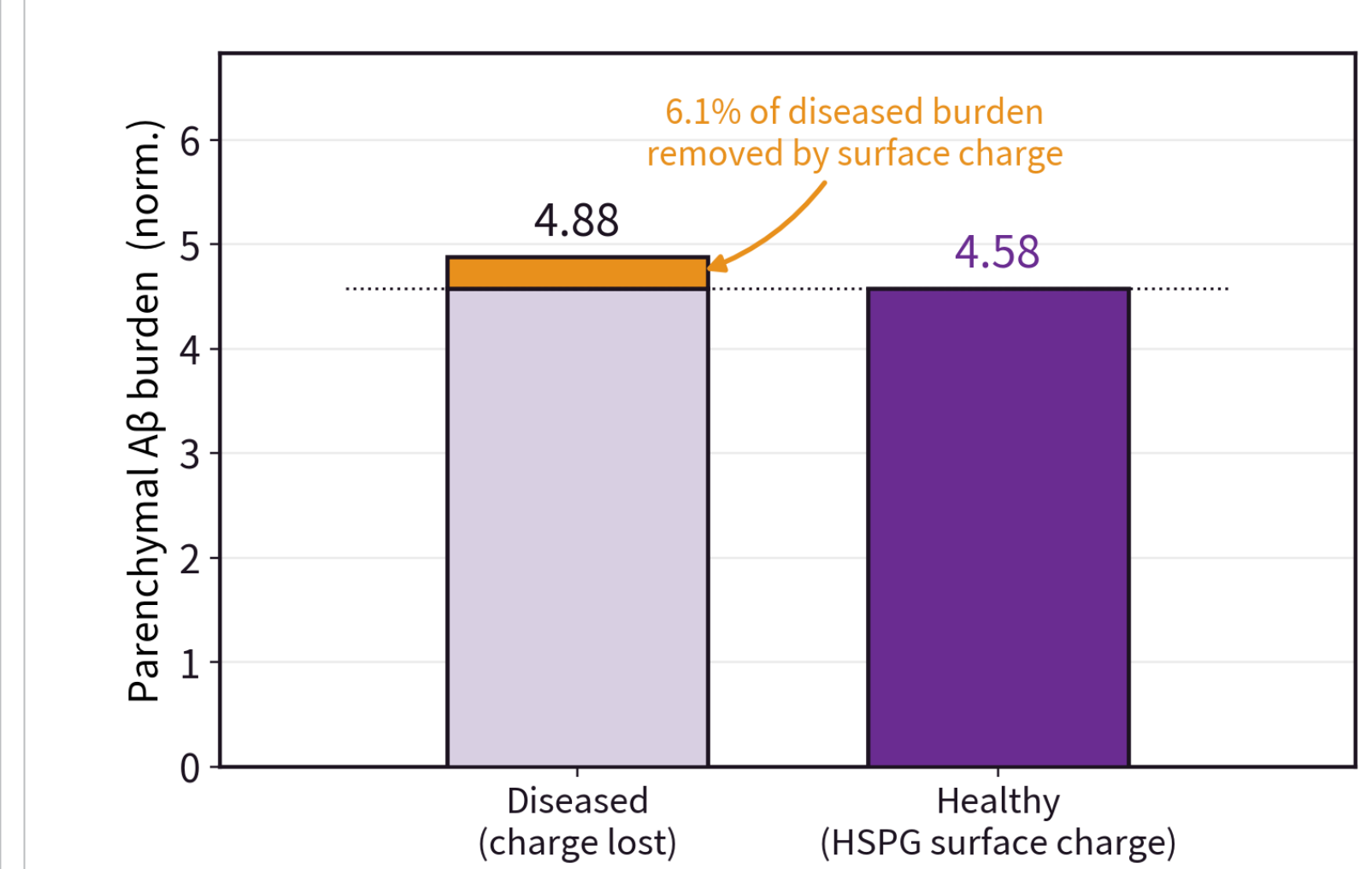


Fig 2. Steady-state parenchymal A β burden (A β retained in the parenchyma; generation = clearance, so higher burden = slower net removal). HSPG surface charge removes 6.1% of the diseased burden (orange slice).

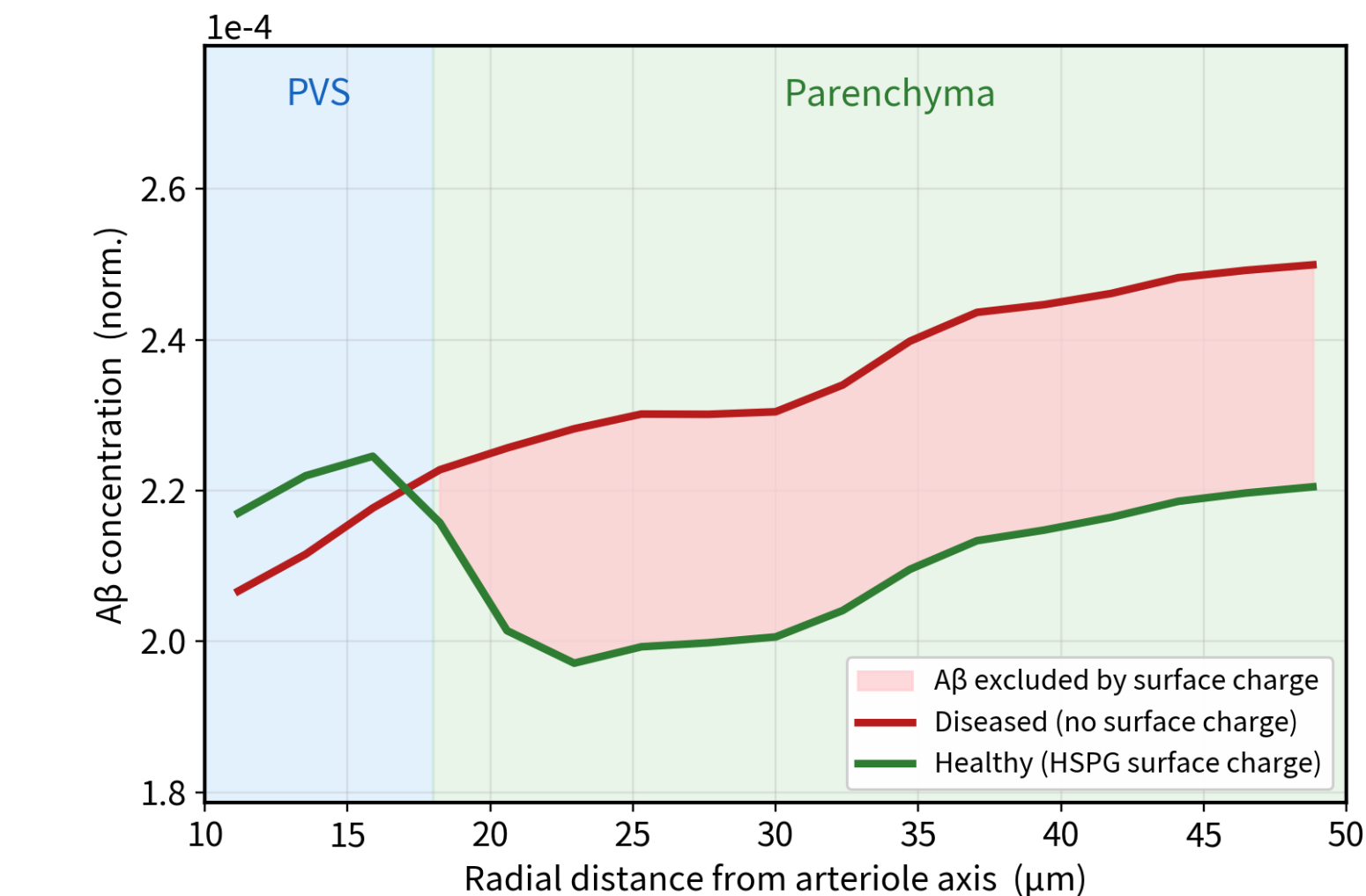


Fig 3. Radial A β concentration. The two states overlap in the PVS (no exclusion) but diverge across the parenchyma — the shaded gap is A β **excluded by surface charge**.

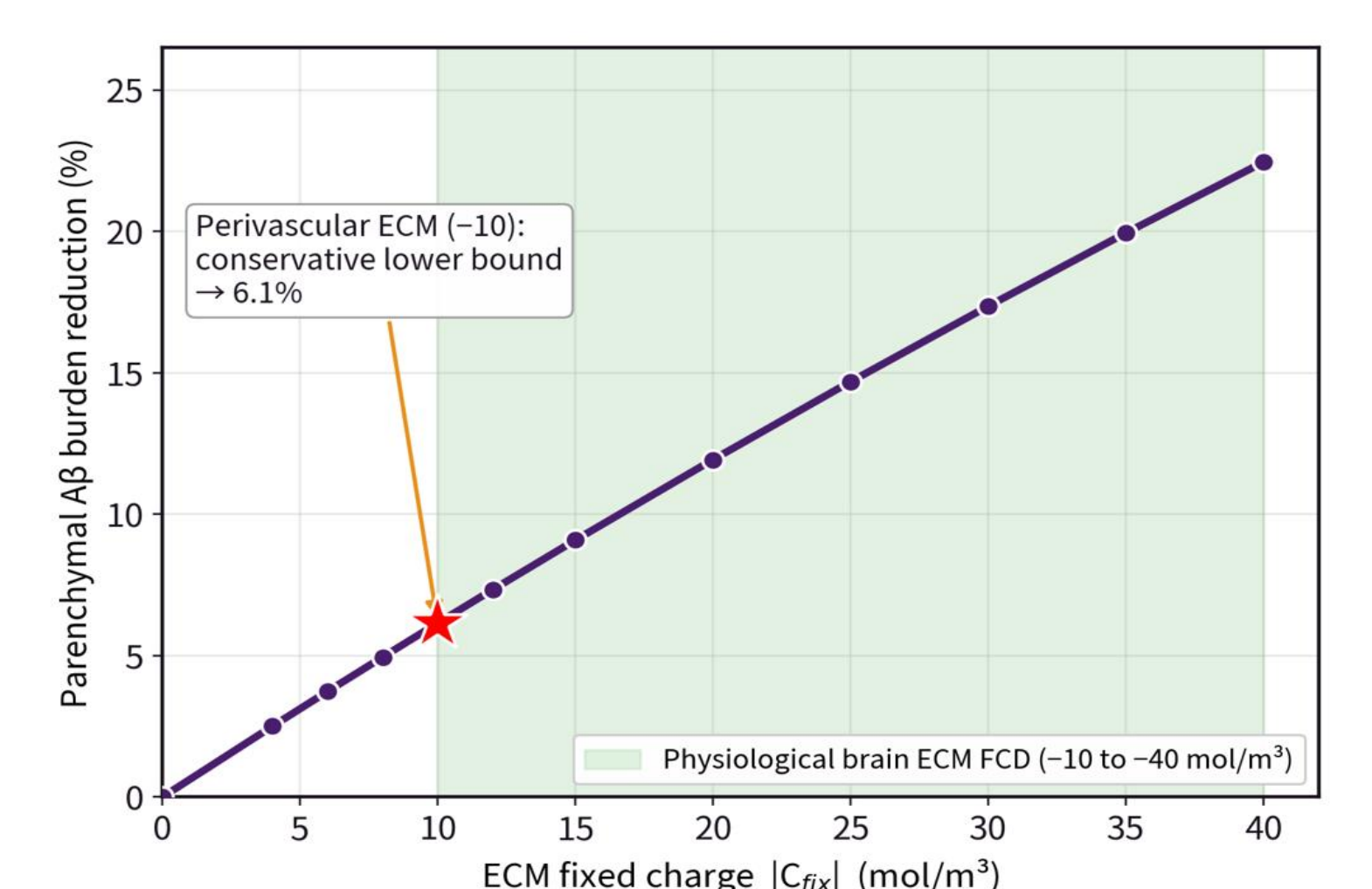


Fig 4. Parenchymal A β burden reduction scales with ECM fixed charge (6.1 % at the perivascular value -10); in aging/AD, HSPG loss collapses the charge (ζ and FCD together) $\rightarrow$ reduction $\rightarrow 0$.

Quantitative findings

- Charged ECM (perivascular Fixed Charge Density(FCD) -10 mol/m^3) retains **6.1 % less A β** than uncharged ($\approx 6\sim 22 \%$ across the physiological range).
- Mechanism:** electrostatic repulsion of anionic A β ($z = -3$) drives the **parenchyma $\rightarrow$ PVS** step; largest where hydraulic flow is limited.
- ζ and fixed charge are the same HSPG charge — both lost in aging/AD (heparanase/MMP) $\rightarrow$ exclusion barrier collapses.

Conclusions

- HSPG surface charge contributes $\approx 6.1 \%$ to perivascular A β clearance — via **electrostatic exclusion**, not bulk-velocity enhancement.
- Greatest in deep, low-flow regions $\rightarrow$ brain tissue **electrical properties as a therapeutic target**.
- Idealized porous-medium PVS: interpretation applies where the PVS is ECM-filled.

Model Geometry & Mesh

- Concentric cylinder architecture**
 - Arteriole lumen ($R \approx 10 \mu\text{m}$)
 - Annular PVS (width $8 \mu\text{m}$)
 - Parenchyma (outer $R \approx 50 \mu\text{m}$)
- Conformal tetrahedral mesh**
- $\approx 56,000$ nodes

Electro-Hydrodynamic Multiphysics

- Brinkman flow (fluid dynamics)**
 - Region-dependent permeability (fast PVS / slow ECM)
 - Vasodilation-driven; $\text{CSF} \approx 20 \mu\text{m/s}$
- Poisson (electrostatics)**
 - Streaming potential from the EDL ($\zeta = -20 \text{ mV}$)
- Nernst-Planck (mass transport)**
 - Anionic A β ($z = -3$)
 - Hindered diffusion/convection (Renkin)
 - Surface-charge partition (K_D) + electromigration

Clearance Setup & Boundary Conditions

- Source / sink**
 - Uniform A β generation in parenchyma $\rightarrow$ cleared via PVS
- Boundary**
 - Clean CSF inflow ($C = 0$)
 - mass-conservative (balance = 1.00)
 - Outer parenchyma boundary: Zero flux (Symmetry)
- Surface charge**
 - ECM FCD at physiological brain range (-10 to -40 mol/m^3)
 - ζ and FCD = same HSPG charge, lost together in aging/AD

REFERENCES