# Supplementary Data

## Supplementary Appendix. Material Models and Properties

Brain tissue and axonal fiber were modeled using anisotropic hyper-viscoelastic materials[1–3]. For the brain tissue matrix material, the isotropic hyperelastic strain energy density function is an isotropic expression of the Holzapfel-Gasser-Ogden (HGO) model [4] as follows:

$$W = \frac{G}{2}\left(\tilde{I}_1 - 3\right) + K\left(\frac{J^2 - 1}{4} - \frac{1}{2}\ln(J)\right) + \frac{k_1}{2k_2}\left(e^{k_2 \tilde{E}_a{}^2} - 1\right) \quad (1)$$

$$\tilde{E}_a = \frac{1}{3}\left(\tilde{I}_1 - 3\right) \quad (2)$$

Where $\tilde{I}_1$ is the first invariant of the isochoric right Cauchy-Green deformation tensor and $J = \det F$ is the volume change ratio. G is the shear modulus, K is the bulk modulus, $k_1$ is a stress-like parameter, and $k_2$ is a dimensionless parameter. The strain energy density function for the axonal fiber is also based on the Holzapfel-Gasser-Ogden (HGO) model[4] and formulated as:

$$W = \frac{k_1}{2k_2}\left(e^{k_2 \tilde{E}_a{}^2} - 1\right) \quad (3)$$

$$\tilde{E}_a = \kappa\left(\tilde{I}_1 - 3\right) + (1 - 3\kappa)\left(\tilde{I}_{4a} - 1\right) \quad (4)$$

$$\tilde{I}_{4a} = \tilde{C}: n_{0a} \otimes n_{0a} \quad (5)$$

Which . $\tilde{C}$ is the deviatoric component of the right Cauchy–Green deformation tensor and $n_{0a}$ is the fiber bundle direction unit vector. The dimensionless structure parameter $\kappa$ accounts for the orientation distribution of the axons in a voxel-scale fiber bundle and can be related with FA values of the fiber bundle elements through equation (6)[5,6], by assuming similarity between mechanical anisotropy and diffusion anisotropy.

$$\kappa = \frac{1}{2}\frac{-6 + 4FA^2 + 2\sqrt{3FA^2 - 2FA^4}}{-9 + 6FA^2} \quad (6)$$

For the lower limit of $\kappa$ ($\kappa = 0$ , equivalently, $FA = 1$), axons are perfectly aligned, and for the upper limit of $\kappa$ ($\kappa = \frac{1}{3}$ , equivalently, $FA = 0$), axons are randomly oriented and isotopically distributed. The temporal response of deviatoric stress was modeled using a quasi-linear viscoelastic (QLV) mathematical framework[7], as the volumetric behavior was assumed to be independent of time.

$$\sigma^d(t) = \int_0^t \left[G_\infty + \sum_{i=1}^{n} G_i e^{-\frac{t-t'}{\tau_i}}\right]\frac{\partial \sigma_e^d}{\partial t'}dt' \quad (7)$$

Where $\sigma_e^d$ is the instantaneous deviatoric elastic response and G is the normalized or reduced relaxation function. A Prony series with one-time constant ($n = 1$) was chosen to model the relaxation behavior[8]. $G_\infty$ and $G_i$ are the steady-state coefficient and normalized relaxation coefficients of the corresponding time decades respectively, and $\tau_i$ are the decay time constants.

To determine the material properties of axonal fiber bundle, the effective stiffness ratio of $R_v$ between the fiber constitutive model and the brain matrix constitutive model was used with the following formulation:

$$R_v = \frac{R}{\gamma_V}\ , \qquad R = \frac{G_{fiber} - G_{matrix}}{G_{matrix}} \quad (8)$$

Where $\gamma_V$ and $\frac{G_{fiber}}{G_{matrix}}$ are the volume fraction ratio and the stiffness ratio of axonal fiber bundle to the brain tissue matrix, respectively. In the HGO material model used in previous studies, the strain energy density functions for the axonal fiber and isotropic brain matrix are coupled and therefore the same volume sizes were considered for both. In this study, the $R_v$ ratio was used to modify the original HGO material model to accommodate for potential excessive material stiffness and volume redundancy associated with the embedded element modeling approach. The stiffness ratio of 3 ($\frac{G_{fiber}}{G_{matrix}} = 3$) and axonal fiber volume fraction of 0.5 ($\gamma_V = 0.5$) experimentally identified by Arbogast, K.B. and Margulies, S.S.[9] for pig brain were used in this study. The detailed material properties of axonal fiber bundles, and brain tissue matrix, skull, lateral ventricle, skull-brain connectors, and falx that were employed in the model are given in Supplementary Table S1.