A Fractional Viscoelastic Model of the Axon in Brain White Matter

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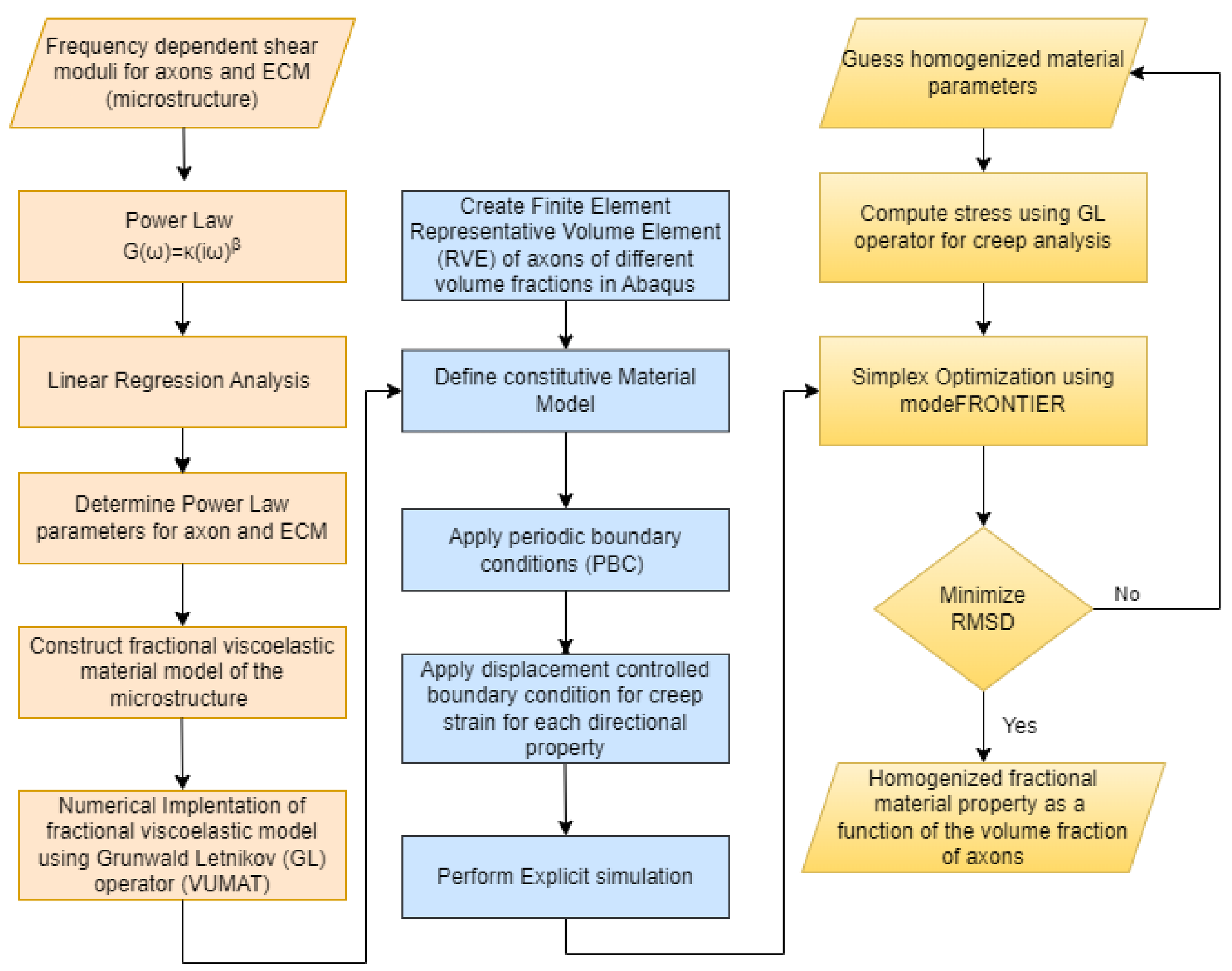
Introduction

Motivation:
Viscoelasticity is a sensitive measure of the composition of brain tissue and is an important marker in predicting neurodegenerative processes.

Objective:

- We aim to develop a numerical framework of the microstructure of brain white matter that incorporates a fractional viscoelastic constitutive material model of the composite white matter comprising of axons and glia.
- Representative volume elements (RVE) of axons embedded in glia with periodic boundary conditions are developed and subjected to a relaxation displacement boundary condition.
- Homogenized orthotropic fractional material properties of axons in glia are extracted by solving the inverse problem.

Fractional Viscoelastic Modeling Framework



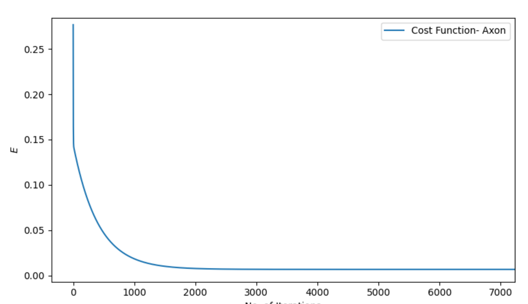
A Logistic Regression Model for Power-Law

The complex modulus of a viscoelastic model following a power law behavior with material constants, κ and β can be written as

$$G(\omega)=\kappa(i\omega)^{\beta}=G'+iG''=\Re(G(\omega))+i\Im(G(\omega))$$

A cost function that minimizes a logistic regression model for a power-law is defined as

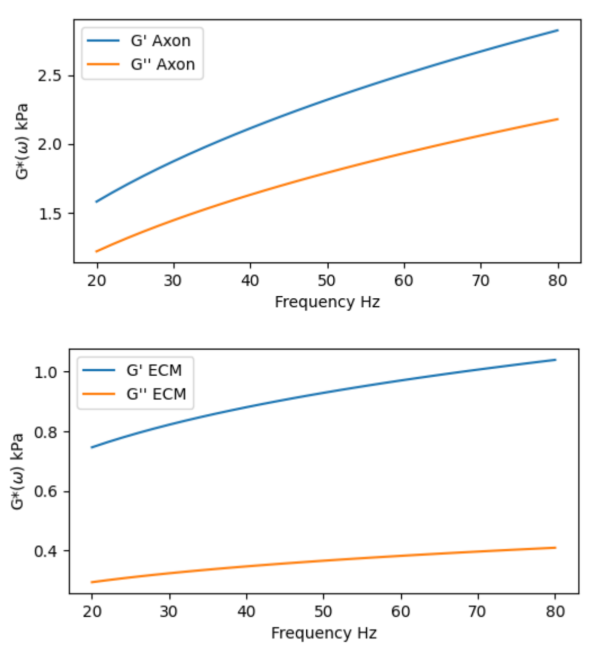
$$E=\frac{1}{2m}\sum_{m}((\ln(\kappa)+\beta\ln(\omega)-\Re(G^{*}))^{2}+(\beta\frac{\pi}{2}-\Im(G^{*}))^{2})$$



Minimization of Cost function for the logistic regression model.

Component	$\kappa\ (Pa\cdot s^{\beta})$	β
Axon	264.115	0.419
Matrix	252.503	0.239

Material constants for Axon and ECM obtained by minimizing the logistic regression cost function.



Storage and loss modulus vs frequency for axon (Top) and ECM (Bottom) using a power-law model.

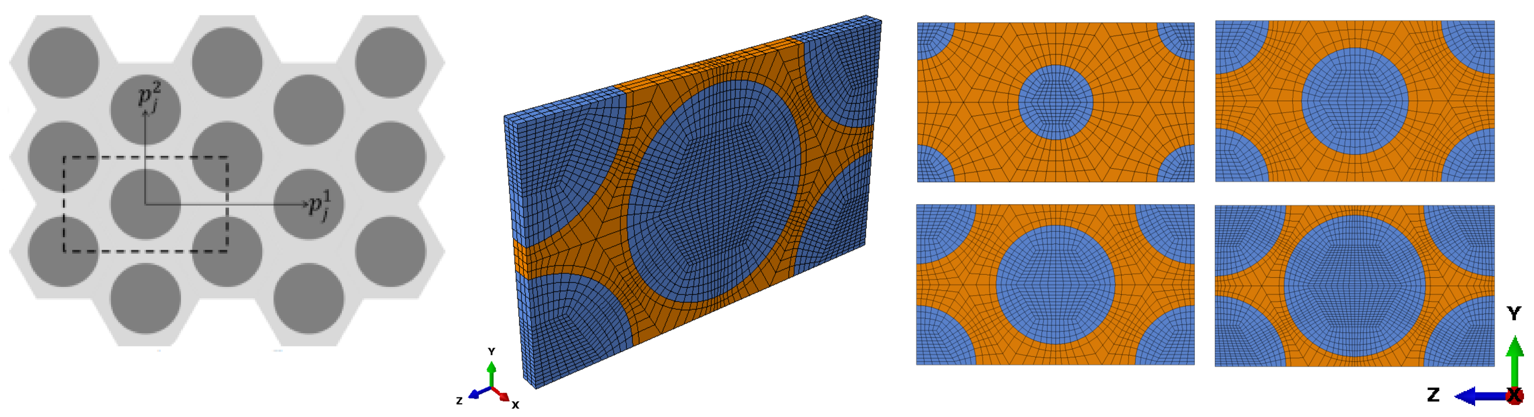
Finite Element Model of the Microstructure

Hexagonally packed RVEs of axons embedded in the ECM of varying volume fractions are developed with a periodic mesh using Abaqus FEA. Periodic boundary conditions (PBC) are enforced between nodes of opposite faces at any coordinate, x_j and periodicity vector, p_j^{α} by

$$u_i(x_j+p_j^{\alpha})=u_i(x_j)+\frac{\partial u_i}{\partial x_j}p_j^{\alpha}$$

u_i is the displacement field in the i_{th} direction. In Abaqus, PBC can be implemented via a set of linear constraint equations with A_n number of coefficients. In the equation below, u_i^p corresponds to displacement variable of node, p and degree of freedom, i.

$$A_1u_i^p+A_2u_j^q+\cdots+A_nu_k^r=0$$



Hexagonally packed periodic unit cell (left). A finite element model of a periodic RVE (center). RVEs with different volume fractions of axon embedded in ECM (left to right: 0.2, 0.4, 0.5, 0.7).

Fractional Viscoelasticity

Definition

The stress for a fractional viscoelastic springpot model is proportional to the β order of strain

$$\sigma(t)=C_{\beta}\frac{d^{\beta}\varepsilon(t)}{dt^{\beta}}\ \forall\ (0\leq\beta\leq1).$$

A generalization of derivatives of non-integer orders can be obtained in a branch of mathematics called fractional calculus using the Liouville-Caputo derivative. The stress is thus

$$\sigma(t)=\frac{\kappa}{\Gamma(1-\beta)}\int_0^t(t-\tau)^{-\beta}\frac{d\varepsilon(\tau)}{d\tau}\ d\tau$$

For a 3D finite element model, writing κ in terms of the volumetric and deviatoric components, the stress equation is

$$\sigma_{ij}=\frac{1}{\Gamma(1-\beta)}\int_0^t(K_{\beta}-\frac{2}{3}G_{\beta})\delta_{ij}\dot{\varepsilon}_{kk}(t)dt+\frac{1}{\Gamma(1-\beta)}\int_0^t G_{\beta}(\dot{\varepsilon}_{ij}(t)+\dot{\varepsilon}_{ji}(t))dt$$

For a 3D state of stress, the Liouville-Caputo derivative can be numerically computed using the Grunwald-Letnikov operator

$$\sigma_{11}^{k+1}=(K_{\beta}-\frac{2G_{\beta}}{3})\left(\frac{1}{\Delta t}\right)^{\beta}\sum_{l=1}^{k+1}\varphi_l\varepsilon_{kk}((k+1-l)\Delta t)+2G_{\beta}\left(\frac{1}{\Delta t}\right)^{\beta}\sum_{l=1}^{k+1}\varphi_l\varepsilon_{11}((k+1-l)\Delta t)$$

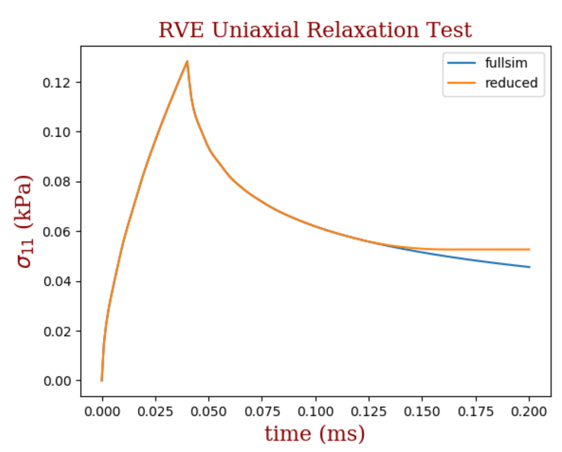
$$k=\frac{Totaltime}{\Delta t}\qquad \varphi_{l+1}=\frac{(k-1-\beta)}{k}\varphi_l,\qquad \varphi_1=1$$

Grunwald Coefficients

$$\frac{d^{\beta}f}{dt^{\beta}}=\left(\frac{1}{\Delta t}\right)^{\beta}\sum_{l=1}^{M+1}\varphi_l f((k+1-l)\Delta t)$$

$$M=\min\{k,\frac{L}{\Delta t}\},\quad L=Memory\ Length$$

Short memory principle for truncating strain history.



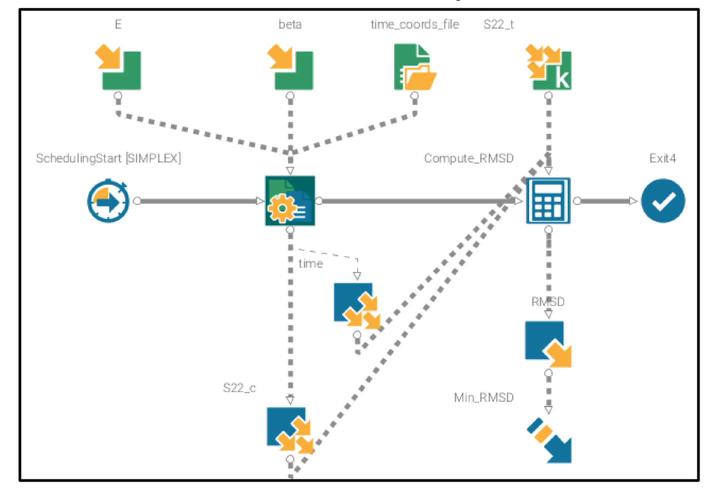
Comparison of σ_{11} vs time computed using entire strain histories (fullsim) and a 60 percent memory length(reduced).

Optimization Workflow

A Nelder-Mead downhill simplex algorithm is used to determine the optimal values

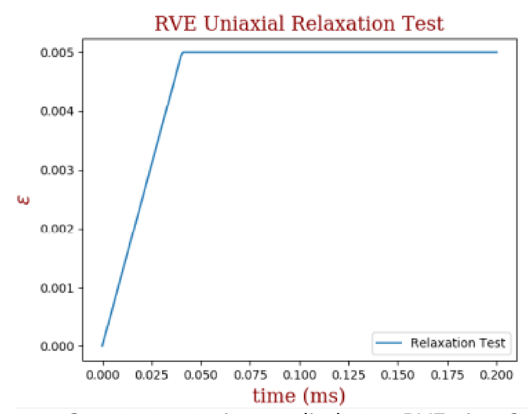
$$\min\quad J=\sqrt{\frac{1}{m}\sum_{n=1}^{m}\frac{(\sigma_{sim}-\sigma_c)^2}{\sigma_{sim}^2}}$$

$$\text{subject to}\quad 0\leq\beta\leq1;\quad m>0$$

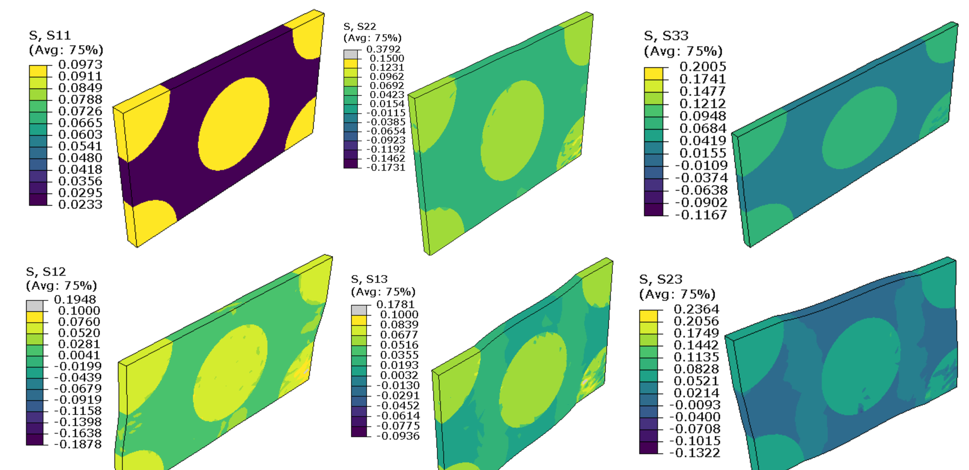


Optimization workflow implemented in modeFRONTIER.

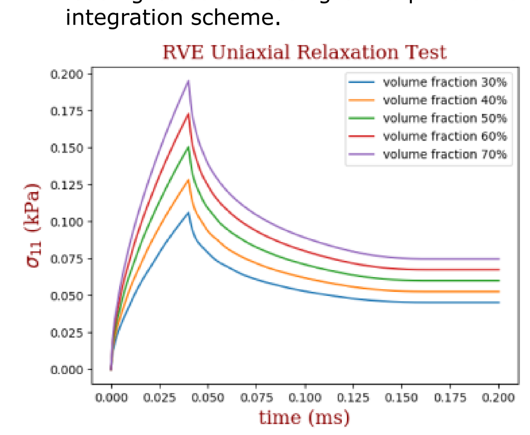
Results



Constant strain applied to RVE in 6 loading directions using an explicit time integration scheme.



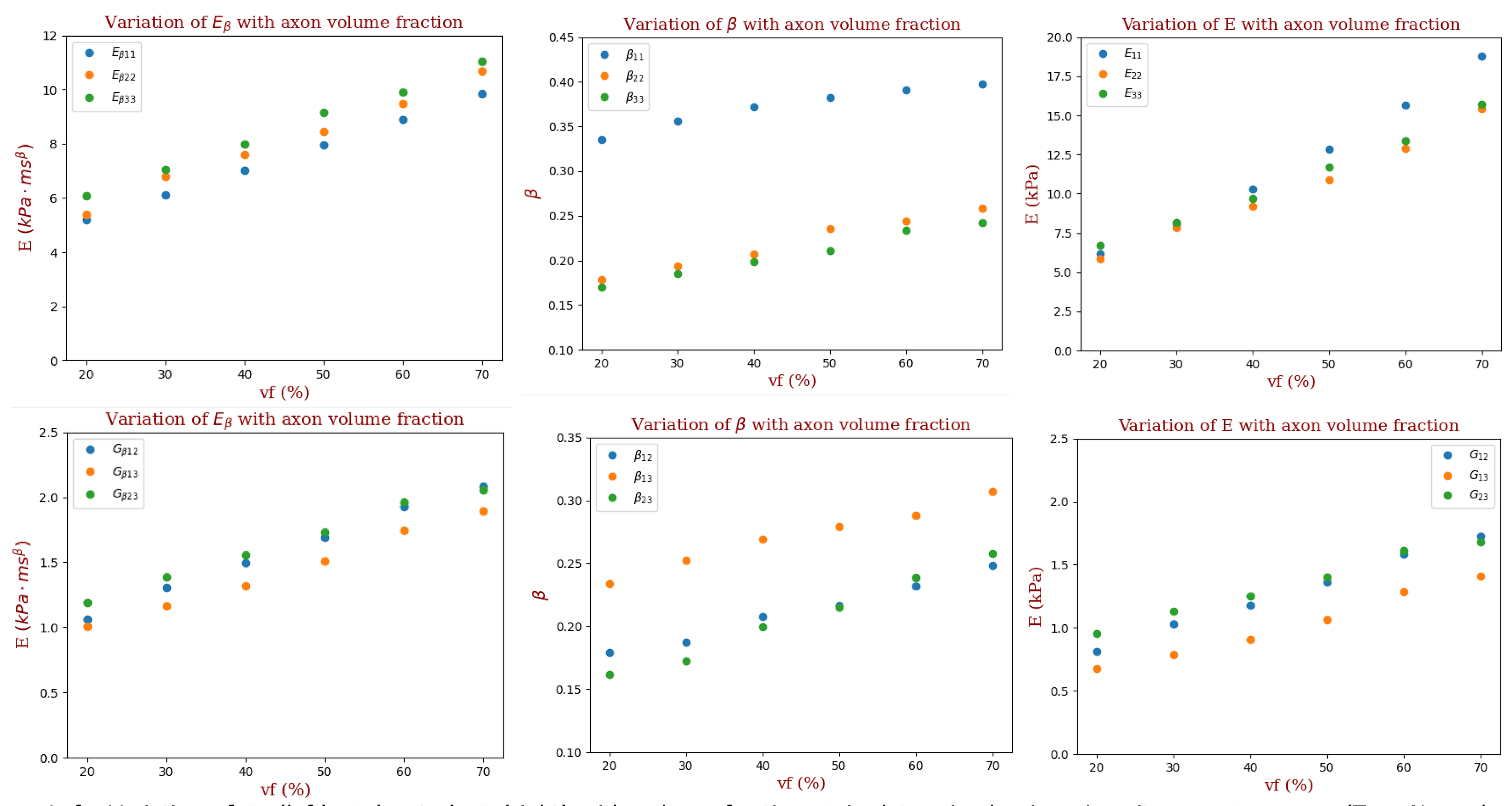
Stress contour and deformation of RVE in 6 loading directions with VF=0.4. The plot is obtained at the end of the creep strain. Stress in kPa.



Homogenized stress along fiber direction for volume fractions 0.3 to 0.7.

E_{β} is cumbersome to interpret due its units $(kPa\cdot ms^{\beta})$. This can be converted to an elastic modulus (kPa) like parameter using the below expression

$$E=(E_{\beta}*\eta^{-\beta})^{\frac{1}{1-\beta}}$$



Left: Variation of E_{β} (left), β (center), E (right) with volume fraction. E is determined using viscosity $\eta=3.7\ kPa\cdot ms$. (Top: Normal directions, Bottom: Shear directions).

Conclusions and Future Work

- Fractional model is phenomenologically easier to interpret in comparison to Prony series models.
- Homogenized structure becomes stiffer and more viscous with higher volume fractions. The variation, however, is not linear.
- In the corpus callosum (VF of axons ~ 0.4 to 0.5), our models predict $\beta\sim(0.21,0.29)$ and shear modulus, $G\sim(1.1,1.37)kPa$.
- Develop RVEs with random distribution of axon diameters, non periodic unit cells.
- Incorporate hyperelasticity for finite strain simulations.

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