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EMULATING THE INTERFACIAL KINEMATICS OF CNS WHITE MATTER WITH FINITE ELEMENT TECHNIQUES

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INTRODUCTION

Axonal injury represents a critical target for TBI and SCI prevention and treatment. Mechanical strain has been identified as the proximal cause of axonal injury, while secondary ischaemic and excitotoxic insults associated with the primary trauma potentially exacerbate the structural and functional damage. Many studies have been attempted to identify the states of stress and strain in white matter using animal and finite element models. These material models employed in finite element simulations of the central nervous system (CNS) of soft tissues heavily depend on phenomenological representations. The accuracy of these simulations depends not only on correct determination of the material properties but also on precise depiction of the tissues' microstructure.

Studies of the kinematic response of white matter axons, based on changes in axon morphology, when the tissue is exposed to controlled stretch, have demonstrated that: 1) axons maintain an initial undulated state that depends on the location of the white matter and stage of development; 2) axons straighten during stretch; and 3) axons do not demonstrate pure affine or non-affine behavior, but instead transition from non-affine dominated kinematics at low stretch levels to affine kinematics at high stretch levels (Bain et al., 2003; Hao et a.l, 2007). This transition and the predominant kinematic behavior have been linked to the natural coupling of axons to each other via the glial matrix, especially oligodendrocytes that interconnect axons through myelination (Shreiber et al., 2009). Naturally, the degree of coupling within the tissue will affect the continuum mechanical properties. Given the complex response of fibers within axon bundles in white matter, a microstructural finite element model (FEM) is necessary for an accurate representation of axon mechanics.

METHODS

The FEM was developed using ABAQUS 6.9 using Python scripting. The purpose of this model is to understand the effect of interaction between the axon and surrounding glial matrix on the overall mechanical behavior of the tissue, such as its continuum level properties, as well as the axon kinematics, such as the change of the axon undulations during loading. A representative volume element (RVE) (Pan et al., 2008) that consists of five serial segments of undulated axons and matrix for the white matter microstructure is generated (Fig. 1). In this simulation, the volume fraction (V_f) of axons is 53%. Each segment can be prescribed a different degree of undulation, defined as the actual length divided by the end-to-end-length for the segment. The average undulation was prescribed as 1.13 (Bain et al., 2003). For this simulation, axons and glia are both represented byOgden's isotropic, large deformation, hyperelastic material model in the strain energy form of (Meaney, 2003):

$$W=\frac{2\mu}{\alpha^2}\left(\lambda_1^{\alpha}+\lambda_2^{\alpha}+\lambda_2^{\alpha}-3\right) \quad (1)$$

where μ and α are material parameters, and λ_i are principal stretches. The material parameters are recorded in Table 1. The overall stress-strain of the RVE of the tissue and the change of the undulations are obtained using the abovementioned model.

The degree of interaction between the axon and glia is controlled by altering the percentage of tied contact area (nodes) at axon/matrix interface. General frictionless surface contact is applied to the interface, but tied constraints are applied to 5%, 15% and 25% of the axon/matrix interfacial area to represent the increasingly affine behavior. For each case, nine models are created by randomly assigning the tied locations along the length of the axon. The RVE is stretched along the axonal direction to 25% strain, and periodic boundary conditions are applied to the RVE. The average stress is identified, and the resulting changes in axon segment undulation are recorded.

RESULTS

The overall averaged uniaxial stress-strain curves obtained from individual simulations are consistent with same percentage of tied area although the tie locations are randomly assigned. The stress-strain curves and fitted data are plotted in Fig. 2. The overall averaged uniaxial stress-strain curves are fitted to the Ogden hyperelastic model, see Eq. (1). The resultant material parameters are also recorded in Table 1. As expected, increasing the interfacial tied area results in stiffer material at the continuum level.

Table 1. Constituents' and fitted material parameters.

	axon	Matrix	25% tied	15% tied	5% tied
μ (Pa)	290.8	96.9	149.6	133.4	107.1
α	6.19	6.19	11.11	10.58	10.69

Properties for the axons and glial matrix were obtained from the literature (Meaney, 2003). Results for the Tied cases were extracted by fitting model results to an Ogden hyperelastic model.

The changes in axons' undulation are documented as a function of stretch. The undulated axons become less wavy when the applied stretch increases as demonstrated in Fig. 3. The experimental data from Bain et al. (2003) and the simulation data from Karami et. al (2009), who also employed an RVE but with fully constrained coupling between axons and glia, are also included for comparison. Clearly, fractional coupling between the axons and glia yields more accurate stretch-undulation data than Karami's model in which axon and glia are perfectly bonded. Although the stretch-undulation curves are close to the experimental data, it is noted that the rate of undulation change obtained by our models at lower stretch are smaller than that of the experimental result. In these simulations, a percentage of tied contact was prescribed and held constant, whereas axon kinematics transition with stretch. We expect that by letting the constrains to evolve with stretch will allow us to capture the non-affine, independent behavior of axons and glia at lower stretch levels and enable a more rapid change in undulation at low stretch levels, consistent with data from Bain et al. (2003) and Hao et al. (2007).

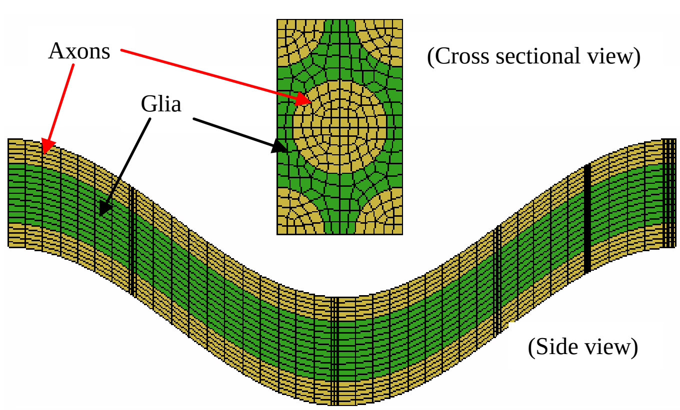

Fig. 1. The RVE of the white matter with undulated axons. (axon V_f: 53%; undulation: 1.13, only one segment is shown.)

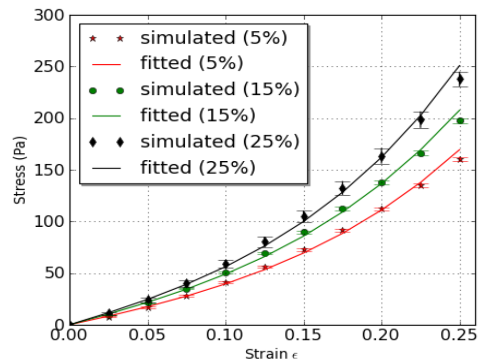

Fig. 2. Predicted stress-strain behaviors.

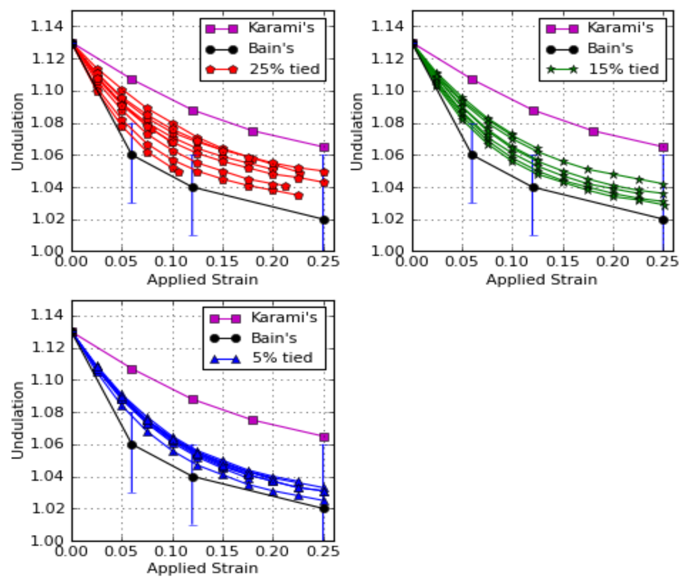

Fig 3. Predicted change in undulation with stretch. Results are compared to experimental results from Bain (2003) and to simulation data from Karami (Karami, 2009).

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