Modeling the influence of cell morphology on tissue mechanical anisotropy via finite element analysis of a soft composite material with ellipsoidal inclusions

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Statement of Purpose Magnetic resonance elastography (MRE) measures the mechanical properties of tissue at the imaging voxel scale (~ 2 mm) [1]. Tissue mechanical properties and whether they vary with orientation (i.e., anisotropy) depend on the mechanical properties of sub-voxel scale components (e.g., cells, extracellular matrix) and their spatial arrangement. Currently there is no reliable method to infer pathological changes in the mechanical properties and morphology of tissue components with MRE. In this study we investigate the relationship between mechanical and morphological properties of the cells and extracellular space on the one hand, and voxel-scale aggregate mechanical properties of the tissue on the other.

Methods Biological tissue was modeled as a soft composite material consisting of uniformly distributed ellipsoidal inclusions, representing cells, embedded in a 3D substrate, representing the extracellular space (ECS). Repeating microscopic units within the composite were subjected to virtual mechanical testing via the finite element method (FEM) to predict tissue-level mechanical properties.

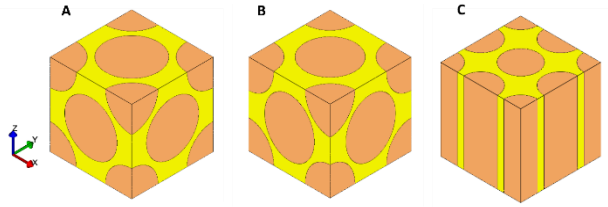

Figure 1. Composite tissue geometries.

The cells (i.e., inclusions) were arranged in a face-centered cubic lattice, and their eccentricity was varied from 0 (spheres) to 1 (cylinders) while preserving cell volume fraction (0.55) (Figure 1). Both the cells and ECS were considered mechanically isotropic elastic solids. Virtual normal and shear loading tests were conducted to determine five independent engineering moduli assuming a single symmetry axis parallel to the cells' major axes.

Results When the cells and ECS were assigned the same mechanical properties, the stress and strain fields in each were uniform and equivalent to those of the composite overall. When the cells were assumed isovolumic (higher bulk modulus and lower shear modulus than the ECS), nonuniform stress and strain fields resulted, particularly within the ECS (Figure 2). During normal extension of the composite, tensile strain was higher in the ECS and increased near cell boundaries. The ECS appears to shield the cells from strain during extension, a potential protective feature of the ECS. When sheared, the cells exhibit higher, nearly uniform shear strain, while the ECS exhibits lower, non-uniform strain.

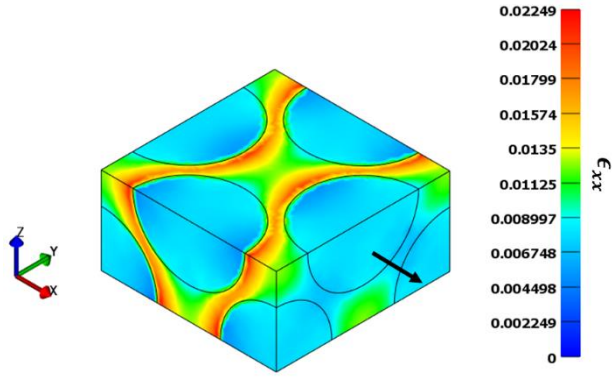

Figure 2. Spatial variation of normal strain in the x-direction

For isovolumic cells, the cell bulk modulus was set three orders of magnitude higher than the ECS. Although cells occupy 55% of the composite's volume, the composite bulk modulus was only about 5 times the ECS bulk modulus. This indicates that even for spherical cells, the composite's mechanical properties are not simply a weighted average of its components' properties, and that tissue microstructure is a factor. As cell eccentricity increased, differences between the longitudinal (E_L) and transverse (E_T) Young's moduli as well as between the longitudinal (G_L) and transverse (G_T) shear moduli increased. For the case of cylindrical cells, the maximum tensile anisotropy predicted was 5.19% and the maximum shear anisotropy was 2.54%. Increasing eccentricity increased E_T and decreased E_L, whereas both G_L and G_T decreased, but G_L less so.

Conclusions The results are by no means intuitive and underscore the need for computational modeling. Our modeling framework can be adapted to make composite property predictions for a wider range of component properties and morphology, including intravoxel heterogeneity and anisotropy which are fundamental features of brain tissue. Such predictions could be the basis for inferring microstructural material properties from voxel-level MRE measurements, which would enhance the sensitivity of MRE to morphological changes that accompany brain cancer [2] and neurodegeneration [3] and increase its diagnostic potential.

References

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