THE EFFECT OF WHITE MATTER ANISOTROPY ON CORTICAL FOLDING DURING DEVELOPMENT

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Human brains and those of other mammals fold during development, giving them their familiar wrinkled appearance. Problems with the development of these folds, called gyri, include the absence of folds, called lissencephaly, and an excess of small shallow folds, called polymicrogyria. The anatomy of the brain is related to its function, and disordered brain folding patterns have been linked to mental and emotional disorders. Despite the importance of this aspect of development, the mechanism that gives rise to these folds is still unknown.

Analytical [1, 2] and finite-element [3, 4] models of the developing brain have been used for decades to investigate the process of cortical folding. Prominent theories have included the role of the skull as a hard constraint [5], differential growth in the brain’s layers [1, 3], and axonal tension drawing strongly interconnected areas of the brain closer together [2]. The last two theories have shown promise in simple simulations, but have failed to conclusively produce geometries or stress patterns that match experimental results [4].

One possible source for this discrepancy is the anisotropic nature of white matter, which is largely made up of axons and their insulating myelin. Axons are the main source of stiffness in white matter, as well as the only component that is known to growth under applied stress or strain [6]. As previous models have modeled white matter as an isotropic or transversely isotropic material, they fail to capture the contribution of axons to the mechanical response subcortex.

Here we introduce a novel material model for cerebral white matter with anisotropy due to axonal fibers, defined by a preferred fiber direction that can vary throughout the domain. We derive the continuum equations for anisotropic growth and demonstrate their computational solution within a nonlinear finite element setting. We motivate our approach through an incompatible growth configuration, which naturally introduces a
multiplicative decomposition of the deformation gradient into an elastic and a growth part. The growth response of the subcortex is stimulated by the stretch felt by the axonal fibers, and is characterized by an internal variable that acts as a growth multiplier in the preferred direction. The behavior of the cortex is governed by a separate isotropic model with morphogenetic growth.

The addition of anisotropy in the white matter results in folded geometries that cannot be achieved with a simpler, isotropic, material model (Fig. 1). Using a range of axonal fiber directions, we demonstrate the potential of our anisotropic growth model to more accurately represent the contribution of axons to the process of cortical folding. Ultimately, this model will be useful in patient-specific geometries and may reveal information about brain development under healthy and diseased conditions.

REFERENCES