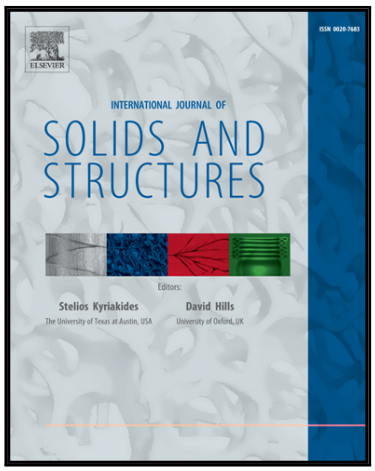

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On the influence of inhomogeneous stiffness and growth on mechanical instabilities in the developing brain

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Abstract

The characteristic surface morphology of the mammalian brain is closely correlated with brain function and dysfunction. During development, the initially smooth surface evolves into an elaborately convoluted pattern. Growing evidence suggests that mechanical instabilities emerging from differential growth between a faster growing outer gray matter and a slower growing inner white matter play a major role in brain morphogenesis. Previous studies assume uniform growth and stiffness; yet, recent experiments indicate that the properties of brain tissue are highly inhomogeneous. Here, we hypothesize that regionally varying developmental pathways across the brain result in nonuniform material properties at the onset of cortical folding. We establish a computational model of brain growth to explore the effects of stiffness and growth variations in gray and white matter tissue to mimic cellular processes and evolving tissue microstructure. We present an effective approach to determine critical growth values from geometrical data and systematically study the effect of inhomogeneous material properties on growth-induced primary and secondary instabilities. Our results reveal that critical growth and wavelength strongly depend on the stiffness distribution in the developing brain. Regional variations in cortical growth affect secondary instabilities and evoke highly irregular folding patterns, but characteristic wavelength and critical growth remain relatively stable. The interplay of different influential factors including cortical thickness, brain geometry, stiffness, and growth explains how primary folds are highly preserved across individuals, whereas secondary and tertiary folds vary significantly. Our findings are directly applicable to imaging data of fetal brains and ultimately enable early diagnostics of cortical malformations to improve treatment of neurodevelopmental disorders including epilepsy, autism, spectrum disorders, and schizophrenia.

Keywords: cortical folding; growth; instabilities; period-doubling; inhomogeneous properties

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