# A Mathematical Model of Cerebral Cortical Folding Development

Kilinc A.[1], Hurdal M.K.[1]
[1] Department of Mathematics, Florida State University, Tallahassee, FL, USA.

**INTRODUCTION**: The cerebral cortex is the outer covering of the brain. In large mammals, it is intricately folded into gyri (hills) and sulci (valleys). To date, there have been three leading biological hypotheses that explain the development of cortical folding. The mechanism behind this folding process is not fully understood yet.

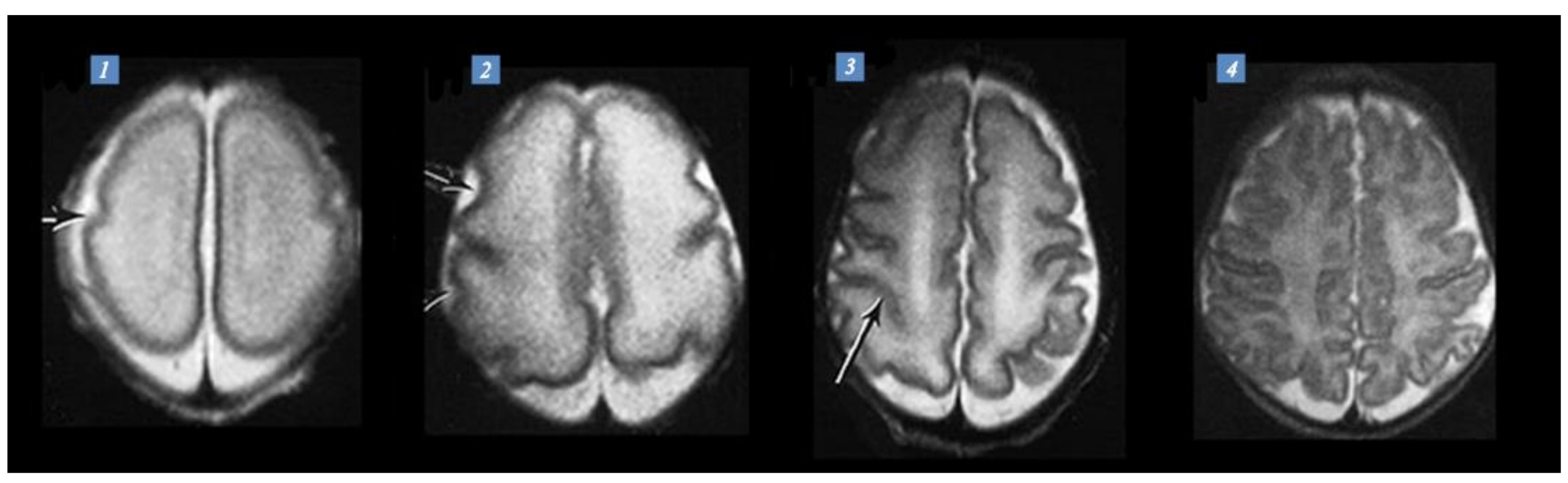


**Figure 1.** MR images of a preterm infant born at the 25th, 28th, 32nd and 40th week of gestational age (GA). The MR images are taken at a supraventricular level in the transverse plane. [1]

**COMPUTATIONAL METHODS**: Finite element simulations are performed using COMSOL Multiphysics software (V.5.4). A 2D, time-dependent scheme is used together with Nonlinear Structural Mechanics module. Brain tissue is assumed to be isotropic, hyperelastic material. A standard neo-Hookean material model [2] is used and the related strain energy density function $W$ is the following:

$$W = \frac{\mu}{2}\left(I_1^* J^{*-\frac{2}{3}} - 3\right) + \frac{\kappa}{2}(J^* - 1)^2$$

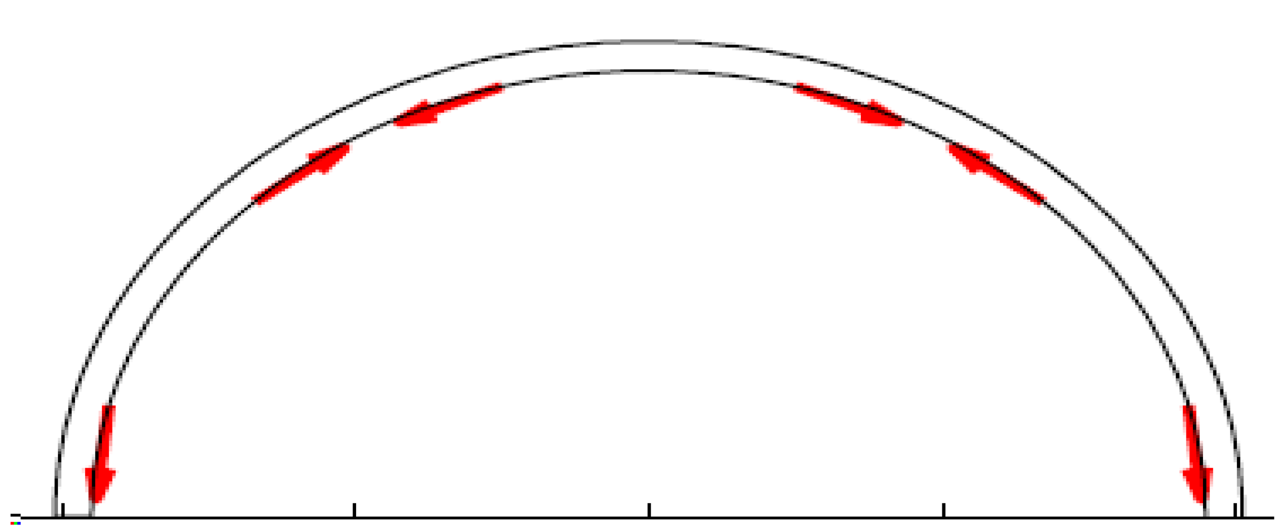

**Figure 2**. An illustration for the place and strength of the applied axonal tension forces based on a Turing pattern [3]

In order to model axonal tension as a force pulling together on the semi-circular and semi-elliptical domains, we use vector $\boldsymbol{f}$ loaded at some nodes as shown in Figure 2.

**PARAMETERS:** The following parameters are used and were obtained from actual data of the human brain:

$\boldsymbol{r}$ = 0.0404 m: radius of brain at 28th week
$\boldsymbol{t}$ = 2.5 mm: thickness of the gray matter
$\boldsymbol{E_g}$ = 1.389 kPa: Young's Modulus of gray matter
$\boldsymbol{E_w}$ = 1.895 kPa: Young's Modulus of white matter
$\boldsymbol{v}$ = 0.4583: Poisson ratio of brain tissue
$\boldsymbol{d}$ = 1.1 $g/cm^3$ : density of brain tissue

**RESULTS**:

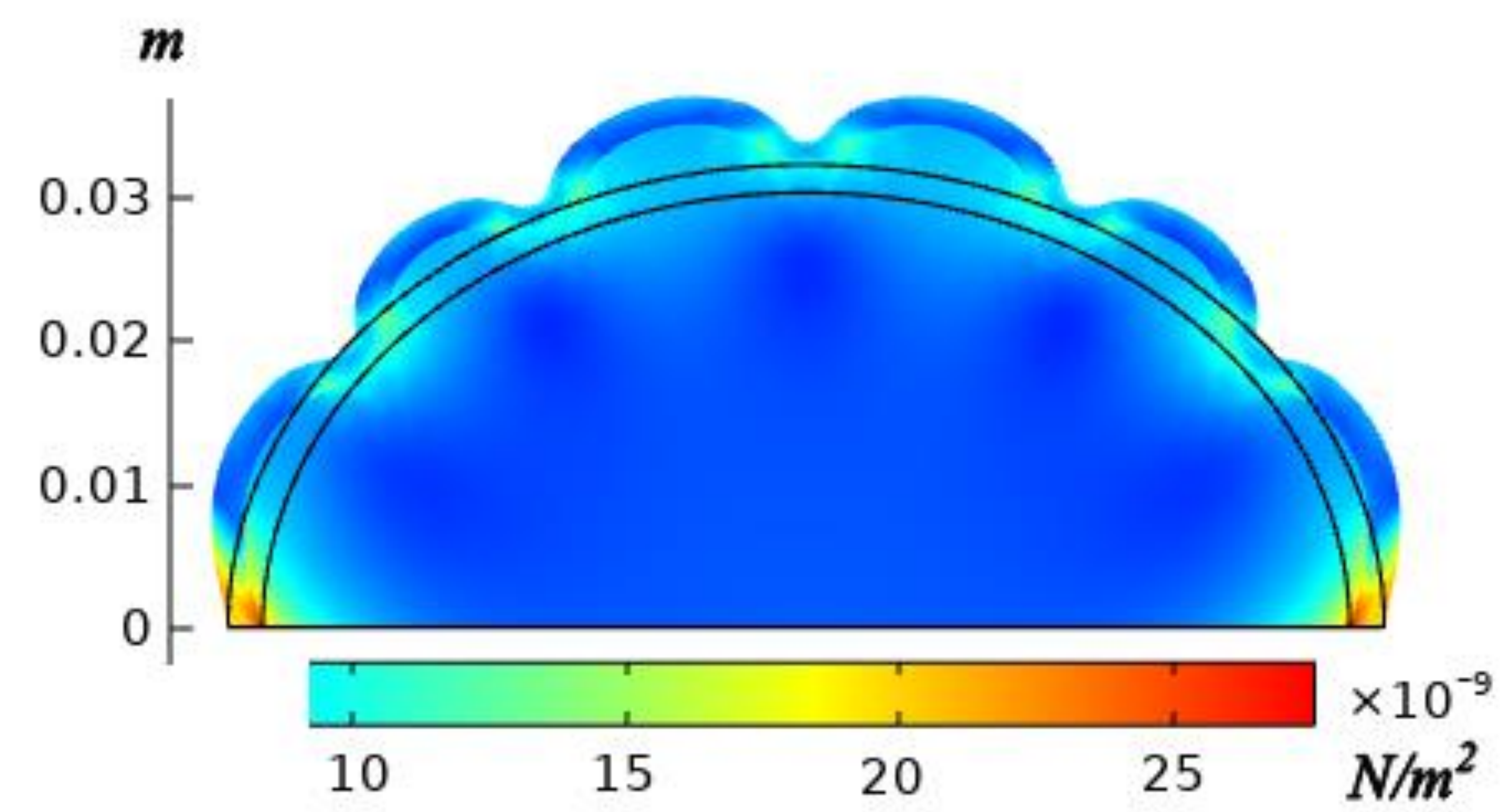


**Figure 3**. Simulation with a 2D semi-elliptical domain. The colors represent the Von Mises stress.

The human brain is more like a semi-ellipsoid. Compared to the MR images shown in Figure 1, Figure 3 demonstrates decent bucklings on the cortex together with volumetric growth. The initial symmetry of the elliptical domain is preserved on the image as well.

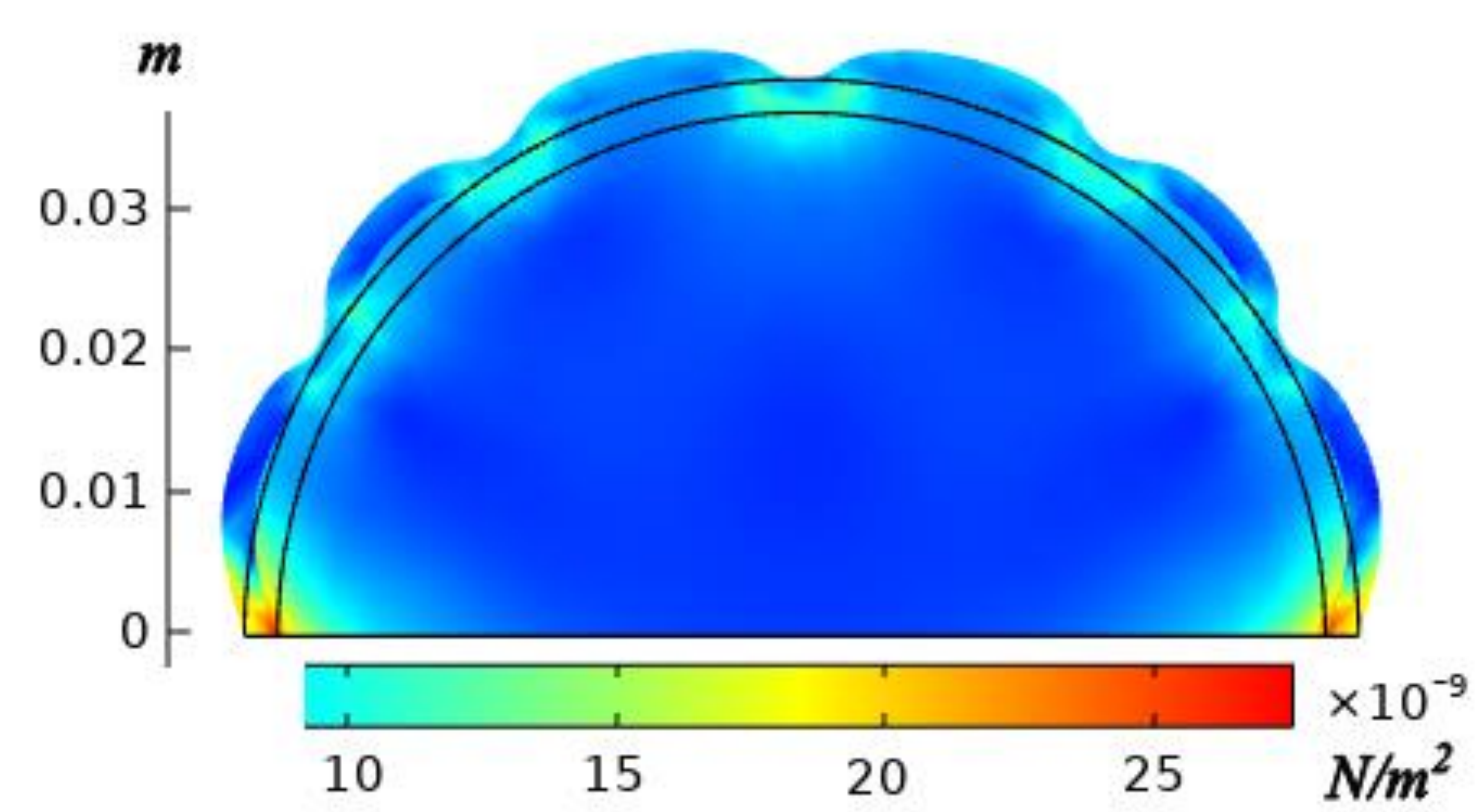


**Figure 4**. Simulation with a 2D semi-circular domain

**CONCLUSIONS**: The current model is distinct from previous models since it utilizes all three leading hypotheses of the cortical folding, and more biologically relevant compared to most other models in terms of being time-dependent, nonlinear, and the fact hyperelastic material is used. Obtaining better patterns and the extension of simulations to the 3D are the next steps.

**REFERENCES**:

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3. Turing A.M., The chemical basis of morphogenesis, *Philos T Roy Soc B*, B 237, 37-72 (1952).