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Modeling Cortical Folding with a Growing Domain Turing System

The brain is one of nature's greatest mysteries, and the cerebral cortex is one of the brain's most striking features. The cerebral cortex is intricately folded into gyri (hills) and sulci (valleys). The folding patterns of these gyri and sulci are unique, both across species and across individuals within a species, much like a fingerprint. Little is understood about how cortical folds form and why they are located where they are. Current biological models of the underlying processes behind cortical folding fall into two main categories; some models highlight the importance of chemical interactions, while others place the primary emphasis on mechanical forces such as tension. We have developed a spatio-temporal mathematical model of cortical folding on a growing domain, expanding upon previous mathematical research on cortical folding conducted using a static domain. A growing domain model of cortical folding may be more realistic than the previous static domain model since it incorporates the growth that inherently occurs as the brain develops. Our model illustrates the importance of including growth in a model of cortical folding and can be utilized to explain certain human diseases of cortical folding. It can help investigate an area of neuroscience where it is difficult to perform human experiments.

Our model utilizes a Turing reaction-diffusion system on an exponentially growing domain. Turing reaction-diffusion systems were originally developed to describe formation of chemical gradient patterns on the developing embryo, and have since been used to model pattern formation associated with various developmental biology phenomena, including leopard spots, zebra stripes, and many more. Turing systems are typically two-equation activator-inhibitor systems that, when certain criteria are satisfied, cause spatially homogeneous systems to generate spatially inhomogeneous patterns. We use the Barrio-Varea-Maini reaction kinetics with parameters that favor striped pattern formation in our Turing system model.

The Turing system in our model can be applied to a growing domain in any of the eleven coordinate systems upon which the Helmholtz equation is separable. This gives the model great flexibility and the potential to be used for mathematical modeling on a geometrically diverse group of domains. To apply the model to cortical folding, we select an exponentially growing prolate spheroid, which approximates the shape of the lateral ventricle (LV) during early stages of cortical development. A prolate spheroid is obtained by rotating an ellipse around its major axis; the focal distance of the spheroid is determined by the length of its semimajor and semiminor axes. In our model, the focal distance of the prolate spheroid grows exponentially so that the spheroid's shape is preserved as it grows isotropically. The Intermediate Progenitor Model (IPM) of cortical folding states that regional patterning of self-amplification of intermediate progenitor cells (IPCs) in the subventricular zone (SVZ) of the LV corresponds with the formation of gyri and sulci. As self-amplification of IPCs is genetically controlled via chemical gradients, a Turing system is a logical choice to create a mathematical representation of the IPM. Our Turing system model uses the exponentially growing prolate spheroid to represent the LV and its surface to represent the SVZ.

Using numerical simulations to compare and contrast patterns generated by our growing prolate spheroid Turing system with those generated by a static prolate spheroid Turing system, we show that the addition of growth causes a significant change in system behavior. While it is well-documented that a static domain Turing system converges to a final pattern like a developing photograph, a growing domain Turing system produces transient patterns that constantly evolve from one pattern to another. We also observe that increasing the exponential growth rate in our system increases the number of stripes in the generated pattern, which can be interpreted as an increase in the number of cortical folds. This result may help explain a form of polymicrogyria (a cortical folding malformation characterized by an excessive number of small gyri) which occurs with hydrocephalus (a build-up of cerebrospinal fluid in the brain causing the LVs to increase in size). Our model could shed more light on the underlying mechanics behind cortical folding and diseases of folding as well as the role of growth in these processes.