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Modelling cortical folding pattern formation of the brain with a Turing system

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Abstract: The folding patterns of the brain vary dramatically across species. Moreover, the location of sulcal (valley) and gyral (ridge) folds differ considerably in terms of their size, shape and extent even within a species. A paradigm for cortical pattern formation within or across species has not become apparent. Discussions as to how cortical folding patterns occur have recently emerged in the literature. Current proposals describe folding through local interactions and include a mechanistic model and a cellular model. In this paper we present a simple and elegant mathematical model that offers a possible explanation as to the formation of cortical folds. Our model takes into account global cortex characteristics and can be used to model folds across species as well as specific diseases that can occur in human brain folding patterns.

Our model uses a Turing reaction-diffusion system to model cortical folding. Turing systems have been used to study pattern formation in a wide variety of biological applications using 1D, 2D and spherical domains. Turing systems use an activator and inhibitor and under certain conditions, a steady state will emerge causing a pattern to form. We employ phenomenological kinetic equations of Barrio-Varea-Maini (BVM) for our reaction-diffusion model.

Due to the shape of the lateral ventrical (LV) in the cortex, we use a prolate spheroidal domain. A prolate spheroid is created by rotating an ellipse about its major axis. The focal distance of the prolate spheroid is determined by the major and minor axes. It has been suggested that cortical pattern formation is due to regional patterns of intermediate progenitor (IP) cells in the subventricular zone (SVZ) of the cortex. During cortical development certain radial glial cells in the ventricular zone (VZ) are activated to create IP cells that travel to the SVZ. Our model approximates the shape of the LV with a prolate spheroid and the VZ with a prolate spheroidal surface.

With our model we are able to predict cortical folding patterns that correlate with cortical observations. As we increase the scaling of our prolate spheroidal domain we observe more elaborate cortical patterns. Additionally, our simulations reveal that the occurrence of the directionality of primary sulci occurring in different species can be accounted for by using the focal distance parameter in our model. Increasing the focal distance corresponds to increasing the shape of the VZ, resulting in changes in the location and type of sulcal pattern observed, By encapsulating global cortex shape characteristics, our model also has the ability to predict why the cortex of certain species may have little or no folding and it can link the evolutionary development of cortical sulcal formation to the eccentricity of the lateral ventrical.

Our model is also able to elucidate reasons as to how certain diseases in cortical pattern formation may occur. Polymicrogyria is a cortical malformation disease that occurs in the human brain and results in an over abundance of cortical folding. This disease is thought to be a neuronal migration disorder and can result in developmental delays, seizures and facial disfigurations. Numerical simulations with our model have enabled us to better understand cortical characteristics which can lead to excessive cortical folding. This application of our model, coupled with patient magnetic resonance imaging (MRI) data of the cortex, may explain how certain cortical pattern formation disease processes develop.

By applying prolate spheroidal harmonics to a Turing system, we have developed a chemically-based mathematical model that predicts the order and directionality of sulcal pattern formation across species based on global shape characteristics. Our model is able to predict and explain the consistency in pattern formation across species. Additionally our model is able to elucidate global cortex characteristics that may result in cortical pattern formation diseases.

Keywords: *Brain, cortical folding, pattern formation, gyrus, polymicrogyria, prolate spheroid, reaction diffusion system, sulcus, Turing pattern*