

POSTER PRESENTATION

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# Toward an in silico models for variation in neuroangiogenesis in retina

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## The problem

Phenotypic variation is ubiquitous. Diversity in behavioral response within a single genotype is ubiquitous. Sources, mechanisms and innovations in variation within a genotype are hardly understood. In neuroscience, the problem of genotype-phenotype relationship is notoriously difficult due to many intermediate layers that mediate between the DNA, the physical structures of cells, and the dynamics of neuroglial and vascular interactions in development and response to environmental stimuli. Neuroangiogenesis in mice retina provides a mechanism that lends itself to detailed study of the relationship between genotype and phenotype.

## Research

The circuitry of the retina is directly affected by genomic perturbations [Markus] Meister et al.. Development of the retinal circuitry plays a fundamental role in the earliest patterns of neuronal connectivity through spontaneous retinal waves [Marla] Feller et al. The branching architectures of nerves and vasculature are also established to develop in parallel. Therefore, it is reasonable to investigate the variation in pattern formation in developing retina as a gateway to understanding variation in fetal brain development and its functional consequences. In this article, we study variations on the branching structures as they occur naturally or due to genomic perturbations, such as gene knockout.

## Results

Angiogenesis is controlled by physical interactions between cells and extracellular matrix as well as

soluble antigenic factors, such as VEGF. Variation in morphology for the wild type is due to modulation of signaling. However, the mechanism by which mechanical signals integrate with other microenvironmental cues to regulate neovascularization in retina remains unknown. This article provides an in silico approach towards exploring morphological variation neuroangiogenesis in the mouse retina for the wild type and certain mutants. Specifically, novel algorithms are designed to quantify natural and perturbed variation in morphology; this is most difficult and laborious step towards analysis of Quantitative Trait Loci (QTL) and other quantitative neuro-genetics methods to determine the genomic and other mechanisms that are responsible for morphological variation.

## Translational medicine

On the clinical side, we elucidate potential applications of the computational models to understanding the mechanism of diseases that are characterized by pathological morphologies in angiogenesis, such as diabetes.

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