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Branching random walk models for cell differentiation in developmental neurobiology.

We model the balance between cell expansion and differentiation in the neurogenesis-to-gliogenesis switch (NGS) regime of developmental neurobiology. Models are developed in the context of Mosaic Analysis with Double Markers (MADM), an advanced imaging technique that tracks cell lineage trees. The stochastic nature of cell differentiation, imaging of only terminal neuron and glial cells, and variability across mice make the inverse problem challenging. We present a branching random walk (BRW) model for the temporal evolution of cell lineage trees based on two fundamental differentiation rules for neural and glial stem cells. Distributions of cell lineage trees are computed via simulations over many realizations and compared to the data. The underlying forward problem is combinatorially complex while the associated inverse problem involves significant uncertainty. Recursive analytical formulas for terminal cell counts were derived for the simpler cases of neuron-only trees and glia-only trees. For the more complex cases of mixed trees, direct numerical simulations were performed using the BRW model. Results are presented to assess how well probabilities in the BRW model can quantify and delineate developmental stages as well effects of deletion of genes implicated in the NGS. (Received September 20, 2017)