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Mathematical Model for Time to Neuronal Apoptosis Due to Accrual of DNA DSBs

We propose a mechanism to explain neuronal aging by tracking the number of non-transient DNA double-strand breaks (DSBs) and repairs over time that may lead to apoptosis. Neuronal apoptosis depends on the amount of space between DSBs as well as time. We derive three models to track the effect of neurodegeneration: a system of autonomous Ordinary Differential Equations (ODEs), a probability model to track the spatial requirement, and a stochastic model that incorporates both the ODE temporal dynamics and a spatial probability model. Using these models, we estimate a distribution for the lifespan of a neuron and explore the effect of parameters on time to death. We identify three possible causes of premature neuronal apoptosis: problems with coding critical repair proteins, issues with the neuron detecting DSBs, and issues with the neuron responding to DSBs.

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