LAWRENCE OPREA, McGill University

Simulation and analysis of white matter in a variably hypomyelinated transgenic mouse model

Demyelination, which causes severe reductions in the quality of action potential transmission, is important in the study of diseases such as multiple sclerosis. Recently, a series of transgenic mouse lines were developed with variable levels of myelin basic protein (mbp) mRNA. Applying semi-automated image segmentation to electron micrographs from these mice, we were able to extract information on myelin thickness, g ratio, myelin volume fraction, and geometric properties from tens of thousands of cells. Additionally, we built an axon packing algorithm to produce simulated 2D and 3D renderings of tracts with varying myelination. Results show clear nonlinear relationships between mbp levels and myelination of axons. These additionally vary across spinal cord regions and age. Compensatory mechanisms that mitigate the effects of low myelination, such as increased cell size and number, appear to occur once a demyelination threshold is reached. These data naturally lead to models investigating the energetics and electrophysiological effects of demyelination in development and maturation.