Compartment and Electodiffusion Models of Myelinated Axon Conduction Reliability J. S. Coggan*[1,3] C.L. Lopreore[1], T.M. Bartol[1], D.X. Keller[1], G.E. Sosinsky[3], T.J. Sejnowski[1, 2], and M.H. Ellisman[3]. [1]The Salk Institute for Biological Studies La Jolla, CA 92037; [2]HHMI; [3]National Center for Microscopy and Imaging Research, Dept. of Neurosciences University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0608.

The node of Ranvier complex is an intricate organization of axonal and glial membranes, small aqueous compartments and ion fluxes. Nodes of Ranvier are distributed at regular intervals along myelinated nerve fibers in the peripheral and central nervous system. The dysfunction of action potential (AP) conduction at node sites in myelinated axons is implicated in many human peripheral neuropathies and motor neuron diseases, including multiple sclerosis and Guillon-Barre syndrome. Factors governing the reliability of AP conduction along a myelinated nerve fiber were analyzed in a computational model cell constructed with the NEURON Simulator (Hines and Carnevale, 2001). The model cell includes a soma and 20 nodes separated by myelinated segments. The dimensions of the model were derived from a serial EM tomographic reconstruction of a peripheral sensory fiber node of Ranvier (Sosinsky et al., 2005). The placement and densities of specific voltage-gated sodium and potassium channels followed from published laboratory experiments. The arrangements of the ion channels were manipulated within nodal and paranodal regions to test location-dependent effects on AP conduction velocity and throughput reliability. Other factors examined include internodal distance, fiber diameter, axial resistance, channel densities and kinetic properties of ion channels. In addition, the role of internodal periaxonal conductance in AP conduction was also examined (Funch and Faber, 1984; McIntyre et al., 2002). Complementary to our myelinated axon model in NEURON, a new computational model was developed for incorporating electrodiffusion of ions in a 3D model node of Ranvier using the same geometrical parameters. Finite volume techniques are used to solve the Nernst-Planck and Poissson equations in a Delaunay/Voronoi mesh was constructed in order to evaluate fluxes of Na^+, K^+, and Cl^-, and the resulting electric potentials. The channels used in the NEURON simulation were converted to discrete-state models and inserted into the electrodiffusion model. Ion fluxes were simulated during propagation of an AP and the results were compared to NEURON model.