

Visualization of axon conduction failure at a node of Ranvier in a multi-scale computational model. J. S. Coggan^{1,2}, C.L. Lopreore³, T.M. Bartol¹, M.H. Ellisman^{4,5}, T.J. Sejnowski^{1, 2,4}, and Charles F. Stevens^{1,2,4}. ¹The Salk Institute for Biological Studies La Jolla, CA 92037; ²HHMI; Tulane University, New Orleans, LA, 70112; ⁴University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093.

The dysfunction of action potential (AP) conduction in myelinated axons is implicated in many human neuropathies and motor neuron diseases. Understanding the causes of conduction failure will require an understanding of axonal electrophysiology over a range of scales. Accordingly, we have developed a multi-scale simulation method for electrodynamic function. Our approach couples a one-dimensional cell-scale model based on cable equations using the NEURON simulator (Hines and Carnevale, 2001) to a three-dimensional (3D) electro-diffusion simulator (Lopreore et al., 2008). This method utilizes finite volume techniques to solve the Nernst-Planck equations and evaluate ion fluxes within a Delaunay/Voronoi 3D mesh. The NEURON model included a soma, axon hillock and initial segment followed by 75 myelin-node segments. Single-node dimensions used in the model were derived from 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 laboratory findings. Variables examined for contributions to conduction failure included the densities of ion channels in nodal compartments and demyelinated segments, internodal distance, changes in the equilibrium potential for K^+ , extra-nodal volume and rate of K^+ clearance from the nodal region. Voltage wave-forms produced by the NEURON model under normal and compromised conditions were injected into the 3D electrodiffusion for evaluation of ion fluxes within subcellular micro- and nano-domains. Supported by HHMI, NIH 1 P20 EB001432-01.