New Metrics of Intrinsic Axonal Excitability from a Computational Model of Demyelination.

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In white matter oligodendrocytes tightly wrap axons at regular intervals to form the myelin sheath. Axonal demyelination diseases represent a devastating group of neurological disorders that affect more than 2 million people worldwide. The process of unraveling the periodic insulation causes axon conduction dysfunction in many diseases of the central nervous system (CNS), as in multiple sclerosis (MS) and infectious encephalomyelitis, or the peripheral nervous system (PNS) as in Guillain-Barré syndrome. Although the etiology of these diseases in most cases is thought to be immunological, the mechanisms of the diverse neurological symptoms are just as poorly understood. These confounding symptoms can present intermittently, resolving and returning, or changing in character and include spasticity, dysfunction of somatic sensation and motor control, impairment of vision and other modalities. These physiological features are accompanied by anatomical and cellular perturbations in affected neurons that include changes in voltage-gated ion channel densities. Here we present a computational model of a demyelinated axon that suggests a simple set of rules that determine the wide range of symptoms observed during demyelination. In addition, the model shows that the moderate, laboratory-measured densities of Na and K channels are optimal for action potential amplitude and conduction velocity in healthy axons – lower or higher densities are less efficient. Taken together our model makes substantial progress towards understanding the cellular and clinical phenomena associated with demyelination diseases.

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