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## A computational study of factors in the evolution of myelin Ann Castelfranco\* and Daniel Hartline

Address: Békésy Laboratory of Neurobiology, PBRC, University of Hawaii, Honolulu HI 96822, USA Email: Ann Castelfranco\* - castelf@pbrc.hawaii.edu

\* Corresponding author

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Myelin is a multilayered, lipid-rich coating of axons that increases the conduction velocity of nerve impulses, contributes to compact nervous systems, and reduces metabolic costs of neural activity. Although usually thought of as a vertebrate adaptation, functionally identical myelin sheaths have evolved in several invertebrate lines. To gain insight into the possible factors in its evolution in the different lines, we undertook a modeling study of different configurations of myelin ensheathment and its physiological parameters. Based on the hypothesis that increased impulse conduction velocity provides a selective advantage that drives the evolution of myelin, we focused on parameters that speed nerve conduction. The myelin sheath was modeled with several levels of complexity using the NEURON simulator, ranging from approximating the effect of myelination by changing the specific capacitance (C<sub>m</sub>) of a uniform cylindrical axon to a double cable model that represented the axon and myelin sheath separately using NEURON's extracellular mechanism. Simulations were performed on a sequence of plausible intermediate stages of myelin evolution from the apposition of membrane from adjacent glial cells to a single layer of myelin surrounding the axon to multiple myelin wraps with well-organized nodes. At each stage the effects of the model parameters on conduction velocity were assessed. We found that a relatively small amount of myelination, even partial coverage by a single layer of glial membrane, produced a substantial increase in conduction velocity. For example, the addition of one myelin wrap (2 membranes) to a small (2 micron) diameter axon resulted in a 70% increase in conduction velocity, suggesting that a substantial advantage of myelin could be available to

the earliest stages in myelin evolution. For the double cable model, conduction velocity increased more rapidly with increasing myelin wraps for larger diameter axons. This suggests that in the transition to a myelinated nervous system, it is large diameter axons that become myelinated first.

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