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Slow axonal transport: Neurofilaments switch between distinct mobile and stationary states during their transport along axons PETER JUNG, Department of Physics and Astronomy, Ohio University, NIRAJ TRIVEDI, Center for Molecular Neurobiology, Ohio State University, LEI WANG, The Burnham Institute, La Jolla, ANTHONI BROWN, Center for Molecular Neurobiology, Ohio State University — According to the stop-and-go hypothesis of slow axonal transport, cytoskeletal and cytosolic proteins are transported along axons at fast rates but the average velocity of movement is slow because the movements are infrequent and bidirectional. To test whether this hypothesis can explain the kinetics of slow axonal transport in vivo, we have developed a stochastic model of neurofilament (NF) transport in axons based on tracking of single NF molecules. Based on this model, we propose that NFs in vivo move in both, anterograde and retrograde directions along cytoskeletal tracks switching between mobile and a stationary states. To verify the proposed stationary state we have developed a novel pulse-escape fluorescence photoactivation technique. We find that on average, the NFs spent 92% of their time in the stationary state and 97% of their time pausing. We speculate that the relative proportion of the time that NFs spend in the stationary state may be a principal determinant of their transport rate and distribution along axons, and a potential target of mechanisms that lead to abnormal NF accumulations in disease.

Peter Jung
Department of Physics and Astronomy, Ohio University

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