SP9 Axonal transport: Bianxiao Cui, Stanford University
Funding Source and Period: NIH Office of the Director, 1DP2NS082125-01, 2012-2017 (Cui, PI)
Associated With: TRD4

Significance: Dynein-dependent transport of organelles from the axon terminals to the cell bodies is essential to the survival and function of neurons. However, quantitative knowledge of the transport process, especially of dyneins and axonal organelles and their collective function during this long-distance transport, is lacking because current technologies to measure these are not available for neurons.

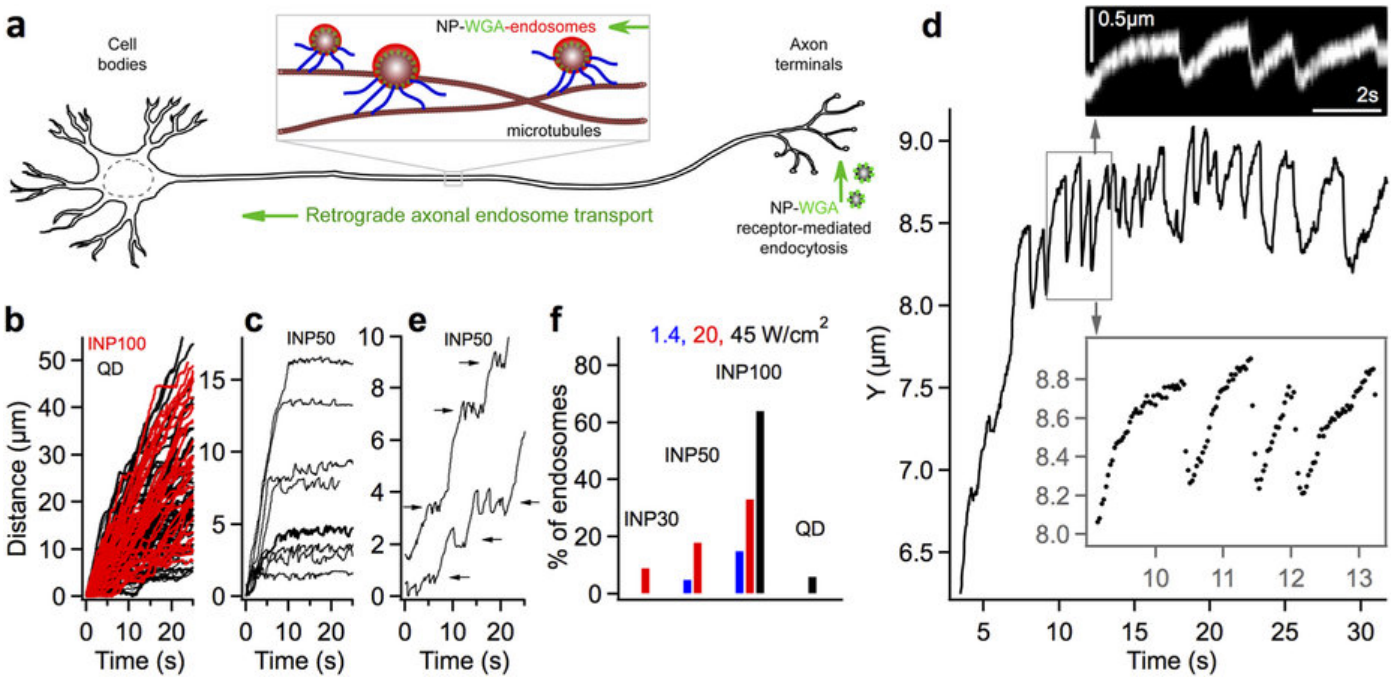

Figure 1. Nanoparticle assisted optical tethering of endosomes in axons. a Schematic of the retrograde axonal transport of nanoparticle-WGA endosomes from axon terminals to the cell bodies in neurons. **b** Unperturbed retrograde transport trajectories of QD-endosomes (black, 45 W/cm2, 32fps) and INP100-endosomes (red/gray, 1.4 W/cm2, 10fps). **c** Retrograde INP50-endosomes (19 W/cm2, 32fps) stochastically becoming stationary within the imaging field of view. **d** Gradual stalling and fast reversals (jumps) exhibited by an affected INP-endosome. Inset zooms in on a few jumps with the corresponding kymograph is also shown. **e** Laser-affected INP50-endosomes exhibiting jumps at different locations along the axon. **f** Percentage of laser-affected endosomes, for different nanoparticles at varying laser powers. [1]

Approach: The Cui lab has developed a new method termed nanoparticle-assisted optical tethering of endosomes (NOTE) that made it possible to study the cooperative mechanics of dyneins on retrograde axonal endosomes in live neurons [1] (Figure 1). The method uses magneto fluorescent particels recently developed by LBRC [3] (Figure 2). In this method, the opposing force from an elastic tether causes the endosomes to gradually stall under load and detach with a recoil velocity proportional to the dynein forces. These recoil velocities reveal that the axonal endosomes, despite their small size, can recruit up to 7 dyneins that function as independent mechanical units stochastically sharing load, which is vital for robust retrograde axonal transport. The Cui group showed that NOTE, which relies on controlled generation of reactive oxygen species, is a viable method to manipulate small cellular cargos that are beyond the reach of current technology.
The Cui lab will further develop techniques beyond NOTE to study axonal transport.

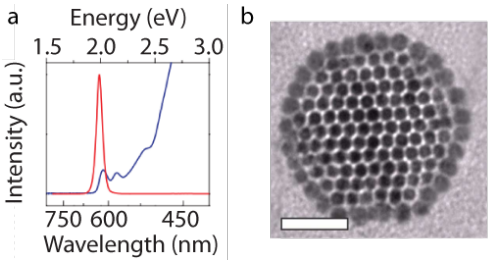

Figure 2. Magneto-fluorescent particles. a Absorbance and fluorescence spectrum of non-blinking, uniform CdSeCdS core-shell QDs with unity QY and narrow emission linewidths [2]. **b** Magnetofluorescent core-shell superparticles compromised of a Fe_3O_4 core and a CdSeCdS shell (Scale bar 15 nm) [3].

Center Offering: LBRC provides novel magneto-fluorescent nanoparticles enabling Cui lab to manipulate small cellular cargos to study mechanochemical transduction of dyneins on the single molecular level.

Literature Cited:

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2. O. Chen, J. Zhao, V. P. Chauhan, J. Cui, C. Wong, D. K. Harris, H. Wei, H.-S. Han, D. Fukumura, R. K. Jain, and M. G. Bawendi, "Compact high-quality CdSe-CdS core-shell nanocrystals with narrow emission linewidths and suppressed blinking.," Nat. Mater. **12**, 445–51 (2013).
3. O. O. Chen, L. Riedemann, F. Etoc, H. Herrmann, M. Coppey, M. Barch, C. T. C. T. Farrar, J. Zhao, O. T. O. T. Bruns, H. Wei, P. Guo, J. Cui, R. Jensen, Y. Chen, D. K. D. K. Harris, J. M. J. M. Cordero, Z. Wang, A. Jasanoff, D. Fukumura, R. Reimer, M. Dahan, R. K. Jain, and M. G. M. G. Bawendi, "Magneto-fluorescent core-shell supernanoparticles.," Nat. Commun. **5**, 5093 (2014).