

Kinesin and dynein respond differently to cytoplasmic drag

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Micron-sized cargoes in living cells are actively transported in opposite directions along microtubules by the molecular motors kinesin and dynein. While these motors have been extensively studied *in vitro*, the conditions in the cell differ substantially. In particular, drag forces cease to be negligible *in vivo*. Previous experiments performed *in vitro* show that opposing loads affect the transport velocity of kinesin and dynein differently, resulting in different force-velocity curves [1, 2].

We have observed evidence for these force-velocity dependences *in vivo*. First, we quantified the cytoplasmic viscous forces experienced by motors in *Drosophila* embryos by using a combination of passive microrheology, and a novel approach to active microrheology, with endogenous lipid droplets as probes. We then treated the embryos with inhibitors or promoters of actin polymerization, thus changing the average rheological properties experienced by motor-driven cargo. This allowed us to measure the effect of cytoplasmic drag on the velocity of those same lipid droplets hauled by kinesin and dynein [3, 4]. We find that kinesin and dynein respond differently to cytoplasmic drag forces, with kinesin being load-sensitive at high opposing forces and dynein at low. Our findings agree with and – to our knowledge – constitute the first *in vivo* validation of the force-velocity curves for kinesin and dynein found *in vitro*.

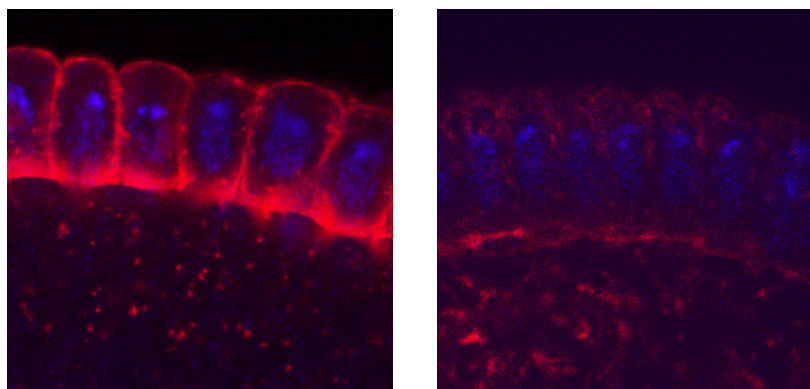


Figure 1: Motor-driven cargoes in an intact embryo (left) face more cytoplasmic drag than in embryos where actin filaments, shown in red, are depolymerized (right).

References

- [1] K. Visscher, M. Schnitzer, S. Block: *Single kinesin molecules studied with a molecular force clamp*. Nature **400**, 184–189 (1999)
- [2] A.K. Rai, A. Rai, A.J. Ramaiya, R. Jha, R. Mallik: *Molecular adaptations allow dynein to generate large collective forces inside cells*. Cell **152**, 172–182 (2013)
- [3] G.T. Shubeita, S.L. Tran, J. Xu, M. Vershinin, S. Cermelli, S.L. Cotton, M.A. Welte, S.P. Gross: *Consequences of motor copy number on the intracellular transport of kinesin-1-driven lipid droplets*. Cell **135**, 1098–1107 (2008)
- [4] C. Leidel, R.A. Longoria, F. Marquez Gutierrez, G.T. Shubeita: *Measuring molecular motor forces in vivo: Implications for tug-of-war models of bidirectional transport*. Biophysical J. **103**, 492–500 (2012)