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Cargo diffusion shortens single-kinesin runs JOHN WILSON, DAVID QUINT, AJAY GOPINATHAN, JING XU, UC Merced — Molecular motors such as kinesin-1 drive active, long-range transport of cargos along microtubules in cells. Thermal diffusion of the cargo can impose a randomly directed, fluctuating mechanical load on the motor carrying the cargo. Recent experiments highlighted a strong asymmetry in the sensitivity of single-kinesin run length to load direction, raising the intriguing possibility that cargo diffusion may non-trivially influence kinesin. To test this possibility, here we employed Monte Carlo-based simulations to evaluate the transport of cargo by a single kinesin. Our simulations included physiologically relevant viscous drag on the cargo and interrogated a large parameter space of cytoplasmic viscosities, cargo sizes, and motor velocities that captures their respective ranges in living cells. We found that cargo diffusion significantly shortens single-kinesin runs. This diffusion-based shortening is countered by viscous drag, leading to an unexpected, non-monotonic variation in run length as viscous drag increases. To our knowledge, this is the first identification of a significant effect of cargo diffusion on motor-based transport. Our study highlights the importance of cargo diffusion and load-detachment kinetics on single-motor function.

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