

# How to measure load-dependent kinetics of individual motor molecules without a force-clamp

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Molecular motors are responsible for numerous cellular processes from cargo transport to heart contraction. Their interactions with other cellular components are often transient and exhibit kinetics that depend on load. Here, we measure such interactions using a new method, “Harmonic Force Spectroscopy.” In this method, harmonic oscillation of the sample stage of a laser trap immediately, automatically and randomly applies sinusoidally varying loads to a single motor molecule interacting with a single track along which it moves. The experimental protocol and the data analysis are simple, fast and efficient. The protocol accumulates statistics fast enough to deliver single-molecule results from single-molecule experiments. We demonstrate the method’s performance by measuring the force-dependent kinetics of individual human beta-cardiac myosin molecules interacting with an actin filament at physiological ATP concentration. We show that a molecule’s ADP release rate depends exponentially on the applied load. This points to Kramer’s Brownian diffusion model of chemical reactions as explanation why muscle contracts with a velocity inversely proportional to external load.

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