Stochastic Mechanochemistry for Processive Motor Proteins: Kinesin Crouches before Sprinting. YOUNG C. KIM, MICHAEL E. FISHER, Inst. Phys. Sci. Tech., University of Maryland, MD 20742 — Experiments by Block and coworkers (2003) applied assisting, resisting, and sideways loads $\boldsymbol{F} = (F_x, F_y, F_z)$ to single-molecules of kinesin as they moved along a microtubule (MT) taking steps of size $d \simeq 8.2$ nm. The velocity, V_x, and the randomness were observed as functions of $\boldsymbol{F}$ and [ATP]. To uncover substeps and intermediate motions from such data, we have extended a discrete-state stochastic model, previously applied to kinesin[1] and myosin V,[2] to allow for the *vectorial* loading of processive motors by invoking a *three*-dimensional "energy landscape" with a potential $\Phi(\boldsymbol{F})$.[3] The size of the attached bead and the resulting angle of the motor's tether relative to the track play a crucial role. The analysis for kinesin then indicates that on binding ATP (and, possibly, catalysing hydrolysis, etc.) the motor 'crouches,' i.e., the point of attachment of the tether moves *downwards* (toward the MT) by 0.5-0.8 nm but *forwards* by only 0.1-0.2 nm, before completing a rapid swing of close to 8 nm. Unlike the scalar, F_x-only, analysis,[1] this is consistent with the observations of Higuchi and coworkers. Furthermore, assisting (*i.e.*, forward) loads are opposed since the 'upwards' component, F_z, is enhanced by $\sim$2 pN which *reduces* the velocity.

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2. A. B. Kolomeisky and M. E. Fisher, Biophys. J. **84**, 1642 (2003).
3. M. E. Fisher and Y. C. Kim, Biophys. J. **86**, 527a, 2738-Plat. (2004).

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Date submitted: 29 Nov 2004

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