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Supplemental information

Simulations suggest robust microtubule attachment of kinesin and dynein in antagonistic pairs

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Supplemental Figures and Tables:

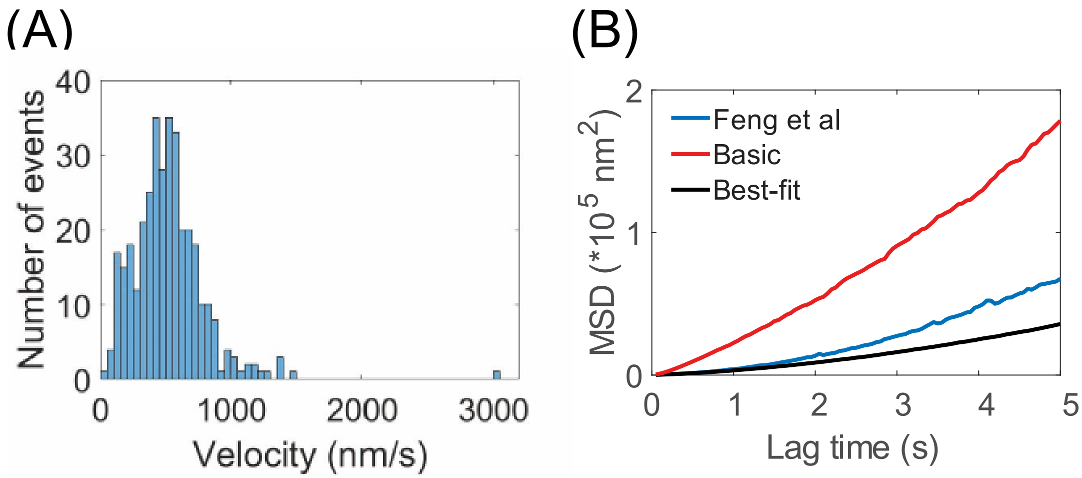

Figure S1. (A) Distribution of trace velocities of isolated kinesin-1 in the dynein motility buffer used in Kin-DDB experiments (1). Dynein motility buffer consists of 30 mM HEPES, 50 mM potassium acetate, 2 mM magnesium acetate, 1 mM EGTA and 10% glycerol, supplemented with 2 mg/ml casein, 20 mM glucose, 37 mM βME, glucose oxidase, catalase, 10 mM Taxol, and 2 mM ATP. The mean velocity of 515 nm/s was used for the unloaded kinesin-1 velocity in the simulations. (B) Mean squared displacement (MSD) analysis of experimental data from Feng et al. (1) and Basic and Best-fit model results from this study. Curves were fit with the equation: $MSD = V^2t^2 + 2Dt$, where V is velocity, D is the apparent diffusion coefficient, and t is the lag time. Fit results are $V = 49\ nm/s, D = 996\ nm^2/s$ for experimental data, $V = 49 nm/s, D = 11{,}800\ nm^2/s$ from the basic model, and $V = 32\ nm/s, D = 1812\ nm^2/s$ from the best-fit model.

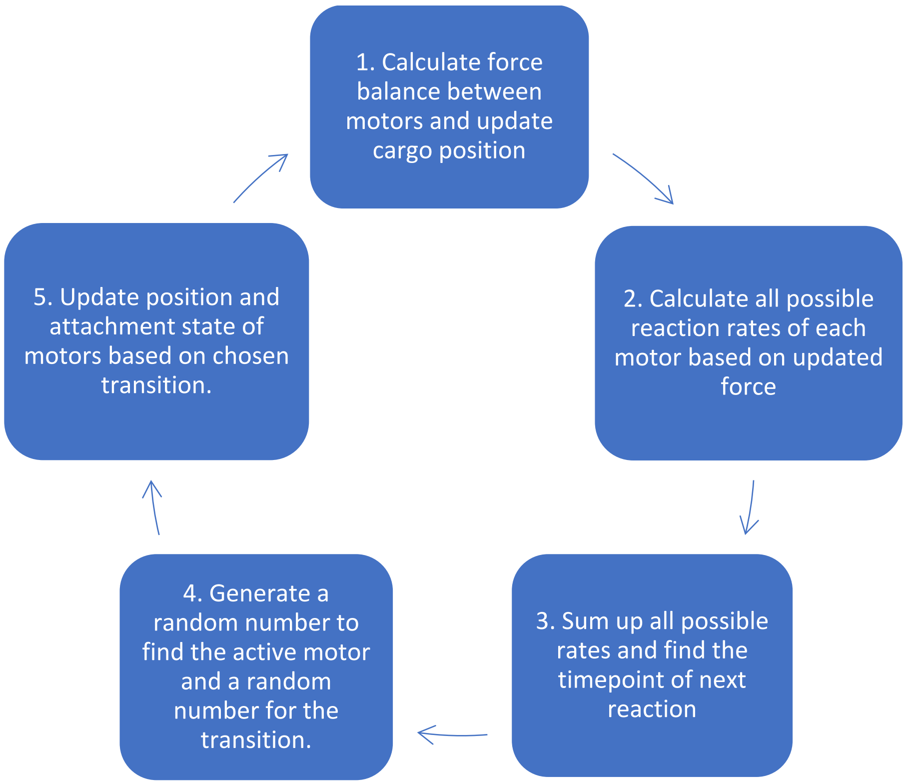

Figure S2. Flow chart for stochastic bidirectional stepping algorithm. The initial positions of both motors and the cargo are at the origin. The first step is to update the force balance between the motors and use this do define the cargo position. The second step is to calculate all possible reaction rates based on the forces applied to each motor. The third step is to use a random number to find the timepoint when the next reaction occurs based on Eq. (2) in Methods. The fourth step is to use one random number to choose which motor is active (i.e., making a transition) and a second random number to choose which transition the active motor will make. Finally, the motor position and attachment states are updated. The steps are repeated until both motors detach from the microtubule or until the maximum simulation time is achieved.

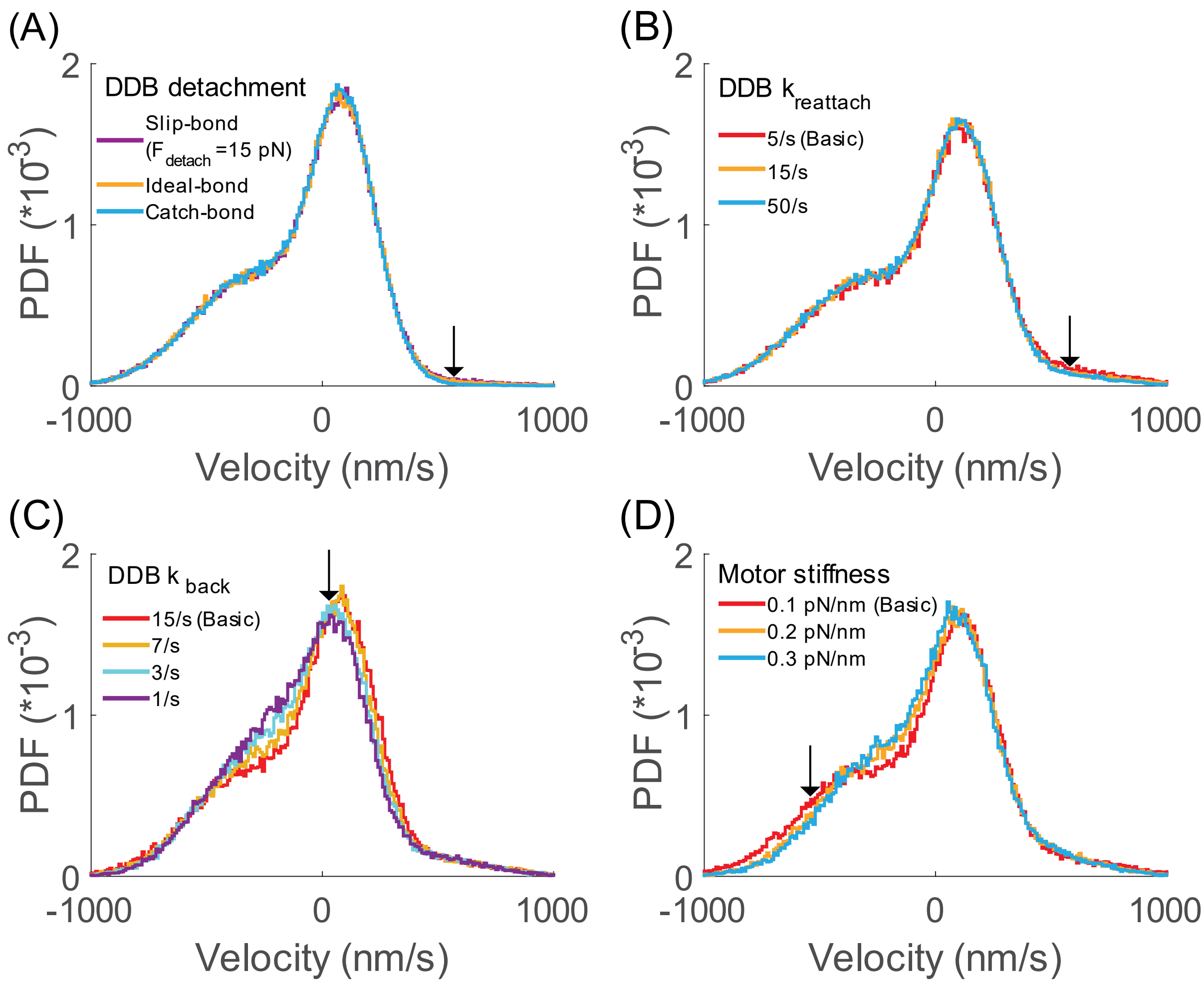

Figure S3. Effect of changing DDB mechanochemical properties and motor stiffnesses on the instantaneous velocity distribution in the 'basic' model. (A) Comparison between different load-dependencies of the DDB detachment rate. The slip-bond with F_{detach} = 15 pN was taken from Fig. 3C, an ideal-bond corresponds to F_{detach} set to infinity, and the catch-bond used F_{detach} = -3 pN such that detachment slows with increasing force. (B) Effect of altering the DDB reattachment rate, showing only a very small effect on the plus-end side peak. (C) Effect of altering the DDB backstepping rate, k_{back}, showing a small leftward shift of the central velocity peak with slower backstepping. (D) Effect of increasing the motor stiffness was to reduce the minus-end velocity peak.

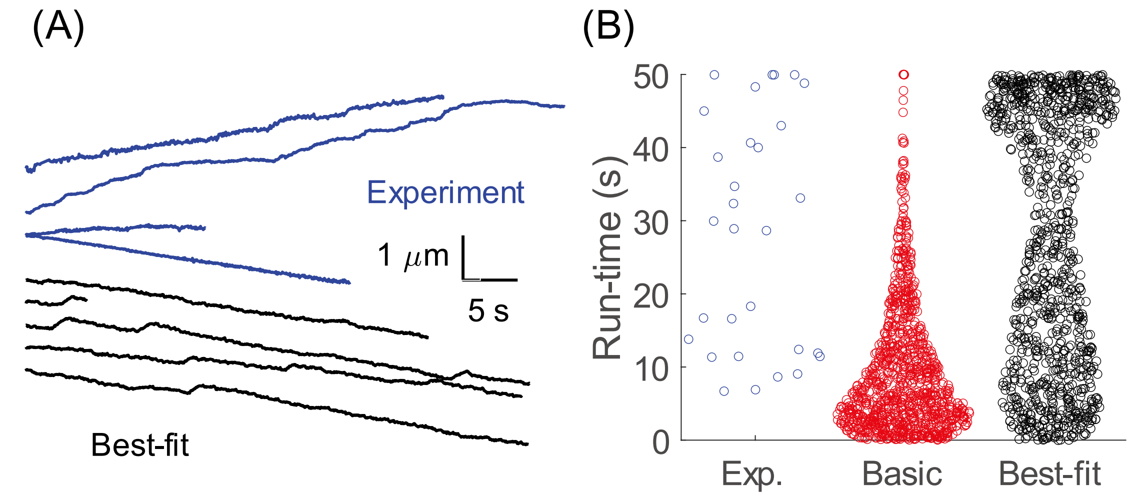

Figure S4. (A) Example 50-second traces from tracking experiment (1) and simulations of the best-fit model. (B) Distribution of run durations from experimental data (blue), basic model (red) and best-fit model (black). The best-fit model had longer run durations that more closely matched the experimental data. Maximum duration of 50 s was set by movie duration from experiments.

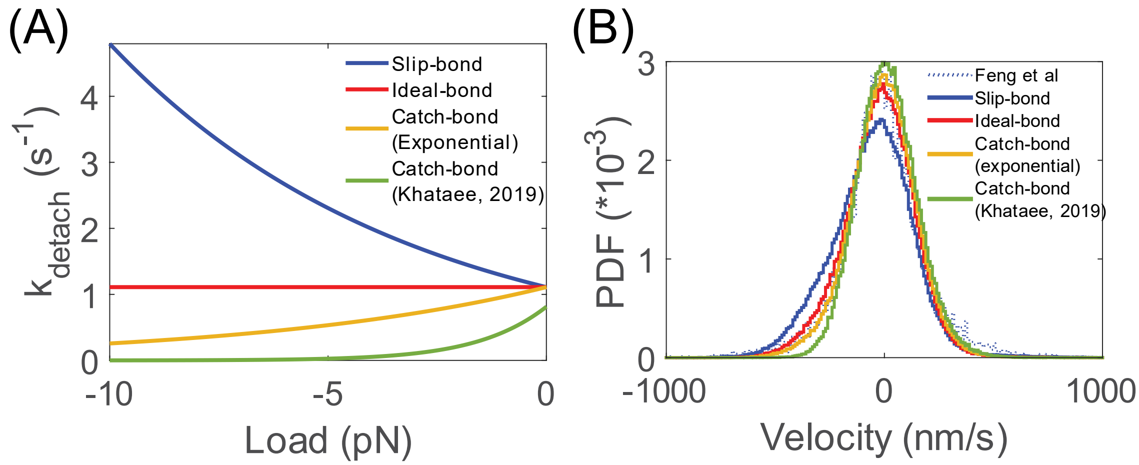

Figure S5. (A) Different models of kinesin detachment under horizontal hindering loads. The slip-bond model (blue) is based on experimental data from Andreasson et al. (2); the detachment rate is $k_{detach}(F) = k^0_{detach} * e^{\frac{|F|}{F_{detach}}}$, where F_{detach} = 6.8 pN. The ideal-bond model (red) used a load-independent detachment rate, $k_{detach}(F) = k^0_{detach}$, where k^0_{detach} = 1.1 s^{-1} is taken from the unloaded detachment rate. The exponential catch-bond model (yellow curve) reverses the sign of the F_{detach}= 6.8 pN used for the slip bond, such that $k_{detach}(F) = k^0_{detach} * e^{\frac{-|F|}{F_{detach}}}$. The alternate catch-bond model (green) is the detachment rate under horizontal load calculated by Khataee et al. (3), where $k_{detach}(F) = \left(\frac{1}{k_1} + \frac{1}{k_2}\right)^{-1}$, $k_1(F) = k^0_1 * e^{-\frac{|F|\delta_{catch}}{k_B T}}$, $k_2 = 7.62$, $k^0_1 = 0.91, \delta_{catch} = 2.9$, and $k_B T = 4.1$. (B) The instantaneous velocity distribution of 'best-fit' kin-DDB model with different kinesin detachment models applied.

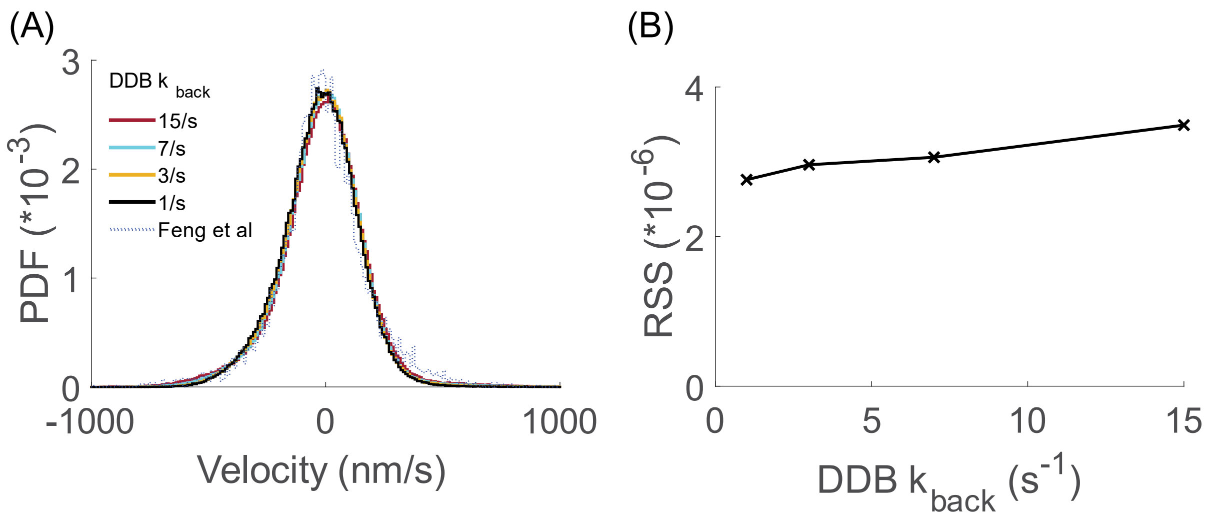

Figure S6. Effect of changing the DDB backstepping rate in the 'best-fit' model. (A) Instantaneous velocity distribution, showing the small effect of changing the DDB backstepping rate. (B) Residual sum of squares between simulation and experiment for 'best-fit' model with different DDB backstepping rates.

	Kinesin-1	DDB
Forward stepping rate under assisting load	$k_{forward}^{0}$	$v(F) = v_{min} * \left[1 - e^{(F_{stall} - F) * \frac{d}{k_B T}}\right]$ $k_{forward}(F) = \frac{v(F)}{8\ nm} + k_{back}$
Forward stepping rate under hindering load	$k_{forward}(F) = k_{forward}^{0} - \left(k_{forward}^{0} - k_{back}\right) * \left(\frac{\lvert F \rvert}{F_{stall}}\right)$	
Forward stepping rate under superstall forces[a]	$0\ s^{-1}$	
Backward stepping rate	Load independent	
Detachment rate	$k_{detach}(F) = k_{detach}^{0} * e^{\frac{\lvert F \rvert}{F_{detach}}}$	
Reattachment rate	Load independent	

Table S1. The models for load-dependent motor mechanisms used in stochastic stepping model.

[a] *Here, superstall is defined as* $F \geq \frac{k_{forward}^{0} * F_{stall}}{k_{forward}^{0} - k_{back}}$.

Parameter	Better-fit model	
	Kinesin-1	**DDB**
Unloaded velocity (nm/s)	515	328
Backstepping rate (s^{-1})	3	15
Stall force (pN)	6[b]	3.6
Unloaded detachment rate (s^{-1})[a]	1.11	0.1
Detachment force (pN)	Ideal	Ideal
Reattachment rate (s^{-1})	50[b]	5
Stiffness (pN/nm)	0.1068	0.1068
Residual sum of squares (RSS)	$4.29*10^{-5}$	

Table S2. Parameters used for the 'better-fit' model.

[a] *For kinesin under assisting loads, the unloaded detachment rate extrapolation was 7.4 s^{-1} and detachment force was 12.8 pN based on (2). For DDB under assisting loads, the unloaded detachment rate and detachment force were identical to the hindering load condition. Ideal bond (load-independent detachment) corresponds to F_{detach} equal to infinity.*

[b] *The parameters used in "better-fit" were established by results of parameter sensitivity tests in simulation.*

Reference:

1. Feng, Q., A. M. Gicking, and W. O. Hancock. 2020. Dynactin p150 promotes processive motility of DDB complexes by minimizing diffusional behavior of dynein. Molecular Biology of the Cell 31:782-792.
2. Andreasson, J. O., B. Milic, G.-Y. Chen, N. R. Guydosh, W. O. Hancock, and S. M. Block. 2015. Examining kinesin processivity within a general gating framework. eLife 4.
3. Khataee, H., and J. Howard. 2019. Force Generated by Two Kinesin Motors Depends on the Load Direction and Intermolecular Coupling. Phys Rev Lett 122.