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Molecular motors are stymied by microtubule lattice defects

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The microtubule surface provides the tracks that molecular motors use to transport cargo throughout the cell. Much like any surface lattice, the microtubule surface may have surface defects such as dislocations or step edges caused by missing tubulin dimers or shifts in the number of protofilaments, respectively. It is an open question as to how microtubule lattice defects affect molecular motors walking along microtubule surfaces. We used the kinesin-1 motor that walks along a single protofilament and has a short step size of only 8 nm to test how lattice defects affect transport. We created microtubule lattice defects by end-to-end annealing microtubules with different protofilament numbers and differential fluorescence labeling, creating a transition in microtubule radius at the annealed site that is directly visualizable. Surprisingly, we observed that kinesin-1 motors are significantly inhibited by protofilament shift defects. GFP-tagged kinesin-1 motors detach at the defect site during at least 70% of encounters with the defect. We find end-to-end annealed microtubules without the additional change in protofilament number at the defect site inhibit at least 50% of kinesin-1 motors at the defect, suggesting that the process of end-to-end annealing creates defects within the lattice. Our results imply that defects within the microtubule lattice can inhibit motility, and must be corrected. Our work sheds light on the biological importance of removing and correcting lattice defects, an activity known to occur by multiple methods in cells.