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New structure and energy cycles of kinesin dimers walking on microtubules revealed from molecular simulations

Xiongwu Wu, Allen Pan, Bernard R Brooks and Alicia Pan
National Institutes of Health Bethesda, USA

Kinesins are motor proteins that move unidirectionally along microtubules as they hydrolyze ATP. Although the general features of the kinesin walking mechanism are becoming increasingly clear, some key questions remain unanswered, such as how they convert the chemical energy of ATP into mechanical energy and walk processively. In this study, through molecular simulations and free energy calculations, we found that in aqueous solution, kinesin favors an extended form with its microtubule-binding interface (MTBI) motif unfolded, as seen in a recent X-ray structure of kinesin-8. Through the flexible fitting of two newly released cryo-electron microscopy (cryo-EM) maps, we derived atomic structures of the kinesin dimer-microtubule complexes in both two-head-bound and one-head bound states. Free energy calculations showed that kinesin bound to microtubules has a lower free energy than the extended form and that the free energy difference is in the range of the free energy released by ATP hydrolysis. The transition between the extended and compact forms, the structural differences of the leading and trailing heads and atomic force simulations lead us to a completely new mechanism by which kinesin dimers walk on microtubules.

Biography

Xiongwu Wu has his expertise in molecular simulation and method development. He has developed Self-Guided Molecular/Langevin Dynamics simulation (SGMD/SGLD) methods that enable molecular simulation to access long-time scale events. He has developed core-weighted grid-threading method for rigid fitting of proteins into low resolution cryo-EM maps and Map-restrained SGLD (MapSGLD) method to flexible fit protein structures into cryo-EM maps. He is also the Developer for both molecular simulation and modeling packages AMBER and CHARMM.

wuxw@nhlbi.nih.gov

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