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Push or Pull? – Cryo-Electron Microscopy of Microtubule's Dynamic Instability and Its Roles in the Kinetochore

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Microtubule is a biopolymer made up of alpha-beta-tubulin heterodimers. The tubulin dimers assemble head-to-tail as protofilaments and about 13 protofilaments interact laterally to form a hollow cylindrical structure which is the microtubule. As the major cytoskeleton in all eukaryotic cells, microtubules have the intrinsic property to switch stochastically between growth and shrinkage phases, a phenomenon termed as their dynamic instability. Microtubule's dynamic instability is closely related to the types of nucleotide (GTP or GDP) that binds to the beta-tubulin. We have biochemically trapped two types of assembly states of tubulin with GTP or GDP bound representing the polymerizing and depolymerizing ends of microtubules respectively. Using cryo-electron microscopy, we have elucidated the structures of these intermediate assemblies, showing that tubulin protofilaments demonstrate various curvatures and form different types of lateral interactions depending on the nucleotide states of tubulin and the temperature. Our work indicates that during the microtubule's dynamic cycle, tubulin undergoes various assembly states. These states, different from the straight microtubule, lend the highly dynamic and complicated behavior of microtubules. Our study of microtubule's interaction with certain kinetochore complexes suggests that the intermediate assemblies are responsible for specific mechanical forces that are required during the mitosis or meiosis. Our discoveries strongly suggest that a microtubule is a molecular machine rather than a simple cellular scaffold.