Poster

Conformational Changes in Tubulin and Implications for Microtubule Self-Assembly

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Basic understanding of fundamental biology and the search for novel treatments for human disease are increasingly taking us to investigations on the nanometer and Ångstrom scales. Atomistic simulations of proteins and their surrounding medium are not just computationally feasible but essential to the understanding of individual proteins and organelles as well as molecular biology in general. In particular, we are interested in microtubules (MTs), an essential component of the cell and important target for anti-cancer drugs.

MTs, found in all eukaryotic cells, are cylindrical organelles 25nm in diameter and up to several hundred μms long. They are one of the three fundamental parts of the cytoskeleton, the key constituent of which is the protein tubulin. Tubulin self-assembles to form a rigid, highly-ordered, helical lattice that forms the wall of the MT. Functionality of microtubules includes providing the structural stability of the cell and transportation of molecular cargo. Arguably, the most important role played is the formation of the mitotic spindle during cell division, requiring self-assembly and dis-assembly of the MT. It is for this reason that MTs have been one of the most successful targets for anti-cancer drugs. By interfering with this process one can prevent the cell from dividing, thereby halting the growth of a tumor and eventually killing the cells.

The precise mechanism for MT self-assembly and dis-assembly has been speculated to arise from the hydrolysis of guanosine-triphosphate (GTP) located at the exchangeable site on the tubulin dimer. After assembly GTP hydrolyzes to guanosine-diphosphate (GDP) causing a conformational change in tubulin and structural stress in the MT. Here we present the conformational changes observed in tubulin through molecular dynamics based computer simulations of the 3D structure of the tubulin dimer. These conformational changes will allow us to understand and simulate the growth of MTs as well as provide *in silico* testing for new anti-cancer drugs that bind to tubulin.