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An atomistic view of microtubule stabilization by GTP

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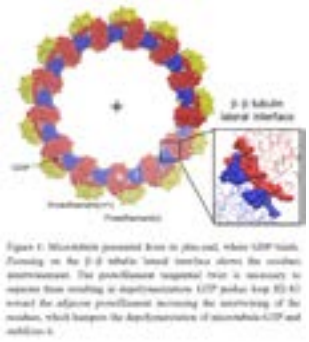
A microtubule is a dynamic system formed of αβ-tubulins. The presence of nonhydrolyzable guanosine-5'-triphosphate (GTP)/guanosine diphosphate (GDP) on the β-tubulins provokes microtubule polymerization/depolymerization. Despite the large number of experimental studies of this dynamical process, its mechanism is still unclear. To provide insights into this mechanism, we studied the first depolymerization steps of GDP/GTP-bound microtubules by normal-mode analysis with the all-atom model. We also constructed a depolymerizing microtubule and compared it to cryo-electron microscopy tomograms (cyro-ET). The results show that during depolymerization, the protofilaments not only curve but twist to weaken their lateral interactions. These interactions are stabilized by GTP, but not evenly. Not all of the interface residues are of equal importance: five of them, belonging to the H2-S3 loop, play a special role; acting as a lock whose key is the γ-phosphate of GTP. Sequence alignments of several tubulins confirm the importance of these residues.



Biography

Liliane Mouawad was always interested in understanding the mechanism of action of proteins or protein assemblies. This understanding may be based on either molecular simulations or on experiments like NMR. But her expertise is primarily in molecular dynamics simulations and more precisely in normal mode analysis (NMA). She has developed several methods going from the calculation of normal modes of very large systems or of images, to the calculation of the pathway between two protein conformations, to the prediction of the compactness of a calcium-binding protein. Recently she was also involved in docking and virtual screening themes, where she has acquired enough expertise to develop a new consensus methodology to overcome some issues observed in these approaches.

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