Box 1 | Microtubule structure and dynamic instability

FROM THE FOLLOWING ARTICLE:

Tracking the ends: a dynamic protein network controls the fate of microtubule tips

Anna Akhmanova & Michel O. Steinmetz

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Microtubules are composed of stable $\alpha/\beta$-tubulin heterodimers that are aligned in a polar head-to-tail fashion to form protofilaments (see figure, part a). The cylindrical and helical microtubule wall typically comprises 13 parallel protofilaments in vivo (part b). The 12-nm helical pitch in combination with the 8-nm longitudinal repeat between $\alpha/\beta$-tubulin subunits along a protofilament generates the lattice seam (red dashed line).
Assembly–polymerization and disassembly–depolymerization of microtubules (panel c) is driven by the binding, hydrolysis and exchange of a guanine nucleotide on the β-tubulin monomer (GTP bound to α-tubulin is non-exchangeable and is never hydrolysed). GTP hydrolysis is not required for microtubule assembly *per se* but is necessary for switching between catastrophe and rescue.

Polymerization is typically initiated from a pool of GTP-loaded tubulin subunits (part c;(1)). Growing microtubule ends fluctuate between slightly bent and straight protofilament sheets. GTP hydrolysis and release of inorganic phosphate occurs shortly after incorporation and is promoted by burial and locking of the partially exposed nucleotide as a result of the head-to-tail assembly of dimers. It has been postulated that GTP hydrolysis changes the conformation of a protofilament from a slightly curved tubulin-GTP to a more profoundly curved tubulin-GDP structure\textsuperscript{125}. This nucleotide-dependent conformational model predicts that the curved tubulin-GDP is forced to remain straight when it is part of the microtubule wall. Growing microtubule sheets are thus believed to maintain a 'cap' of tubulin-GTP subunits to stabilize the straight
tubulin conformation within the microtubule lattice. Closure of the terminal sheet structure generates a metastable, blunt-ended microtubule intermediate (part c; (2)), which might pause, undergo further growth or switch to the depolymerization phase. A shrinking microtubule is characterized by fountain-like arrays of ring and spiral protofilament structures (part c; (3)). This conformational change, which is presumably directed by tubulin-GDP, may destabilize lateral contacts between adjacent protofilaments. The polymerization–depolymerization cycle is completed by exchanging GDP of the disassembly products with GTP (part c; (4)).