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S E M I N A I R E

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" *Mechanobiology of microtubule self-assembly: deciphering the physical principles behind microtubule force generation and sensing* "

At the heart of many cellular processes, microtubule filaments are responsible for actively organizing the cellular interior, enabling directed intracellular transport and providing force stroke during cell division. The latter is achieved by the mitotic spindle, primarily using microtubules that exert forces on kinetochore complexes attached to the chromosomes. Notwithstanding its importance, the mechanisms of microtubule assembly and force transduction remain elusive. Microtubule-driven force generation is a challenging topic to study experimentally because molecular-level dynamic properties remain hidden to ensemble averaging methods like cryo-electron microscopy, while time-resolved optical laser trapping and microscopy assays do not provide sufficient spatial resolution. Furthermore, we lack multiscale theoretical models that would explain how the shape of fluctuating microtubule ends affects the generated force and exactly how the dynamics of microtubule ends change upon contact with a cargo. Thus, there is an urgent need to reconcile experimental and computational finding in a predictive physical model of microtubule force generation. To this end, we developed a minimal coarse-grained model of microtubule dynamics and parametrized it using free-energy matching with our previous all-atom simulations of tubulin oligomers and whole microtubules. Our model demonstrates that (1) the balance between spring-like elasticity of and interactions between curling tubulin oligomers at the microtubule end drives the assembly; and (2) the flare microtubule end enables proper kinetochore-microtubule attachment in a nucleotide-dependent manner and capable of bearing physiologically relevant mechanical loads.

Jeudi 25 janvier 2024

14h00

Salle des conférences