Microtubule tug-of-war and stochastic kinetochore oscillations

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We investigate the cooperative dynamics of microtubules, which are elastically coupled to kinetochores in the mitotic spindle. The model includes the dynamic instability of microtubules, forces on microtubules and kinetochores from elastic linkers and, eventually, an external force on the kinetochore. We use stochastic simulations and analytical solutions of Fokker-Planck equations to first analyze one hemisphere of the mitotic spindle consisting of an ensemble microtubules coupled to one kinetochore under a constant external force. In simulations of this one-sided spindle model, kinetochore movement exhibits bistable behavior as a function of the applied force [1]. Solving the Fokker-Planck equations for the microtubule-kinetochore distance distribution, we derive bistable behavior and conditions for the occurrence of bistability analytically. This allows us to quantify the bistable regime in the parameter plane of linker stiffness and microtubule numbers. In the full two-sided spindle model, two such bistable systems are coupled in a tug-of-war. This leads to stochastic chromosome oscillations in metaphase, which have been observed in several experiments.

[1] E.J. Banigan et al., Proc. Nat. Acad. Sci. U.S.A. 112, 12699 (2015).