Dynamic instability of microtubules

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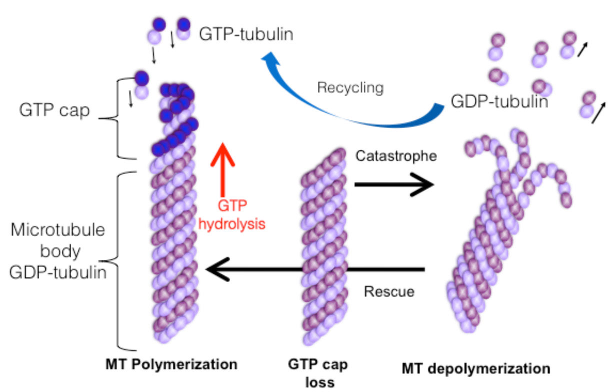
Microtubules (MTs) are long tube polymers of tubulin, found throughout the cytoplasm. MTs are very important in a number of cellular processes as maintaining structure of the cell, formation of the cytoskeleton, providing platforms for intracellular transport. They also segregate the chromosomes during cell division, and regulate substrate adhesion dynamics and cell polarity during cell migration, all crucial cellular processes in cancer progression. A key property of MTs necessary for almost all of these activities is their highly dynamic behavior at their plus end, called dynamic instability.

Indeed, MT plus ends alternate between phases of assembly and disassembly. MT polymerizes through the addition of GTP bound tubulin at the MT tip. GTP is hydrolysed in GDP shortly after incorporation. Thus, a MT has a tiny GTP cap at the tip while its body mainly composed of GDP bound tubulin. During polymerization MT can loss the GTP cap, if the rate of hydrolysis exceeds the rate of polymerization. In this case the MT undergoes a disassembly. The switch from growing to shrinking phases of MT is called catastrophe. There is also a possibility that a shrinking MT returns to the growing population, this situation is called a rescue event.

We propose a new deterministic mathematical model inspired by the work of Hinow et al.[1] to simulate the behavior of a MT population. It accounts for the principal reactions involved in dynamic instability such as polymerization, depolymerization, GTP hydrolysis, catastrophes and rescues. It couples transport equations with ordinary differential equations with nonlocal terms endowed with suitable boundary conditions for both catastrophe and rescue. The mathematical model is built from biological observations obtained by the pharmacologist of our interdisciplinary research group. Namely, there is an evidence that GTP hydrolysis rate may depend on the microtubule "age" under the influence of anti-microtubule drugs. The concept of MT aging has been incorporated in the mathematical model presented in this work.

Experimental data and computational simulations will illustrate the diverse concepts. Numerical results are obtained in MATLAB by using upwind scheme with adaptive time step for the partial differential equations and the explicit Euler method for the ordinary differential equations. This new model will allow us to better understand the pharmacological action of anti-microtubule drugs.



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Références

[1] Hinow P., Rezania V. and Tuszynski J. A. *A continuous model for microtubule dynamics with catastrophe, rescue and nucleation processes.* Phys. Rev. E 80 (2009).

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