

## Complexity miniproject 2014: **Simulation of tip structure evolution on dynamic microtubules**

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### **Background:**

Microtubules are dynamic, cylindrical filaments that serve as the intracellular transport network and fulfil vital structural and signalling roles in the cell.

Microtubules are assembled from  $\alpha\beta$ -tubulin dimers that attach head-to-tail into protofilaments, 13 of which form a hollow tube of ~25nm diameter. Assembly and disassembly of microtubules occurs at the ends of the microtubules [1]. Microtubules do not assemble with blunt ends, thus the length of individual protofilaments varies. It has been proposed that the evolution of more extensive tip structures precedes microtubule catastrophes, i.e. the change from assembly to disassembly [2]. We have reconstituted microtubule dynamics in vitro from purified components [3] and obtained high-resolution data of microtubule length and the fluorescence decay at the microtubule tip (a measure of protofilament length variability).

In this project we aim to simulate a microtubule dynamics experiment with known microtubule and protofilament length changes to determine the accuracy of our image and data analysis routines.

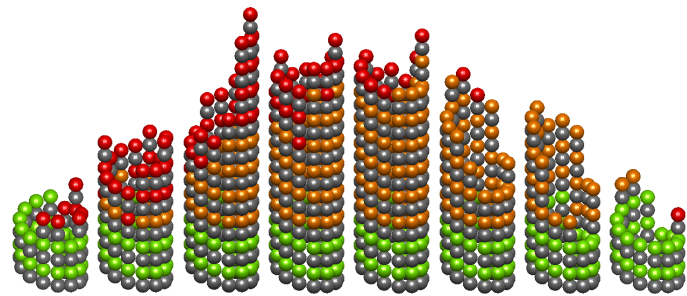


Fig. 1: Tubulin assembly from a stabilised seed. A cap of GTP-tubulin (red) protects the growing microtubule end during growth. Catastrophe occurs when the GTP cap is lost and GDP-tubulin (yellow) is exposed at the end.

### **Objectives:**

You will develop a simple model of microtubule dynamics based on existing literature [4-7] to generate realistic synthetic data of microtubule length fluctuations and evolving tip structures. The resulting synthetic images of microtubules will be convolved with the experimentally determined point spread function from our microscope setup. You will then be able to test our image analysis and statistical data analysis routine to determine which features of microtubule dynamics and tip structure can be robustly extracted from experimental data.

### **Potential PhD project:**

The project can expand to fitting experimental data to a dimer-scale microtubule dynamics model with inclusion of new features, such as a 3<sup>rd</sup> state of tubulin (the GTP/Pi-tubulin intermediate), which is recognised by the microtubule plus end tracker EB3. Correlated data for microtubule length, taper and EB3 intensity distribution at the plus end will directly inform such a model. A further layer of complexity would see addition of the plus end tracking proteins and their interactions with microtubules to the model.

### **References:**

- [1] Howard and Hyman. Growth, fluctuation and switching at microtubule plus ends. *Nat Rev Mol Cell Biol* (2009) 10: 569-74
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- [3] Straube. How to measure microtubule dynamics? *Methods Mol Biol* (2011) 777: 1-14
- [4] VanBuren et al. Mechanochemical model of microtubule structure and self-assembly kinetics. *Biophys J* (2005) 89: 2911-26
- [5] Gardner et al. Rapid microtubule self-assembly kinetics. *Cell* (2011) 146: 582-92
- [6] Margolin et al. The mechanisms of microtubule catastrophe and rescue: implications from analysis of a dimer-scale computational model. *Mol Biol Cell* (2012) 23: 642-56
- [7] Piette et al. A thermodynamic model of microtubule assembly and disassembly. *PLoS ONE* (2009) 4: e6378