Mechanical Properties of Microtubules under Various Chemical Conditions

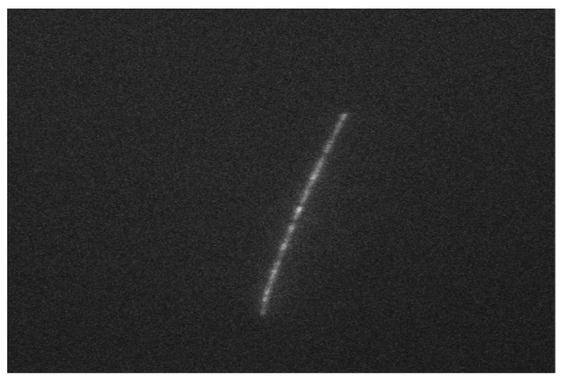
Kuang Wei
Mentor: Dezhi Yu, Faculty Advisor: Dr. Megan T. Valentine
Department of Mechanical Engineering, University of California - Santa Barbara

Introduction

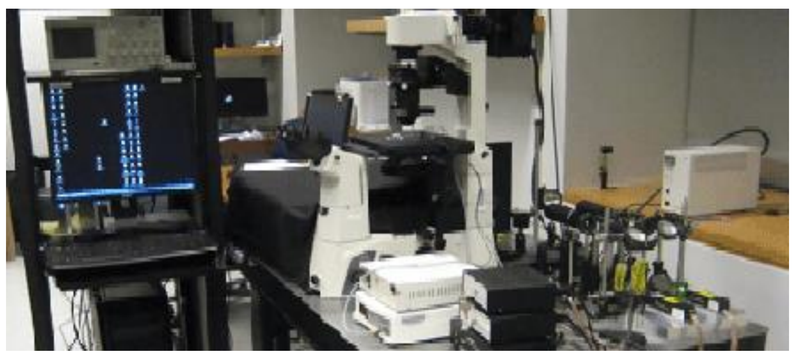
Microtubules are responsible for cell organizations, intracellular transport, and cell division. Many chemotherapeutic drugs inhibit microtubules' dynamics in order to prevent tumor cells from dividing. We suspect that the side effects associated with chemotherapy might be due to the structural and mechanical changes of microtubules induced by chemotherapeutic drugs. Therefore, in this project, we study the synergetic effects of various chemicals on microtubules' mechanical properties in hope to improve chemotherapy.

Experimental Methods

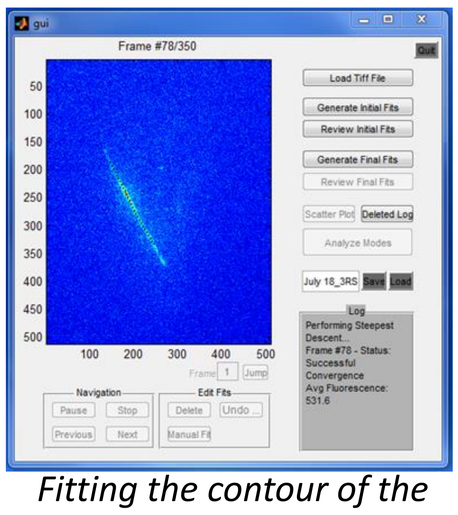
We synthesize microtubules with taxol, a microtubule stabilizer that is commonly used as a chemotherapeutic drug, and tau proteins, which not only stabilize microtubules but are critical to the development of healthy nervous system. We record movies of microtubules' thermal fluctuations and analyze the movies with pre-established MATLAB algorithms to fit the contour of microtubules with orthogonal polynomials and further obtain the persistence lengths of the microtubules using the worm-like chain model.



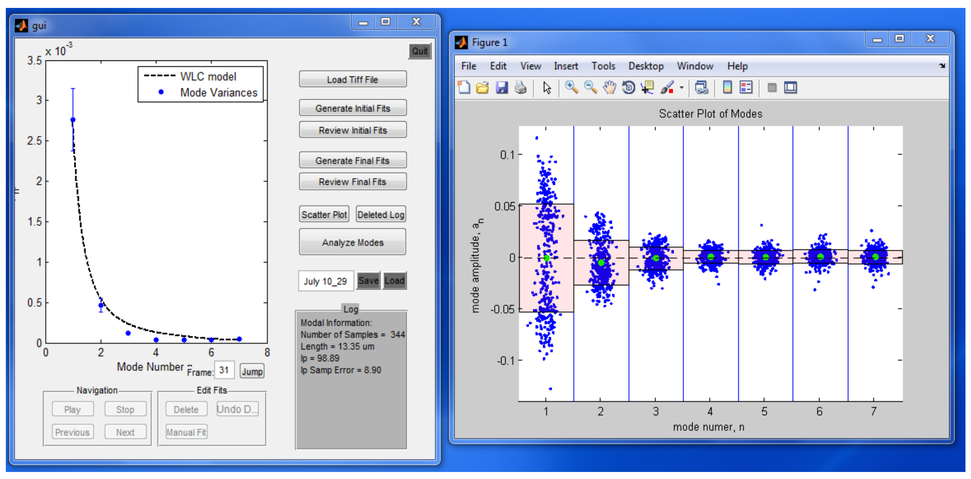
Snapshot of a microtubule movie



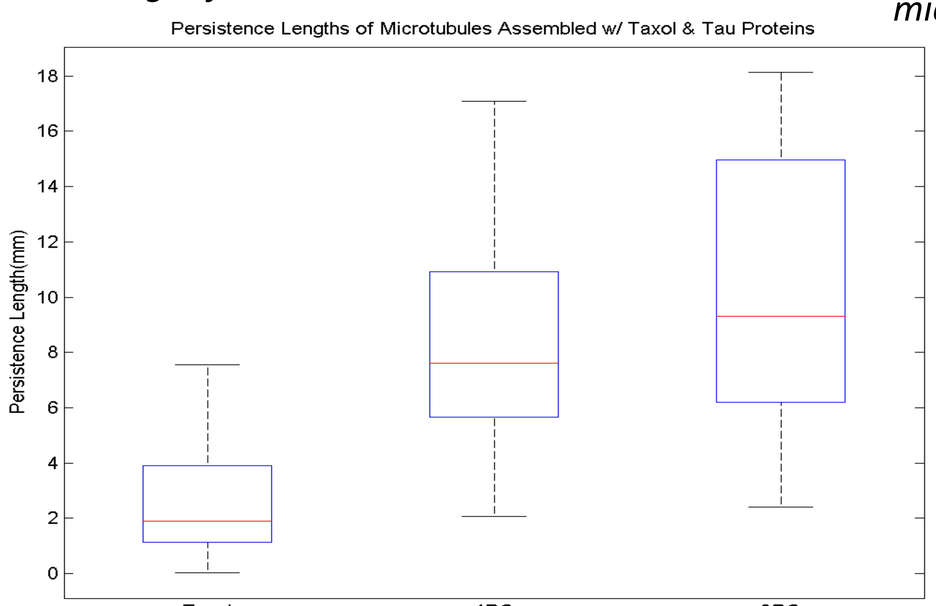
Customized TIRF microscope with the movie-recording software



Fitting the contour of the microtubule



Worm-like chain model and the variances of each mode



Data

We use persistence length to quantify the stiffness of microtubules. We found the median of the persistence length of taxol assembled microtubules to be 1904 µm, which matches with the previous study closely. We also found that the microtubules which were assembled with tau proteins have significantly higher persistence lengths than taxol assembled microtubules. The median persistence lengths of the 4RS tau protein assembled and 3RS tau proteins assembled microtubules came out to be 8135 µm and 9306 µm, respectively.

Discussion and Conclusion

In the previous study, it was found that tau proteins have little to no effect on the stiffness of microtubules if coated after the microtubules are polymerized with the presence of taxol. However, we have found that the stiffness of tau proteins assembled microtubules is significantly higher than taxol assembled microtubules. The result suggests that taxol might induce significant structural and mechanical changes on microtubules that are overriding tau proteins' effects on microtubules. This finding could lead us to gain a better understanding of the effects of taxol on microtubules' mechanical properties on a molecular level.

References

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Kuei, S., Pessino, V., Valentine, M. T., and Yu, D. 2013. Mechanical and functional properties of epothilone-stabilized microtubules. *Cytoskeleton*. 70:74-84

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