McGill

Department of Anatomy and Cell Biology

Seminar Series

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Hosted by: Dr. Susanne Bechstedt

Wednesday, April 17, 2019

11:30 am

Room 1/12

Strathcona Anatomy Building
3640 University Street

"Integrated 3D tomography and computational modeling to study forces in metaphase spindles"

The faithful segregation of chromosomes during mitosis is a fundamental and important process. Errors in mitosis have severe implications and are often detrimental to development, health and survival of the organism. We know that microtubules, in particular kinetochore microtubules, exert forces on chromosomes to initially position them on the metaphase plate and consequently divide them to the two daughter cells. The forces generated by microtubules are in balance during metaphase resulting in a mechanical steady-state and a stable long-lived spindle shape and length. Previous studies have identified the proteins involved in metaphase spindle assembly. Yet, we do not understand how those proteins lead to force generation through interactions of microtubules, motor proteins and chromosomes in submicron scale, and the collective effect of these forces on spindle shape function at larger scales. One major barrier in answering this question is the limitation of light microscopy in visualizing details of spindle microstructure in submicron resolutions. We have developed a novel approach of visualizing entire spindles in 3D by electron tomography and automatic microtubule segmentation. Using this approach, we can resolve single microtubules, which provides a unique perspective and offers a plethora of completely new information about the microstructure of spindles. Specifically, we can resolve chromosome surfaces, identify microtubules that are in contact with chromosomes (kinetochore microtubules), determine microtubules' nucleation profile, length distribution and local curvature. We combine electron tomography, light microcopy, biophysical modeling and large-scale simulations to develop a detailed and unprecedented understanding of force generation inside the spindle from individual microtubules to the mitotic spindle composed of thousands of microtubules.