Workflow:

Simulating microtubule dynamics 🡪 relating microtubule dynamics to the “mitotic force” magnitude and direction(mitotic force will be represented by the “stretch” at the kinetochore ) 🡪 relating mitotic force to the changes in the geometrical constrains in NDc80 protein 🡪 relating the changes in the geometrical constrains to the changes in the possibility of SAC activation using a feedback loop [This is essentially to link a biochemical model to a mechanical model].

Introduction

In paper <@ISI:000531629100001>, the authors used a model in which ensembles of parallel microtubules are attaching to a kinetochore via elastic linkers. This is similar to the model I propose in the sense that Ndc80s are my protein of interest and their elastic linkers. However, this paper is more focused on the observation of chromosome movement, while I am more interested in the change of the kinetochore. Nonetheless, I believe the methods and analytical thinking in the paper is of similar type.

In paper<@000491549200011>, the authors used CRW-like PDEs to model the spatial distribution of the tubulins. The distribution of the tubulin influences the dynamics of the microtubule polymerization and thus the magnitude and the direction of the mitotic force.

The paper<@000433291900011> considers the lifetime of the attachment between microtubules (MT) and kinetochores (kt). More importantly, the authors extend the formalism to model the stochastic kinetics of an attachment formed by a bundle of

multiple parallel microtubules with a single kt, which is closer to the actual biological phenomenon. This paper will help me consider the bundle effect of MTs in the MT-Kinetochore interface.

The paper <@ ISI:000440134000018> is a review on the molecular mechanism responsible for the chromosome motion associated with dynamic microtubule tips at the single-molecular level. The paper introduces me a new concept called the couplers, which are multimolecular ensembles.

The paper<@ISI:000388449500002> is a review on various approaches to simulate microtubule dynamics, from statistical chemical kinetics models to molecular dynamics models. This is a good starting point for the project: starting by **simulating the microtubule dynamics**.

The paper<@000365801600053> reports the development of mathematical models that can be fitted to high-resolution kinetochore tracking data, thereby estimating the model parameters and allowing us to indirectly compute the (relative) force components (K-fibre, spring force and PEF) acting on individual sister kinetochores in vivo. This is similar to the kind of data I want to collect. What’s different is that I am working on the collection of data of tracking single kinetochore. Multiple papers have made important advances by demonstrating that “force” at kinetochore depends on changes within the kinetochores rather than relative changes between the two sister kinetochores.

The paper < ISI:000338507200005>, provides an overview of dynamics and mechanical properties of the mitotic spindle. This paper will provide me a big idea of what’s known and what’s unknown in the field of MT-Kinetochore interaction.

In the paper <ISI:000332501300004>, a mathematical model that predicts the force generated at the kinetochore using 1) flexible kinetochore binder elements and 2) the shape of shortening microtubule tips. This is similar to what I am attempting in the second step of my workflow: being able to predict mitotic force using the “single kinetochore shape change information”.

The paper <ISI:000289575400011>, provides a review on the existing model of chromosome motion in the context of recent advances in our understanding of kinetochore molecular biology. This is good review paper in which I can find more relevant references.

The paper <ISI:000296584100013>, compares to paper < ISI:000332501300004>, provides an alternative way to model force generation at the kinetochore-microtubule interface. Here, spatial distribution of tubulin and polymerizing rate-altering enzymes inside the Kt are used to main varibales.

The paper < ISI:000275837800006> incorporates a molecular scale model of kinetochore-microtubule interactions into a negative feedback loop between spindle forces and local kinetochore biochemical reactions. This is exactly the method I want to use in order to link the force at kinetochore to the signaling at the kinetochore.

The paper < ISI:000278776500010> is an easy read for a biologist like me to get into modeling

The paper < ISI:000236080600005> provides a nice review for current models of spindle assembly, positioning, maintenance and elongation; of chromosome capture and congression; and of the spindle assembly checkpoint. The paper has a nice section on the SAC system.

The paper < ISI:000174501400001> discusses the diffusion approximation model of microtubule assembly. This can be related to the diffusion process we are talking right now in the class.