Title of Project	An integrated mathematical and cell biological approach to understand tension sensing at the kinetochore
Cell Mechanism Supervisor Name	Adele Marston
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Summary of project

During mitosis and meiosis, chromosomes must attach to microtubules from opposite poles, a state known as biorientation. The ability to sense tension that is thereby generated provides a signal that chromosomes are properly aligned and segregation can proceed. However, the mechanism by which this state of tension is sensed and signalled is poorly understood. Work in the Marston lab (*eLife* 2014*, Genes Dev* 2014) discovered that the conserved shugoshin protein is responsive to the state of tension in budding yeast. Shugoshin associates with chromosomes that are not under tension, but dissociates upon tension establishment. A major outstanding question is how shugoshin converts positional cues into a biochemical response to tension. This project will address this question by combining genetics and cell biology with mathematical modelling to gain mechanistic insight into how kinases and phosphatases control shugoshin localization and how this, in turn influences the response to tension.

The project will take advantage of synergy between the Marston lab, with traditional cell biological expertise and the Goryachev lab, with extensive experience in modelling the spatial regulation of cellular complexes. It will use state of the art live cell imaging and quantitative genomic methods, together with mathematical modelling to (1) measure the abundance and dynamics of shugoshin and its regulators (kinases, phosphatases); (2) determine how these parameters are altered by perturbation of the regulators and (3) define thresholds and triggers for the tension response.