**1885-Pos**

**A Mechanomolecular Model for Chromosome Movement During Mitosis**

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During mitosis chromosomes attach to dynamic microtubules in order to move to the cell equator. Kinetochores facilitate chromosome movement by maintaining a floating grip on inserted polymerizing or depolymerizing microtubules. In many vertebrates, chromosomes experience striking oscillatory movement both close to a pole and around the equator. Several chemical species that affect microtubule dynamics as well as proteins that bind to the microtubule lattice have been localized at kinetochores. Yet, there is no clear understanding of the force producing mechanism at microtubule attachment sites, and of how movement is controlled and coordinated at kinetochores so that a chromosome pinpoints the cell equator. Here we develop a mathematical model of chromosome motility that addresses the above two questions. First, we consider force production at kinetochores by developing a molecular motor model that describes molecular scale interactions between several kinetochore binders and an inserted microtubule. We find that for weak binding and low activation energies, the motor produces velocities that are fairly insensitive to loads and depend on the inserted polymer growth/shortening rates, in agreement with chromosome movement data. Then, we incorporate the molecular motor into a chromosome movement model in which motility results due to feedback between mechanical loads that arise from spindle-chromosome interactions and kinetochore chemical reactions that involve a force sensing kinase and a microtubule depolymerase.

Numerical simulations show that kinetochore chemical control of movement is a robust mechanism for chromosome oscillations and centering at the equator. Further, we observe that proper transition between mitotic stages is strongly influenced by kinetochore reactions, which indicates that motility does not solely result from ''tug of war'' between opposing forces. We find that our proposed mechanism is sufficient to recreate chromosome movement from prometaphase to anaphase, in good agreement with experimental data.

**1886-Pos**

**Probing the Force-Balancing Mechanism of the Meiotic Spindle in Xenopus Egg Extracts**

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During cell division, the meiotic spindle equally segregates replicated genomes into two daughter cells. Errors in this process cause birth defect and cancer. Spindles are mainly composed of microtubules (MTs) and molecular motors. Various studies have revealed key regulators, such as Kinesin-5 (plus-end directed kinesin tetramer), depolymerizing kinesins and microtubule-associated proteins (MAPs). These exert forces for sliding MTs or regulating MT dynamics in the spindle, so that the spindle maintains a rugby ball-like structure at metaphase. These forces are also known to generate a poleward flux of spindle MTs. At metaphase, size and shape of the spindle are maintained constant in spite of the dynamic nature of spindle MTs. This indicates forces exerted by molecular motors and MTs are well balanced in the spindle.

In this study, we developed micromanipulation techniques for changing spindle shape to disrupt steady state force balance of the spindle without any changes in molecular components of the spindle. Spindles spontaneously assembled in Xenopus egg extracts were stretched along their pole-to-pole axis using two glass micro-needles. When the spindles were briefly stretched, they recovered their original size and shape after a while. In contrast, when spindles were kept stretched, they gradually recovered their original shape with the increase in the spindle width, resulting in the enlargement in size. This result indicates that the meiotic spindle has an ability to adjust its size and shape to the externally applied force. Our findings provide new insights into the force-balancing mechanism of the spindle.

**1887-Pos**

**A Mechanical Model of Actin Stress Fiber Formation and Substrate Elasticity Sensing in Adherent Cells**

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Tissue cells sense and respond to the stiffness of the surface on which they adhere. Precisely how cells sense surface stiffness remains an open question, though various biochemical pathways are critical for a proper stiffness response. Here, based on a simple mechanochemical model of biological friction, we propose a mechanical model for cell mechanosensation as opposed to previous more biochemically-based models. Our model of adhesion complexes predicts that these cell-surface interactions provide a viscous drag that increases with the elastic modulus of the surface. Using the force-velocity relation of myosin II, we show that myosin generates greater force the slower the adhesion complexes slide. Then, using a simple cytoskeleton model, we show that an external force applied to the cytoskeleton causes actin filaments to aggregate and orient parallel to the direction of force application. The greater the external force, the faster this aggregation occurs. As the steady-state probability of forming these bundles reflects a balance between the time scale of bundle formation and destruction (due to actin turnover), more bundles are formed when the cytoskeleton time-scale is small (i.e. on stiff surfaces), in agreement with experiment. As these bundles seem related to stress fibers, large bundles of actin that appear preferentially on stiff surfaces, our mechanical model provides a mechanism for stress fiber formation and stiffness sensing in cells adhered to a compliant surface.

**1888-Pos**

**Dynamic Adaption of Actin Stress Fibers in Response to Stretch**

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Actin stress fibers are mechanosensitive structural elements that respond to stretching to regulate cell morphology, stress fiber alignment, signal transduction and cell function. Adherent cells maintain a level of prestress largely dependent on myosin contractility, suggesting that stress fibers self-adjust to an equilibrium level of stress. Here a quantitative model is developed to describe a potential mechanism for fibers to re-establish stress equilibrum in response to changes in fiber length. The model involves dynamic changes in fiber reference length regulated by myosin-actin cross bridging, where the force-velocity relationship for individual sarcomeres is expressed as a hyperbolic Hill-type model. Under static conditions, the basal level of fiber tension and pre-extension are determined by the number of sarcomeres bundled together in the fiber and the stall force of the constituent myosin filaments. Following a step increase in fiber length, tension initially increases elastically, but then relaxes with a characteristic time constant dependent on the rate of myosin cross bridge dynamics. Returning the fiber to the original length results in a drop in tension below equilibrium, followed by a relatively rapid return to equilibrium.The model predicts that stress fibers respond to cyclic stretch in a manner dependent on frequency, ATP concentration, equilibrium sarcomere length, and sarcomere stiffness with relaxation times ranging from 0.02 to 0.8 sec based on model parameter values extracted from the literature. The modeling results are consistent with various experimental findings and provide molecular insight into how stress fibers determine and maintain mechanical equilibrium in response to changes in length.

**1889-Pos**

**Spatially Dissecting the Viscoelastic Recoil and Cell Shape Contributions of Actomyosin Stress Fiber Bundles**

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The ability of a living cell to distribute contractile stresses against the extracellular matrix (ECM) in a spatially heterogeneous fashion underlies many fundamental behaviors, including motility, polarity, and assembly into multicellular tissues. Here we investigate the biophysical basis of this phenomenon at unprecedented spatial and mechanical resolution by using femtosecond laser ablation to sever contractile stress fibers located in specific cellular compartments and measure regional variations in fiber viscoelastic retraction and contribution to cell shape stability. Upon photodisruption, myosin light chain kinase-dependent stress fibers located along the cell periphery recoil much more slowly than rho-associated kinase-dependent stress fibers located in the cell center, with severing of peripheral fibers uniquely triggering a dramatic contraction of the entire cell. Remarkably, selective pharmacological dissipation of peripheral fibers significantly accelerates the retraction of central fibers, suggesting transference of tensile loads from one population of stress fibers to another in order to stabilize cell shape. These results suggest that stress fibers regulated by different myosin activators exhibit different mechanical properties and cell shape contributions. These data also illustrate the potential of femtosecond laser ablation to spatially map the microscale contractile mechanics of living cells.