2401-Pos Board B387
A Model for the Motion of Listeria in Curved Paths
Yuan Lin, Vivek Shenoy.
The movement of certain pathogens, such as Listeria monocytogenes, is commonly believed to be driven by actin polymerization. By hijacking the actin machinery of the host cell, these pathogens can move in the cytoplasm with a speed in the order of 0.1 μm/s. Several microscopic or macroscopic models have been proposed to account for the force generation by actin polymerization, however, a theoretical explanation for the rich trajectories traced out by the pathogens, including circles, winding S curves, translating figure eights, and serpentine shapes etc., is still lacking.
Here we show that the non-uniform polymerization of actins behind Listeria could be responsible for these fascinating trajectories. Specifically, we will demonstrate that if polymerization is fast at one side of the comet tail and slow at the other, then Listeria will move in circles. Stress profiles corresponding to different polymerization conditions will also be presented and, interestingly, we found that, depending on the degree of the non-uniformity in polymerization rate, some actin filaments might generate propelling forces pushing the bacteria forward while others might exert forces opposing the movement of Listeria, which is consistent with recent experimental observations.
In addition to a propelling force normal to the load surface, our model also predicts the generation of a tangential force by polymerizing filament. Consequently, a torque can be generated within the comet tail, causing Listeria to spin, if the symmetry of the actin network is broken. We will further demonstrate how various trajectories observed in experiments, such as winding S curves and translating figure eights, can be related to the asymmetric structure of the actin network, as well as the non-uniform polymerization of actins.

2402-Pos Board B388
Micro-Fabricated Substrates to Study Mechanotransduction
Jimmy Le Digabel.
Cellular processes imply an important coordination of interactions with the extracellular medium. Accumulating evidences demonstrate that cell functions can be modulated by physical factors such as the mechanical forces acting on the cells and the extracellular matrix, as well as the topography or rigidity of the matrix. These extracellular signals can be sensed by mechanosensors on the cell surface or in the cell interior to induce various cell responses. We have developed an original approach based on micro-fabricated substrates of PolyDimethylSiloxane (PDMS) to study cell migration. We used a closely spaced array of flexible micropillars of different sizes to measure the forces exerted by cells on their substrates and to modify the effective rigidity of the substrate. In particular, we performed durotaxie experiments using substrates with a well defined frontier between two regions of different rigidities. We observed that a cell arriving to the frontier is more inclined to go to the more rigid region than to the softer one. We propose also to analyze the cell response to an external applied stress by a well-controlled actuation of the substrate. To do so, we developed magnetic pillars. Using polyacrylamide hydrogels doped with ferromagnetic iron oxide particles or ferrofluids, we can make magnetic pillars with diameters of 4 to 10 μm while a magnetic field can be locally applied with a magnetic needle. With such a technique we can exert forces of the range of several nN. Those substrates can be helpful to study the mechanical response of cells to an external force or to local changes in their microenvironment.

2403-Pos Board B389
Controlling Dorsal Ruffles in Cells Through Substrate Stiffness and Mechanical Stimulation
Yukai Zeng, Philip R. LeDuc, Keng Hwee Chiam.
Circular dorsal ruffles (CDRs) are actin rich structures formed in mammalian cells in response to stimulation with growth factors, such as platelet-derived growth factor (PDGF). CDR formation is a possible mechanism by which the actin cytoskeleton in cells is remodeled relating to migration. We have found that CDRs form immediately after PDGF stimulation, before persisting and disappearing after tens of minutes in fibroblast cells seeded on underlying polydimethylsiloxane (PDMS) substrates coated with fibronectin. Increasing the PDMS stiffness with the same PDGF stimulation in NIH 3T3 fibroblasts increases the percentage of cells in a population which contain CDRs. Increasing PDMS substrate stiffness also results in a biphasic response of the average persistence time of CDRs formed in a cell population. This biphasic response reveals that the percentage of cells with CDRs increases at low stiffnesses while decreasing at higher stiffnesses. Not only does the substrate stiffness affect the CDRs, but by applying biaxial stresses to the cells through stretching the PDMS substrates, we observe an increase in the average persistence time of CDRs formed in a cell population with similar PDGF stimulation. Our results suggest that the functionality of CDRs in cells after stimulation with PDGF is linked to substrate stiffness and also the mechanical environment of the cells. We believe that this work is of interest to a wide variety of fields including physics, biology, material science, and mechanics.

2404-Pos Board B390
The Mechanism of Gut Loops Morphogenesis
Thierry Savin.
The small intestine has a remarkably complex morphology. It exhibits a distinguished coiled shape, with a succession of loops and twists. The latter allow for the long transit times required for digestion and nutrients absorption that characterize its function. Given this peculiar configuration, understanding development and morphogenesis of the gut appears to be a challenging, yet important task. I will show how we explain the formation and shape of gut loops by using a simple mechanical model, based on the differential growth between the gut tube and the mesentery, that is the membrane tissue that holds the intestine in place.

2405-Pos Board B391
Mechanical Control of Epithelial Growth: Distinct Morphogenetic Regimes
Oswaldo A. Lozoya, **Sharon R. Lubkin**.
We develop a model of transport and growth in epithelio-mesenchymal interactions. Analysis of the growth of an avascular epithelial spheroid inside a passive mesenchyme shows that sustained volumetric growth requires four generic mechanisms: (1) growth factor, (2) protease, (3) control of cellularity, and (4) swelling. The model reveals a bifurcation delineating two distinct morphogenetic regimes: (A) steady epithelial growth, (B) epithelial growth arrested by capsule formation in the mesenchyme. In both morphogenetic regimes, growth velocity is constant unless and until a complete capsule forms. Comprehensive exploration of the parameter space reveals that the bifurcation is determined by a ratio of the relative strengths of growth and proteolytic activity. Growth velocity is determined only by the strength of growth signaling, independent of proteolytic activity. There is a continuum of bulk versus surface growth, with fastest growth at the surface. The model provides a theoretical basis for explaining epithelial growth arrest despite proteolysis of surrounding tissue, and gives a quantitative framework for the design and interpretation of experiments.

2406-Pos Board B392
Influence of Substrate Thickness and Stiffness on Cell Behavior
Srikanth Raghavan, Aravind R. Rammohan, Martial Hervy.
It is known that various cell types can sense and respond to the mechanical properties of their microenvironment. Specifically, cells have been known to spread more when cultured on stiff substrates and are able to match their internal stiffness to that of the substrate. It has also been recently reported that even some cells are cultured on soft but thin coatings attached to stiff supports, they can perceive an effective stiffness that is much larger than that of the bulk coating. Building on earlier models [1,2], we present a model and invoke arguments based on energetics that explain why stiff and thin substrates encourage some cells to spread more easily and why these cells can match their internal stiffness to external stiffness more efficiently than others.

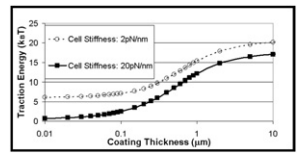

Figure : Traction energy as a function of coating thickness for different cell stiffnesses

Reference:
1. U. S. Schwarz et al, Biosystems, **83**, 225 (2006).
2. J. M. Maloney et al, Phys. Rev. E, **78**, 041923 (2008).

2407-Pos Board B393
Mechanosensing Directs Mitotic Signaling Proteins to Sites of High Mechanical Stress to Regulate Cytokinesis Through a Feedback Control System
Yee Seir Kee, Richard Firtel, Pablo Iglesias, Douglas Robinson.
Cytokinesis is the process by which a cell divides into two daughter cells and must be well regulated to prevent aneuploidy. The mitotic spindle is commonly viewed to initiate cleavage furrow formation through spindle signaling to the polar and furrow cortices. However, a number of studies have shown that the furrow can form independently of the mitotic spindle. Using *Dictyostelium discoideum*, our lab found that cellular mechanosensing is important for cell shape control during cytokinesis. Using micropipette aspiration (MPA) to apply mechanical stress to the cell cortex, we discovered that mechanical stress stimulates accumulation of myosin-II (a force-generating protein) and cortexillin-I (an actin-bundling protein) to the deformation site to correct cell shape. Both myosin-II and cortexillin-I localize to the cleavage furrow and are essential for mechanosensing. Here, we investigated how the spindle signals and mechanosensing work together to control cytokinesis. We found that the kinesin-6-family protein Kif12 can be recruited to mechanically stressed regions in a manner that is dependent on myosin-II and IQGAP2, a signaling effector of cortexillin-I. However, Kif12 is not required for myosin-II mechanosensing. Using agar overlay, we applied a uniform mechanical stress on the cortex. Previous studies showed that dividing cells under this condition have an enhancement of myosin-II localization at the cleavage furrow. In our study, we found