migration speed and cytoskeleton organization. Furthermore, cellular migration is monitored on polymer-tethered bilayer substrates with a sharp boundary or lateral gradient in lipopolymer concentration.

874-Pos Board B629
Modeling Follicle Cell Length Oscillations During Tissue Elongation in Drosophila Egg Chamber
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Periodic processes are an indispensable part of biological phenomena. Circadian rhythms, heart rhythms, neuronal oscillations, cell cycle, and cytoskeletal structures such as the axonemes of cilia are all examples of systems exhibiting oscillatory dynamics. The underlying mechanisms of several such processes can be explained by understanding the origins of these oscillations and characterizing them. One particular example is the follicle cell basal surface area oscillations observed in Drosophila egg chamber during oogenesis. It has been suggested that these oscillations restrict the egg chamber width, and thus help in elongation of the tissue. In this work, we attempt to model these oscillations in follicle cell length using a mechano-chemical model. Our model predicts an increase in oscillation period, upon removal of the basement membrane, which has been observed experimentally upon collagenase treatment of the egg chamber. The model also predicts an inverse relationship of maximum contractile force and oscillation period.

875-Pos Board B630
Coupling up: How Interactions between Cell Stresses and Intracellular Biochemistry Affect Cell Spreading
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We present a two-dimensional mathematical model and finite element simulations that allow us to better understand how local cellular deformations must be coupled to the evolution of an intracellular plaque protein that controls the formation of focal adhesions. Specifically, we explore effects of alternate formulations for coupling cellular response to substrate mechanics. Further, we also investigate the effect of initial cellular shape on cell spreading and intracellular stresses. Our aim is to determine whether the initial anisotropy of a cell predisposes it to remain anisotropic during spreading. In addition, we examine the role of focal adhesion strength in maintaining anisotropy. In the models for cell and substrate mechanics we assume that the cell is an active hypoelastic material and the substrate is linearly elastic. Focal adhesions are modeled as a collection of discrete springs that can be added and removed dynamically. This work aims to unearth some of the fundamental mechanisms in cell-substrate interactions.

876-Pos Board B631
Calculating Intercellular Stress in a Model of Collectively Moving Cells
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Cells move together in groups during development, wound healing, and cancer metastasis. It remains unclear how collectively moving cells coordinate their motion. In addition to external chemoattractants and exchanging signaling molecules, cells may also respond to mechanical cues. We developed a model of collective cell migration under the assumption that cells align their motility force with the direction of their velocity. This simple mechanism leads to large scale velocity correlations, swirling motion in the bulk of monolayers, and finger-like protrusions at the edge [1]. In experimental studies, the inter- and intracellular stress in the monolayer has been calculated from measured traction forces between the cells and the substrate. Stress builds up successively towards the center of the tissue as the majority of the cells pull outwards [2]. While one dimensional stress profiles are based on a simple force balance, two dimensional stress maps require the additional assumption of an elastic tissue [3], and the validity of this assumption remains disputable. In our model simulations, both the forces on the substrate and the intercellular forces are accessible. We can therefore apply a second method to calculate the stress based on forces between cells. Stress patterns calculated with both methods agree, showing that recovery of the intercellular stress is indeed mostly independent of specific material properties.

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877-Pos Board B632
Combination of Chemotaxis and Differential Adhesion Leads to Robust Cell Sorting During Tissue Patterning
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Robust tissue patterning is crucial to many processes during development. The ''French Flag'' model of patterning by instructive morphogen concentrations has been the most widely proposed model for tissue patterning. However, recently, cell sorting has been found to be an alternative model. In this article, we used computational modeling to show that two mechanisms, namely chemotaxis and differential adhesion, are needed for robust cell sorting. We assessed the performance of each of the two mechanisms by quantifying the fraction of correct sorting, the fraction of stable clusters after correct sorting, time taken for correct sorting and the size variations of the cells having different fates. We found that chemotaxis and differential adhesion confer different advantages to the sorting process. Chemotaxis leads to high fraction of correct sorting whereas differential adhesion leads to high fraction of stable clusters. A combination of both chemotaxis and differential adhesion yields cell sorting that is both accurate and robust. Thus, we propose that both mechanisms are used for cell sorting during tissue patterning in development.

878-Pos Board B633
Catching up on Slip: Focal Adhesion Composition and Mechanosensing
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Unlike slip bonds, catch bonds experience reinforcement under tension. Cell adheres to the surface, using integrins forming both catch- and slip- bonds with the surface receptors. How will the catch and slip bonds interact with each other on a single adhesion scale? How does the intracellular structure vary depending on the extracellular matrix stiffness? I discuss the implications of single catch-bond characteristics for the behavior of a load-sharing cluster of such bonds: these are shown to possess a regime of strengthening with increasing applied force, similar to the manner in which focal adhesions become selectively reinforced. In addition, I present numerical simulations of mixtures of catch and slip bonds within single focal adhesion, and propose a model of how they can influence cytoskeletal reorganization, force generation and adhesion growth, interacting indirectly through applied force. Our results may shed new light on the fundamental processes that allow cells to sense the mechanical properties of their environment and in particular show how single focal adhesions may act, autonomously, as local rigidity sensors.

879-Pos Board B634
Influence of Substrate Stiffness and Thickness on Cell Traction Forces
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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 [1-3] and are able to match their internal stiffness to that of the substrate [2, 3]. Recent works have reported on dynamics of cellular properties such as cell shape, cell spread area, and focal adhesion area, as functions of environmental properties such as substrate stiffness, thickness, and chemistry. Building on earlier models [4, 5, 6], we present mathematical models that enable us to replicate some aspects of experimentally reported time-dependent cell behavior. Our models investigate the adaptation of internal cell stiffness through increase in number of focal adhesion complexes and temporal build-up of traction force. Our models crucially invoke the ability of some cell types to adapt their internal stiffness and show that substrate stiffness and thickness can strongly assist in rapid build-up of traction forces and formation of multiple cooperative focal adhesion complexes. Further using our models we generate some mechanistic insights into why certain cell types under the influence of specific substrate properties exhibit the kind of dynamics that has been

experimentally reported. We attempt to establish correlation between the mechanistic models presented here and an earlier heuristic model that we have developed [6].
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880-Pos Board B635
Water Potential of Cell Microenvironments Modulates their Proliferation
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Microenvironmental conditions in interstitial spaces can change rapidly after inflammatory insults. Hydration potential shifts of *50-150 mmHg* occur during burn and ischemia-reperfusion injury in dermal and myocardial extracellular matrices, respectively, presumably due to increased mechanical tension, fluid flux, and water activity as edema accumulates (McGee et al., *Biophys J 2012;Circ Res 2012a;Wound Rep Reg 2013*).While cell responses to mechanical and flow-related components of the hydration potential are increasingly studied and understood, responses to concomitant changes in water's chemical potential are not. Here, we explore its effects on *HL60*, an anchorage-independent, human leukemia cell line that readily differentiates towards various cell lineages. Cells *(10^5 /ml)* were grown in static suspension cultures at *37 °C*, in liquid media supplemented with *2.5%* fetal calf serum and at colloidosmotic pressures adjusted to between *1-100 mmHg* with inert polymers. After 24 hours, the cells' growth rate changed with the water chemical potential in direct proportion to the colloidosmotic pressure of the growth solution. Linear regression analyses showed that the slope of the growth rate versus pressure was *(2.4%)/day/mmHg(R^2 = 0.875)*. The observed rate changes were independent of the physicochemical characteristics of the inert polymer; *polyethyleneglycol 8000* or *dextran 10* enhanced cell proliferation. Cell differentiation pathways also appeared to change as determined by the cells morphology and size in Giemsa stained cytocentrifuge preparations and further suggested by a shift to the right in the frequency-distribution of their nucleus/cytoplasm ratios. These results show that changes in water's chemical potential modulate proliferation regardless of media-stiffness or flow sensing by the cell. Hydration potential components other than the mechanical play significant roles in cells' adaptation to changes in their microenvironment.

881-Pos Board B636
Rapid Disorganization of Mammary Acini Driven by Long-Range Mechanical Interaction
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Cells and multicellular structures can mechanically align and concentrate fibers in their extracellular matrix (ECM) environment but can also sense and respond to mechanical cues by differentiating, branching, or disorganizing. Mechanically induced collagen concentration and alignment into arrangements variously referred to as fibers, tracts, cables, straps or lines has been seen in experimental systems ranging from single cells and tumor explants to human clinical samples. Here we show that pairs or groups of Ras-transformed mammary acini with thinned basement membranes and weakened cell-cell junctions can generate collagen lines that then coordinate and accelerate transition to an invasive phenotype. When two or more acini mechanically interact by collagen lines, the pairs or groups of acini begin to disorganize within 12.5 ± 4.7 h in a spatially coordinated manner, whereas acini that do not interact mechanically with other acini disorganize more slowly (21.8 ± 4.1 h) and to a lesser extent ($p<0.0001$). Overall, disorganization of mechanically interacting pairs of acini is more probable, rapid, and extensive than of single acini. When the directed lateral mechanical interconnections between paired acini were laser-severed, the acini reverted to the slow disorganization phenotype. When acini were mechanically isolated from other acini and also from the bulk gel by box-cuts with a side length below 900 μm, transition to an invasive phenotype was blocked in 20 of 20 experiments. Thus, pairs or groups of mammary acini can interact mechanically over long distances through the collagen matrix and these directed mechanical interactions are necessary for rapid transition to an invasive phenotype.

882-Pos Board B637
Dorsal Adhesion Slows Glioblastoma Migration in Perivascular Mimics
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Glioblastoma multiforme (GBM), the most prevalent primary brain cancer, is characterized by diffuse infiltration of tumor cells into brain tissue, which severely complicates surgical resection and likely gives rise to the almost universal tumor recurrence. This diffuse infiltration is frequently guided by anatomical "tracks" in the brain in the form of blood vessels or white matter tracts, which give rise to the highest migration speeds observed in vivo. Despite this observation, little is known about the biophysical and biochemical mechanisms through which these tissue interfaces promote invasive motility, which in turn may derive from a lack of appropriate culture paradigms. To address this need, we developed a culture system in which tumor cells are sandwiched between a ventral fibronectin-coated dorsal surface representing vascular basement membrane and a dorsal hyaluronic acid (HA) surface representing brain parenchyma. We find that inclusion of the dorsal HA surface induces formation of adhesive complexes and significantly slows cell migration relative to a free fibronectin-coated surface. This retardation is amplified by inclusion of integrin binding peptides in the dorsal layer and expression of CD44, suggesting that it acts through biochemically specific mechanisms rather than simple physical confinement. Moreover, both the reduction in migration speed and assembly of dorsal adhesions depend on myosin activation and the stiffness of the ventral layer, implying that mechanochemical feedback directed by the ventral layer can influence adhesive signaling at the dorsal surface.

883-Pos Board B638
Length Scale Dependent Micro-Rheology of Cellularized Type I Collagen Gels
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Collagen gels are commonly used as the substrate for experiments on cell mechanics because collagen is the most abundant protein in the extracellular matrix of most animals. The gels are commonly approximated as homogeneous elastic materials; however, on smaller length scales, the inhomogeneity of the collagen fiber network becomes very apparent. During gelation, collagen fibers can group together to form larger fiber bundles, with the size, shape, and distribution of these bundles depending on the collagen concentration and the temperature during gelation. In addition, when cells are embedded in the collagen substrate, the cell adhesion forces deform the collagen and alter its elastic properties. We study local variation in the elastic modulus of type I collagen gels and characterize inhomogeneity caused by cell adhesions and fiber bundles in the collagen network. We expect the cell adhesions and the collagen fiber bundles to each have distinct length scales over which the elastic properties will vary. These length scales will be calculated by separating the gel into domains in which the elastic properties of the collagen change in a characteristic way. We map the local elastic modulus of type I collagen gel using active two-point micro-rheology. Optical tweezers are used to perturb microscopic particles embedded in the gel and in-line holographic particle tracking is used to calculate the particle displacements. The local elastic properties are calculated by cross-correlating the trajectory of the perturbed particle with the trajectories of the surrounding particles. Then confocal reflection microscopy is used to image the collagen fiber network, showing the locations of cells and fiber bundles. These images are used to compare the distribution of cells and fiber bundles to the results of the local micro-rheology calculations.

884-Pos Board B639
Intermediate Filament Structure, Assembly and Nanomechanics
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Intermediate filaments (IFs) consist of two-stranded coiled coils that form anti-parallel, half-staggered tetramers. By time-lapse electron microscopy, complemented with total internal reflection fluorescence (TIRF) microscopy, we have investigated the in vitro assembly of vimentin to define the assembly pathway for vertebrate cytoplasmic IFs. First, we have characterized the physical and structural state of the soluble vimentin subunits by analytical ultracentrifugation (AUC) and X-ray crystallography. Assembly is induced by a change in the ionic strength and starts with the lateral association of tetramers to full-width unit-length filaments (ULFs) driven by the interaction of the