

structure, we find that despite the chirality of the ciliary structure, cilia can in principle generate clockwise as well as anticlockwise twirling beat patterns. However, our results show that the axoneme's chirality leads to one sense of rotation being selected dynamically for given parameter values and properties of dynein motors. This dynamic selection of asymmetric states is analogous to how the direction of motion of a motor protein moving along a filament.

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Cellular Potts Modeling of Matrix-Dependent Endothelial Cell Networking

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¹Institute for Medicine & Engineering, University of Pennsylvania, Philadelphia, PA, USA, ²Department of Architecture, University of Pennsylvania, Philadelphia, PA, USA, ³Department of Pathology & Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, USA. Networking of endothelial cells during fetal and post-natal development relies upon dynamic remodeling and subsequent stabilization of cell-cell and cell-extracellular matrix (ECM) interactions. Herein, we investigate lung endothelial cells network dynamics on thin films of engineered ECM. These systems adhere to the Differential Adhesion Hypothesis and their behaviors are well reproduced with a Cellular Potts Model. In order to gain insight on the profound effect external environment has on cell behavior, our model explicitly includes the ECM, as we explore particular changes in networking dynamics with changes in substrate parameters. Further, we describe specifics of the system Hamiltonian governing the Monte Carlo methods with addition of experimentally derived rules that can simulate both normal and non-networking cells systems. The biological significance of derived cell-cell and cell-matrix adhesion and cohesion energies that most appropriately model our experimental data is discussed.

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Accelerated Proliferation and Migration of Keratinocytes, Fibroblasts and Macrophages Isolated from H2-Calponin Knockout Mice

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Section of Molecular Cardiology, NorthShore University Health System and Northwestern University Feinberg School of Medicine, Evanston, IL, USA. Calponin is a family of actin-associated regulatory proteins that play a role in modulating smooth muscle contractility and actin cytoskeleton functions. The h2 isoform of calponin is found in smooth muscle and certain non-muscle cells. Keratinocytes, fibroblasts, and macrophages express h2-calponin at significant levels. To investigate the function of h2-calponin in these cell types that are key players in wound healing, we studied primary cultures of epidermal keratinocytes, dermal fibroblasts and peripheral macrophages isolated from h2-calponin knockout mice recently developed in our laboratory (Huang et al., *J. Biol. Chem.* 283:25887-99, 2008). Cell proliferation studies revealed faster growth rates of all of the three cell types from h2-calponin knockout mice as compared with that of wild type control cells. Similarly, the three types of cells exhibited faster migration in vitro wound healing experiments when h2-calponin is absent. The results suggest that h2-calponin may be a regulatory factor in the balance of cell proliferation and migration during wound healing. We have previously observed that mechanical tension built in the cytoskeleton regulates h2-calponin expression and degradation in cells including keratinocytes and fibroblasts (Hossain et al., *J. Biol. Chem.* 280:42442-53, 2005; *Biochemistry* 45:15670-83, 2006). Therefore, experiments are underway to investigate the role of h2-calponin in the effect of mechanical tension on keratinocyte differentiation and skin wound healing.

3238-Pos Board B285

How deep cells feel: Mean-field Computations and Experiments

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Most cells in solid tissues exert contractile forces that mechanically couple them to elastic surroundings and that significantly influence cell adhesion, cytoskeletal organization, and even cell differentiation. However, strains within the depths of matrices are often unclear and are likely relevant not only to the fact that some matrices such as so-called basement membranes are thin relative to cell dimensions but also to defining how far cells can 'feel'. Here we present experimental results for cell spreading on thin, ligand-coated gels and for prestress in stem cells in relation to gel stiffness. Spread area on thin and soft gels was found to resemble cells on thick and stiff gels. Matrix thickness also affects focal adhesions and cytoskeleton organization in stem cells, which we will compare to differentiated cells. We introduce a finite element computation in which a cell is placed on an elastic matrix, while matrix elasticity and thickness are varied in order to compute and compare elastostatic deformations within the matrix. Average interfacial strains between cell and matrix show large deviations only when soft matrices are a fraction of the height

and width of a cell, proving consistent with experiments. Three-dimensional (3D) cell morphologies that model stem cell-derived neurons, myoblasts, and osteoblasts show that a cylinder-shaped myoblast induces the highest strains, consistent with the prominent contractility of muscle. Groups of such cells show a weak crosstalk in matrix strains, but the cells must be much closer than a cell-width - experimental tests of this are emerging. Cells thus feel on length scales closer to that of adhesions than on cellular scales or larger.

3239-Pos Board B286

Interactions Between Lipid Bilayer And Protein Skeleton In Erythrocyte Deformations

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We study mechanics of a red blood cell in large deformations by using a multi-scale modeling approach, in which the interactions between the lipid bilayer and the protein skeleton are considered as two parts: vertical contact and lateral sliding. The sliding is caused by the mobility of the transmembrane proteins (e.g. band 3 and glycophorin C). Our model consists of a complete-cell model which depicts the cell membrane as two continuous shells, and a molecular-detailed model of a junctional complex (JC) that provides the constitutive properties of the inner layer (the skeleton). The folding/unfolding reactions of the spectrin are also considered and incorporated into the JC model. This multi-scale model is validated by comparisons with other modeling approaches and experiments about micropipette aspirations and optical tweezer stretching. Applying this method, we numerically duplicated the boundary-value problem associated with cell deformation in a flow channel. The critical contact force, i.e. the maximum contact force that can exist between the bilayer and the skeleton without inducing skeleton-bilayer disassociation, is extracted. This critical force is then applied to predict conditions of vesiculation in other mechanically-induced cell deformations.

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Measurement of Adhesion Force between a Human Neutrophil and a *Candida albicans* Hyphae Using a Micromanipulation Technique

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Yeast infection (candidiasis) is a common and persistent threat to human health. Normally harmless, the fungus *Candida albicans* is present in 40-80% of normal human beings, but in immune-compromised individuals, it can proliferate and cause a variety of health problems including pneumonia, septicemia, or endo[[Unsupported Character - Codename -]]carditis. The fundamental mechanism towards the control of candidiasis and other fungal infections involves understanding how human neutrophils interact with β -Glucan, a polysaccharide present in fungal cell walls, at the single cellu[[Unsupported Character - Codename -]]lar level. We hypothesize that the complement receptor 3 (CR3), a member of the integrin family, can recog[[Unsupported Character - Codename -]]nize the β -Glucan on the *C. albicans* hyphae, initiating neutrophil adhesion and caus[[Unsupported Character - Codename -]]ing a respiratory burst. We test this hypothesis using a two-pipette micromanipulation technique to measure the adhesion force between a single neutrophil and a *C. albicans* hyphae. A micromanipulator attached to a suction pipette is used to trap a single *C. albicans* hyphae that is attached by a single neutrophil to a second, flexible pipette. The micromanipulator slowly pulls up on the hyphae, exerting an increasing force and causing the flexible pipette to bend until the hyphae detaches from the neutrophil. By measuring the deflection of the flexible pipette at the instant the hyphae detaches, Hooke's law can be used to calculate the adhesion force between the hyphae and the neutrophil. By measuring the average adhesion force of neutrophils from knock-out mice missing CR3 and compare with that from the wild type animals expressing CR3, we can determine the mechanical role the receptor plays in neutrophil adhesion.

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Mechanical Computation in Neurons

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Motility is a major function of cells, playing a fundamental role in development and embryogenesis. Growth cones are the major motile structures usually located at the tip of neurites and are composed of a lamellipodium from which thin filopodia emerge. We have analyzed the kinetics and dynamics of growth cones from a computational point of view with the aim to understand two major issues: firstly, the strategy used by filopodia and lamellipodia during their exploration and navigation; secondly, which kind of mechanical problems neurons need to solve during their operation. Filopodia grow and retract following