polysaccharides, secreted by the bacteria provide protection from harmful chemical elements, such as chlorhexidine digluconate, commonly found in medical grade soap. Much is known about the biological and chemical mechanisms of chlorhexidine digluconate as an antiseptic, whereas the physical response of the bacterial biofilm to the chemical is poorly understood. In this investigation, we used force spectroscopy to analyze the physical effects of varied concentrations of chlorhexidine digluconate on a robust biofilm-forming Escherichia coli strain. Preliminary data suggest a correlation between the stiffness (spring constant) of the biofilm and the concentration of chlorhexidine digluconate.

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Increased Cytoskeletal Stiffness of Schlemm's Canal Endothelial Cells in Glaucoma
Rocio Vargas-Pinto, Mark Johnson.
Northwestern University, Evanston, IL, USA.
The elevated intraocular pressure characteristic of glaucoma has been associated with a decreased pore density in the cells of the inner wall of Schlemm's canal (SC). SC cells form these pores in response to a transcellular pressure drop, facilitating the flow of aqueous humor across this endothelium. We hypothesize that impaired pore formation in glaucoma is due to an elevated stiffness of SC cells.
Atomic force microscopy (AFM) measurements of elastic modulus were performed using pyramidal or spherical (4.5 or 10 μm) tips on SC cells isolated from 6 healthy and 5 glaucomatous human eyes. Using finite element modeling and AFM experiments with latrunculin-A (an F-actin depolymerizing agent), we previously showed that sharp pyramidal tips characterize the cortex stiffness while larger, spherical tips characterize the stiffness of the subcortical cytoskeleton. The geometry of an SC cell was reconstructed based on electron microscopy images and used to model cell deformation under pressure (3-6 mmHg). When probed with spherical tips, the modulus of glaucomatous cells (1.36 ± 0.14 kPa) was significantly higher ($p<0.02$) than that of healthy cells (0.89 ± 0.10 kPa). No significant difference was detected between healthy and glaucomatous cells using sharp tips (7.40 ± 1.33 vs. 7.99 ± 0.97 kPa). The higher modulus measured on glaucomatous cells using spherical tips suggest that the altered stiffness is likely in the subcortical cytoskeleton and not in the cell cortex. Preliminary studies using finite element modeling predict a 34-40% decrease in cell deformation solely due to the increased cell stiffness measured on glaucomatous cells. This is consistent with our hypothesis that cell deformation is likely a precursor to the pressure-driven pore formation process and that increased cell stiffness may inhibit this process.
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Cell Viscoelasticity as a Function of Substrate Stiffness
Rachel Brunetti[1], Gawain Thomas[2], Qi Wen[2].
[1]Physics, Scripps College, Claremont, CA, USA, [2]Physics, Worcester Polytechnic Institute, Worcester, MA, USA.
While it is known that cells respond to the mechanical properties of their environment, limited information is available regarding mechanosensing and the means by which such stimuli are transduced. The cytoskeleton, a critical component used by cells to sense substrate stiffness, determines the viscoelasticity of cells. Information on cell viscoelasticity as a function of substrate stiffness and vimentin levels can lead to a larger composite model of the mechanism through which cells respond to external mechanical stimuli.
3T3 fibroblasts were grown on collagen-coated polyacrylamide gels, of which the stiffness was controlled by varying both the concentrations of acrylamide and bisacrylamide. An atomic force microscope (AFM) was used to perform dynamic micromechanical tests. The force-mapping mode was employed to obtain 24 by 24 maps of force curves. For each force curve, the AFM first indents a cell with a 700 pN force and then applies a 10 Hz sinusoidal strain to the cell. The storage, E', and loss modulus, E'', were calculated by fitting the sinusoidal portion of the applied force and resulting indentation to obtain the amplitude and phase offset.
Both E' and E'' increase with substrate stiffness. While the increase in E' is consistent with literature, we found that the ratio of E'' to E' decreases as substrate stiffness increases. This agrees with our hypothesis that cells become more solid-like as the elastic modulus of the extracellular matrix increases. Additionally, the value of E' was higher in vimentin null cells, suggesting that cells change their cytoskeletal composition to adapt to the loss of vimentin. This may involve an increase in the concentration of actin filaments, which contribute more to the elasticity than vimentin. Further experiments will investigate the potential link between vimentin expression and the mechanosensing ability of the cells.

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A Systematic, High Resolution Mapping of the Elastic Modulus of Mouse Cartilage Matrix
Preethi L. Chandran[1], Jessica Yuan[1], Ferenc Horkey[2], Edward Mertz[3], **Emilios K. Dimitriadis**[1].
[1]BEPS, NIBIB, NIH, Bethesda, MD, USA, [2]STBB, NICHD, NIH, Bethesda, MD, USA, [3]SPB, NICHD, NIH, Bethesda, MD, USA.
Hyaline cartilage cushions bone at articular joints and is responsible for elongation and mechanical integrity of growing bones. The major components of cartilage matrix are the collagen mesh and the highly charged proteoglycan aggrecan entangled in and swelling the mesh. In growing cartilage, the composition and organization of these components varies across both growth plate and articular cartilage and in the vicinity of chondrocytes. Mice are extensively used as model system for a wide range of pathologies including arthritis, but there are limited studies mapping matrix nanomechanics across different regions. Nanomechanical studies, typically performed by indenting tissue sections, are subject to errors due to matrix collapse, surface roughness and diffusional loss aggrecan loss from the section surface. Moreover, there are often issues of data interpretation when the probe size and indentation depth are comparable to the mesh and aggrecan sizes.
We performed a high-resolution (~1um) nanoindentation elasticity mapping of extracellular matrix material of mouse growing cartilage across different regions of both cartilage types in physiological solution. We used an AFM with microsphere probes whose radii and indentation depth exceeded mesh and molecular sizes. We mildly fixed the cartilage to prevent aggrecan loss. We developed a new method for obtaining the Hertzian contact points on rough surfaces. We applied large-strain indentations and force corrections to remove the error due to surface roughness and to select the linear regime of the force data. The latter greatly improved the consistency of our elasticity results. Tissue collapse was partially corrected using the cartilage height mapping. Matrix regions were extracted by correlation with optical images. The matrix elasticity across the growing cartilage showed interesting difference between the two cartilage types and correlations with previous studies of matrix composition at the same locations.

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Cell Adhesion on Silicon Nanowires
Anna Murello[1], Laura Andolfi[2], Damiano Cassese[1], **Marco Lazzarino**[1,2].
[1]laboratorio TASC, IOM-CNR, Trieste, Italy, [2]Consorzio per la Biomedicina Molecolare (CBM), Trieste, Italy.
Understanding nanostructured materials - cell interactions is essential for the development of innovative substrates for cell culture, differentiation and precise electrical stimulation. In this framework, silicon nanowires (SiNWs), characterized by high aspect ratio and a broad range of mechanical, optical and electrical properties, are interesting nanomaterials for innovative cellular engineering. We investigated and quantified, using single cell force spectroscopy (SCFS), the interaction of murine embryonic fibroblast with two mechanically different SiNW substrates, and two reference substrates, collagen gel which is generally used for cell culture, and flat glass which has the same chemical reactivity of SiNWs. We observed comparable adhesion values on SiNWs substrates and on gel substrate, while flat glass generate a 10-times weaker interaction. A closer analysis of the adhesion curves revealed significant differences between soft and hard SiNW, suggesting that a different cell membrane organization is developed depending on the mechanical and geometrical properties of the substrate.
In conclusion SiNW substrates are compatible with cell engineering and thanks to their high range of mechanical and geometric properties, a fine tuning of cellular response can be achieved.

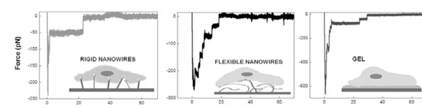

Figure 1: representative SCFS curves for rigid NWs, flexible NWs and collagen-coated coverslips.

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Characterization of Mechanotransensitivity of Articular Chondrocytes
Whasil Lee, Holly Leddy, Farshid Guilak, Wolfgang Liedtke.
Duke University Medical Center, Durham, NC, USA.
Articular cartilage is a protective soft connective tissue lining the ends of bones in weight-bearing joints. It sustains numerous cycles of mechanical loading during normal joint activity. Recent studies showed that mechanical factors not only play a critical role in the pathology of cartilage, e.g. initiation of degenerative joint disease such as osteoarthritis (OA); but also influence the metabolic response of chondrocytes, the only cellular element of cartilage. One of the early events implicated in chondrocyte mechanotransduction is a