observed. These results suggest that wound healing is predominantly a mechanical process that is modified, but not produced, by cell-cell signaling.

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Video Force Microscopy (VFM): A New Technique that Allows Cell-Level Driving Forces to Be Determined from Time-Lapse Images
G. Wayne Brodland, Vito Conte, P. Graham Cranston, Shane Hutson, Florian Ulrich, Buzz Baum, Mark Miodownik.
For purposes of video force microscopy (VFM), the forces in the cells of an embryonic epithelium are assumed to consist of active forces, which can be mathematically resolved into equivalent forces along cell boundaries, and passive forces associated with deformation of the cytoplasm and its contained organelles and intermediate filament network, which are represented by an equivalent viscosity, mu. All triple junctions in the time-lapse images are tracked over time and finite element techniques are used to estimate the forces that must act on the passive components of each cell to deform them as observed. A mathematical inverse method is then used to determine the forces that must act along each cell edge in order to produce the net forces needed at each triple junction to drive the observed deformations. The technique has been successfully applied to multi-photon cross-sections of Drosophila embryos undergoing ventral furrow formation. There, it revealed that the ventral furrow is produced by contractions that vary smoothly with time and position in the apical surface of the presumptive mesoderm, by apical-basal contractions in the cells of this tissue and, surprisingly, by spatially more uniform basal contractions in the ectoderm. It was also able to quantify the sometimes subtle force modifications present in mutants that generate abnormal phenotypes. The indicated force alterations are consistent with known genotype-specific structural protein changes. When applied to wound healing in embryonic epithelia, it was able to quantify the forces generated in the purse string that closes the wound and the surrounding cells. It both of these contexts, VFM was able to quantify the forces that drive observed morphogenetic movements and to do so with sub-cellular spatial detail and sub-minute temporal resolution.

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The Role of the Scar/WAVE Complex in the Mechanics of Cell Migration
Effie Bastounis, Ruedi Meili, Baldomero Alonso-Latorre, Juan-Carlos del Alamo, Richard Firtel, Juan Lasheras.
Cell motility is integral to a wide spectrum of biological phenomena. It requires the spatiotemporal coordination of underlying biochemical processes, resulting in cyclic shape changes associated with mechanical events (*themotility cycle*). A major driving force of cell migration is the dendritic polymerization of actin at the leading edge, regulated through the nucleation activity of the Arp2/3 complex, activated by the Scar/WAVE complex. Our aim is to understand the effect of the different components of the Scar/WAVE complex in the mechanics and in particular the motility cycle of migrating cells.
For this purpose, we acquired time-lapse recordings of cell shape and traction forces of *Dictyostelium* cells migrating on deformable substrates. We compared results for wild-type cells and cells lacking the Scar/WAVE complex proteins PIR121 (Sra-1/CYFIP/GEX-2) (*pirA*-) and SCAR (*scrA*-). We find that mutantcells move slower than wild-type, while maintaining the overall characteristics of the mechanical interaction with the substrate, attaching at front and back and contracting inwards. Although the distribution of applied forces is unchanged, their magnitude is lower than in wild-type for *scrA*- cells and higher for *pirA*- cells. This correlates with the F-actin content of the different cell lines corroborating a role for F-actin in determining the level of the traction stresses. In *pirA*- cells regularity of the motility cycle (quasiperiodic repetition of shape changes and strain energy deposited) seems to be reduced compared to wild-type. This suggests that proper regulation of the Scar/WAVE complex and its role in F-actin turnover is essential for amoeboid motility.

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Conceptual Models for Synthetic Bipedal Motors
Sara Sadeghi, Nancy R. Forde, Gerhard A. Blab, **Martin J. Zuckermann**, Heiner Linke.
Biomolecular nano-motors have provided the inspiration for the design and construction of artificial nanoscale motors and machines based on several types of molecule including DNA. However, no synthetic nano-motors have yet been constructed from building blocks of protein-based material even though biomotors themselves are proteins. The HFSP motor group (1) are in the process of developing a bottom-up approach to the understanding of bio-motors by designing and constructing synthetic protein motors and numerically simulating their kinetic properties. One such concept is the ''tripedal tumbleweed'' motor (1) and another is the ''Inchworm''. In this context we present the results of numerical simulations for a bipedal motor with two connected peptide legs and a simple model for the ''inchworm'' motor in terms of harmonic bonds. These motors walk on a one-dimensional track of periodically arranged binding sites. The sequence of binding sites on the track of each motor is AB-AB-AB..... and the motors are powered by a temporally periodic sequence of composite washes which modulate the ligand concentrations and the leg angles. The washes cause the motors to undergo directed motion by a hand-over-hand mechanism and an inchworm mechanism, respectively, on a track with asymmetric spacing between the AB and the BA binding sites. We will show simulation results for two-dimensional motor action which includes stepping diagrams, stall forces processivity and first passage times for a range of parameters. These motor has the following properties observed for biological molecular motors: binding, power stroke and diffusional search. Extensions of the model will also be discussed. 1. E. Bromley et al. HFSP Journal Vol. 3 pp.204-212, (2009).

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Mechanical Control of Bacterial Cell Shape
Hongyuan Jiang, Fangwei Si, William Margolin, Sean X. Sun.
The most visible phenotype of an organism is its geometrical shape, yet a mechanistic connection between genotype and the organismal shape is elusive. For bacterial cells, several genes have been implicated in cell shape determination, including the cytoskeletal filaments bundles such as MreB, which controls whether the cell takes on a spherical or a rod-like shape. Here we describe the role of cell wall growth, mechanics and cytoskeletal filaments in determining the bacterial cell shape. We show that a growing rod-like cell by itself is mechanically unstable. But this growth-induced instability can be suppressed by cytoskeleton filaments such as MreB. We propose that MreB exerts an additional force on the cell wall. We use simulation and experiments to demonstrate the negative control of cell shape by MreB. In the process, we demonstrate that our model explains a range of MreB function, including: (a) Depletion of MreB leads to a reversible transformation from a short rod to a sphere. (b) Over-expression of MreB results in the filamentation of bacterial cells. (c) The depolymerization of MreB helix around the septum is a prerequisite for cell division. (d) Partial disassembly and non-uniform distribution of MreB can lead to the bulging of a filamentous cell.

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Cells CRAWL from Soft to Stiff Surfaces as Myosin-II Polarizes the Cytoskeleton
Matthew D. Raab, Dennis E. Discher.
Scarring in the heart after a myocardial infarction, or scarring in the skin after wounding - lead to rigidification of tissue through extensive collagen crosslinking and can also lead to homing of adherent mesenchymal stem cells (MSCs). 'Durotaxis' describes the tendency for a cell to crawl from a soft, collagen-coated gel to an adjacent stiff matrix, but clear evidence for accumulation of any cell type has been lacking as has insight into molecular mechanisms. We cultured human MSCs on matrices with scar-like gradients in elastic modulus (stiffness) that are on order of 10 Pa/micron and document a bias in migration toward the stiff matrix with proliferation-independent accumulation taking just a couple of days. As found with other cell types, MSCs on stiff substrates show myosin-IIB is polarized toward the rear while the centrosome and microtubule (MT)-network are polarized toward the front, but such polarization is surprisingly absent from cells on soft substrates. With myosin-II inhibition, we find cells on stiff matrix crawl faster whereas cells on soft matrix are initially impeded but then transition to motile cells as their centrosomes and MT-networks polarize as they would on stiff matrix. While myosin-II is required for contractility but not migration, MTs are required for any migration - including durotaxis - but contractility on gels remain intact after destabilization of MTs. The model gel results thus show that the progressive polarization of myosin-II on stiff substrates is particularly key to durotaxis. The broader relevance of this conclusion is tested with decellularized heart tissue that permits an examination of MSC adhesion, contraction, and migration. Decellularized heart tissue was stiffened with chemical crosslinking to increase elastic modulus measured with atomic force microscopy. We see that this increased stiffness alters cell migration behavior.

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How Deeply Cells Feel: From Soft Matrices of Controlled Thickness to Nuclear Readouts
Amnon Buxboim, Edward C. Eckels, Dennis E. Discher.
Tissue cells constantly probe their surroundings. They lack eyes to see and ears to hear but sense their microenvironment by adhering and physically deforming, which allows cells to feel into the depths of a matrix. To address how deeply cells feel we cultured mesenchymal stem cells, as prototypical but particularly sensitive adhesive cells, on collagen-coated gels-made microfilms of controlled elasticity (E) and thickness (h). After just 36 hrs in culture, cell spread area was distinctively smaller on thick and soft compared to either thin or stiff films, correlating well with nuclei morphology. Transition from small-to-large spread area was obtained at <5 microns gel thickness, which defines a tactile length scale for mechanosensitivity. Matrix-dependent cytoskeletal organization exhibits