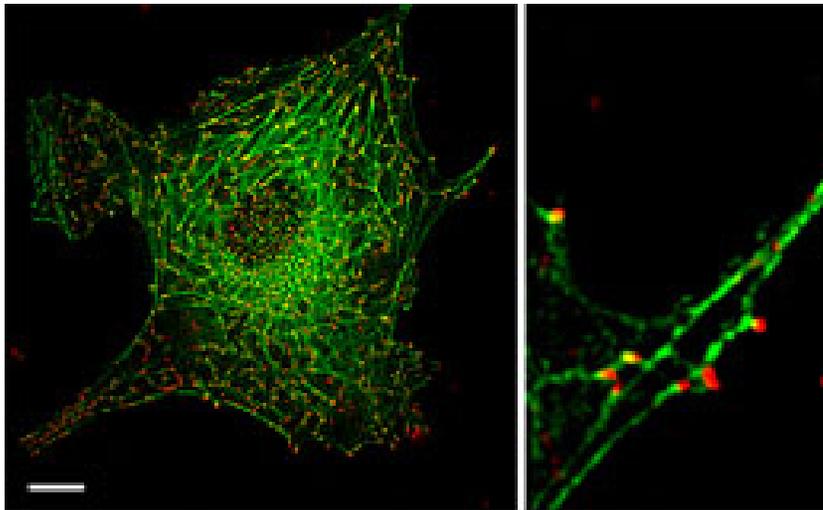


Helmke Research Group



Living cells and tissues adapt to their environment by altering structure, gene and protein expression, and biochemical functions. However, the mechanisms by which cells transduce mechanical stimuli into biochemical signals are not well understood. Our laboratory employs a multidisciplinary biomedical engineering approach to understand the relationship between intracellular mechanics and cell function. We employ several tools for investigating cellular mechanotransduction as are described below.

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“Our goal is to elucidate cellular mechanotransduction mechanisms as candidates for therapeutic cellular engineering.”



Image Analysis of Living Cells

Directed cell migration plays an important role in many physiological and pathological processes, including angiogenesis, wound repair, and cancer metastasis. Persistently migrating cells must first acquire spatial symmetry and directionality, an active process dependent on polarized remodeling of the cytoskeleton. During the initial stages of cell polarization, cells actively probe the composition and rigidity of the extracellular matrix by extending actin-rich lamellipodia at cell edges in search for spatial cues. These structures contain a meshwork of polymerized actin filaments that may extend smoothly outward or perform wavelike motions known as edge ruffling. Identifying the underlying mechanisms that guide directional edge ruffling and the establishment of cell polarity in response to external chemical and mechanical stimuli remains a critical challenge in developing strategies to engineer and control cell migration. We have implemented a novel technique to quantitatively measure edge ruffling dynamics and actin-mediated planar cell polarity in living cells. Compared to manual methods, the image analysis technique we have devised provide rapid, more objective, and more consistent readouts at improved spatial resolution.

Cellular Structural Dynamics Analysis

Mechanical stresses such as tension, compression, and shear play important roles in regulating cell growth and function. Since many cellular component experience tension, a variety of mechanotransducers have been proposed, including integrins, focal adhesion (FA) proteins, and the cytoskeleton. However, mechanisms by which cells transduce external physical cues into biochemical communication remain elusive. We have designed a new stretch device optimized for high-resolution live-cell imaging during the application of arbitrary spatio-temporal strain profiles. Our tool is proving to be very useful for measuring dynamic structural remodeling under mechanical strain.

RECENT RESEARCH DEVELOPMENTS

- Learning how cells in arteries adapt to the mechanics of blood flow is leading to more effective treatments for brain aneurysms
- A new medical device for the pediatric intensive care unit will help prevent hospital-acquired infections

RECENT GRANTS

- Hartwell Foundation-Ciliated Pediatric Endotracheal Tube for Active Prevention of Ventilator-Associated Pneumonia
- NIH- Engineering an Atherosclerosis-Resistant Endothelium

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