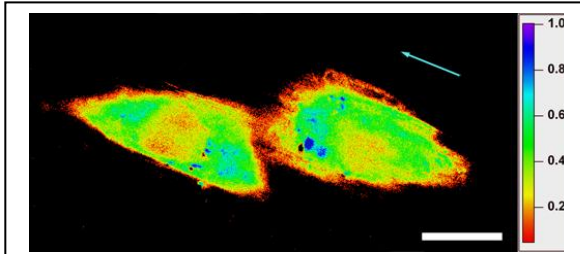


# How Cells Deal with (Mechanical) Stress

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Mechanical forces acting on a living cell can have a profound impact on its biological function. From embryonic development to controlled cell death, cellular responses to the mechanical properties of the environment have been recognized to play an important role in a plethora of biological functions and cellular regulation. Not surprisingly, perturbations of the mechanisms that couple mechanical signals into



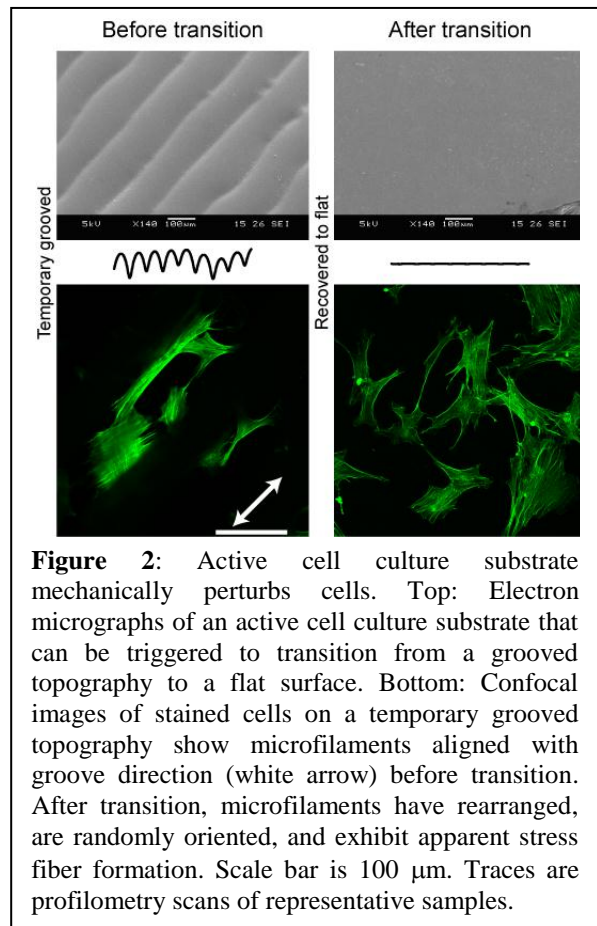
**Figure 1:** False color image representing the relative stresses in a cell growing on a surface with parallel grooves (groove direction indicated by arrow). Scale bar: 15 $\mu$ m.

the biochemical signaling pathways of cells are indicative of many diseases. In addition, the detailed understanding of cellular mechano-biology in the context of stem cell differentiation and tissue formation is pivotal to make significant progress in tissue and prosthetics bioengineering. Yet, currently there are still many open fundamental questions regarding the mechano-biology of living cells. One of which is the coupling between external mechanic stimuli, changes in cellular mechanics, and cell behavior. The particular questions that this experimental project tries to answer are: How are the stress fields within a cell distributed in space and how

do they change over time? How fast and where do cells dissipate stresses arising from external stimuli and changes in their environment? How do these responses depend on the mechanical history?

The successful execution of this project necessitates the synergetic application of methods from Biology, Physics, and Material Sciences. Firstly, the cellular stress fields need to be determined with high spatial and temporal resolution. To that end, a fluorescence based sensor is introduced in cells of interest. Using multicolor fluorescence microscopy and image analysis one can thus visualize local stresses within those cells (Figure 1). Secondly, in order to induce mechanical perturbation, bio-functionalized active cell culture surfaces of shape memory polymers will be used (Figure 2). These surfaces will change their surface from flat to grooved depending on temperature. This allows for well controlled changes in surface topography and, consequently, mechanical action on surface adhered cells.

With the successful completion of this research project, several aspects of cellular biomechanics will have been illuminated. Firstly, we will have arrived at general insights in cellular stresses and how they relate to functions such as motility. Furthermore, we will have gained insight in the spatial and temporal mechanisms of externally induced stress dissipation in living cells. These insights are expected to provide unprecedented new understanding of tissue development, maintenance, and disease states. As a result, important new advances in diagnosis and treatment of diseases as well as regenerative medicine can be anticipated.



**Figure 2:** Active cell culture substrate mechanically perturbs cells. Top: Electron micrographs of an active cell culture substrate that can be triggered to transition from a grooved topography to a flat surface. Bottom: Confocal images of stained cells on a temporary grooved topography show microfilaments aligned with groove direction (white arrow) before transition. After transition, microfilaments have rearranged, are randomly oriented, and exhibit apparent stress fiber formation. Scale bar is 100  $\mu$ m. Traces are profilometry scans of representative samples.