Why Mechanical Forces Matter in Health and Disease: proteins as mechano-chemical switches

Viola Vogel, *Laboratory for Biologically Oriented Materials, Department of Materials,* ***ETH*** *Zurich, Switzerland. (viola.vogel@mat.ethz.ch)*

Ample evidence exist that bacteria, cells and tissues sensitively respond to mechanical stimuli. But how can shear forces enhance bacterial adhesion? How can eukaryotic cells sense and transduce a broad range of mechanical forces into distinct sets of biochemical signals that ultimately regulate cellular processes, including adhesion, proliferation, differentiation, and apoptosis? New nanotechnology and computational tools begin to reveal novel mechanisms how the structure/function relation of proteins can be switched if proteins are mechanically stretched and partially unfolded. Some bonds that the adhesins of some cells form with their respective ligands can be activated rather than weakened by tensile force (i.e. catch bonds versus slip bonds). Some bacteria thus adhere more firmly to surfaces under flow conditions and we will give insights into the structural mechanisms how force can switch their nanoadhesives to a high binding strength. Other structural mechanisms are at work by which fibroblasts and other cells can stretch, unfold and switch the chemical display of extracellular matrix molecules. Deciphering the underlying engineering design principles by which proteins can serve as mechano-chemical switches is not only essential to learn how cells sense and respond to mechanical forces. It has far reaching implications in systems biology and medicine. Illustrative examples will be discussed, from microbiology to drug discovery to tissue engineering.

Selected References:

M. Antia, G. Baneyx, K. Kubow, V. Vogel, ***Fibronectin in aging extracellular matrix fibrils is progressively unfolded by cells and elicits an enhanced rigidity response.*** Faraday Discussions 139 (2008) 229.

Vesa P. Hytönen, Viola Vogel, ***How force might activate talin's vinculin binding sites: SMD reveals a structural mechanism,*** PLOS Computational Biology, 4 (2008), e24, 1-15.

Little, W. C., M. L. Smith, U. Ebneter and V. Vogel. ***Assay to mechanically tune and optically probe fibrillar fibronectin conformations from fully relaxed to breakage.*** Matrix Biol **27** (2008) 451-61.

Smith, M.L., D. Gourdon, W.C. Little, K.E. Kubow, R.A. Eguiluz, S. Luna-Morris, and V. Vogel. 2007. ***Force-Induced Unfolding of Fibronectin in the Extracellular Matrix of Living Cells.*** PLoS Biol. 5 (2007) e268

Sokurenko, E., V. Vogel, and W.E. Thomas. 2008. ***Catch bond mechanism of force-enhanced adhesion: counter-intuitive, elusive but … widespread?*** *Cell Host & Microbe*. October issue.

Thomas, W.E., V. Vogel, and E. Sokurenko. 2008. ***Biophysics of catch bonds***. *Annu Rev Biophys*. 37:399-416.

Vogel V, Sheetz MP. ***Local force and geometry sensing regulate cell functions***. Nature Rev Mol Cell Biol, 7 (2006) 265-275

Vogel, V. ***Mechanotransduction involving multimodular proteins: converting force into biochemical signals***. Annu Rev Biophys Biomol Struct **35** (2006) 459-88.