STABILIZATION OF MEMBRANE PROTEINS BY COMPATIBLE SOLUTES: SINGLE MOLECULE FORCE SPECTROSCOPIC STUDY

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Mechanical single molecule techniques offer exciting possibilities for investigating protein folding and stability in native environments at sub-nanometer resolutions. The single molecules without inherent symmetry can directly be monitored in their physiological conditions using atomic force microscopy (AFM). Recent developments in AFM enable us to go beyond the ensemble average and measure the behavior of individual molecules. In nature, compatible solutes (organic osmolytes) are used for protecting cells against high osmotic stress. They are compatible with cell metabolism even at molar concentrations. The influence of ectoine, betaine and taurine on the mechanical properties of bacteriorhodopsin (BR) has been investigated by single molecule force spectroscopy. Unfolding experiments taking BR as a model system revealed that these compatible osmolytes increase the tendency of the polypeptide to coil, thus decreasing its persistence length. This allows us to conclude the mechanism of interaction between the unfolded polypeptide chain and the osmolyte. The osmolytes are expelled from the protein surface due to the increase in chemical potential of the stretched state forcing the protein into a more compact structure.

These information and approaches provide basis for our further studies regarding the effects of compatible solutes on other membrane proteins of medical importance (particularly in case of liver diseases) which can directly resolve transient intermediate states and multiple reaction pathways, and thus are uniquely powerful in characterizing the complex dynamics of protein folding. Thus, this study is set to provide exciting possibilities in the field of drug development for liver diseases including in vitro rescue of the misfolded proteins and to directly analyze and correlate their structural and functional properties at the sub-molecular level.