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## AFM as a Tool to Probe the Mechanics and Kinetics of Integrins on Living Cells

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Lymphocyte recruitment from the bloodstream plays an important role in a variety of physiological and pathological processes. Intercellular adhesion mediated by the integrin VLA-4 and its endothelial ligand VCAM-1 precedes the extravasation of the lymphocytes to the target tissue. Integrins participate in all adhesive steps between tethering and rolling and firm adhesion. To match this bridging position, these cell surface receptors are subject to insight-out and outside-in signaling, by which the kinetics and mechanics of adhesion under the shear force in the blood stream is regulated.

Here, atomic force microscopy experiments are employed to investigate the attachment of VLA-4 bearing cells to VCAM-1 coated surfaces. We introduce a combined interpretation of classical force spectroscopic parameters, such as forces and rupture lengths, with a new analysis of curve shape and bond formation rate. Based on the assumption that the force-distance curves describe the extrusion of membrane tethers, our interpretation of the data gives insight into a multitude of kinetic and nano-rheological parameters. We show that AFM can be used to simultaneously measure the physiological off-rate under force and the two-dimensional on-rate of proteins immobilized on different surfaces, as well as nano-viscoelastic parameters of the receptor anchoring membrane. We show that the careful analysis of these parameters in combination with flow chamber experiments allows us to fully describe the effect of an VLA-4 activating agents in living cells.