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Deciphering and filming molecular recognition at the nano-scale with AFM

In molecular recognition force microscopy (MRFM), ligands are covalently attached to atomic force microscopy tips for the molecular recognition of their cognitive receptors on probe surfaces. Interaction forces between single receptor-ligand pairs are measured in force-distance cycles. The dynamics of the experiment is varied, which gives insight into the molecular dynamics of the receptor-ligand recognition process and yields information about the binding pocket, binding energy barriers, and kinetic reaction rates. Combination of high-resolution atomic force microscope topography imaging with single molecule force spectroscopy provides a unique possibility for the localization of specific molecular recognition events. The identification and visualization of receptor binding sites on complex heterogeneous bio-surfaces such as cells and membranes are of interest in this context. Considered as the paradigm for molecular recognition are antibodies. They are key molecules for the immune system of vertebrates. The Y-shaped antibody type IgG exhibits C2-symmetry; its Fc stem is connected to two identical Fab arms, binding antigens by acting as molecular callipers. Bivalent binding of the two Fab arms to adjacent antigens can only occur within a distance of roughly 6 to 12 nm. AFM (Atomic force microscopy) cantilevers adorned with an antibody can measure the distances between 5-methylcytidine bases in individual DNA strands with a resolution of 4 Å, thereby revealing the DNA methylation pattern, which has an important role in the epigenetic control of gene expression. Moreover, due to their nano-mechanical properties antibodies exhibit “bipedal” walking on antigenic surfaces. The walking speed depends on the lateral spacing and symmetry of the antigens. Importantly, the collision between randomly walking antibodies was seen to reduce their motional freedom. It leads to formation of transient assemblies, which are known to be nucleation sites for docking of the complement system and/or phagocytes as an important initial step in the immune cascade.

Biography

Peter Hinterdorfer performs advanced nanoscopic techniques in nano-bio technology, life science, and medical diagnostics, and has been working on antibody/antigen interactions, transmembrane transporters, virus/membrane interactions, cells of the immune system, nuclear envelope membranes, and bacterial surface layers. He has done pioneering work in single molecule force spectroscopy and has invented a combined topography and recognition imaging technique. Recently he did research with high-speed bio-AFM.

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