Multiple surface associations of oligomeric proteins to control ligand-receptor recognition

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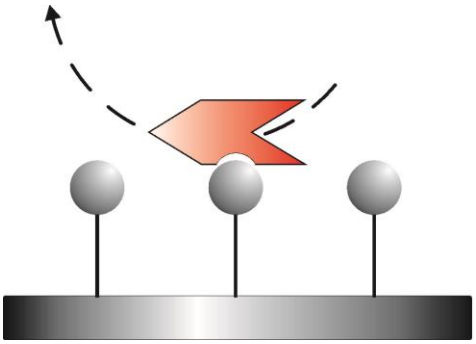
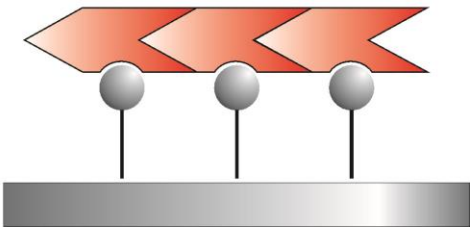
Background:

Biological molecules (e.g. adhesion proteins; lectins) show enhanced binding to cell surface receptors upon well-organized multivalent presentation. Collagen triple helices, coiled coil conformations and receptor clustering result from subunit assembly and generate a variation of binding sites that changes binding kinetics and ligand valency. Multivalent systems are far more complex than the classical 1:1 stoichiometry of receptor-ligand interactions. To explore the relevance of the oligomerization process for the multivalent interactions synthetic multivalent ligands will be used to study the ligand influence on oligomerization and to mechanistically investigate this phenomenon in molecular detail.



Weak binding,
fast association, dissociation



Strong multivalent binding,
very fast association, slow dissociation

Abstract:

Multivalent interactions of monomeric and defined dimeric, trimeric and higher low-n oligomeric forms of protein will be studied by quarz crystal microbalance (QCM), surface plasmon resonance (SPR) and microscale thermophoresis (MST). The respective binding studies will be performed with pre-formed clusters purified by size-exclusion chromatography. To enable the study of multisite interactions of defined biological polymers with the cell surface, multivalently functionalized microparticles will be produced. Receptor clustering induced by binding of multivalent ligands will be analyzed by proximity ligation assays (PLA). Stoichiometry of clusters, kinetics, ligand valency and binding competition of monovalent receptors will be studied by SPR.