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Nano-positioning of supramolecular ligands on DNA origami for multivalent protein recognition

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Supramolecular ligands like Guanidiniocarbonylpyrrole (GCP) and the molecular tweezer CLR01 are small molecules for protein recognition, in contrast to the commonly used large antibodies. This is mainly based on their ability to bind proteins via non-covalent interactions at accessible residues of the protein surface which can be localized, for example, by X-ray crystallography or molecular dynamics simulations. The design of a modular platform with many precisely positioned low-affinity protein-binding supramolecular ligands and an overall high avidity could be the next step for protein recognition in biomedical applications. The molecular recognition of proteins with GCP is based on the residue specific binding of carboxylates while the Janus-type tweezer binds with its aromatic cavity, the apolar chain of lysin and arginine and the side chain cation with the hydrogen phosphate anion. The combination with a programmable DNA origami platform enables the binding of proteins in their native states via nano-positioned supramolecular ligands resulting in high avidity. The controlled deposition of the ligands on the DNA origami is achieved by hybridizing complementary ssDNA strands: One stands out of the DNA origami and another free ssDNA strand, which is linked optionally to an ExoS-peptide or a supramolecular ligand. As a gold standard for binding 14-3-3 with high affinity, a short peptide derived of the binding motif of the ExoS enzyme (*Pseudomonas aeruginosa*) is used. In first proof-of-principle experiments, the association of the protein 14-3-3 with DNA origami is tested by Total Internal Reflection Fluorescence microscopy (TIRF) as well as Atomic Force Microscopy (AFM) with the short ExoS peptide as a gold standard for a selective binding motive.

Biography

Michael Erkelenz has completed his Biology (BSc) from Heinrich-Heine-University Düsseldorf. He has completed his MSc in Medical Biology from University Duisburg-Essen and is a PhD student in Physical Chemistry with Prof. Sebastian Schlucker. He is the Member of the Graduate School of the Collaborative Research Center 1093 founded by the German Research Foundation.

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