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Antibody Adsorption Over Graphene: An Atomistic MD and MF-AFM

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Tunable Binding Reactions on DNA Origami Nanostructures

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Two-dimensional DNA origami shows promise as scaffolds for the assembly of nanoscopic electrical or photonic devices and studies of individual molecular reactions. Maximal binding of functional materials to pre-defined sites on all origami is essential for robust applications and reliable measurements. However, the two-sided nature of the scaffold and its randomly adsorption onto surfaces have proved limiting in the production of identically oriented complexes on practically or technologically useful solid substrates. We have discovered that the holes within DNA origami scaffolds are ~1nm, sufficiently large for the passage of ssDNA. Ligands attached to long ssDNA spacers initially on one side of the origami are thus able to go through the block to the other side, obviating any dependence on the substrate-binding site for subsequent binding reactions. Direct monitoring of single-molecule reactions by using atomic force microscopy, we find that the spacer lengths of 5 bases are enough for helping ligands, here biotins, from one side origami surface to the other side, consistent with expectations, and spacer lengths of 10 bases are with the maximal streptavidin-biotin binding efficiency and rate.

Antibody Adsorption Over Graphene: An Atomistic MD and MF-AFM

Antibody Adsorption Over Graphene: An Atomistic MD and MF-AFM Study

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Protein-surface interaction has great technological relevance for the development of biocatalysts, implants and biosensors. Recent advances on both molecular-dynamics (MD) simulations and atomic-force-microscopy(AF), allow studying such large systems with atomistic detail. Here we have combined MD simulations with high-resolution multi-frequency-AFM experiments to study the adsorption of the IgG antibody (150kDa) over graphene. IgG provides the majority of antibody-based immune response. Therefore studying its biocompatibility/activity over graphene is of interest to address the graphene usage as an implant material as well as to develop more sensitive immunoassays.

We have developed a protocol combining steered-MD simulations and long (>150ns) equilibration runs to address several key open questions concerning protein adsorption: the interaction mechanisms behind the adsorption, the role of the water molecules in such process, and under which conditions the protein unfolds due to the interaction with the substrate. Moreover we determine the most favorable adsorption orientation of the IgG, which in turn allows us to set up a strategy to control the IgG adsorption over graphene. Both the bioactivity and adsorption orientation statistics are in good agreement with experiments.

[1] Antibody adsorption over graphene; submitted to NanoLetters

Molecular Mechanisms of Misfolding of Amyloid Peptides

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The current model for the development of Alzheimer’s, Parkinson’s, Huntington’s, prion, and other neurodegenerative diseases involves protein misfolding as the early step followed by spontaneous aggregation, with specific proteins identified as the primary initiators for disease development. Therefore, elucidating the properties of the disease-prone misfolded states, understanding the mechanism of their formation, and identification of their most toxic forms will open prospects for the development of early diagnostics and specific therapeutics for these diseases. We have developed single molecule AFM force spectroscopy (SMFS) experimental approach enabling us to probe interprotein interactions and to identify those interactions that correspond to misfolded protein states. Using SMFS, we have discovered that the misfolded dimers are very stable and have a lifetime in a second time scale. Such a long lifetime of dimers suggests that the formation of dimers is the mechanism by which the protein misfolded state is stabilized. We hypothesize that the formation of highly stable misfolded dimers is a critical step in the entire process of the peptide self-assembly into aggregates. The Molecular Dynamics (MD) simulation performed at the μs timescale demonstrated that isolated non-structured monomer upon approaching to each other changed dramatically their initial conformation and formed dimers with antiparallel beta-sheet structures. Steered MD approach showed that the dimers dissociated cooperatively resulting in a sharp rupture peak corresponding to breakage of the beta-sheet structure. Altogether, the SMFS experimental study and computational analysis revealed a critical role of the interpeptide interaction in the misfolding process and highlighting the key role of the dimerization in the amyloid aggregation process.

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