Revealing secrets of material specific peptide adhesion: From advanced NMR analysis to computational process modeling

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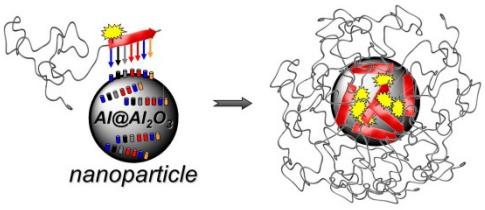
Complex of topics: B3 Analysis tools for dynamic interfaces to understand nanostructures

Short version (~150 words)



The adhesive system of marine mussels stimulated intensive interdisciplinary research.[*Science* **1981**, *Annu. Rev. Mater. Res.* **2011**] Mussels adhere onto virtually any hard substrate in hostile environments and outperform technical wet-glues. Besides these universal and complex protein based adhesives, 12*mer* peptides can be selected by biocombinatorial means to exhibit highly specific adhesion onto material surfaces.[*Nature* **2000**] Those material specific adhesives promise a scope of next generation applications from nanoengineering of nanoparticle surfaces, to specific glues for nerve surgery.[*ACS Macro Lett.* **2012***; J. Am. Chem. Soc.* **2012**] The effects on the molecular scale, which originate the material specific adhesion of peptides are, however, by far not understood. Soft multipoint interactions, surface related docking, locking of peptide conformations and surface induced folding processes are discussed.[*JACS* **2011**]

Objectives of the present project are the development of analytical tools and their companion with computational methods to gain insight into material specific adhesion. Advanced NMR analytics such as solution-based nuclear Overhauser and saturation transfer difference (STD) spectroscopies under transient binding conditions as well as surface enhanced local Raman spectroscopy (SERS) probing will be combined with modern molecular simulation to investigate dynamic interactions of peptides with material surfaces and thus elucidating mechanisms of recognition.

Focus will be set on the understanding of three recently selected peptides, showing specific adhesion onto surfaces of (i.) gold, (ii.) aircraft aluminum and (iii.) magnesium fluoride. The adhesive processes will be analyzed by advanced NMR techniques revealing insight into peptide surface contacts and contact developments throughout the adhesion process. The results will be accompanied with SERS-probing to analyze changes of vibrational dynamics of the surface adhered peptides. Based on those analytical data, molecular modeling of peptide conformation on the surface and conformational pathways during peptide adhesion process will be performed and reveal the origin of material specific adhesion on the molecular level. The discussed opinions about specific peptide adhesion should be modeled and validated. With the aid of atom-based models of surfaces and peptides (parametrization inside the software package GROMACS) and by using a sophisticated statistical thermodynamics software platform ZIBMolPy with domain decomposition and free-energy estimation [SIAM JMMS **2007**, Lecture Notes **2013**], adhesion scenarios can be analyzed thermodynamically. Moreover, kinetic effects have to be simulated and recent non-thermodynamic effects such as "rebinding effects" [JCP **2012**] will be taken into account requiring new computational method developments.

Overall goal of the project

The project aims to establish analytical tools and companion those with computational methods to understand material specific adhesion of peptides onto 2D and 3D surfaces. While several peptide sequences have been described, which were selected via biocombinatorial means to strongly or even highly specifically adhere onto surfaces of interest, the molecular origin for specific adhesion still needs to be revealed.

Major challenges in Analytical Sciences result from the fact that adhesion processes occur at rather ill-defined interfaces and binding is heterogeneous in nature. Analytical methodologies established for investigating defined peptide-receptor interactions have to be transferred to heterogeneous systems with less defined binding events. Saturation transfer difference (STD) NMR spectroscopy and solution-based nuclear Overhauser spectroscopy experiments (NOESY) will be used to elucidate transient peptide-surface contacts and contact developments during binding processes. SERS sensors should be used to probe the different states of peptide binding via changes of vibrational states of the peptide while adhering on the surface of interest. Curvature dependency of adhesion modes and interaction strengths should be analyzed, as well.

The experimental studies should go along with theoretical investigations of the adhesion process. Especially, the suggested, existing opinions about specific peptide adhesion should be modeled and compared with experimental data for validation/falsification. Soft multipoint interactions, surface related docking, and locking of peptide conformations are connected to a thermodynamics point of view. Surface induced folding processes could be analyzed thermodynamically, too, but they are also connected to a kinetics point of view. In this context, the "rebinding effect" should be discussed. The adhesion processes can be analyzed by new computational methods developed (and still developing) in the working group of Marcus Weber at the Zuse Institute Berlin.

This project meets the challenges of “complex B3”, where analysis tools for dynamic interfaces are developed with the aim to understand nanostructured materials.

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