Interactions at the ZnO/peptide interface

Adsorption of binding peptides on ZnO - Towards a quantitative understanding of organic-inorganic interactions

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In Short

- Interactions at the ZnO/peptide interface
- Calculation of binding free energies from advanced sampling methods and steered molecular dynamics.
- Circular dichroism spectroscopy as joint observable for simulations and experiments.

The specific binding of peptides to biomolecular receptors is key to the regulation of biological processes such as cell adhesion or antibody recognition. In the 1990s seminal works by Stanley Brown exported the concept of molecular recognition to the field of materials science with individual peptide sequences that selectively bind to inorganic mineral phases.[1]. Extending this concept further, sequences that recognize certain materials classes, inorganic compounds or even crystallographic facets of the same material have been identified [2]. leading to highly promising applications in bio-nanotechnology.[3].

By comparison, our knowledge of biomolecular recognition heavily relies experiementally on precise structure determination for instance by nuclear magnetic resonance (NMR) methods.[4]. In this context, atomistic simulations can be of great help, as they can complement the accessible indirect experimental information, e.g. the binding free energy or the adhesion forces between surfaces and peptides, with precise structural details. Precise steering of the structure and thus the properties (e.g. optical or catalytic) of ZnO/peptide hybrids necessarily requires quantification of the interactions at the bio-inorganic interfaces that dictated the relative stability of the various morphological phases. With this project, we aim for a quantitative determination of the binding characteristics (binding free energy, adhesion forces) of ZnO-binding peptides interacting with the non-polar (10-10) surface of ZnO. They will be interpreted in terms of both the primary peptide structures and of changes of peptide conformation (secondary structure) after adsorption.

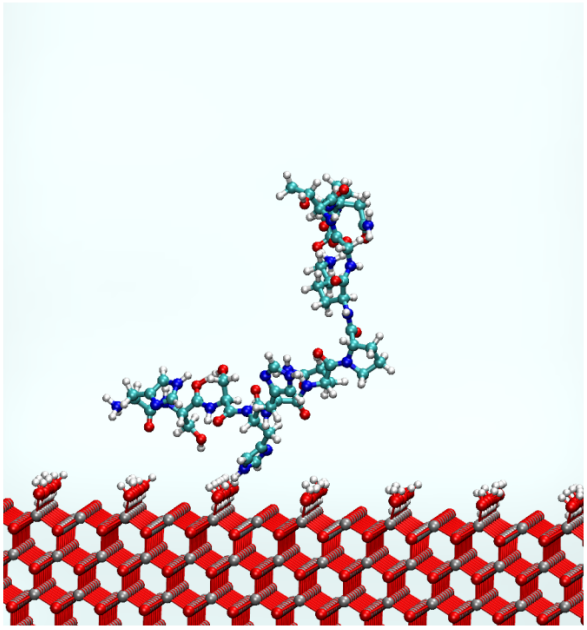

***Figure 1:** Possible input structure of a zinc oxide binding peptide approaching the ZnO(10-10) surface in water.*

This proposed project is based on recent work studying the non-polar zinc oxide surfaces (10-10) and (1-210) preparing realistic surface models with the correct terminal groups [5,6]. These models have been used to develop a classical force field describing the interactions of these surfaces with amino acids and peptides in larger-scale systems[7], which will be the starting point of this project.

The calculations regarding the conformational ensambles of five ZnO binding peptides will be based on classical all-atom Molecular Dynamics simulations, coupled to techniques that enable a computational prediction of free energy profiles for the interactions across hybrid interfaces, such as Metadynamics (MetaD) and Replica Exchange with Solute Tempering (REST).[8]. In order to compare this simulations to experiments, the CD spectra of the peptides in solution are computed, which was shown to lead to a quantitative agreement with experimental measurements [9]. In a second step this approach will be used to charaterize the interactions of the peptides with the non-polar zinc oxide surfaces (10-10) (see 1 for an example of such model).

Additionally, non-equilibrium, steered MD will be used to extract the free energy of adsorption from the dependence of the experimentally measured adhesion forces (already performed in our group) on

the applied AFM loading rates using an approach introduced by [10].

We believe that these simulations will help us elucidate the influence of the primary peptide structures and of changes of peptide conformation (secondary structure) upon the interaction with the non-polar ZnO surface (10-10) and allow the quantification of the interactions at the interface.

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http://www.hmi.uni-bremen.de

More Information

[1] S. Brown, *Nat. Biotechnol.* **15**, 269-272 (1997) doi:10.1038/nbt0397-269

[2] S. R. Whaley, D. S. English, E. L. Hu, P. F. Barbara and A. M. Belcher, *Nature* **405**, 665-668 (2000) doi:10.1038/35015043

[3] K. Shiba, *Curr. Opin. Biotechnol.* **21**, 412-425 (2010) doi:10.1016/j.copbio.2010.07.008

[4] D. Rothenstein, B. Claasen, B. Omiecienski, P. Lammel and J. Bill, *J. Am. Chem. Soc.* **134**, 12547-12556 (2012) doi:10.1021/ja302211w

[5] S. grosse Holthaus, S. Koppen, T. Frauenheim, L. Colombi Ciacchi, *J. Chem. Phys* **140**, 234707 (2014) doi:10.1063/1.4882280

[6] S. grosse Holthaus, S. Koppen, T. Frauenheim, L. Colombi Ciacchi, *J. Chem. Theory Comput* **8**, 4517-4526 (2012) doi:10.1021/ct3007106

[7] S. grosse Holthaus, Dissertation, University of Bremen (2014)

[8] J. Schneider, L. Colombi Ciacchi, *J. Am. Chem. Soc.* **134**, 2407 (2012) doi:10.1021/ja210744g

[9] R.H Meissner, J. Schneider, P. Schiffels, L. Colombi Ciacchi, *Langmuir* **30**, 3487-3494 (2014) doi:10.1021/la500285m

[10] R.H. Meissner, G. Wei, L. Colombi Ciacchi,*Soft matter* **11**, 6254-6265 (2015) doi:10.1039/C5SM01444A