ABSTRACTS

of talks at the

NTZ-Workshop on

Protein Folding and Substrate Specificity: Computational and Experimental Approaches for Studying Biological Macromolecules

ProtFold05

**Institut für Theoretische Physik,
Universität Leipzig, Germany**

16 June 2005

http://www.physik.uni-leipzig.de/~janke/ProtFold05

Supported by the Theoretical Sciences Center (NTZ) of the Center of Higher Studies (ZHS), Universität Leipzig, and the DAAD-PPP-Exchange Programme with Sweden.

ProtFold05 Timetable

June 16, 2005 - Vor dem Hospitaltore 1, Large (''Grosser'') Seminar Room 1L12/13

15:15-15:30		**- Welcome Coffee -** 
15:30-16:00	**Anders Irbäck**	Protein folding and unfolding studied using a simplified atomic model
16:00-16:20	**Sandipan Mohanty**	Oligomerization with an all-atom model
16:20-16:50	**Bernd A. Berg**	A biased Metropolis scheme for simulations of biomolecules
16:50-17:10	**Thomas Vogel**	Simple protein models
17:10-17:30	**Hans-Jörg Hofmann**	Folding in homologous peptides
17:30-18:00		**- Coffee Break-** 
18:00-18:20	**Robert Günther**	Molecular docking of small ligands to proteins
18:20-18:50	**Annette G. Beck-Sickinger**	Chemical modification and immobilisation of proteins
18:50-19:00	**Marius Grundmann**	Interaction of organic material with semiconductors
19:00-19:20	**Karsten Goede**	When molecules recognize their substrate: Selective peptide binding to semiconductors
19:20-19:50	**Michael Bachmann**	Minimalistic models for substrate adsorption of polymers and peptides
20:30		**- Dinner at "Vodkaria" - Bar & Restaurant (Gottschedstr. 15)** 

Wolfhard Janke - Tue Jun 14 09:34:34 CEST 2005 - Sat May 14 19:32:24 CEST 2005

Minimalistic models for substrate adsorption of polymers and peptides

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The interest in understanding polymer adsorption at substrates has grown quite recently with the development of high-resolution experimental equipment allowing for single-molecule microscopy and the technologically important question of substrate-binding specificity of synthetic or biopolymers concerning future nanosensory devices.

In our study, we investigate how solubility of the surrounding solvent and temperature influence the substrate-binding of non-grafted homo- and heteropolymers in a cavity with an attractive surface. Extending our multicanonical chain-growth algorithm, we performed extensive simulations and obtained the entire temperature-solubility pseudo-phase diagram within a single simulation. In the case of the homopolymer we clearly separated the expected thermodynamically stable phases dominated by the respective adsorbed and desorbed collapsed and random-coil conformations. Another central aspect of our study is the discussion of pseudo phases that specifically depend on the precise number of monomers in the polymer chain. Although most of the pseudo-phase transition lines are expected to disappear in the thermodynamic limit, effects like layering transitions in three dimensions as well as hierarchical structural dissolution of the completely adsorbed polymer approaching the two-dimensional Θ transition line could become essential for future technological applications. This is also of enormous interest for peptide recognition by nanoscale devices, where the specificity of the substrate and the peptide sequence determine the binding properties of the hybrid system. In a first preliminary study we investigated a simple heteropolymer model and its adhesion to three different substrates: entirely attractive, hydrophobic, and polar. In particular, we found a rich variety of pseudo phases in the regime of the adsorbed and collapsed heteropolymer, where the substrate–specificity is responsible for the different dominant heteropolymer conformations.

Chemical modification and immobilisation of proteins

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A biased Metropolis scheme for simulations of biomolecules

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The Rugged Metropolis (RM) algorithm is a biased updating scheme, which aims at directly hitting the most likely configurations in a rugged free energy landscape. Details of the one-variable (RM1) implementation of this algorithm are presented. This is followed by an extension which includes simultaneous updating of two dynamical variables (RM2). For the test case of Met-Enkephalin in vacuum at 300 K the RM1 version improves conventional Metropolis simulations by a factor of two and another factor of two is gained by switching to RM2. We also investigate multi-hit Metropolis scheme, which spends more CPU time on variables with large autocorrelation times.

When molecules recognize their substrate: Selective peptide binding to semiconductors

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One of today's physics major challenges is bridging the gap between anorganic matter, i.e., the prime working field of previous physics, and living matter which until recently was mostly looked upon by biologists and chemists. Yet merging these two research fields may promote both a better understanding of the world that surrounds us and an unimagined range of applications from *smart* protheses or quick organics detection and coated functionalised surfaces to true nanoscale opto-electronics and data processing in single molecules. However, given the nanometer size of organic building blocks and their necessary number for a single device, the true potential of such hybrid organic-anorganic nanostructures will remain under-utilised until there are appropriate self-assembly techniques. In this regard, using DNA or amino-acid based molecules like peptides or proteins is one of the most promising approaches. In nature, recognition and assembly capabilities driven by amino acids or base pairs govern the replication of all living structures. We have devoted ourselves to the fundamentally new field of applying these self-assembly principles to peptide clusters on surfaces of classic, anorganic semiconductors. By taking AFM micrographs and

subsequently analysing them, we have quantitatively shown that on the one hand the adhesion rate (the percentage of surface covered by peptide clusters) of a specially selected 12-mer peptide on nine different semiconductor surfaces ranges from 25% to 0% under the same standard conditions. On the other hand, different peptides adhere rather different to equal surfaces. In this talk, I shall discuss these experimental findings together with an atomic-scale explanation which is based on the interplay between polar amino-acid side chains and the surface atoms with their respective electronegativity.

Interaction of organic material with semiconductors

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The research directions in the semiconductor physics group are briefly reviewed. Several concepts and materials such as nanostructures, electronic devices and ZnO allow future devices for biosensing, cell manipulation and biologically directed self-assembly.

Molecular docking of small ligands to proteins

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Interactions between biomolecules are fundamental to the obvious majority of biological processes. Based on these interactions, living organisms maintain complex regulatory and metabolic interaction networks that together constitute the processes of life. Understanding of biomolecular interactions is the key in solving the biological phenomena and is of great importance for the design of novel theurapeutics. Molecular Docking is a computional approach to answer the question: "Given the structure of a protein and that of a potential ligand, can the two form a favorable complex? What are the bases for binding and specificity?" Like many molecular recognition questions, molecular docking is difficult because of the many states accessible to macromolecules and their ligands, and the problem of calculating accurate energies. In this talk, I will give a short overview on basic methodologies suitable to solve the docking problem.

Folding in homologous peptides

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It has been assumed for a long time that oligomers composed of homologous amino acids (iβ-, γ-, δ-amino acids) are unable to form definite secondary structures comparable with those in native peptides and proteins because of a higher flexibility of the peptide backbone. Contrary to this, a wide variety of characteristic secondary structure elements (helices, sheets, turns) was found in experimental studies and predicted by theory. Thus, such structures have got attention as peptidomimetics and in material sciences.

Here, an overview is given on the helix formation in homologous peptides on the basis of systematic conformational analyses employing ab initio MO theory.

Protein folding and unfolding studied using a simplified atomic model

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Using an all-atom model with a simplified interaction potential, we study the folding of several peptides with different native geometries. The same model is also used to investigate the force-induced unfolding of ubiquitin, which was studied in recent single-molecule constant-force experiments. An aggregation study based on this model will be discussed by Sandipan Mohanty in his talk.

Oligomerization with an all-atom model

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Formation of small oligomers is studied with an all-atom model with a simplified interaction potential. Exactly the same potential has been used to study folding and thermodynamics of several small peptides with different native geometries, as well as the mechanical unfolding of ubiquitin. We identify several interesting shapes for oligomers consisting of 3 to 10 chains of Alzheimer's Abeta (16-22) peptide.

Related paper exists and can be obtained from Biophysical Journal, Vol 87, pages 3657–3664.

Simple protein models

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