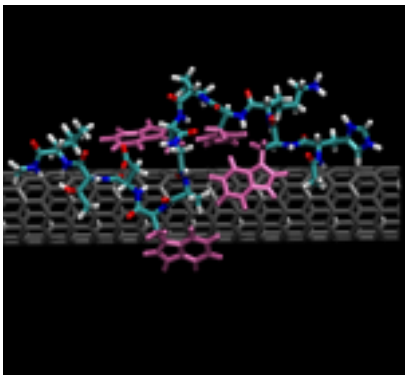
Modelling the Interaction of Biomolecules with Inorganic Surfaces



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October 2, 2007

1 Workshop Details

1.1 Details

Timing
Number of days : 3
Start : 2007-07-25
end : 2007-07-27

Location of the activity
CECAM
46 allé e d'Italie
69007 Lyon
France

1.2 Description

The pioneering work of Stanley Brown [1] first showed that it was possible to identify, out of billions of possibilities, peptide sequences that could specifically bind to one inorganic material over a range of others. Since this influential paper was published, hundreds of similar experiments have been reported, publishing peptide sequences (aptamers) for recognising a range of inorganic materials (see the reviews of Refs [2,3] for examples) including metals, oxides and semi-conductors. At present, advances in experimental methods far outpace corresponding progress in theory and simulation in this emergent research area. Furthermore, although significant progress has been made in identifying sequences that possess specificity for a variety of targets, the underlying mechanisms of this specificity at the molecular level are at present unknown.
Recent experimental advances in aptamer selection techniques both in-vivo (phage-display, cell-surface display) and in-vitro (messengerRNA display) have opened up new vistas for combining biological and traditional materials via controlled interactions at the biointerface. Furthermore, advances in characterization techniques such as nuclear magnetic resonance (NMR), neutron reflectometry, surface-enhanced raman scattering (SERS), surface plasmon resonance (SPR) and isothermal titration calorimetry (ITC) are fast gathering pace in this area. Depite this, at present structural detail at the molecular level remains scarce for these biointerfaces. However, interpretation of these characterization experiments would be aided significantly if partnered with corresponding atomistic simulations of such biointerfaces. Furthermore, given that aptamer selection typically is taken from a limited and/or biased peptide library, there is ample scope for optimization of peptides via bioinformatics approaches that are based on 'scoring matrices' not yet fine-tuned for application to peptide-inorganic interfaces. Atomistic simulation data may conceivably be used in future to achieve this goal. In addition, very recent experiments [4] have revealed that aptamers can nucleate the inorganic materials that the peptides were initially selected against, opening the issue of how to simulate nucleation of inorganic material (such as biomineralization) in the presence of these peptides. The modelling of these biointerfaces should not be confined to the atomistic level alone. Very recent experimental work has revealed that multimers (e.g. trimers) of aptamers form regular, hierarchical nanoscale patterns when adsorbed onto the target inorganic surfaces against which the peptides were selected. This ag-

gregation and patterning behaviour could be modelled using coarse-grained potentials, derived from atomistic simulations.
While the peptide/inorganic-surface interface is currently a ’hot topic’ experimentally, and in principle amenable to study by simulation approaches, the meeting also has the broader remit of considering any type of biomolecule/inorganic-surface interface. This may include lipids and membranes, proteins, and pharmaceuticals in the biomolecule category. Target inorganics may encompass a range of models aside from flat surfaces, and cover shape effects ranging from surface steps and terraces to nanoparticle shape and size.

2 Requested Support

CECAM

Simbioma

EPSRC Materials Modelling Consortium

3 Participant List

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4 Presentation List

A computational approach to the interaction between proteins and gold surfaces
Stefano Corni
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Abstract
Combinatorial biotechniques have shown that it is possible to identify proteins that bind a given inorganic surface, ranging from insulators to metals. However, the basic principles regulating such specific interactions cannot be disclosed via these combinatorial approaches alone. In the framework of the European project PROSURF ("Computational toolbox for protein surface interaction"), that involves groups with theoretical/computational and experimental expertise, we have started a systematic recognition of the interaction between the natural amino acids (and water) with the gold (111) surface. In particular, I shall present DFT calculations on small model molecules, representative of the natural amino acids functionalities, adsorbed on the gold surface, and calculations on larger systems including gold, water and model peptides. The nature of the adsorption (chemi- vs physi-sorption) on gold of the natural amino acids will be discussed, together with the strategy for the use of these quantum mechanical results to parameterize classical force fields for protein-surface interactions.

Ab-initio QM study of hydroxyapatite (001) and (010) surfaces in interaction with water
Marta Corno
University of Torino, Dipartimento di Chimica I.F.M., Italy
Abstract
Hydroxyapatite [HA, Ca10(PO4)6(OH)2] is the principal constituent of the mineral phase of bone as well as of teeth enamel. Much recent work has investigated the role of calcium hydroxyapatite within the wide range of biomaterials, both experimentally and theoretically. Considering bioglasses, it was shown by Hench and coworkers that a thin crystalline layer of a material, very similar in structure to HA, is formed on the surface of a bioglass when it is immersed in body plasma solution (in vivo tests) or in SBF (Simulated Body Fluid, usually used for in vitro studies). Due to the fundamental function carried out by HA, the knowledge of its structure at the atomic level is considered of great importance. In the present work, ab-initio B3LYP periodic electronic methods using the CRYSTAL06 code have been applied to study the most common HA (001) and (010) surfaces. Actually, HA crystals are elongated in the [0001] direction in both bone matrix and tooth enamel, but some proteins bind preferentially to the (010) crystal faces. Surface models with different thickness have been characterised, both free and in interaction with water. The computed water binding energy is $\sim$ 20/30 kcal/mol, in agreement with microcalorimetric data. The vibrational frequencies of adsorbed water molecule show a blue shift of the bending mode (average value $\sim$ 80 cm-1), and a red shift ($\sim$ 100-1200 cm-1) of the OH stretching modes, as consequence of the hydrogen bond between water and the surface oxygens of the phosphates groups. These results are in remarkable agreement with the experimental IR data. For the future, we will aim at modelling amino acids adsorptions and at simulating the interaction between HA and silica based materials, with the purpose to better understand the formation of the thin HA layer at the bioglasses materials.

Conformations vs. Interaction energy: adsorption of flexible (bio)molecules on inorganic substrates

Luca Ghiringhelli
Max Planck Institute for Polymer Research, Germany

Abstract
For flexible molecules near to inorganic surfaces the understanding of the adsorption process requires the analysis of the interconnection between molecular conformations and chemical or electrostatic interactions with the substrate. Conformations are sampled according to the flexibility of the molecule when restricted by the surface confinement, while the adsorption of the molecule is dominated by the chemical nature of the substrate. Here we present a DFT study of an amino acid, namely the phenylalanine, interacting with different substrates for which the role is either a confining wall or an actively interacting substrate. We will show how the various aspects of conformation and selective interaction combines by going from an inert graphene surface, to an electrostatic-like interacting surface as Silver and finally to the highly chemical interactive Platinum. This is a unique route to understand the basic aspects of molecule-surface interaction and can be next used for modelling pourpose for larger, multiscale-like approaches. (see the presentation of our collaborator N.van der Vegt).

Experiments on specific adhesion and clustering of peptides on semiconductor surfaces

Karsten Goede
University of Leipzig, Germany

Abstract
In nature, recognition and assembly capabilities driven by amino acids or base pairs govern the replication of all living structures. Studying peptide behaviour on surfaces of anorganic semiconductors can thus bridge the gap between classic physics and novel nano-biotechnology. We investigate self-assembly, clustering, and conformational transitions of small peptides on semiconductor surfaces, both in experiment (mainly by atomic-force microscopy) and simulation [1, 2, 3]. We have experimentally shown that the adhesion coefficient (the percentage of surface covered by peptide clusters) of a specially selected 12-mer peptide on nine different semiconductor surfaces ranges from 25% on GaAs (100) to 1% on Si (100) under the same standard conditions [1]. Yet different peptides adhere differently to equal surfaces. The cluster ensembles have surface-specific properties: The larger, higher and softer clusters generally appear on the surfaces with lower peptide adhesion [2]. Quantitative details and qualitative explanations of these specificity and clustering phenomena will be presented. The influence of sample preparation-solution parameters, such as pH value, temperature and peptide concentration, will be considered. Simulations are applied to better understand the affinity of the molecules to adhere to solid substrates [3]. Within the pseudo-phase diagram of a suitable lattice-polymer hybrid system, thermodynamically stable phases dominated by adsorbed or desorbed collapsed conformations can be clearly distinguished from random-coil conformations.

References

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[3] K. Goede, M. Bachmann, M. Grundmann et al., Bioforum 2005, 10, 53-55.

Guiding theory: Materials genomics and lessons learned from polypeptide "interactions" with natural and artificial inorganic solids.

John Evans
Professor, Chemistry, New York University, United States

Interaction of glycine with isolated hydroxyl groups at the silica surface: first principles B3LYP periodic simulation

Piero Ugliengo
University of Torino, Italy

Abstract
The adsorption of glycine molecule on a model of silica surface terminated by isolated hydroxyl group has been studied ab-initio using a double-z polarized gaussian basis set, the hybrid B3LYP functional and a fully periodic treatment of the silica surface/glycine system. The hydroxylated silica surface has been simulated using either a two dimensional slab or a single polymer strand cut out from the (001) surface of an all silica edingtonite. A number of B3LYP optimized structures have been found by docking glycine on the silica surface exploiting all possible hydrogen bond patterns. Whereas glycine is generally adsorbed in its neutral form, two structures show glycine adsorbed as zwitterion, the surface playing the role of a "solid solvent" whereas intra-strand hydrogen bond cooperativity stabilize the zwitterions. The adsorbed zwitterionic structures are no longer formed at a lower glycine coverage as simulated by enlarging the unit cell so to break intra-strand hydrogen bonds, showing the importance of H-bond cooperativity in stabilizing the zwitterionic forms. Each structure has been characterized by computing its harmonic vibrational spectrum at G point, which also allowed to calculate the free energy of adsorption. The experimental infrared features of chemical vapour deposited glycine on silica surface are in agreement with those computed for glycine adsorbed in its neutral form and engaging three hydrogen bonds with the surface silanols, two of them involving the C=O bond and one originating from the glycine OH group. The NH2 group only plays a minor role as a weak hydrogen bond donor.

Mechanisms and dynamics of protein clustering on a solid surface

Paul Mulheran
University of Reading, United Kingdom

Abstract
A methodology for discovering the mechanisms and dynamics of protein clustering on solid surfaces is presented. In-situ atomic force microscopy images are quantitatively compared to Monte Carlo simulations using cluster statistics to differentiate various models. We study Lysozyme adsorption on mica as a model system and find that all surface-supported clusters are mobile, not just the monomers, with diffusion constant inversely related to cluster size. The monomer diffusion constant is measured to be D1 $\sim$ 9x10-16 cm2s-1, such a low value being difficult to measure using other techniques.

Meso/MM/QM modelling of biomolecules on self-assembled monolayers

Maria Sushko
UCL, United Kingdom

Abstract

Local control of polymer chain conformation upon adsorption onto surfaces is one of the central issues in biosensing, biomineralization and biocompatability. One of the possible ways of controlling the conformation of adsorbed biomolecules is via engineering the properties of the surface. Self-assembled monolayers, with a well developed patterning protocols, offer a versatile system for designing different surface functionalities. We have considered the specific adsorption of DNA molecule on a surface of patterned self-assembled monolayers and studied the dependence of the conformation on the size of the pattern. Due to the size and heterogeneity of the system, the problem requires the developments of new simulation techniques. We propose the following method. In order to model the interactions of large organic molecules, such as DNA or proteins, with surfaces it is essential to adequately describe short- and long-range interactions with the surface. We will show that the long-range forces can be described on the mesoscopic level of theory. The comparison of the results of mesoscopic calculations, based on the mean-field DLVO theory, with the experimental data for DNA on mica surface in aqueous salt solutions shows that the theory is able to capture the conformational behaviour of the DNA molecule on the surface. The theory also predicts the solvent composition, at which the transition from the compressed to extended conformation of DNA on mica takes place. This suggests that the analytical expressions for the interaction energies and forces, obtained using the mean-field approach can be used in the combined coarse grained/atomistic calculations for the description of the long-range interactions of the molecule and the surface. In order to treat the short-range part of interactions, responsible for specific binding of biomolecules to surfaces, we have developed an embedded cluster model. In this model the region of interest is considered quantum mechanically, while the rest of the atomistic system is treated on the molecular mechanical level. Most force-field are fitted to reproduce the van der Waals interactions between organic molecules and the segments of polymer molecules, which in many cases largely determine the conformational properties of biomolecules. However, the density functional methods are known to fail to describe the dispersion interactions correctly. Therefore, in order to overcome this deficiency of density functional methods, we have introduces classical corrections to the quantum region. This embedded cluster model has been tested for self-assembled monolayers on gold surface. Combining the mesoscopic and the embedded cluster approaches allows us modelling biomolecules on surfaces. Using this technique we have found the optimum size of pattern of mixed self-assembled monolayers required for DNA adsorption in almost unperturbed solution conformation, while maximising the density of DNA molecules on the surface.

Microcanonical Analyses of Peptide Aggregation Processes

Wolfhard Janke
Institut für Theoretische Physik, Universitä t Leipzig, Germany

Abstract

We propose the use of microcanonical analyses for numerical studies of peptide aggregation transitions. Performing multicanonical Monte Carlo simulations of a simple hydrophobic-polar continuum model for interacting heteropolymers of finite length, we find that the microcanonical entropy behaves convex in the transition region, leading to a negative microcanonical specific heat. As this effect is also seen in first-order-like transitions of other finite systems, our results provide clear evidence for recent hints that the characterisation of phase separation in first-order-like transitions of finite systems profits from this microcanonical view.

References

Ch. Junghans, M. Bachmann, and W. Janke,
Phys. Rev. Lett. 97, 218103 (2006).

Modelling affinity of peptides at inorganic surfaces: the role of solvent

Tiff Walsh
University of Warwick, United Kingdom

Abstract

Considerable experimental advances are being made in the study of organisation of peptides on inorganic surfaces. In contrast, comparable advances in the modelling of these interfaces lags behind substantially. In this contribution, the information that can be gathered from molecular simulation of these interfaces will be outlined, with particular attention paid to the contrast in solvation behaviour seen at both hydrophobic and hydrophilic interfaces, and the impact this has on peptide adsorption and dynamics at the interface. Two types of interface will be illustrated. First, adsorption on an archetypal hydrophobic graphitic surface will be covered, outlining our recent work on modelling graphite-peptide and nanotube-peptide systems [1]. In the second case, the 'structure-making' effects of solvent on the rutile TiO2 surface, and the consequences this has for peptide dynamics, will also be discussed in detail [2].Both cases serve to illustrate general issues surrounding the impact of solvation structure at the peptide-surface interface.

References

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[2] A. A. Skelton and T. R. Walsh, in preparation.

Modelling Biomolecules close to Metal Surfaces

Nico van der Vegt
Max-Planck-Institute for Polymer Research, Germany

Abstract

The adsorption of organic molecules, including polymers of synthetic and biological origin, onto solid surfaces is an important problem in many modern scientific and technological fields. For example, adsorbed proteins may foul membranes in filtration/fractionation devices and biosensors, or clog hemodialysis membranes and artificial arteries. On the other hand, the formation of active biopolymer monolayers at metal surfaces is an essential step in the fabrication of a number of important bioanalytical devices such as biochemical sensors, bioelectronic switches and gates, chemical separation and purification surfaces, and enzymatically controlled electrochemical interfaces. Theoretical modelling, on the one hand, needs to account for local, chemistry-specific interactions, while on the other hand it must account for a statistically repre-

sentative description of a vast configuration space. These two requirements are usually not met simultaneously, therefore, multiscale modeling methods must be used, which link together first-principle quantum mechanics methods, classical force-field-based (atomistic) descriptions, as well as coarse-grained ”effective particle” descriptions. I will discuss our multiscale modelling methods based on some examples recently studied in our group, including the interaction of liquid water with metal surfaces, and the adsorption of biomolecules at water/metal interfaces.

References

P. Schravendijk, N. van der Vegt, L. Delle Site, K. Kremer, ChemPhysChem 6, 1866 (2005).

P. Schravendijk, L.M. Ghiringhelli, L. Delle Site, N.F.A. van der Vegt, J. Phys. Chem. C 111, 2631-2642 (2007).

Post-selection Genetic Engineering of Inorganic-Binding Peptides

Candan Tamerler
Istanbul Technical University, Turkey

Abstract

Prediction of switching in alpha-helical polypeptides at solid surfaces

Mark Biggs
University of Edinburgh, United Kingdom

Abstract

The behaviour of proteins at solid surfaces is of relevance to biosensors, prostheses (e.g. stents, artificial heart valves) and biomimetic assembly of nanoparticles amongst many other things. The design of such technologies would be greatly assisted by the availability of physics-based molecular modelling tools that predict the three-dimensional structure and properties of proteins when at solid surfaces. We at Edinburgh are developing such tools. In this presentation, we will outline the tools we have developed to date and will report on some key results obtained using them including our study of switching behaviour in an alpha-helical polypeptide on solid surfaces, which maybe of relevance to molecular computing and nano-machines.

Protein/Solid Interfaces: Designed Marriage of Biology and Materials for Technology and Medecine

Mehmet Sarikaya
Professor, Materials Science, University of Washington, United States

Specific polymer and peptide adsorption to attractive solid substrates

Michael Bachmann
Complex Systems Division, Lund University, Sweden

Abstract

The interest in understanding polymer adsorption properties to attractive substrates has grown quite recently, since today's high-resolution experimental equipment allows for single-molecule microscopy at the nanometer scale. The question of substrate-binding specificity of synthetic or biopolymers is of essential relevance for future nanosensory arrays.

In our studies of simple hybrid models, we have investigated how solubility of the surrounding solvent and temperature influence the substrate-binding of nongrafted polymers in a cavity with an attractive surface [1,2]. Applying a suitably adapted variant of the multicanonical chain-growth algorithm for self-avoiding walks [3], we performed extensive computer simulations of lattice polymers with up to 200 monomers and obtained the entire temperature-solubility pseudo-phase diagram of the hybrid system within a single simulation. We clearly separated expected thermodynamically stable phases dominated by the respective adsorbed and desorbed collapsed and random-coil conformations. Another central aspect is the discussion of subphases that depend on finite-size properties such as the precise number of monomers. For protein-like hydrophobic-polar heteropolymers, we have also investigated the dependence of the pseudophases on the specificity of substrates which are attractive to selective monomer types only [4].

References

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The absorption of polysaccharide molecules onto calcite surfaces

John Harding
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Thermodynamics of adsorption in polymer-nanoparticle mixtures

Dmytro Antypov
University of Cambridge, United Kingdom

Abstract

We present a novel numerical method which combines multcanonical Wang-Landau sampling with a technique normally used in grand-canonical simulations to study a polymeric lattice system also containing two types of interacting sites, with the lower volume fraction species representing nanoparticles and the majority representing solvent. Unlike polymer adsorption on a flat surface or adsorption on fixed randomly dispersed particles, the positions of mobile adsorbate species are strongly coupled with conformation of the polymer chain, whose statistics in turn depend on the solvent properties. We calculate free energy and a number of properties for a single polymer chain as a function of adsorption strength and solvent properties to identify the phase behavior. Addition of particles with slightly higher than solvent affinity for the polymer resulted in swelling within a narrow window of interaction parameters. If the difference in affinity was large, localization of attractive interactions led to a collapse of a polymer chain, even in good solvent. Due to a high entropic penalty, there was no extended adsorbed phase, and

strong adsorption of nanoparticles always led to a polymer collapse. However, if such particles were added to a polymer in poor solvent, the already collapsed globule swelled by adsorbing them from the solution. In total, four thermodynamically distinct phases were observed, each separated into two regions corresponding to different polymer degrees of freedom.

Towards a Molecular Level Understanding of Peptide-Mineral Interactions: a Computational and Experimental Study

Siddharth Patwardhan
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Abstract

Please see attached file.

5 Poster List

Ab initio modelling of complexes between biomolecules and synthetic inhibitors

Mark Robinson
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Abstract

Recent advances in linear scaling DFT methods have opened up systems of many thousands of atoms to ab initio study. One group of systems now within range are biological macromolecules such as enzymes and the complexes they make with nonbiological nanomolecules. We have studied one such system, the metalloenzyme Carbonic Anhydrase, and the complexes it makes with a number of novel synthetic inhibitors. Using DFT we are able to calculate their binding energies and so compare their affinity to the enzyme.

Chemical Reactivity in Biological Systems: implementation of a hybrid QM/MM Method in the DFT code SIESTA

Pablo Ordejon
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Abstract

We have developed a hybrid Quantum Mechanics - Molecular Mechanics (QM/MM) implementation, which couples the DFT code SIESTA to describe the QM part, and the AMBER force field to describe the MM system [1-3]. Because of the efficiency of the SIESTA package (and, in particular, its linear scaling with system size), the method can deal with large molecular complexes. It is particularly suited to study large systems in which the environment effects are important, as in the case of an enzyme active site immersed in a protein matrix, or a solute in a condensed phase. We will present results obtained with this scheme for the some problems involving local chemical reactions in active sites of enzymes and heme proteins. Extensions of the methods to introduce classical force fields to describe the interaction between bio and

inorganic systems are now under consideration.

References

[1] Damiá n A. Scherlis, Marcelo A. Martí , Pablo Ordejó n and Darí o A. Estrin, “Environment Effects on Chemical Reactivity of Heme Proteins”, International Journal of Quantum Chemistry, 90, 1505− 1514 (2002)
[2] Marcelo A. Martí , Damiá n A. Scherlis, Fabio A. Doctorovich, Pablo Ordejó n and Darí o A. Estrin, “Modulation of the NO trans effect in heme proteins: implications for the activation of soluble guanylate cyclase”, J Biol Inorg Chem 8, 595− 600 (2003)
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DFT based calculations of D-alaninol molecule interaction with Cu(100) surface

Amedeo Palma
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Abstract

Core level shift (CLS) spectroscopy constitutes an efficient and powerful tool to investigate the chemical changes induced by chemical reaction on surfaces. Inspired by an experimental study [1] we performed plane waves DFT calculations [2] on the adsorption of D-alaninol chiral molecule on the Cu(100) surface. We have found several adsorption geometries (local minima) for a single molecule of D-alaninol on a 461620;4 surface cell (intended to represent the experimental low-coverage situation) where both Oxygen and Nitrogen are covalently bound to Cu surface atoms. N(1s) CLS’s evaluated [3] between different conformations are much lower than the shift observed in experimental spectra when passing from low to high coverage. Only when a change in N oxidation (deprotonation) is supposed to occur, the calculated CLS’s reasonably reproduce the measured core shift, even if the oxidated configuration is energetically unfavored. This finding suggests that supramolecular chemistry effects should be responsible of the deprotonation of N and of the resulting alaninol self-assembling on the Cu(100) surface. Further studies are in progress on this topic.

References

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DFT study of the interaction between the gold(111) surface and small molecules modeling aminoacidic functional groups.

Francesco Iori
University of modena and reggio emilia, Italy

Abstract

The interaction between proteins and the surfaces of inorganic materials is of great importance

in natural systems and a long studied topic[1,2]. What is yet to be fully understood is the mechanism that determines such interactions, in particular, for a given surface, which aminoacid, if any, binds and, in that case, what is the nature of the binding. I have studied the interaction between all the natural aminoacids and a gold(111) surface, to systematically address the issue of their chemisorption or physisorption. In particular I have performed plane waves DFT calculations, in the supercell approach, on small molecules adsorbed on a gold surface, each of them representative of an aminoacidic functional group. For example, the peptide bond, asparagine and glutamine can be represented by formamide. The results obtained have shown the predominant presence of interactions of physical nature, weak or strong depending on the electrostatic feature of the functional group involved. Two exceptions were observed: cysteine, already studied by our group in a previous work[3], and imidazole, both showing chemisorption on the gold surface.
[1] M. Sarikaya et al., Nat. Mat. 2, 577 (2003) and refs. therein. [2] J. J. Gray, Curr. Op. Struc. Bio. 14, 110 (2004) and refs. therein. [3] R. Di Felice, A. Selloni, J. Chem. Phys. 120, 4906 (2004).

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[3] R. Di Felice, A. Selloni, J. Chem. Phys. 120, 4906 (2004).

Effective potential between a nano-cylinder and a planar wall

Michael Allen
University of Warwick, United Kingdom

Abstract
Using classical density functional theory, the structure of a molecular fluid around a cylindrical nanoparticle near a solid substrate is studied. The solvent mediated force between the nanoparticle and the substrate is calculated in both the nematic (N) and isotropic (I) phases of the solvent.

Hydrogen bond and dispersion: the driving forces of the adsorption of amino acids on silica surfaces

Albert Rimola
Autonomous University of Barcelona, Spain

Abstract
The interaction of a silica surface with 14 different amino acids (Gly, Ser, Thr, Cys, Phe, Tyr, His, Lys, Arg, Met, Asn, Gln, Asp and Glu) has been addressed theoretically. Hydroxylated silica has been used to simulate the surface. This consists with a large model cluster cut out from the (001) surface of an all-silica edingtonite. The systems have been treated following the ONIOM2 strategy, the high level zone at the B3LYP/6-311++G(d,p) level whereas, for the real zone, the MNDO semiempirical approach has been employed. The adsorption of the amino acids takes place via hydrogen bonds with the terminated silanol groups of the surfaces. The interaction energies have been computed for every system, in which the basis set superposition

error has been accounted for by applying the counterpoise correction scheme. Additionally, since dispersive interactions are expected to be significant, post-DFT corrections proposed by Grimme has been carried out and added to the interaction energies in a posterior fashion. Results show that the most favourable adsorptions are given by large amino acids because they establish multiples hydrogen bonds with the surface and because of the dominant role of dispersion forces.

Molecular Simulations of Hydration Structures around the Carboxylate Group in Aqueous Solvation

Taining Liang
University of Warwick, United Kingdom

Abstract
The hydration structure of carboxylate groups of the dipeptide Aspartyl-alanine and Glycyl-alanine in aqueous solution are studied by molecular dynamics simulations with the polarizable force-field AMOEBAPRO and conventional force-fields Amber using TIP3P water or POL3 polarizable water. The radial distribution functions (RDF) and hydration numbers corresponding to the water-carboxylate interaction are calculated for carboxylate groups for all force-fields used. The polarizable force-field is shown to yield terminal group RDFs that agree with DFT data, and also yields a hydration number that is consistent with experimental results. It is also found the hydration number and RDFs around the carboxylate group are affected by the molecular structure and conformation change. The sensitivity of the variety of the hydration number relies on the local molecular structure and the force-field used in the simulations.

Molecular Simulations of the Interactions of Dimethylsulfoxide (DMSO) with Model Membranes of the Skin

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Abstract
The lipid layers of the stratum corneum constitute the main barrier to penetration of exogenous substances. One approach to overcoming this barrier, for example in transdermal drug delivery, is to use penetration enhancer molecules that interact with the skin lipids to facilitate the transport of the molecule through skin. Dimethylsulfoxide (DMSO) enhances drug penetration at high concentrations however its precise mechanism of action remains elusive [1]. In this study we investigate the effects of DMSO on the properties of ceramide bilayers by means of molecular dynamics simulation. In our earlier work we observed spontaneous pore formation in phospholipid bilayers with high concentrations of DMSO [2]. Hence, we have also carried out calculations to characterise the free energy barrier to pore formation in the presence and absence of DMSO. Our results show that DMSO acts primarily through interactions at the bilayer/water interface. At high concentrations (>30%), DMSO induces a transition in the bilayer from the ordered, tightly-packed gel phase, which is characteristic of the skin lipids, to the disordered, loosely-packed liquid crystalline phase [3]. We find that the free energy barrier to pore formation is significantly reduced in the presence of high concentrations of DMSO. Both fluidisation

and pore formation may be important mechanisms by which DMSO enhances the diffusion of molecules through the skin.

References

[1] A. C. Williams and B. W. Barry, Adv. Drug Del. Rev. 56, 603 (2004)
[2] R. Notman, M. G. Noro, B. O'Malley and J. Anwar, J. Am. Chem. Soc. 128, 13982 (2006)
[3] R. Notman, W. K. den Otter, M. G. Noro, W. J. Briels and J. Anwar, Biophys J. 93, 1 (2007)

Mutation studies of peptide-nanotube interactions using a polarizable force-field

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Abstract

The strong binding affinity of several peptide sequences is investigated using molecular dynamics (MD) simulations with a polarizable force field [1]. Phage-display experiments have demonstrated that peptides containing tryptophan (W) strongly bind to carbon nanotubes (CNTs), compared with control sequences [2]. Our previous simulation work recovered these observations [3]. Here we report mutational studies to explore if the role tryptophan plays is due to aromaticity alone, or if intramolecular stabilisation between residues is also a factor. To this end, we mutate two strong-binding tryptophan-rich sequences, such that each tryptophan is replaced with either tyrosine (Y) or phenylalanine (F). Loss of binding affinity for the mutant sequences would suggest that factors additional to pi-stacking are at work in these systems.

References

[1] P. Ren and J. W. Ponder, J. Phys. Chem. B, 126, 344 (2004)

[2] S. Wang and E. S. Humphreys and S-Y. Chung and D. F. Delduco and S. R. Lustig and H. Wang and K. N. Parker and N. W. Rizzo and S. Subramoney and Y-M. Chiang and A. Jagota, Nature Materials, 2, 196 (2003)

[3] S. de Miranda Tomasio and T. R. Walsh, Mol. Phys., 105, 221, (2007)

The Modulation of peptide binding by structured water on the TiO2 surface.

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Abstract

Molecular dynamics simulations of a hexapeptide (RKLPDA) close to the rutile TiO2 (110) surface dissolved in water are performed. Z-density profiles, lateral-density profiles, residue-surface distances, angular distributions of water, peptide-surface interaction energies and peptide-water interaction energies are analyzed. This is in order to elucidate how the highly structured water layers close to the surface influence the behaviour of the peptide and how the peptide in turn changes the water structure.

Ultrathin Cholesterol films on water

Stephen Cromie
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Abstract

Structural and dynamical properties of cholesterol monolayers adsorbed on the surface of liquid water have been investigated by MD and MC simulations, using an empirical atomistic potential.

The simulated system consists of a slab of liquid water occupying the central slab of an orthorhombic cell, periodically repeated in 3D. A variable number of cholesterol molecules are adsorbed on one of the two exposed water surfaces, with up to monolayer coverage.

The bonding energies and geometries have been first analysed in the case of a single cholesterol molecule on a large water surface. The cholesterol layer at monolayer coverage appears to be well ordered(solid like) at room temperature. We determined the structure and a few characteristic dynamical excitations for this interface, and we computed the free energy of selected defects (vacancy and interstitials, etc.) as well as the free energy barrier to nucleate a second cholesterol layer on top of an ordered monolayer.

The results are compared to the experimental data reported in the literature for the same system, and provide insight on the nucleation of cholesterol micro-crystals in a water environment, as well as the thermodynamic data for the mesoscopic modelling of cholesterol/water micelles and inverted micelles.

6 Program

Day 1: July 25 2007

Session : 1
08:55 to 09:00 : Welcome

09:00 to 09:45 : Presentation
Protein/Solid Interfaces: Designed Marriage of Biology and Materials for Technology and Medecine
Mehmet Sarikaya

09:45 to 10:15 : Presentation
Interaction of glycine with isolated hydroxyl groups at the silica surface: first principles B3LYP periodic simulation
Piero Ugliengo

10:15 to 10:45 : Presentation
Conformations vs. Interaction energy: adsorption of flexible (bio)molecules on inorganic substrates
Luca Ghiringhelli

10:45 to 11:15 : Coffee Break

11:15 to 11:30 : Presentation
Ab-initio QM study of hydroxyapatite (001) and (010) surfaces in interaction with water
Marta Corno

11:30 to 12:00 : Presentation
A computational approach to the interaction between proteins and gold surfaces
Stefano Corni

12:00 to 12:30 : Discussion

12:30 to 14:00 : Lunch Break

14:00 to 14:30 : Presentation
Modelling Biomolecules close to Metal Surfaces
Nico van der Vegt

14:30 to 15:00 : Presentation
Modelling affinity of peptides at inorganic surfaces: the role of solvent
Tiff Walsh

15:00 to 15:30 : Coffee Break

15:30 to 16:00 : Presentation
The absorption of polysaccharide molecules onto calcite surfaces
John Harding

16:00 to 16:30 : Presentation
Towards a Molecular Level Understanding of Peptide-Mineral Interactions: a Computational and Experimental Study
Siddharth Patwardhan

16:30 to 17:00 : Discussion

Day 2: July 26 2007

Session : 2
09:00 to 09:45 : Presentation
Guiding theory: Materials genomics and lessons learned from polypeptide "interactions" with natural and artificial inorganic solids.
John Evans

10:15 to 10:45 : Presentation
Prediction of switching in alpha-helical polypeptides at solid surfaces
Mark Biggs

10:45 to 11:15 : Coffee Break

11:15 to 11:45 : Presentation
Experiments on specific adhesion and clustering of peptides on semiconductor surfaces
Karsten Goede

11:45 to 12:15 : Presentation
Mechanisms and dynamics of protein clustering on a solid surface
Paul Mulheran

12:15 to 12:45 : Presentation
Meso/MM/QM modelling of biomolecules on self-assembled monolayers
Maria Sushko

12:45 to 13:15 : Discussion

13:15 to 15:00 : Lunch Break

15:30 to 16:30 : Poster Session

19:30 to 22:00 : Dinner

Day 3: July 27 2007

Session : 3
09:00 to 09:45 : Presentation
Post-selection Genetic Engineering of Inorganic-Binding Peptides
Candan Tamerler

09:45 to 10:15 : Presentation
Microcanonical Analyses of Peptide Aggregation Processes
Wolfhard Janke

10:15 to 10:45 : Coffee Break

10:45 to 11:15 : Presentation
Thermodynamics of adsorption in polymer-nanoparticle mixtures
Dmytro Antypov

11:15 to 11:45 : Presentation
Specific polymer and peptide adsorption to attractive solid substrates
Michael Bachmann

11:45 to 12:15 : Discussion

12:15 to 12:30 : Closing word

7 Organizer's report

7.1 Conclusions.

The effect of water may sometimes be important in determining the structure and dynamics, and thermodynamics, of peptide-surface systems.

Progress has been made, exploiting both simplicity in the model interactions and consequent efficiency in exploring configuration space, on the one hand, and highly accurate, but expensive, interatomic potentials, on the other.

Interesting thermodynamic information is available from both simulation and experiment; for example, adsorption isotherms and phase diagrams. However, the emphasis seems to be mainly on energetic aspects rather than entropic ones.

There is a rapidly growing body of experimental data for material-specific peptides. Rationalizing these data presents an enormous challenge for the simulation community.

Although the experimental aspects of this research area are rapidly progressing, advances in theory and simulation are in relative infancy. The workshop environment was profitable for both experimentalists and simulators: both an international network and a future workshop would be highly desirable. In the short-term, bilateral contacts (both pre-existing and those established in the workshop) are likely to be fruitful.

Although it is a field in relative infancy, it is apparent that most groups are making progress in predicting affinity between a peptide and an inorganic surface. However, in terms of technological applications affinity in itself is not as useful - rather it is the prediction of peptide-binding specificity of a material. No attempts of modelling specificity appear to have been published, and none were mentioned at this meeting.

7.2 Recommendations.

More attention needs to be paid to the introduction of structured water models in place of implicit water in some simulations.

More needs to be done in bridging the two extremes of accurate and grossly-simplified models. For example, it would be helpful to discuss coarse-graining procedures more widely in this context.

Simulation approaches that address energetics, mobility and aggregation together are needed; for example, to tackle structural rearrangements within an adsorbed peptide layer.

More systematic methods are needed for identifying trends and communicating these to the simulation community. For example, in a typical experimental scenario, peptides are isolated against a particular crystallographic orientation of a surface (e.q. quartz 001), but the subsequent characterization experiments may be performed on, e.g., an amorphous surface (say, silica). This procedure helps to identify generic elements that contribute to binding affinity. Better control of surface chemistry in experiments would be of enormous benefit to modellers.

Participants should follow up bilateral contacts made during the workshop. Some participants should begin the coordination activities for both an international network and a follow-up workshop.

Simulation groups should be encouraged to make use of recent experimental identifications of materials-specific peptides (e.g. a sequence that preferentially binds to silica but not hydroxyapatite).

8 Key references

[1] S. Brown *Metal-recognition by repeating polypeptides*, Nature Biotechnology **15** 269 (1997)

[2] M. Sarikaya, C. Tamerler, A. K. -Y. Jen, K. Schulten and F. Baneyx *Molecular biomimetics: nanotechnology through biology*, Nature Materials **2** 577 (2003)

[3] J. J. Gray *The interaction of proteins with solid surfaces*, Current Opinion in Structural Biology **14** 110 (2004)

[4] H. X. Dai, W. S. Choe, C. K. Thai, M. Sarikaya, B. A. Traxler, F. Baneyx and D. T. Schwartz *Nonequilibrium synthesis and assembly of hybrid inorganic-protein nanostructures using an engineered DNA binding protein*, Journal of the American Chemical Society **127** 15637 (2005)

[5] E. E. Oren, C. Tamerler, M. Sarikaya *Metal recognition of septapeptides via polypod molecular architecture*, Nano Lett. **5** 415 (2005)