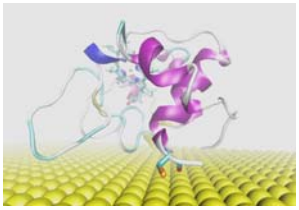
CECAM-ESF Workshop ProSurf
Modeling Protein Interactions with Solid Surfaces and Nanoparticles
CECAM HQ, Lausanne, 9-11 May 2011



Summary

The aim of the workshop was to bring together computational scientists of different backgrounds (e.g., condensed matter physicists, chemists, biochemists, biologists) working on the central common theme of protein-surface interactions to foster the exchanging of ideas, the set up of new collaborations and, in summary, the creation of a computational scientific community able to deal with the complex and relevant problem of protein-surface interactions.

The emphasis was on the development of computational methodologies and the related tools needed to reliably simulate highly complex systems composed of proteins, water, and inorganic components, such as extended surfaces and nanoparticles. This includes the need to extend the existing computational methods to make them suitable for study of these systems (e.g. the development of force field parameters for protein-surface interactions), as well as to work out viable strategies for multiscale modeling. Moreover, the interaction with experimentalists working in the field allowed understanding of the experimental state-of-the-art and the open further fundamental questions to be addressed by computational simulations. The workshop topics included:

• Atomistic ab initio simulations for studying protein-surface and protein-nanoparticle systems
• Development and use of force field parameters to describe protein-surface or protein-nanoparticle interactions in water
• Enhanced sampling techniques applied to protein-surface simulations
• Coarse-grained and continuum solvation models for protein-surface and protein-nanoparticle interactions
• Development of sequential and concurrent multiscale models for protein-surface and protein-nanoparticle interactions
• Modeling the interface between water and inorganic surfaces/nanoparticles

Description of the scientific content and discussion at the event

Main outcomes of key presentations

-Modeling protein-surface interactions at multiple scales

In most of the presented works, the multiscale description of protein-surface interactions follows a sequential multiscale approach: typically, ab initio methods are used to parameterize classical force fields (as shown by Luigi Delle Site, Lucio Colombi Ciacchi, Giorgia Brancolini, Tiff Walsh, Dominique Costa) and also to predict reasonable geometries and structures for amorphous oxide surfaces (Lucio

Colombi Ciacchi). Only Giorgia Brancolini and Daria Kokh described a further level of modeling, i.e., derivation of a continuum implicit model to be used for rigid protein-surface docking simulations. An exception to sequential multiscale was the AdResS (Adaptive Resolution Strategy) presented by Luigi Delle Site, where not only different levels of description (e.g., QM, atomistic MM and coarse-grained) co-exists for a given system, but the level of description of water molecules can change depending on their position in space.

-*What can we learn from ab initio calculations?*
The potency of DFT to help interpreting experiments on well-controlled systems (amino acids on hydroxyapatite) was shown by P. Ugliengo. Limitations related to the treatable system size and the problem of properly simulating solvation were also discussed.

-*Exploring and exploiting classical force field methods*
The classical atomistic MD simulations in explicit solvent appear at present the most useful single level of description to simulate protein-surface interactions (as mentioned, among others, by Robert Latour, Tiff Walsh, Colin Freeman, Kay Gottschalk, Paul Mulheran).
Klaus Schulten remarked the importance of classical force field –based MD as a tool to provide qualitative insights and thus new ideas on the complex systems under study, that cannot be directly accessed by experimentalists but can be of use to them.

-*Coarse-grained description of protein-surface interactions*
Stefan Auer described a tube-like model of peptides aggregation and condensation on surfaces, while Mike Allen presented an exhaustive MD study of on-lattice peptide models adsorbed on surfaces. They both put the accent on the capability of this model to catch the range of different qualitative behaviors for the peptide and peptides-on-surface systems

-*Experimental characterization of protein-surface interactions: structures*
Gil Goobes and Luigi Calzolai described how NMR techniques (solid state and solution NMR respectively) can provide structural information for peptides and proteins on solid supports and nanoparticles. Kartsen Goede discussed IR spectroscopy to characterize peptide structures on semiconductor surfaces.

-*Experimental characterization of protein-surface interactions: energies and kinetics*
Gideon Schreiber discussed SPR measurements of binding strength of fusion proteins on Au surfaces. He remarked the kinetics nature of the measurements and the fundamental and not understood role of pH.

-*Highlighting the role of protein-surface interactions in material and biomedical science*
Mehmet Sarikaya discussed the enormous potential of practical applications in material science of peptides specific for inorganics. They also appear relatively well-characterized systems to compare calculations with. Pier Paolo Pompa and Luigi Calzolai stressed instead the importance of protein-nanoparticle interactions in the field of nanotoxycology and nanomedicine.

Report on selected discussions
For each morning and afternoon section, we reserved time in the schedule for a general discussion that supplemented the Q&A sections following each talk.

- It has been identified a need to define systems on which both experiments and calculations can converge. In particular, it has been suggested to focus on two classes of systems: peptides specific for inorganic surfaces and protein-nanoparticle adducts important for biological and nanotoxycological studies.

- To understand the predictive quality of computational methods, it has been proposed to set up initiatives similar to CASP and CAPRI (for protein structure and protein-protein docking, respectively), where calculations should predict the properties (structure, energetic) of experimental targets before the actual experimental data are made of public domain. In this way, any bias in the computational prediction would be prevented.

- While classical atomistic MD appears as the best compromise to treat protein-surface system, it has been remarked that its accuracy is at present poorly assessed (and probably not high) for peptides in solution. Better force field (e.g., including polarization) may be needed to accurately describe the structure and behaviour of peptide systems.

-A general agreement on the necessity to develop specific implicit solvation models for proteins at surfaces has been expressed. In fact, implicit models for bulk solution appear inadequate to describe surfaces as they disregard effects of ubiquitous water structuring at solid surfaces. For ionic solutions, the distribution of ions at surfaces (including description of specific and unspecific adsorption) is also an issue. While no conceptual problem hinders the development of such models, extensive data from more accurate simulations or from experiments are required. This may set the basis for collaborations among groups producing these experimental data and groups developing the models.

- Understanding the molecular basis of peptide specificity for solid surfaces has been recognize as a pivotal goal for the field, as it represents a scientific challenge and also has important technological applications.

Assessment of the results and impact on the future direction of the field

To what extent were the objectives of the workshop achieved?
The main objectives of the workshop were achieved:
- It included participants from several disciplines: condensed matter physicists, computational chemists, material scientists, biochemists. Both computational and experimental scientists attended.
- It attracted many applicants, also by overseas. Not all the applications could be accepted due to reached capacity.
- The discussion was always very lively, and a clear sense of representing a scientific community is arising. An example is the idea of giving ourselves long term goals (such as setting up a CASP-like initiative).
-Coordination with the following workshop "Grand challenges", including a joint session among the two workshops, was quite successful. The overlap between

workshops participants was not very high, which however was a way to reach a larger community (both workshops were oversubscribed early).

Suggestions for new workshops/tutorials/conferences
While the fields may be premature for tutorials, as computational methodologies are still not well settled and developments are in fieri, the large number of applicants and the lively interactions among them may indicate that a conference larger than a workshop could be appropriate in the next years.

Final programme

Day 1 - May, 9th 2011

Monday morning

- 08:30 to 09:00 - Registration
- 09:00 to 09:10 - Welcome
- 09:10 to 09:50 - **Luigi Delle Site**

  Multiscale Modeling organic-inorganic interfaces: Methods and Applications

- 09:50 to 10:30 - **Lucio Colombi Ciacchi**

  The effect of charged surface sites on the adsorption of peptides on inorganic materials

- 10:30 to 11:00 - Coffee Break
- 11:00 to 11:40 - **Tiff Walsh**

  Investigating molecular-level control at peptide-inorganic interfaces using molecular simulation.

- 11:40 to 12:20 - **Karsten Goede**

  Specific behaviour of peptides at interfaces to semiconductors

- 12:20 to 13:00 - Discussion
- 13:00 to 14:00 - Lunch Break

Monday afternoon

- 14:00 to 14:40 - **Colin Freeman**

  The role of the Surface in Controlling Molecular Interactions

- 14:40 to 15:05 - **Cynthia Lo**

  Steered molecular dynamics simulations to model photosynthetic protein assemblies on well-defined surfaces

- 15:05 to 15:35 - Coffee Break
- 15:35 to 16:15 - **Stefan Auer**

  A Condensation-Ordering Mechanism in Nanoparticle-Catalyzed Peptide Aggregation

- 16:15 to 16:55 - **Michael Allen**

  Monte Carlo Simulations of Confined Lattice Polymers and Peptides

- 16:55 to 17:30 - Discussion
- 17:30 to 19:00 - Poster Session

Day 2 - May, 10th 2011

Tuesday morning

- 09:00 to 09:40 - **Gideon Schreiber**

  A quantitative, real-time assessment of binding of peptides to gold surfaces

- 09:40 to 10:20 - **Kay Gottschalk**

  The Adhesion of Amino Acids and Proteins on Gold

- 10:20 to 10:45 – **Stefano Corni**

  The interaction of Cytochrome C with a gold surface investigated by molecular dynamics simulations

- 10:45 to 11:15 - Coffee Break
- 11:15 to 11:40 - **Alexandra Carvalho**

  Charge transfer from silicon nanocrystals to organic acceptors: a first-principles study

- 11:40 to 12:20 - **Daria Kokh**

  Modeling of protein thermodynamics and kinetics on a gold surface using atomistic Brownian dynamics simulations

- 12:20 to 13:00 - Discussion
- 13:00 to 14:00 - Lunch Break

Tuesday afternoon

- 14:00 to 14:40 - **Gil Goobes**

  Using Solid State NMR to Study Adsorbed Proteins: From Site-Specific Structural Constraints to Extensive View of Surface-Bound Proteins

- 14:40 to 15:20 - **Luigi Calzolai**

  Identification of Protein-Nanoparticle Interaction Site

- 15:20 to 16:00 - **Giorgia Brancolini**

  Multi-step computational scheme for Ubiquitine-gold interactions in water

- 16:00 to 16:30 - Coffee Break
- 16:30 to 16:55 - **Robert Latour**

  Force Field Comparisons for Simulation of Protein Adsorption Behavior

- 16:55 to 17:35 - **Paul Mulheran**

  Lysozyme adsorption at charged surfaces

- 17:35 to 18:00 - Discussion
- 19:30 to 22:00 - Dinner

Day 3 - May, 11th 2011

Wednesday morning

- 09:00 to 09:40 - **Pier Paolo Pompa**

  Nano-biointeractions: influence of nanoscale features on the response of biological systems

- 09:40 to 10:05 - **Dominique Costa**

  Adsorption of small biomolecules on metal and oxide surfaces: insight from ab initio studies

- 10:05 to 10:45 - **Piero Ugliengo**

  Molecular Recognition at the Surfaces of Hydroxyapatite Modeled by Periodic DFT Methods Based on Localized Orbitals

- 10:45 to 11:15 - Coffee Break
- 11:15 to 11:55 - **Mehmet Sarikaya**

  Mechanisms of Self-assembly of Genetically-Engineered Short Peptides on Atomically-Flat Solid Materials

- 11:55 to 12:35 - **Klaus Schulten**

  Computer Modeling in Biotechnology, a Partner in Development

- 12:35 to 13:00 - Discussion

- 13:00 to 14:00 - Lunch Break

JOINT SESSION WITH Grand Challenges

- 14:00 to 14:10 - Welcome
- 14:10 to 14:45 - **Jeffrey Gray**

  Design of peptide-biomimeral interactions using protein structure prediction approaches

- 14:45 to 15:20 - **P. U. P. A. Gilbert**

  Experiments at the cutting-edge of biomineralization: theory must boldly go where no experiment has been before, and probably never will

- 15:20 to 16:00 - Discussion