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Computational challenges about nanostructures and biosystems at surfaces

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Summary. — The interaction between nano-objects and extended solid surfaces is of paramount importance in the context of nanoscience and nanotechnology. It plays a role both in investigating the properties of nanoscale materials and in exploiting such properties. We overview selected examples inspired by experimental facts. We focus on bio-nano cases such as the adsorpion of small polypeptides and nucleotides on metal surfaces, including the role of an aqueous environment. We highlight evidences that call for interpretation, computational approaches based on density functional theory and molecular dynamics that are currently available to face the open problems, and desired theoretical/computational developments that may increase the potentialities of theory to guide and interpret technology progress.

PACS 68.43.-h – Chemisorption/physisorption: adsorbates on surfaces.
PACS 81.16.Fg – Supramolecular and biochemical assembly.
PACS 71.15.Pd – Molecular dynamics calculations (Car-Parrinello) and other numerical simulations.

1. – Why nano-bio objects at surfaces?

These hybrid systems have a potential impact in a variety of timely research fields, such as: nano-electronics, nano-medicine, controlled drug delivery, diagnostics and health care (*e.g.*, biosensors). In addition, the adsorption of organic molecules and bio-molecules on inorganic surfaces is the natural condition in some experimental measurement setups, for instance in imaging/spectroscopy techniques such as scanning tunneling microscopy (STM) and atomic force microscopy (AFM). In such methods, the molecules or other target objects must be deposited onto a supporting substrate in order to be probed. Envisaged applications of molecule/surface interactions are also in the construction of self-assembling circuits and in the production of new materials. Specifically, the last two hypotheses are based on the concept of recognition between a protein and a surface. If a protein binds to a given face of a material preferentially with respect to other faces, one may exploit this recognition property to design an object in which a given face (or some given faces) is preferred, thus tailoring the shape.

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At S3 we study a number of molecule/surface interfaces in which the interaction between the adsorbate and the substrate can be chemical (*e.g.*, thiolate bonds related to contacts in nano-junctions and other conditions) [1, 2] or physical or intermediate (*e.g.*, aromatic molecules on metal surfaces) [3]. In this short article we describe only a couple of selected cases in which the adsorbate is a bio-object (amino acids, peptides or DNA) and the substrate is a metal surface.

2. – Selected examples

2˙1. *Protein-surface recognition.* – It is well known that proteins specifically recognize biological partners. Are they capable of recognizing inorganic surfaces as well?

The interaction between proteins and the surfaces of inorganic materials has been studied for a long time [4]. Recently, it has been demonstrated that different combinatorial biotechniques are efficient to select proteins able to specifically bind to a given inorganic surface. However, to date the demonstration of specific protein-surface associations has not been accompanied by an understanding of the mechanisms that determine the partnership and the resulting function. What features of the surface and of the proteins determine which protein is able to bind to a given surface and how? Are electronic, structural, morphological or dynamic factors most relevant?

The systems of interest to answer the above questions are a real computational challenge, for various aspects. They contain a large number of atoms of materials with diverse chemical nature, namely a protein, the inorganic surface and the solvent. They require statistical sampling or dynamical simulations over long times. They involve interactions of different origin, including chemical bonding, Coulomb and van der Waals interactions, for which different theoretical levels are needed to achieve accuracy.

Given the complexity of the systems from a fully *ab initio* point of view, we tackle the problem by a two-fold approach. On the one hand, we adopt a multi-scale approach: i) *ab initio* determination of the force fields for the interaction of amino acid side chains with inorganic surfaces [2, 5]; ii) use of the thus determined force fields in classical molecular dynamics simulations; iii) use of the classical trajectories to model score functions for docking codes. On the other hand, we identify model systems for full quantum molecular dynamics simulations [6], massively exploiting the power of supercomputers. In the left panel of fig. 1 we show a three-dimensional (3D) view of Azurin adsorbed on a Au(111) surface in the presence of the water solvent, that we normally simulate at the classical level after choice of suitable force fields [7]. In the right panel of fig. 1 we show the unit bulding block of a 3D-periodic *ab initio* molecular dynamics simulation based on density functional theory (DFT) [8]. The specific elements of the system, with the poly-serine peptide on Au(111), were chosen because it is known that a serine-rich portion is responsible for the adsorption on gold of the gold-binding protein (GBP), and at the same time the β-sheet motif allows us an easy implementation of periodic boundary conditions. We carried out a 20-ps-long dynamical run. We analyzed the trajectories in terms of correlation functions and other structural quantities, atomic charges, densities of states (DOS) and electronic wave functions. We find that poly-serine and water do not chemisorb on Au(111); however, a weak interaction is indeed present, as revealed by changes in the DOS of the adsorbed peptide relative to the free peptide.

2˙2. *Scanning tunneling spectroscopy of single DNA molecules.* – DNA is an appealing material for the development of molecular electronics because it has fantastic structuring and recognition capabilities [9]. However, its conductivity is still questionable [10]. In the

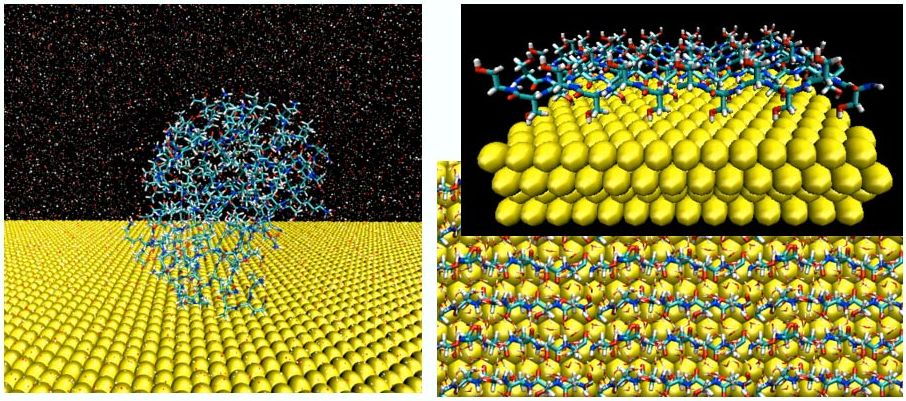

Fig. 1. – (Colour online) Left: an Azurin protein adsorbed on Au(111) through a thiol group and surrounded by water. Right: top and side view of the periodic system chosen for a Car-Parrinello simulation of a poly-serine peptide adsorbed on Au(111) in the presence of water; the unit supercell contains 4 layers of Au(111) in a $2\sqrt{3}\times 7$ periodicity, an interstitial water layer, the peptide and then water molecules on top for a thickness of 15 Å, for a total of 587 atoms and 2552 electrons. The Au atoms of the substrate are represented as yellow spheres and the molecules are rendered in a stick representation with standard colors (O red, C cyan, N blue, H white).

quest for unraveling the electronic structure of DNA in specified sequences and lengths, different experimental routes are pursued, ranging from detection of electron transfer rates in solution, to measurement of current-voltage curves of single molecules or aggregates suspended between electrodes or deposited on surfaces, to scanning tunneling spectroscopy (STS) caharacterization.

STS measurements on single DNA molecules deposited on a gold substrate recently revealed the presence of reproducible peaks with a fundamental energy gap in the $(\mathrm{d}I/\mathrm{d}V)$-$V$ curves [11]. The conductance curves measured in a scanning tunneling setup are proportional to the DOS of the sample. Hence, it is extremely desirable to perform density functional theory calculations of the DOS. In principle, one should compute the quantum conductance of a system shown pictorially in the left of fig. 2, composed of a DNA molecule lying longitudinal on a surface and surmounted by the metal STM tip. Given the complexity of the system and the lack of knowledge of experimental geometrical details (what is the structure of adsorbed DNA molecules? what is the exact shape of the tip when interacting with the molecule?), we carried out a DFT structural optimization and frozen electronic structure calculation [8] of a free-standing poly(dG)-poly(dC) periodic polymer. The unit building block of the periodic calculation contained the backbone and counter-ions but the solvent was excluded (right of fig. 2). This simplified system is representative of a situation of weak molecule-substrate coupling and can be complemented by modeling of the whole substrate-DNA-tip system by modeling tight-binding Hamiltonians for the Keldysh Green's Function computation of the quantum conductance [12]. Our results (right of fig. 2) [11] allow us to interpret the experimental peaks in terms of contributions by guanine (magenta), cytosine (cyan), backbone and counter-ions. Despite the approximations implicit in the choice of the model system that may affect the fine details of the DOS, this is an important step towards the interpretation of STS results.

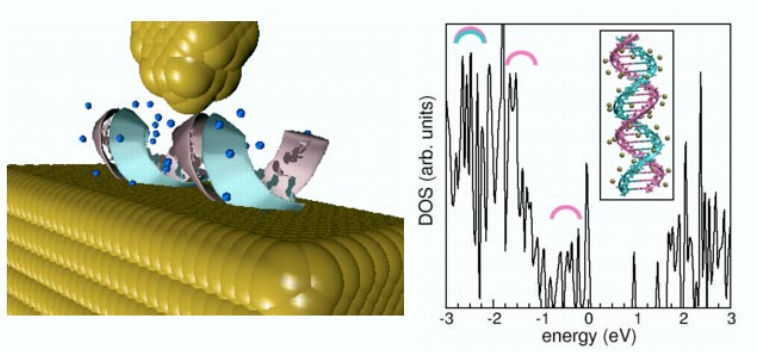

Fig. 2. – Left: scheme of the experimental scheme at an atomistic level. Right: calculated DOS and structure of the simulated periodic poly(dG)-poly(dC) polymer. (Adapted from [11] with permission; copyright 2008 by Nature Publishing Group.)

3. – Desirable follow-up and development

The expected progress of the above activities is towards the simulation of real experimental conditions and measurable quantities: Environment and measurement geometry (electrodes, substrates, etc.), Excited-state quantities (optics, transport), Biological processes. The desired developments necessary to attain this goal are manyfold: Theory (*e.g.*, developments of efficient algorithms beyond the ground state), Software (*e.g.*, optimal scaling on parallel computers and implementation of new theoretical tools) and Hardware (RAM, Disk, speed).

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REFERENCES

[1] Di Felice R., Selloni A. and Molinari E., *J. Phys. Chem. B*, **107** (2003) 1151.
[2] Iori F., Corni S. and Di Felice R., *J. Phys. Chem. C*, **112** (2008) 13540.
[3] Ferretti A., Calzolari A., Di Felice R., Ruini A., Molinari E., Baldacchini C. and Betti M. G., *Phys. Rev. Lett.*, **99** (2007) 046802.
[4] Sarikaya M., Tamerler C., Jen A. K.-Y., Schulten K. and Baneyx F., *Nature Mater.*, **2** (2003) 577; Gray J. J., *Curr. Opin. Struct. Biol.*, **14** (2004) 110.
[5] Corni S., Di Felice R., Iori F. and Molinari E., *J. Comput. Chem.*, **30** (2009) 1465.
[6] Corni S., `http://www.deisa.eu/science/deci/projects2006-2007/PSI-Wat`.
[7] Setty-Venkat A., Corni S. and Di Felice R., *Small*, **3** (2007) 1431.
[8] Scandolo S., Giannozzi P., Cavazzoni C., de Gironcoli S., Pasquarello A. and Baroni S., *Z. Krist.*, **220** (2005) 574; `http://www.quantum-espresso.org`.
[9] Seeman N. C. and Lukeman P. S., *Rep. Prog. Phys.*, **68** (2005) 237; Keren K., Berman R. S., Buchstab E., Sivan U. and Braun E., *Science*, **302** (2003) 1380.
[10] Porath D., Cuniberti G. and Di Felice R., *Top. Curr. Chem.*, **237** (2004) 183.
[11] Shapir E., Calzolari A., Cavazzoni C., Ryndyk D., Cuniberti G., Kotlyar A. B., Di Felice R. and Porath D., *Nature Mater.*, **7** (2008) 68.
[12] Ryndyk D., Shapir E., Porath D., Calzolari A., Di Felice R. Cavazzoni C. and Cuniberti G., to be published in *ACS Nano*, published online July 2, 2009. DOI 10.1021/nn800238g.