Ab-initio calculations and molecular dynamics simulations of peptide adsorption onto metal oxide surfaces

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INTRODUCTION

Peptides that bind inorganic surfaces are of great interest for the self- or directed assembly of nanodevices, with wide ranging applications such as electronics, biomaterials, energy production, and medicine. These surface-binding peptides can be identified by phage-display peptide libraries, but little experimental information is available for developing an understanding of the relationships between the peptide sequence, its structure at an inorganic surface, and its surface adhesion. To aid in this development, first principles simulations based on Density Functional Theory (DFT) and classical Molecular Dynamics (MD) simulations are carried out to investigate the structure and stability of single amino acids and of the full peptide adsorption on TiO2 anatase (101). Our results shed light on the role played by some amino acids that are known to be essential in selective adsorption on TiO2[1], as well as their structural conformation upon the surface. The critical role for the adhesion mechanism played by the water molecules at the organic-inorganic interface adhesion is also revealed by our results.

DFT CALCULATIONS

Our study is based on DFT in the generalied gradient approximation (GGA) of Perdew, Burke, and Ernzerhof (PBE)[2], and the plane-wave pseudopotential scheme as implemented in the Quantum-ESPRESSO package. Vanderbilt-type ultrasoft pseudopotentials[3] have been used with a plane-wave energy cutoff of 30 and 300 Ry for the electronic wave functions and the total charge density, respectively. The optimized geometries are obtained using the Hellman-Feynman forces with the Broyden-Fletcher-Goldfarb-Shanno algorithm to minimize the total energy with respect to the atomic positions. By the above method, we firstly optimized pure anatase TiO2. The Brillouin zone was sampled using a (4×4×4) Monkhorst-Pack k-point grid[4]. We utilized a (2×3) periodic slab to model the surface structure and properties, which contained four O-Ti-O trilayers and was separated by a vacuum gap of 20 Å thickness. The top two trilayers were relaxed, while the bottom two tri-layers were kept fixed to mimic the bulk region.

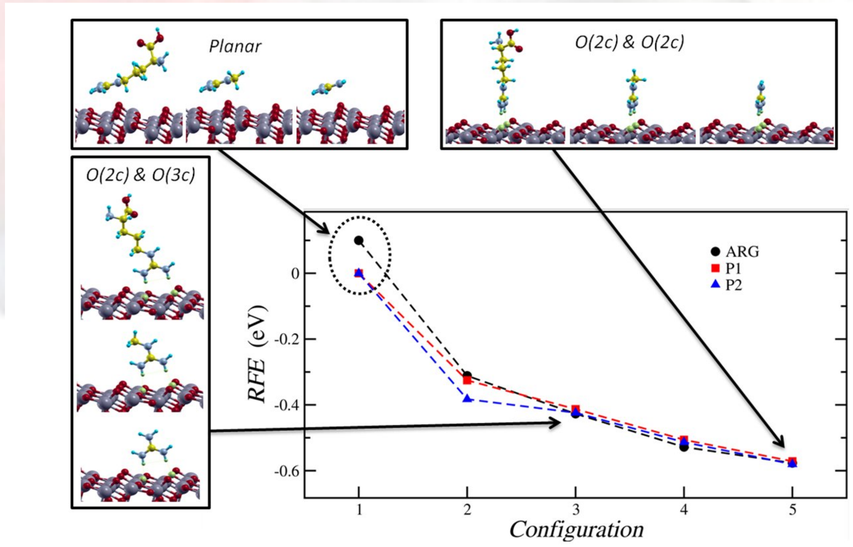

Fig 2: Analysis of the possible adhesion configurations of arginine (Arg or R) onto TiO2 surface, to be compared with R analogues obtained by successive truncation of its lateral chain. The Relative Formation Energy (RFE) at each binding configuration concerning with arginine is very close to those related to the analogues.

MOLECULAR DYNAMICS SIMULATION

The MD simulations of the system composed by the peptide, the TiO2 anatase (101) surface and the solvent are performed with GROMACS v4.5.4 following the simulation protocol of Kang *et al.*[5] by using the OPLSAA force field[7] modified by introducing the nonbonded parameters for TiO2 surface[7,8] (Table I). The water solvent molecules are modeled by the simple point charge SPC model[9]. The system composed by about 4400 atoms is energy minimized and after 200 ps of initial equilibration, data collection is started with trajectory saved every 0.2 ps. The simulation consists of a total run of 15 ns. Analyses of the trajectories were performed with GROMACS tools.

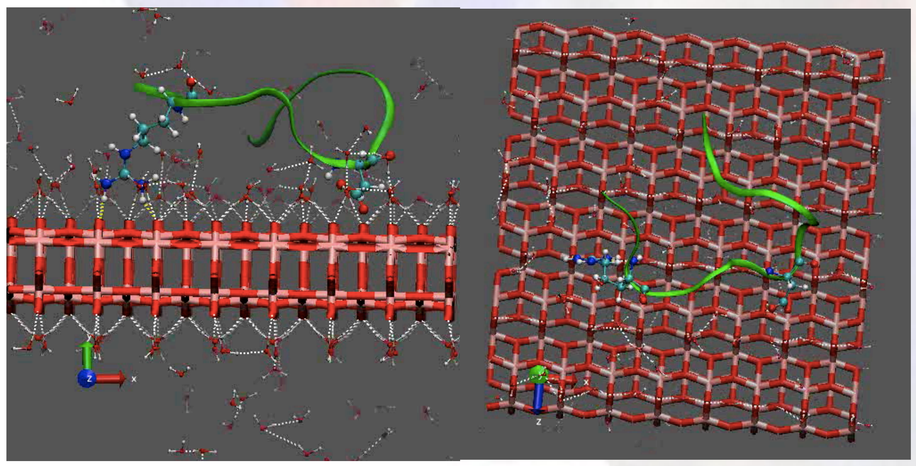

Fig 4: Snapshots of side view and top view of the adsorbed peptide adsorbed onto TiO2 (101) anatase surface taken at 5 ns. The peptide backbone is shown as a green ribbon while the relevant amino acids for adhesion mechanisms are represented through CPK model. Only the interfacial water molecules are shown for clarity. The hydrogen bonding network among them are displayed as white dashed lines. The hydrogen bonding network among the atoms of the peptide and those of the surface are also shown in yellow dashed lines.

Table I: Lennard-Jones parameters and atomic charges of TiO2 surfaces used in our simulations

atom	σ_i (nm)	ε_i (kJ/mol)	q_i
Ti	0.19565	2.5466	2.196
O	0.29273	0.5866	- 1.098

Table II: Protein – Surface Interaction Energy (kJ/mol), the adsorbed residues (within 0.2 nm of the TiO2 surface and the Hbonds

system	ΔE_{int}	adsorbed residues	H_{bonds}
WT	- 165	R3, D7	Arg 3 – OT1 335; Arg 3 – OT1 359

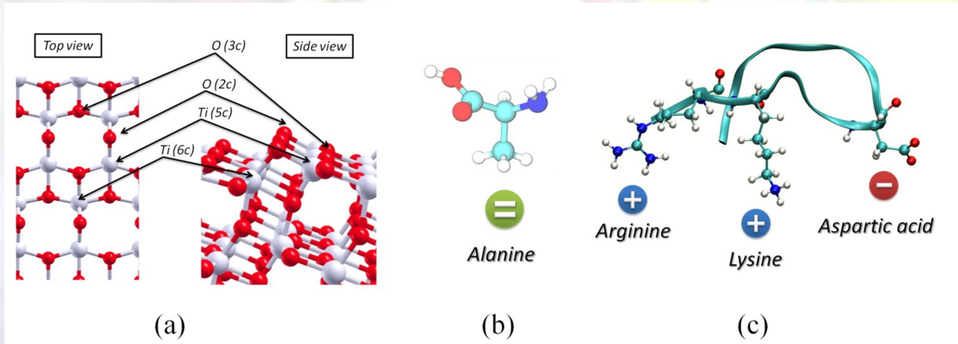

Fig 1: Top and side view of TiO2 (101) anatase surface reconstruction: low coordinated Ti(5c) and O(2c) atoms play a crucial role onto peptide adhesion mechanisms (a). Alanine (Ala or A) is a neutral amino amino acid that does not bind to the TiO2 surface: it is used as a term of comparison (b). TiO2-binding peptide: the peptide backbone is shown as a ribbon while the relevant amino acids for adhesion mechanisms: arginine (Arg or R), lysine (Lys or K) and aspartic acid (Asp or D) are represented through balls and sticks (c).

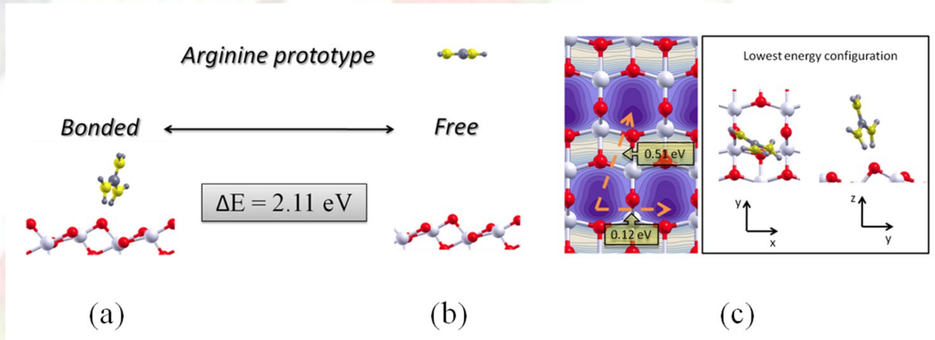

Fig 3: The binding energy of Arg analogue to the TiO2 anatase (101) surface has been evaluated as the total energy difference between the bonded (a) and the unbonded (a) configuration of the entire TiO2-Arg system. Topological map of the TiO2-Arg bonding energy (c).

RESULTS

-The metal surface (Fig1a) is formed by Ti(5c) and Ti(6c) coordinated Ti atoms and by O(2c) and O(3c) oxygen atoms. Each O(2c) is bonded to one Ti(5c) atom and one Ti(6c) atom forming a Ti-O-Ti angle of nearly 102 degrees. The orbital rearrangements of the dangling bonds of the Ti(5c) and O(2c) atoms determines a negative and a positive charge localized around the O(2c) and Ti(5c) atoms, respectively. The positively charged Arg and Lys residues of the peptide are attracted by O(2c) atoms and the negatively charged Asp residue is attracted by Ti(5c) ones (Fig1c).

-The Relative Formation Energy (RFE) calculated at five different equilibrium configurations, shows that both Arg and its analogues are characterized by the same bonding chemistry and that most stable configuration is characterized by a vertical orientation of Arg with the terminal charged part oriented on O(2c) atom, as expected (Fig 2).

-The Potential Energy Surface (PES), shows the global minimum at the O(2c) site (dark blue in Fig 3c) and the global maximum along the Ti(6c)-O(3c) bridge. We proposed two pathways (see arrows in Fig 3c) between global minima along which Arg can diffuse.

- MD simulation of the adsorption of the full peptide onto the metal surface indicate that the peptide-surface interaction energy (Table II) is similar to that found in the work of Kang[5]. The adsorbed residues are, as expected, Arg and Asp. Fig.4 shows the configuration of the adsorbed peptide onto surface after 5 ns of simulation. The interfacial water molecules are quite stable and orientationally structured on TiO2 forming an hydrogen bonding network induced by the surface and the side chain of the Asp residue adsorbs onto the surface mediated by the interfacial water layer. The side chain of the Arg residue forms two H-bonds with the O(2c) atoms (Table II). As predicted by DFT calculation the Arg residue is allowed to diffuse along one of the surface pathway (data not shown, for details see movies at: http://www.afs.enea.it/project/cmast/FLV/hybrid_pos1close_side2.html, http://www.afs.enea.it/project/cmast/FLV/hybrid_pos1close_top1.html).
The DFT study will be extended to Lys, Asp and the neutral Ala for comparison. These energy scales will allow us to determine the best amino-acid choice in adhesion and to shed light on the great number of experimental results relative to the individuation of TiO2-selective binding peptides.
By comparison we will also perform simulations of mutants of the peptide which are known to lose their ability to bind the metal surface[1]. In addition MD simulations using realistic model of the TiO2 surface in oxidizing aqueous environment (hydroxylated surface) will be also performed in order to better elucidate the solvent-mediated effects that governs the adsorption behavior of the peptide on the TiO2 surface

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