Adsorption of Modified Arg, Lys, Asp, and Gln to Dry and Hydrated ZnO Surface: A Density Functional Theory Study

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Adsorption of Modified Arg, Lys, Asp, and Gln to Dry and Hydrated ZnO Surface: A Density Functional Theory Study

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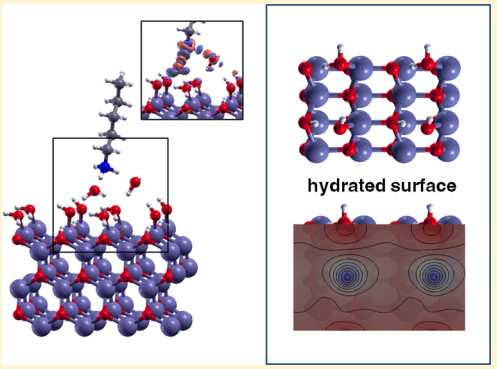
Supporting Information

ABSTRACT: The interface of biological molecules with inorganic surfaces has been the subject of several recent studies. Experimentally some amino acids are evidenced to play a critical role in the adhesion and selectivity on oxide surfaces; however, detailed information on how the water molecules on the hydrated surface are able to mediate the adsorption is still missing. Accurate total energy *ab initio* calculations based on dispersion-corrected density functional theory have been performed to investigate the adsorption of selected amino acids on the hydrated ZnO$(10\bar{1}0)$ surface, and the results are presented and discussed in this paper. We have also investigated the role played by water in the determination of the most energetically favorable adsorption configurations of the selected amino acids. We have found that for some amino acids the most energetically favorable configurations involve the deprotonation of the molecule if the water screening is not effective.



1. INTRODUCTION

Recently, great attention has been focused on bioinorganic interfaces and their possible applications in biomedical and nanotechnological areas.[1−3] Nowadays, several experimental techniques are able to design engineered peptides that have demonstrated the ability to adhere selectively on specific inorganic surfaces. Moreover, metal-based materials are the most considered for this kind of interface due to their extensive utilization in several technological applications including biomedical ones. Nevertheless, a fundamental understanding of the adhesion mechanism of the engineered peptides on the inorganic surfaces is still elusive because many physicochemical phenomena are concurrently involved in the adhesion process: both structure and charge of the amino acids, amino acids sequence, amino acids cooperation/interactions, and overall peptide conformation. The story is even more challenging due to the presence of water molecules that mediate the interaction between peptide and surface. Among the others, both titanium and zinc are considered inorganic materials of great interest to play the role of support to biological functionalizations due to their biocompatibility and extensive use in many optical and optoelectronic applications.

Artificial peptide sequences with specific affinities for titanium and zinc oxide have been identified by using combinatorial library methods (cell and phage display techniques)[4−7] and computationally assisted peptide screenings.[8] A deep understanding of both structural features and binding affinity is requested in order to exploit the properties of the selected peptides. The interactions of single amino acids and of peptides to titanium have been investigated[9−11] also in our group.[12,13] It was supposed that chemical and physical effects contribute to the binding strength of a peptide to an inorganic material. Ionic interactions of charged atoms are one of the major governing forces in addition to polar interactions of neutral atoms (hydrogen bond, van der Waals, and hydrophobic effects). On the contrary, very little is known about the molecular rules governing the ZnO-binding peptide and zinc oxide interactions. Two classes of peptides, based on conserved amino acid residues, have been identified to display high and selective affinities to ZnO. The two classes are characterized by the HXXH (H = histidine, X = any amino acids) and RXXR (R = arginine) tetrapeptide putative binding motif. Most of the peptide sequences are hydrophilic, highly basic, often carry a positive charge, and show high values of isoelectric point. The

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interactions of selected single amino acids residues, histidine (H), glycine (G), alanine (A), and tryptophan (W), to ZnO have been investigated.[14−17] In these studies the adsorption mode was found to be driven by the carboxyl and/or amino groups of the amino acids. However, in a peptide chain these groups react with the amino and carboxyl groups of other amino acids (condensation reaction process) to form the backbone of the peptide chain. Hence, the adsorption of an inorganic binding peptide is supposed to be mediated by the lateral groups of the amino acids which are responsible for the affinity and selectivity of the binding. The nature of the interaction at atomic level between a specific class of peptides and ZnO nanoparticle has been determined by means of NMR spectroscopy.[18] This class of peptide is characterized by an enrichment of histidine residues (HXXH) which have been clearly demonstrated to be the binding partners for ZnO nanoparticle. Rothenstein et al.[18] have demonstrated that the binding is strongly dependent by the peptide charge (the protonation state of the amino acids side chains), which is mainly dependent on the pH of the solution. Peptides lacking histidine residues and characterized by an enrichment of positively charged residues (RXXR) were also identified as strong ZnO binders.[6,8] The molecular basis of the ZnO binding by RXXR class of peptides has not been yet clarified. We focused our attention on the RQIRK motif extracted from the dodecapeptide sequence (RIGHGRQIRKPL) isolated by Thai et al.[6] which was demonstrated to selectively bind electrodeposited ZnO.

In the present paper we have studied by first-principles calculations based on the dispersion-corrected density functional theory (DFT) the adsorption to the ZnO$(10\bar{1}0)$ surface of the following amino acids: arginine (R, Arg), glutamine (Q, Gln), lysine (K, Lys), and aspartate (D, Asp). Indeed, Arg, Gln, and Lys are in the preferential binding sequence for ZnO,[6] while Asp is not. We have additionally considered Asp to make a comparison with a similar study conducted for titania.[12] The ZnO$(10\bar{1}0)$ surface has been found to be the energetically most favorable surface.[19] The binding mechanisms will be analyzed in terms of structural information, charge density, and binding energies. Arg, Lys, and Asp were modeled in their corresponding charge states due to the protonation (Lys and Arg) and deprotonation (Asp) of the side chains occurring in water solutions at physiological pH. The goal is to describe the binding mechanisms of the single amino acids with the surface in the ground state configurations, where we have focused on the specific amino acids that are supposed to favor the adhesion of the peptide to the metal oxide. Currently, it is not clear what role water plays in the interaction between peptide and surface. For this reason our model goes further the investigation of the interaction with a dry surface by including explicitly in the model also the intermediation of the water molecules that deeply affect the selectivity and the strength of adhesion. The comparison with our results for the interaction with $TiO_2(101)$ surface within the same methodology[12] will allow to get more insights into the specificity of adhesion on different surfaces.

2. CALCULATION DETAILS

Our study is based on a pseudopotential plane-wave method using PWSCF code as implemented in the QUANTUM-ESPRESSO package.[20] All calculations have been performed using the generalized gradient approximation (GGA) with the Perdew, Burke, and Ernzerhof (PBE) correlation functional.[21] The pseudopotential plane-wave calculations were performed using Vanderbilt ultrasoft pseudopotentials.[22] The convergence of the total energy has been checked by varying cutoffs to reach a good compromise between accuracy and computational times. Vanderbilt-type ultrasoft pseudopotentials have been used with a plane-wave energy cutoff of 60 and 420 Ry for the electronic wave functions and the total charge density, respectively, allowing a convergence of the total energy below 0.0002 Ry/atom. 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. The dispersion forces have been included through a semiempirical correction term.[23]

After optimization of the bulk ZnO cell by sampling the Brillouin zone using a 12 × 12 × 12 Monkhorst−Pack k-point grid, we obtained the crystallographic parameters a = 3.280 Å, c = 5.290 Å, and u = 0.379 which are close to the experimental values a = 3.258 Å, c = 5.220 Å, and u = 0.382, respectively.[24] Next, the ZnO$(10\bar{1}0)$ surface was modeled by the repeated slab geometry with the in-plane 4 × 2 unit cell, which contains three ZnO bilayers and counts 96 atoms. The layers were separated by a vacuum gap of 20 Å thickness in such a way to neglect the interactions among the periodic images of the system in the vertical direction. The supercell has been fully optimized starting from the bulk atom positions, resulting in a size of 13.12 × 10.58 × 35 Å^3. The top two bilayers were relaxed, while the bottom bilayer was kept fixed to mimic the bulk region. Given the size of the supercell, all calculations have been done in the Γ-point. The supercell has been used to optimize the ground state adsorption configurations of the amino acids; in particular, charged structures containing either protonated or deprotonated amino acids have been fully optimized in a uniform charged background to make the supercell neutral. We have relaxed several starting geometries chosen by changing the adsorption site of each amino acid and holding the molecule perpendicular to the surface. In this paper we will discuss the most stable configurations among the calculated ones. To calculate the adsorption energy of charged structures, the total energy of the ground state configurations has been calculated on a neutral supercell obtained by adding to the ground state configuration a counterion placed in the vacuum region far from both the amino acid and the surface. This is done in order to avoid all the difficulties related to the Ewald sums in such inhomogeneous systems. In all cases, the artificial electric field across the slab induced by the periodic boundary conditions has been corrected.[25] However, the supercell used to model the surface of the isolated dry and hydrated surfaces, presented in section 3.1, had size of 6.56 × 10.58 × 27 Å^3 and contained 48 atoms. For this system the Brillouin zone was sampled with a 2 × 1 × 1 Monkhorst−Pack k-point grid.

We are interested in getting insights into the nature of the interaction of each amino acid in the peptide's sequence with the surface, so we focus on the interaction of the side chain with ZnO.

For this purpose, we have compared the ground state adhesion configurations obtained with templates where the −COOH and $-NH_2$ were removed from the amino acids (modified amino acids). Our calculations evidenced that Lys and Arg, which are the amino acids with the longer alkyl chains, have the same binding energy and adhesion geometry of the modified amino acids. For Asp and Gln which, on the contrary, have short alkyl chain, we have found that the removal of the −COOH and $-NH_2$ groups lowers a little the binding energy but at such an extent that does not alter the scenario drawn. As a consequence, because we wanted to exclude possible artifacts due to the

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presence the −COOH and $-NH_2$ groups (which in the peptide chain are constrained by deformations of peptide bonds), we have preferred to remove the carboxyl and the amino groups, and the resulting dangling bonds have been passivated with H atoms. Then the modified amino acids can be assumed correct for the side chain configuration of the amino acid during the adhesion if we want to model the interaction of the amino acids when they are in the peptide sequence.

The charge density related to the adsorption for each structure has been investigated. We calculated the electron charge density difference for each configuration, defined as the difference between the electron charge density of the full system and the sum of the electron charge densities associated with the slab and the amino acid, considered as isolated.

3. RESULTS AND DISCUSSION

3.1. Dry and Hydrated Surfaces. In the relaxed geometry of the dry ZnO(10$\bar{1}$0) surface the outermost atoms form rows of tilted Zn−O dimers, with a 0.23 Å relative displacement in the direction perpendicular to the surface between the outward O and the inward Zn atoms. The structural properties of the surface are shown in Figure 1. The deposition of water molecules is

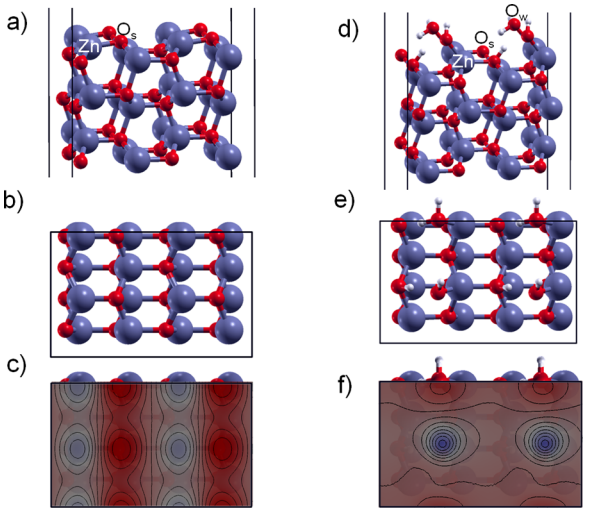

Figure 1. Side view of relaxed geometry of (a) dry and (d) hydrated ZnO(10$\bar{1}$0) surfaces (Zn in violet, O in red). The corresponding top views are shown in (b) and (e), respectively. Top views of the electrostatic potential color maps are shown in (c) and (f) (red (blue) color corresponds to the highest (lowest) value), respectively.

favored by the rows of acidic-like Zn and basic-like oxygen atoms as well as by the tilting of the "dimers". We have considered as hydrated surface the one fully covered by one monolayer of water, in the most stable configuration calculated by Calzolari[26] and Yan,[27] in which the water molecules saturated the bonds available on the surface, with the formation of an ordered 2 × 1 superstructure where half of the water molecules are dissociated. The partial dissociation of water on the ZnO(10$\bar{1}$0) surface has been observed in ZnO nanoparticles powder exposed to water, yielding coexistent H_2O and OH species.[28] We have alternated rows of undissociated and dissociated water molecules along the [12$\bar{1}$0] direction. In Figure 1, the geometrical configuration of the hydrated surface is also shown, where the adsorbed water layer rearranges in order to optimize the H-bond path both with the surface and among molecules. The geometrical parameters reported in Table 1 agree well with those calculated in previous

Table 1. Geometry Parameters for Dry and Hydrated ZnO(10$\bar{1}$0) Surfaces (Lengths in Å)

	d(Zn−O_s)	d(Zn−O_w)	d(O_w−O_s)
dry surface	1.871		
hydrated surface		2.057[a]	2.663[a]
		1.967[b]	2.667[b]

[a]Undissociated water. [b]Dissociated water.

papers.[26,27] The calculated adsorption energy for the saturated surface (calculated as $E_{ads} = 1/n[E_{tot}(\text{water/ZnO}) - E_{tot}(\text{ZnO}) - n^*E_{tot}(\text{water})]$) is −1.14 eV/molecule, comparable to −1.16 and −1.30 eV/molecule calculated by Calzolari[26] and Yan,[27] respectively. In the following, we label O_w and O_s the oxygen atoms from the water molecule and from the surface, respectively. The dry surface offers a good adhesive substrate for the side chains of the amino acids. Arg, Lys, and Asp have charged side chains, so that the electrostatics of the surface play a crucial role in the adsorption process. In Figure 1 the electrostatic potential at a fixed distance of 2.0 and 7.0 Å from the substrate is mapped for the dry and hydrated surfaces, respectively. For the dry surface, the electrostatic potential forms regular alternated rows of proton-attracting O_s and electron-attracting Zn, in correspondence of the potential local extrema. The topology of the electrostatics potential of the hydrated surface changes completely with respect to the dry surface. There, the O_w of the undissociated water will be proton-attracting and the H atom bond to dissociated water will play an acidic-like role in place of Zn. In this way the hydrated surface is still good for the adsorption of the amino acids, but the surface density of the reactive sites is the half compared to the dry surface.

3.2. Adsorption on the Dry Surface. The ground state adsorption configurations of protonated Lys and Arg, deprotonated Asp, and neutral Gln on the dry ZnO(10$\bar{1}$0) surface are reported in Figures 2 and 3, while the geometrical parameters are

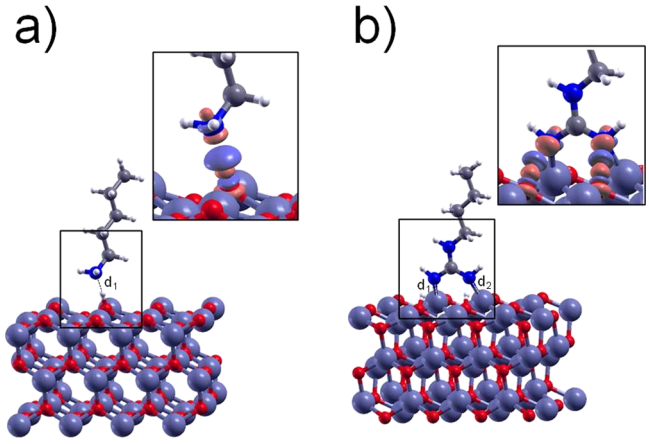

Figure 2. Relaxed geometry of (a) lysine and (b) arginine on the dry ZnO(10$\bar{1}$0) surface (Zn in violet, O in red, C in gray, H in white, N in blue). In the insets the red (blue) isosurface corresponds to the electron-charge accumulation (depletion) region.

collected in Table 3. Lysine adsorption occurs via amino acid deprotonation: indeed, an H atom is detached from the $-NH_3^+$ side chain terminal group and forms a covalent bond with an oxygen atom of the surface (d = 1.09 Å). Then, the deprotonated lysine sticks on the surface through the formation of a hydrogen bond (d_1 = 1.485 Å, Figure 2a) between the H atom captured by the surface and the N atom of the resulting $-NH_2$ terminal

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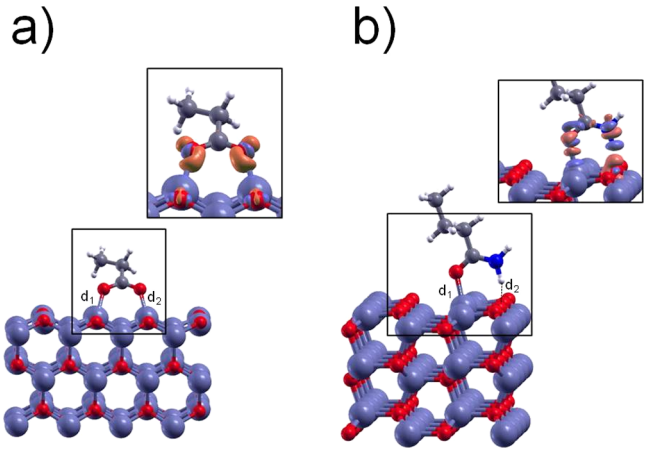

Figure 3. Relaxed geometry of (a) aspartate and (b) glutamine on the dry ZnO(10$\bar{1}$0) surface (Zn in violet, O in red, C in gray, H in white, N in blue). In the insets the red (blue) isosurface corresponds to electron-charge accumulation (depletion) region.

Table 2. Adsorption Energies (in eV) of Amino Acids on the Dry, One-Layer Hydrated and Two-Layers Hydrated ZnO(10$\bar{1}$0) Surfaces

	Lys	Arg	Asp	Gln
dry	−3.531	−4.385	−2.769	−1.431
one layer hydrated	−3.027	−2.856	−1.327	−0.942
two layers hydrated	−2.837	−2.640		

Table 3. Geometrical Parameters for Dry, One-Layer Hydrated and Two-Layers Hydrated ZnO(10$\bar{1}$0) Surfaces (Lengths in Å)

	systems	d_1	d_2	d_3	d_4
Arg	dry surface	2.050	2.050		
	hydrated surface	1.883	1.710	1.898	
	two layers hydrated surface	1.648	1.742	1.829	1.759
Lys	dry surface	1.485			
	hydrated surface	1.619			
	two layers hydrated surface	1.588	1.739	1.682	1.591
Gln	dry surface	2.026	1.552		
	hydrated surface	1.765	1.737	2.122	2.257
Asp	dry surface	2.002	2.002		
	hydrated surface	2.185	1.712	2.222	

group. The same phenomenon occurs in the Arg case where two H atoms are detached from the protonated side chain $-C(NH_2)_2^+$ terminal group and are bonded to two O_s atoms (with bond length d = 1.01 Å each) with N−H distances of d = 1.884 and 1.828 Å. In this way, two N−Zn covalent bonds are formed each with length d = 2.050 Å (d_1 and d_2 in Figure 2b). N is electron attracting in both cases, and the most of the charge transferred to the amino acids is located there. We estimated a 0.043 (0.27) e charge transfer to N atom(s) for Lys (Arg) by Löwdin charges calculations, reported in the Supporting Information. We specify that here positive electron charge transfer to an atom must be regarded as negative charge that moves toward that atom, and negative electron charge transfer to an atom must be regarded as negative charge that moves away from that atom. On the contrary, the negative charged Asp is adsorbed on Zn atoms via two Zn−O bonds each with length d = 2.002 Å (d_1 and d_2 in Figure 3a) and the neutral Gln is adsorbed by means of a Zn−O covalent bond with length d_1 = 2.026 Å and a hydrogen bond between a hydrogen of the NH_2 terminal group and a O_s oxygen (d_2 = 1.552 Å), as shown in Figure 3b. Although Asp is negatively charged, we found that the electron charge moves toward the CO^- terminal groups because of the bond formation. We estimated an electron charge transfer of 0.26 and 0.27 e to Asp's O atoms and 0.10 (−0.06) e to Gln's O (N) atom.

The adsorption energies for the charged amino acids have been calculated including a counterion (OH^- for the Lys and Arg molecules and H_3O^+ in the Asp case) in the relaxed adsorption configuration, as

$$E_{ads} = E_T - E_S - E_{amino} - E_{CI} \quad (1)$$

where E_T and E_S are the total energies of the full system and of the isolated ZnO slab, respectively, while E_{amino} and E_{CI} are the total energies of the isolate amino acid and its corresponding counterion, respectively. The adsorption energy values for the dry surface are reported in the first row of Table 2. The amino acid with the strongest adhesion is the arginine with a binding energy of −4.385 eV due to the strong interaction with the surface of the two NH_2 groups, followed by the lysine with −3.531 eV. The aspartate is bound with −2.769 eV and the neutral glutamide with −1.431 eV is the less adhered amino acid among those investigated, so that the binding energy of Asp is twice the binding energy of Gln. Therefore, the considered amino acids can be easily adsorbed from the dry ZnO(10$\bar{1}$0) surface due to the ZnO dimers prone to chemically interact with the side chains and the electrostatic interaction of charged groups. Arg and Lys, which are positively charged, exhibit an interaction with the surface stronger than Asp, which is negatively charged. In this way we can infer that proton-attracting O_s give rise to an interaction with positive charges stronger than that of Zn with negative charges. The neutral Gln is the amino acid with the weakest interaction among those investigated. The binding energies are larger than the thermal energy at room temperature, so that adhesions are stable in standard conditions.

3.3. Adsorption on the Hydrated Surface. In the experiments, amino acids and peptides usually interact with metal oxides surfaces in aqueous environment. One or more layers of water are separating the biological molecules from the inorganic substrate, forming a hydrated surface. We studied how the water molecules influence the adsorption by considering one monolayer and two monolayers of water for all of the considered amino acids and the two strongest interacting configurations, respectively; the first monolayer is adsorbed as in the partial dissociation 2 × 1 superstructure reported in Figure 1.

The ground state adsorption configurations on one-monolayer hydrated surface obtained after full relaxation are shown in Figures 4 and 5, and the geometrical parameters are reported in Table 3. One H atom detaches from the $-NH_3^+$ side chain terminal group of Lys to bind to O_w of a water with a bond length d = 1.00 Å; contextually, a H atom is detached from the water molecule and forms a covalent bond with O_s. The net effect of this atom transfer is the deprotonation of the amino acid and the protonation of the substrate. In this way the interaction of the amino acid with the surface is mediated by a hydrogen bond between N of amino acid and H of the water (d_1 = 1.619 Å, Figure 4a). We observe that this configuration is 0.2 eV lower in energy than the nearest configuration without deprotonation. The protonated side chains of arginine sticks on the hydrated surface through two hydrogen bonds with O_s and O_w with bond lengths d_1 = 1.883 Å and d_2 = 1.710 Å, respectively, as shown in Figure 4b. Moreover, the molecule is tilted in such a way to form also one

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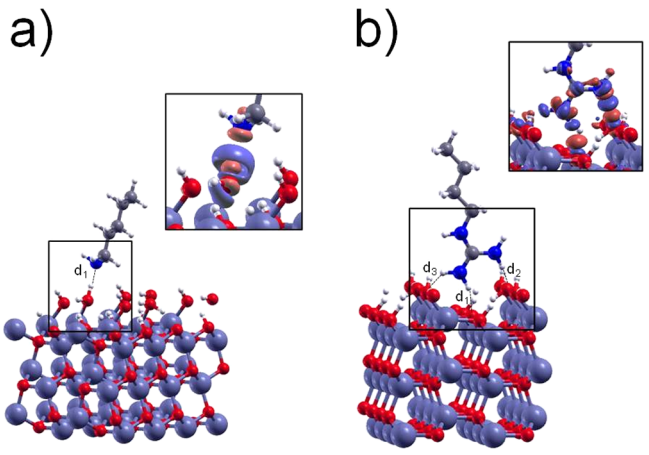

Figure 4. Relaxed geometry of (a) lysine and (b) arginine on the hydrated ZnO($10\bar{1}0$) surface. In the insets the red (blue) isosurface corresponds to electron-charge accumulation (depletion) region.

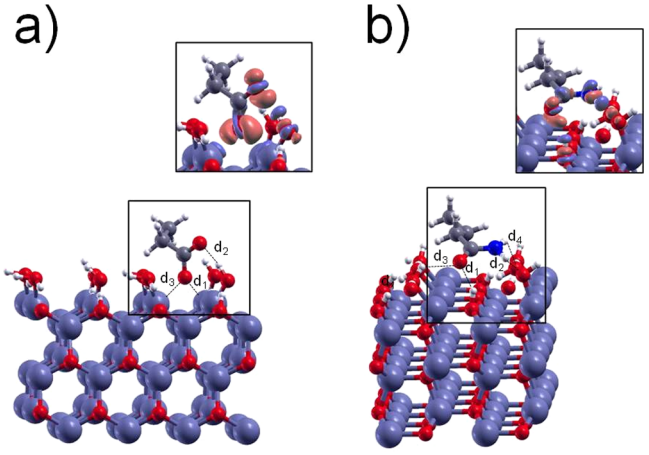

Figure 5. Relaxed geometry of (a) aspartate and (b) glutamine on the hydrated ZnO($10\bar{1}0$) surface. In the insets the red (blue) isosurface corresponds to electron-charge accumulation (depletion) region.

hydrogen bond with O_w (d_3 = 1.898 Å). We observe that the interaction of the Arg with the surface is not completely mediated by water. This happens also for the aspartate, for which one O atom of the carboxyl group points toward two Zn atoms with bond lengths d_1 = 2.185 and d_3 = 2.222 Å and the other one forms a hydrogen bond with a hydrogen of the dissociated water (d_2 = 1.712 Å), as shown in Figure 5a. The carboxy−ammine side chain of glutamine sticks to the hydrated surface by means of two hydrogen bonds of the O atom and two hydrogen bonds of the NH_2 terminal group. The O atom of the carboxy−ammine points toward two H atoms: one H atom bound to O_s and the other one from the dissociated water with O−H lengths d_1 = 1.765 Å and d_3 = 2.122 Å, respectively. The H atoms of the NH_2 terminal group point toward two O_w's of the dissociated and undissociated water, with O−H lengths d_2 = 1.737 Å and d_4 = 2.257 Å, respectively, as shown in Figure 5b. Therefore, the interaction of Gln with the surface is mediated by water. The investigation of the charge density difference shows that water layer of hydrated surface does not change the charge transfer toward Lys, Asp, and Gln observed on the dry surface, while for Arg the charge transfer is reversed when compared to the dry surface adsorption, with a charge transfer of −0.02 *e* away from the N atom nearest to the surface. On the other side, we estimated the following charge transfers: 0.07 *e* to N atom for Lys, 0.31 and 0.15 *e* to Asp's O atoms, and 0.04 (−0.05) *e* to Gln's O (N) atom.

The adsorption energy values are lower than the corresponding values calculated on the dry surface. They have been calculated again through eq 1 where E_S must be replaced by $E_{S+(H_2O)_4}$ and reported in Table 2. The bonds formed by Lys are stronger than the H-bonds formed by Arg, so that the binding energy hierarchy on the hydrated surface is reversed with respect to the dry one, with the Lys forming the strongest bond to the hydrated surface with −3.03 eV. The adsorption energy difference between Lys and Arg is 0.17 eV, while it was 0.85 eV for the dry surface. The adsorption energies of Asp and Gln on the hydrated surface are very much reduced compared to the dry case; indeed, the Asp binding energy is 0.38 eV larger than that of Gln. The reduction of the binding energies can be related to the hydrogen bonds formation and to the electrostatic interaction screening due to the water layer. We compared the binding energies to dry and hydrated surfaces with those calculated with the PBE correlation functional, not including the dispersion forces parametrization. Their values are reported in the Supporting Information. We have found that the binding energies calculated by including dispersion forces are greater than that estimated by PBE functional, meaning that van der Waals interactions play a substantial role in the adhesion. By resuming, we can distinguish two well distinct kinds of interactions for amino acids with hydrated ZnO: the strong positive charged side-chain adhesion of Lys and Arg and the less strong negative charged and neutral side-chain adhesion of Asp and Gln.

We have investigated the role played by a second water layer on the amino acid adhesion. We have limited this study just to Arg and Lys that resulted to have the most stable adhesion to the surface. We applied the same approaches described in a previous paper[12] to study the fully hydrated amino acids. We used the same MD simulation of Lys and Arg solved in water solution, and we considered only the direct links between the first monolayer water molecules and the two molecules closest to the protonated terminal group. Those two molecules represent the second layer of water that interacts with Lys and Arg. The structures obtained by DFT total energy optimization are shown in Figure 6 and resulted in an adsorption energy of −2.84 and −2.64 eV for Lys

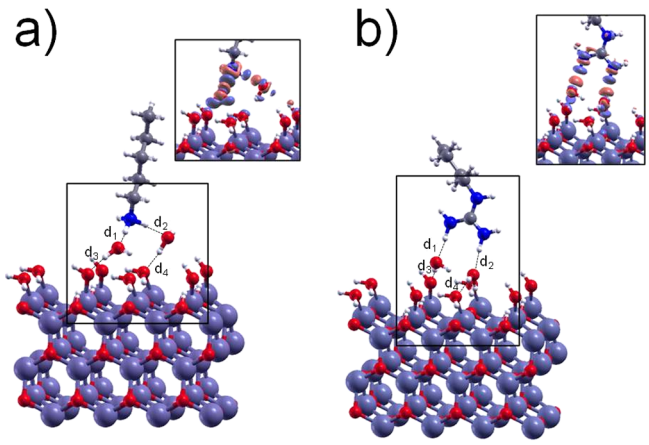

Figure 6. Relaxed geometry of (a) lysine and (b) arginine on the two-layers hydrated ZnO($10\bar{1}0$) surface. In the insets the red (blue) isosurface corresponds to electron-charge accumulation (depletion) region.

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and Arg, respectively, each one with the formation of two hydrogen bonds (d_1 = 1.588 Å and d_2 = 1.739 Å for Lys and d_1 = 1.648 Å and d_2 = 1.742 Å for Arg). The geometrical parameters are collected in Table 3. Notably, the deprotonation of the amino acid and the protonation of the substrate do not occur for neither of them. It is evident that a considerable surface adhesion is still present also when the amino acid are separated by two water layers. We can infer that the screening of the closest hydration shell reduces the adsorption energy of Arg and Lys, but the interaction remains basically electrostatic. The charge density exhibits just small changes compared to the case with only one layer of water so that the effect of the second layer of water on the charge transfer is negligible.

The adhesion of amino acids on the anatase $TiO_2(101)$ surface with and without one monolayer of water has been also investigated in a previous work,[12] where the ground state configurations were calculated for Lys, Arg, and Asp. Thus, we can compare the adhesion properties of Lys, Arg, and Asp to $ZnO(10\bar{1}0)$ and $TiO_2(101)$ surfaces. On the $TiO_2(101)$ dry surface, Arg exhibits the strongest adhesion with a binding energy of −2.4 eV, followed by Lys. Asp was the less adhered amino acid with −1.3 eV. This hierarchy was confirmed on the $TiO_2(101)$ hydrated surface, even if the binding energies are remarkably reduced, with the highest adsorption energy of −1.9 eV.

The two surfaces behave differently with respect to the amino acid adhesion in water mainly because the two hydration patterns are quite different: while water on TiO_2 does not dissociate, on ZnO the hydration pattern consists of alternating rows of undissociated and dissociated water. As a consequence, the polar behavior of the two surfaces, and thus the electrostatic interaction with biological materials, are quite different. For instance, the z-dipole induced by the charge redistribution upon formation of a water layer is nearly zero (i.e., $\Delta d = -0.12$ D) in the ZnO case while in the (101) TiO_2 case is $\Delta d = -1.17$ D. Moreover, besides the different polarity, the surfaces interact differently with the amino acids also because of the different hydration patterns: consider the Arg case, for instance, where the two layer models of the water mediated interactions are quite different in the two cases: in the ZnO case three waters and one dissociated water are involved that stay just below the amino acid so that the interaction is quite localized; in the TiO_2 case, instead, four waters are involved but they are located in a wider area so that the water density is locally reduced.

Thus, we have established that except for the different specific details discussed above, the results found for $ZnO(10\bar{1}0)$ and $TiO_2(101)$ are very similar; consequently, the adhesion of the amino acids is strong enough that significant preferences are not found. However, peptides that are specific for anatase and are not for ZnO, and vice versa,[29] were evidenced in the experiments. The discrepancy between the above-reported results concerning the amino acid adhesion onto the $TiO_2(101)/ZnO(10\bar{1}0)$ surfaces and the experimental results indicating some selectivity property is mainly related to the fact that the experiments were performed with peptides, not isolated amino acids.

Then, we can argue that this discrepancy might be related to the much more complex structure that characterizes the peptides, such as their conformation changes and the way the conformation affects the adhesion on the two surfaces. Moreover, because the hydration pattern considered for the two surfaces are quite different (in the anatase case no water dissociation was observed), and the surfaces too, the ground state conformation of the adsorbed peptides might also depend on them. Only specific peptides with a suitable sequence of amino acids can dispose of the correct arrangement that makes the adhesion stable. Thus, the experimental results concerning selectivity of specific peptides on the anatase or ZnO surface are most likely related to the specific peptide conformation instead of to the specific adhesion properties of the isolated amino acids. The comparison of the results obtained on the interaction of the isolated amino acids with ZnO surface with those previously obtained on TiO_2 surface seems to indicate that the adsorption properties of isolated amino acids cannot explain the selectivity of the peptides. The surrounding environment, induced by neighboring residues, may indeed influence on the properties of individual amino acids of the peptide. The less demanding classical molecular dynamics simulations would be more suitable to study the complicated time- and temperature-dependent correlations involved in biological systems interfaced with inorganic surface, but this requires suitable and reliable potential parameters to model the force field and the interactions between the surfaces and the charged amino acids. However, the parametrization of the classical force fields should be accurate enough to take into account eventual protonation processes that can happen on zinc oxide surfaces when the screening of water molecules is reduced. Further studies are in course to evidence the role of the peptide conformation in the adhesion properties.

4. CONCLUSIONS

In conclusion, DFT can clarify the nature of the interaction of peptides with inorganic surfaces, including the effects of the water environment. However, the adhesion of peptides is not simply related to the adhesion of every single amino acid in its sequence, but rather it is ruled by the presence of particular groups. We have found that Arg and Lys are the amino acids in the preferential binding sequence for ZnO surface with the larger adhesion energy. We have found from the structural properties and binding energetics that the mediation of water can influence the interaction of amino acids with $ZnO(10\bar{1})$ surface. Indeed, we have seen that the binding energy hierarchy is inverted for Lys and Arg: Arg is the amino acid with the strongest adhesion on the dry surface, while Lys is the most stable on the hydrated surface. The reduction of the binding energies for the hydrated adsorption that we observe can be attributed, in general, to the screening by the water layer of the electrostatic interactions and to the formation of hydrogen bonds. However, we have found that both Lys and Arg as hydrated have comparable binding energies: −3.0 eV for Lys and Arg is just 0.2 eV less stable. The adhesion to the hydrated surface is probably more relevant in the practical applications, where the adhesion of the peptide to the metal oxide is experimented in aqueous solution. On the other hand, we have calculated the structure in the ground state of single amino acids as static systems, and we have just included a few layers of water. Therefore, the study and understanding of the adsorption mechanisms require to model the full sequence in the water environment by using the appropriate computational approaches.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcb.5b05584.

Additional test case details; adsorption energies without dispersion forces; Löwdin charge tables; full set of coordinates for the structures studied in this work (PDF)

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Notes

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