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Published on: 22 Feb 2008 - ChemPhysChem (John Wiley & Sons, Ltd)

Topics: Alanine, Hydrogen bond, Molecule and Molecular dynamics

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Investigating alanine - silica interaction by means of first-principles molecular-dynamics simulations

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December 12, 2007

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Abstract

In our attempts to achieve a detailed understanding of protein - silica interactions at an atomic level we have, as a first step, simulated a small system consisting of one alanine in different protonation states, and a hydroxylated silica surface, using a first-principles molecular-dynamics technique. The simulations were carried out in vacuo as well as in the presence of water molecules. In the case of a negatively charged surface and an alanine cation, an indirect proton transfer from the alanine carboxylic group to the surface takes place. The transfer involves several water molecules revealing an alanine in its zwitterionic state interacting with the neutral surface through indirect hydrogen bonds mediated by water molecules. During the simulation of the zwitterionic state the ammonium group eventually establishes a direct –N–H$\cdots$O–Si interaction, suggesting that the surface–amino group interaction is stronger than the interaction between the surface and the carboxylic group. In vacuum simulations, the amino group exhibits clearly stronger interactions with the surface than the carboxylic group.

Keywords: density functional theory, hydrogen bonding, molecular dynamics simulation, peptide-surface-interaction, silica

1 Introduction

Studying the interaction between biomolecules and inorganic materials is of interest for various reasons. On the one hand, mineral surfaces might have served as catalysts for peptide bond synthesis in prebiotic chemistry and, thus, might have made possible the synthesis of first small polypeptides. [1] On the other hand, the interaction of proteins and nucleic acids with solid surfaces is of importance to many applications for biomaterials or in nanotechnology. [2] Examples for such applications are the integration of an implant with tissue or the assembly of biosensors. [3, 4] On the experimental side, catalytic efficiency of hydroxylapatite surfaces, [5] of silica-rich surfaces like zeolites or feldspars, [6, 7] or of silica and aluminosilicate surfaces [8] on peptide bond formation has been demonstrated.

The interaction of proteins with silica surfaces has been studied using various spectroscopic techniques such as NMR-, [9] IR-, [10] or ATR-IR-spectroscopy. [11] Basiuk et al., [12] for example, suggested on the basis of IR spectroscopy that the formation of linear glycine oligomers is catalyzed by the silica surface through formation of a silica-glycine anhydride via an esterification reaction, as manifested by the appearance of an IR-absorption band at 1760 cm^{-1}. In contrast, no covalent interaction between glycine and a silica surface was found in studies by Lomenech at al. [13] and Meng et al. [14] The latter work suggests that the adsorbed molecule interacts with the surface through the formation of specified hydrogen bonds, which gives rise to small shifts of the infrared frequencies of the affected groups.

The interaction of one amino acid molecule (or of small molecules capable of forming a peptide bond like ammonia and formaldehyde or methyl amine and acetaldehyde) with different surface models has also been explored using computational methods. Due to the relatively small size of such systems,

ab initio and DFT calculations could be carried out for these computational studies. [15, 16, 17] Of particular interest to the present contribution is the work of Rimola et al. [16] These authors claimed that a direct interaction glycine - silica is possible without the need of having water molecules as a solvent. Moreover, the hydroxylated silica surface was shown to stabilize the glycine zwitterionic form. However, all these quoted studies generally suffer from two shortcomings: first, the calculations are statically, i.e. structures of complexes, reaction coordinates, and possible transition state geometries were assumed and were subject to a minimization protocol. Second, these calculations were generally performed for conditions in vacuo, i.e. the effects of water as a solvent with possible hydrogen bonding interactions or even as a reaction partner were neglected.

Key questions in the context of protein-surface interaction are how protein conformations might change due to the adsorption and what the nature of the contact is at the molecular level. An intriguing topic here concerns the question whether stabilization of a protein-surface complex is achieved through direct interaction or indirectly, mediated by water molecules.

Protein-silica systems are by far too large and too complex to be treated using high-level quantum chemical methods. Thus, only semi empirical [18, 19, 20] and classical molecular dynamics studies [21, 22, 19, 20] are available in the literature. While the results of classical dynamics simulations largely depend on the applied force field, the probability of artifacts could be reduced by treating the complete simulation system quantum chemically.

To shed some light on the peptide-silica interaction at the atomic level, we have, therefore, carried out first-principles molecular-dynamics simulations on a system consisting of an alanine molecule, a hydroxylated silica surface, and water molecules. To our knowledge, this is the first investiga-

tion of a silica - amino acid system that accounts *(a)* for dynamical effects and *(b)* includes explicit solvent molecules. The size of the simulation systems containing explicit water molecules is large for running extended first-principles molecular dynamics simulations. We can, therefore, at this point only monitor first steps of adsorption processes by placing the alanine at short distance of the silica slab and running relatively short simulations of several picoseconds. In order to reach equilibrium conditions, much longer simulations would have to be run which, currently, are not affordable at this level of theory.

In periodic simulation systems electrostatic interactions are efficiently treated using Ewald summation. [23, 24] For that purpose, the simulation cell needs to have a zero net charge. [25] In order to not being obliged to add ions to fulfill this requirement and, thereby, increasing the complexity of the simulation system needlessly, we have confined ourselves to the following three simulation setups for this investigation: *(a)* the alanine molecule had a charge +1 and the surface a charge of -1, *(b)* the alanine was unionized and the surface was uncharged, and *(c)* the alanine was a zwitterion and the surface uncharged. All three simulation systems were treated with explicit water molecules and in vacuo. Primarily the following questions are addressed:

- Does the simulation predict a direct amino acid - surface interaction or is the interaction mediated by one or several water molecules?
- Could the formation of a silica-alanine anhydride, as proposed by Basiuk et al., [12] be observed?
- How much do simulations in vacuum differ from those carried out in the presence of water molecules?

2 Computational Methods

2.1 Generation of the simulation systems

As suggested by Civalleri et al. [26] we have used the edingtonite structure to model a silica surface. In order to have a proper start structure, the geometry of a structural unit of edingtonite was first optimized at the Hartree-Fock level using the GAUSSIAN03 suite of programs [27] and a standard 6-31G* basis set. [28] Then, a three dimensional box of such units was generated. Depending on the application, slabs can either be cut out directly from this box or, in the case of classical MD simulations, the box can first be adapted to the applied force field using 3D periodic boundary conditions. For the present application, a slab with a surface corresponding to a (001) crystal plane was cut out, completely hydroxylated, and immersed in a box of water molecules of a density of $1 g/cm^{-3}$. Centered with respect to the slab and about 6 Å above the slab, an alanine molecule was finally placed. Using the program X-PLOR,[29] water molecules within a distance of 2.5 Å of the slab or the alanine were cut out. This resulted in a simulation setup as shown in Figure 1.

Before starting any calculations, the system had to be tailored by either deprotonating one of the central silanole groups of the top layer of the slab and adding this proton to the carboxylic group of alanine or by generating an unionized or zwitterionic alanine molecule. The simulation system created that way consists of 16 silicon, 3 carbon, 1 nitrogen, 42 oxygen atoms, 67 water molecules, and 23 hydrogen atoms, and thus a total of 286 atoms.

With this choice we have generated 6 different simulation systems: *(i)* a system consisting of a negatively charged slab (i.e. deprotonation of a centered hydroxyl group) and a positively charged alanine cation. We will

refer to this system with explicit water molecules to system $\mathbf{A}^{Sol}$ and to the corresponding vacuum system to system $\mathbf{A}^{Vac}$, *(ii)* a second simulation system consists of a neutral slab and an alanine molecule in its zwitterionic form. This system is refered to as system $\mathbf{B}^{Sol}$ (with water molecules) and $\mathbf{B}^{Vac}$ (vacuum system), and *(iii)* a system consisting again of a neutral slab, but this time with the alanine in its unionized form. $\mathbf{C}^{Sol}$ refers to this system with water molecules and $\mathbf{C}^{Vac}$ to the one in vacuum.

For the analysis of structures as well as for the generation of figures, the program VMD [30] was applied. The standard parameters within VMD for the detection of hydrogen bonds (distance cutoff of 3.0 Å and angle cutoff of 20°) have been applied. Figures were generated using the raytracing program POVRAY. [31]

2.2 Simulation

All simulations were carried out using the QUICKSTEP module of the CP2K package. [32, 33, 34, 35, 36] DZVP basis sets were applied [35] in combination with PBE functionals [37] and Goedecker-Teter-Hutter (GTH) pseudopotentials. [38, 39] This simulation setup resulted in 356 electrons or 178 doubly occupied orbitals and 921 basis functions in the case of the vacuum simulations and in 892 electrons or 446 doubly occupied orbitals and 2462 basis functions in the case of the simulations with water molecules. While QUICKSTEP uses Gaussian type basis functions to describe the wave function, the density is described using an auxiliary plane wave basis. [35]. The plane wave cutoff was 280 Ry. The simulation cell was periodic in the x- and y-direction with edges of 13.928 Å. The extension of the simulation box in z-direction has to comply with the method used for treating the electrostatics of the system. We have applied the Martyna-Tuckerman

poisson solver which requires a z-edge which at least doubles the extension of the molecular system in this direction. [40] As long as this condition is fulfilled, the particles are free to move in z-direction and the system can be considered as open. As soon as a particle should violate this prerequisite, however, the simulation would become meaningless. Using a z-edge of 35 Å, we never had a problem to fulfill this condition. The need of a large z-edge, however, causes a relatively large plane wave basis. Due to the requirements discussed above, no control of pressure was possible. The simulations were carried out in the NVT-ensemble using a thermostat. The step size during the simulations was 0.5 fs.

In a first step we minimized the structures. After minimization, the systems were equilibrated at 100 K for 1 ps. During equilibration, the α-carbon of alanine was restrained in its mobility by applying a harmonic potential. Furthermore, the positions of 31 atoms of the bottom of the slab were kept fixed during equilibration and following dynamics simulation. After the short equilibration, the restraint on the alanine carbon atom was released and a free dynamics simulation was run, first during 2.5 ps at 100 K, followed by 13 ps (unionized and zwitterion) or 14 ps (charged system) at 300 K. In the case of the vacuum simulations, which all ended up in the same simulation configuration,the dynamics at 100 K had been extended to 5.5 ps.

3 Results and Discussion

3.1 Vacuum Simulations

3.1.1 Simulation $\mathbf{A}^{Vac}$

After releasing the restraints potential on the alanine α-carbon at the end

of the equilibration the alanine molecule quickly moves towards the surface owing to the strong electrostatic interaction. About 65 fs after the start of the 100 K free dynamics simulation, a hydrogen bond Si–O^- – H_3N^+- to the originally deprotonated silanol group S_a (see Figure 2) is formed and about 10 fs seconds later the proton is completely transfered to this silanol. Hereby, a simulation system corresponding to $\mathbf{C}^{Vac}$ according to the definitions given above is created which persists during the continuation of the simulation. The pursued dynamics is dominated by i) a strong interaction between the two silanol groups S_a and S_c, ii) an occasionally appearing hydrogen bond between S_a and the nitrogen atom of the alanine amino group, and iii) occasional hydrogen bonds between the carboxylic group of alanine and silanol groups S_c and S_d at a later stage of the simulation. During the remaining part of the trajectory at 100 K, the structure is dominated by these three hydrogen bond interactions as depicted in Figure 2.

The temperature was changed to 300 K following 3400 steps (1.7 ps) of simulation at 100 K. The added energy disturbs the system considerably, breaking up the hydrogen bonds between the carboxylic group of the alanine and the two silanol groups S_c and S_d. Only the interaction between the amino group and the surface is retained most of the time. During the ongoing simulation, the alanine moves considerably, forming short living hydrogen bonds from the carboxylic group to the silanol groups S_c and/or S_d and, more rarely, between a proton of the amino group and the oxygen of silanol S_b. After about 3.3 ps of simulation at 300 K, a relatively stable structure similar to that found at 100 K is formed which is dominated by a hydrogen bond from nitrogen of the amino group to the proton of the central silanol S_a. Occasionally, hydrogen bonds from the carboxylic group to silanol groups S_b or S_d are also created. At this elevated temperature,

however, hydrogen bonds between the carboxylic group and the surface are even less stable than at 100 K. This interactions are mostly retained during the rest of the trajectory, although, the alanine occasionally undergoes some larger conformational changes.

We can conclude that the formation of relatively stable complexes between an amino acid molecule and a silica surface is feasible through direct hydrogen bonding interaction. This interaction is governed by the interaction between the amino group of the amino acid with the surface.

Our findings can be quantified in terms of root mean square (rms) deviations of each averaged position of the amino acid atoms. We determined this motional property during the last 5 ps of the trajectories of simulations $\mathbf{A}^{Vac}$ and $\mathbf{A}^{Sol}$ and obtained the results shown in Figure 3. Atomic mobilities of the alanine molecule in the vacuum simulation are given in the upper part of this figure. The smallest mobility has been determined for atom HT2 (0.29). This proton had been transfered to the surface and is bound to silanol S_a. As discussed above it forms a stable hydrogen bond to the amino nitrogen of alanine thus reducing the mobility of this atom. This is reflected in a relatively small rms value of 0.51 for N. Compared to the amino group the oxygens OT1 and OT2 of the carboxylic group show considerably larger rms values of 1.41 and 1.17, which reflects their larger mobility owing to their weaker interaction with the surface.

We can compare our results with recent work of Rimola et al. [16] There, glycine was interacting with the surface through two or three hydrogen bonds, which were directed towards two silanol groups. In our dynamics simulation, however, alanine is interacting with three different silanol groups. Two factors might cause the different interactions: first, we are using a larger simulation cell containing 8 silanol groups whereas the cells of Rimola et al.

contained 2 (high coverage) or 3 (low coverage) such groups. Second, alanine contains a methyl group and has thus a slightly bulkier side chain than glycine which might affect the interaction with the surface.

Regarding the hydrogen bonding pattern, we find some striking differences to the results provided by Rimola et al. [16] In all their structures, except in structure SG-1, they find hydrogen bonding between a proton of the amino group and an oxygen of a silanol. In our simulations, however, the interaction between the nitrogen of the amino group and a silica OH proton is clearly favored.

We may also compare our results to the work presented in Ref. [15] Here, the reaction between a silanol group with glycine in its unionized state (NH_2–CH_2–COOH) was investigated using static density functional methods. The reaction resulted in a structure Si–O–(C=O)–CH_2–NH_2 and the release of one water molecule, i.e. the silanol reacted with the carboxylic part of glycine. However, our simulations suggest the interaction between silanol and amino groups to be favored as compared to the one between silanol and carboxylic groups, thereby reducing the probability for such a reaction.

In order to check for a possible influence of the start structure on the progression of the simulation, we have rerun the vacuum simulations at 100 K with six additional start structures. These structures were constructed as follows: the origin of the coordinate system was moved onto the α-carbon of alanine and the molecule was rotated by plus and minus 90° around the x-, y-, and z-axis, respectively. Five of these six structures showed a similar dynamic behavior as the structure we have discussed in detail above, i.e. the alanine quickly moves towards the silica slab, followed by a proton transfer from the ammonium group to S_a. In one structure, however, due to the short distance between surface and amino acid, an interaction between

the carboxylic group and the surface is formed during the equilibration step. During the succeeding dynamics simulation the carboxylic group approaches the surface and transfers its proton to site S_a, followed by an intramolecular proton transfer from the ammonium group to the carboxylic group. During the ongoing simulation, this structure is dominated by an intramolecular hydrogen bond which weakens the alanine - surface interaction. Placing the alanine only 1 Å further away from the surface, however, prevents the formation of the COOH - surface interaction and allows the ammonium group to orient towards the surface, as in the other structures. Averaged z-coordinates of the N atom together with their standard deviations during the simulation at 100 K are also depicted in Figure 2. The exemplary trajectory we have discussed above agrees well with the averaged trajectory and, thus, provides a reasonable basis for analyzing the dynamical behavior.

3.1.2 Simulation $\mathbf{B}^{Vac}$

Already during the minimization of structure $\mathbf{B}^{Vac}$, a proton transfer from the -NH_3^+ group of alanine to its -COO^- takes place, i.e. the zwitterionic form is not stable without solvent molecules. This observation is consistent with a series of investigations on the stability of glycine in the gas phase (see for example Jensen and Gordon [41] and references given therein). Also, the alanine zwitterion is too far away from the surface in order to be stabilized by interaction with surface hydroxyl groups as was suggested by Rimola et al. [16] Simulation $\mathbf{B}^{Vac}$ thus very quickly switches into configuration $\mathbf{C}^{Vac}$.

3.1.3 Simulation $\mathbf{C}^{Vac}$

Due to the lack of electrostatic interaction between the surface and the unionized alanine molecule, the adsorption process is too slow when the simulation

is started from the original position. Moving the alanine closer to the surface manually ends up in a structure similar to that found after the deprotonation of the alanine cation in simulation $\mathbf{A}^{Vac}$. We therefore expect the same behavior as discussed above in section 3.1.1.

3.2 Simulations with explicit solvent molecules

3.2.1 Simulation $\mathbf{A}^{Sol}$

During equilibration a three dimensional network of hydrogen bonds has been formed. As in the vacuum simulation, following equilibration we first carried out a short dynamics simulation at 100 K. After the restraint on the alanine carbon atom has been released, the electrostatic attraction causes a movement of the alanine towards the surface. However, due to the hydrogen bonding network, this movement is restricted and a relatively stable structure is obtained after about 1 ps in which the amino interacts indirectly with the deprotonated silanol S_a involving two water molecules. Again we take the z coordinate of the alanine nitrogen as a relative measure for the distance of this respective atom to the surface. The z coordinates of the surface oxygen atoms are between 2.14 and 2.71 Å in the vacuum simulation and between 2.11 and 2.69 Å in the simulation with solvent molecules. Figure 4 shows the time development of the z coordinate of the amino group nitrogen in vacuum compared with that in the explicit solvent simulation.

It should be noted that during the whole simulation at 100 K in solution the alanine keeps its protonation state. The carboxylic moiety of the alanine interacts with neighboring water molecules as well. The –O–H part forms a strong hydrogen bond to the oxygen of one water molecule over the whole trajectory. The –C=O group forms weaker, short living hydrogen bonds to

one or two water molecules. Here, the hydrogen bonding partners of the alanine change during the trajectory. The deprotonated silanol S_a interacts with the proton of silanol S_c and with one water molecule which in turn is involved in the bridging between S_a and the alanine. At 100 K no direct interaction between the alanine cation and silanol S_a is found.

After running the dynamics simulation at 100 K for 2.5 ps, the temperature was raised to 300 K. Snapshots of the ongoing simulation are given in Figure 5. After 370 fs, we find a temporal direct interaction between the amino group of alanine and silanol S_a which lasts for about 200 fs (Fig. 5 a). About 60 fs later a water molecule diffuses in between, forming strong hydrogen bonds with the amino group and site S_a (Fig. 5 b). After 845 fs of the simulation, the water molecule releases a proton to S_a, and, only about 30 fs later, the hydroxide ion accepts a proton from the amino group of alanine. The system now consists of a neutral, unionized alanine, a water molecule and a neutral, uncharged surface (Fig. 5 c). The structure obtained at this point corresponds to our system $\mathbf{C}^{Sol}$ and is stable for about 1.715 ps. During these 1.715 ps we do not observe any spontaneous transition of the unionized alanine to its zwitterionic form. Such a proton transfer on the sub-picosecond time scale had been described by Leung and Rempe. [42]) In order to clarify whether this observed stabilization of the unionized form of alanine might be caused through interactions with the surface over hydrogen bonds, we have carried out a dynamics simulation of an unionized alanine in a box of 100 water molecules. Also under these conditions no such proton transfer could be found during 3.0 ps of simulation at 300 K.

After 2578 fs of simulation at 300 K, the amino group is being reprotonated through proton transfer from the same water molecule, and, nearly instantly, the created $^{-}$OH ion accepts the proton from S_a. After several

proton transfers among the groups –NH_2 – H_2O – S_a these three groups become separated from each other. At this point, we are back at a system consisting of a negatively charged surface and the positively charged alanine cation. This structure is now stable for nearly 1 ps.

After this period the carboxylic group releases its proton to a water molecules and, after a series of proton transfers over several water molecules, a proton is released to site S_c (Fig. 5 d) after 6023 fs. The following 4865 fs sees the system to consist of an uncharged surface and an alanin zwitterion that forms hydrogen bonds to various water molecules. This system corresponds now to the simulation system $\mathbf{B}^{Sol}$. Occasionally, the alanine also forms one or two indirect hydrogen bonds through water molecules to the surface (Fig. 5 e). A direct interaction between an amino group proton and the S_a-oxygen appears after 10889 fs (Fig. 5 f). This interaction is manifested in a rapid decrease of the distance of the nitrogen atom from the surface as shown in the upper half of Figure 6.

In the course of the rest of the trajectory, the distance between the amino group proton and the silanol oxygen varies between about 1.6 and 2.5 Å and occasionally, the relatively strict criteria for the formation of a hydrogen bond are fulfilled. As one recognizes in Figure 5 f, at 11.015 ps, this direct interaction is often accompanied by an indirect –N–H $\cdots$ water $\cdots$ silanol interaction.

The stabilization through hydrogen bonds causes the mobility of the alanine atoms to vary to a lesser extent than in the vacuum simulation (see Figure 3). With the exception of the methyl protons, rms values are between 0.55 and 0.89, reflecting a more uniform stabilization of the amino acid than in the vacuum system. On the other hand, we can also notice that the rms value of the amino group nitrogen is considerably larger in solution

than in vacuum, indicating that the direct interaction between the amino group and the surface is smaller in solution than in the vacuum.

3.2.2 Simulation $\mathbf{B}^{Sol}$

At the end of the short equilibration at 100 K, the carboxylic group of the alanine interacts indirectly with the surface via two water molecules. After releasing the constraint of the alanine carbon atom an interaction COO^- – H_2O – surface is formed within 165 fs which stays stable during the remaining time of the dynamics simulation at 100 K. During this part of the trajectory, the ammonium group forms hydrogen bonds to one or two nearby water molecules. No direct or indirect interaction between this group and the surface is found.

Having raised the temperature to 300 K, both the carboxylic and the ammonium group of alanine start to interact indirectly with the surface, each one through one water molecule. The system behaves now like system $\mathbf{A}^{Sol}$ during that part of the trajectory, when alanine was in its zwitterionic state. However, in contrast to simulation $\mathbf{A}^{Sol}$ we do not find any direct interaction with the surface. As a measure for the distance of the alanine from the surface, we again monitor the time development of the z coordinate of the nitrogen atom. This quantity is shown in Figure 6 for all three simulations.

As becomes clear from Fig. 6, the distance between the surface and the amino group in the two simulations is very similar during about 8750 fs of the simulation, although in simulation $\mathbf{A}^{Sol}$, the system undergoes various changes during this period. We conclude that the network of hydrogen bonds is strong enough such that it can not be broken by the attractive electrostatic interaction. The largest difference between trajectories $\mathbf{A}^{Sol}$ and $\mathbf{B}^{Sol}$ is found after about 10 ps of simulation time at 300 K or 12.5 ps of

total dynamics simulation time. Even though both systems were in the same zwitterionic state during the preceding 3.75 ps, suddenly, in simulation $\mathbf{A}^{Sol}$, a direct interaction surface - amino acid is created which involves the formation of a hydrogen bond between one proton of the amino group and the oxygen of group S_a.

3.2.3 Simulation $\mathbf{C}^{Sol}$

After releasing the constraint on the alanine α-carbon we observed only indirect interactions through two water molecules between the amino group of the unionized alanine and the surface at 100 K.

Raising the temperature to 300 K does not alter the structure considerably. Only indirect interactions between alanine and the surface over at least two water molecules are found. Here, the chains of hydrogen bonds are completely absent during longer periods of time. These hydrogen bonds must therefore be less stable than in the previously discussed simulations $\mathbf{A}^{Sol}$ and $\mathbf{B}^{Sol}$. Again, as discussed in section 3.2.1, the unionized alanine seems to be stable and does not spontaneously undergo a proton transfer in order to form the zwitterion.

Already in simulation $\mathbf{A}^{Sol}$ no direct conversion from the unionized alanine to the zwitterion was found. There, the intramolecular proton transfer was catalized by the surface through a proton transfer from the surface to the amino group of the unionized alanine followed by a proton transfer from the –COOH group of alanine to the surface.

4 Conclusion

Using a first-principles molecular-dynamics method we studied the evolution of molecular interactions and structural changes during the adsorption process of an alanine molecule on a hydroxylated silica surface. The simulations were performed under vacuum conditions and in the presence of water molecules.

The strongest electrostatic interactions are present in a system consisting of a positively charged alanine ion and a negatively charged silica slab. In the vacuum simulation (denoted as simulation $\mathbf{A}^{Vac}$), the electrostatic attraction causes the amino acid to move rapidly towards the surface. Once being in contact with the surface, the cation transfers a proton from its ammonium group to the surface revealing an unionized neutral alanine interacting via direct hydrogen bonds with the surface. The dynamics simulation at 300 K is dominated by the interaction between the nitrogen atom of the amino acids amino group and the proton of a silanol group. Only occasionally, interactions between an amino group proton and a silanol oxygen are also found.

Treating the same system in the presence of solvent molecules (simulation $\mathbf{A}^{Sol}$) reveals a different picture. In early stages of the simulation, the alanine cation interacts with the negatively charged surface indirectly through water molecules. After a series of deprotonation and reprotonation steps, the system ends up in an alanine molecule being in the zwitterionic state interacting either indirectly through water molecules or through direct hydrogen bonds with the neutral surface. The finding of different mechanisms for the proton transfer reactions and of different final structures in the two simulations suggest that computational studies without the inclusion of explicit solvent molecules are only of limited value.

Comparing simulations $\mathbf{B}^{Sol}$ and $\mathbf{C}^{Sol}$ we find stronger amino acid - surface interaction in the case of system $\mathbf{B}^{Sol}$, i.e. in the simulation of the zwitterion. Here, the ammonium group interacts stronger with the surface than the carboxylic group, although both interactions are indirect through one water molecule. The attractive interaction between ammonium groups and silica surfaces described in this contribution is known and of technical importance. E.g., poly-d-lysine (PDL) and poly-l-lysine (PLL) are molecules that are incorporated into cells in order to enhance cell attachment to glass surfaces. [43]

5 Acknowledgment

Computations were performed on the Matterhorn Cluster of the University of Zurich. We thank Jürg Hutter and Joost VandeVondele for helpful discussions concerning the program CP2K, the CP2K developers team for providing this software, and J. Robert Huber for critically reading the manuscript. Financial support by Schweizerischer Nationalfonds (SNF) is gratefully acknowledged.

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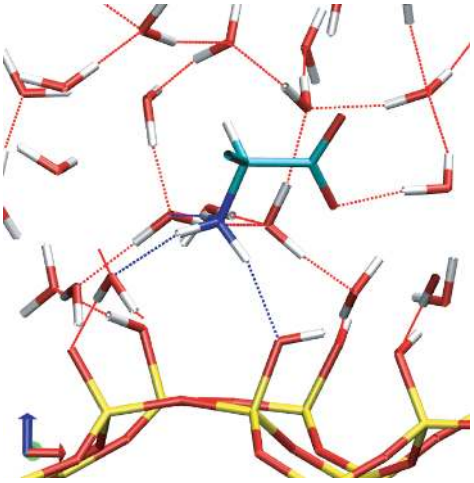

Protein-surface interactions are of importance for various reasons. The microscopic nature of such interactions is investigated using first-principles molecular-dynamics techniques with including solvent molecules. The picture shows a snapshot of a trajectory at 300K with the two dominant amino acid - surface interactions, i.e. a direct hydrogen bonding of one amino hydrogen to the oxygen of a surface silanol and an indirect hydrogen bonding through one water molecule.

Keywords:

density functional theory, hydrogen bonding, molecular dynamics simulation, peptide-surface-interaction, silica

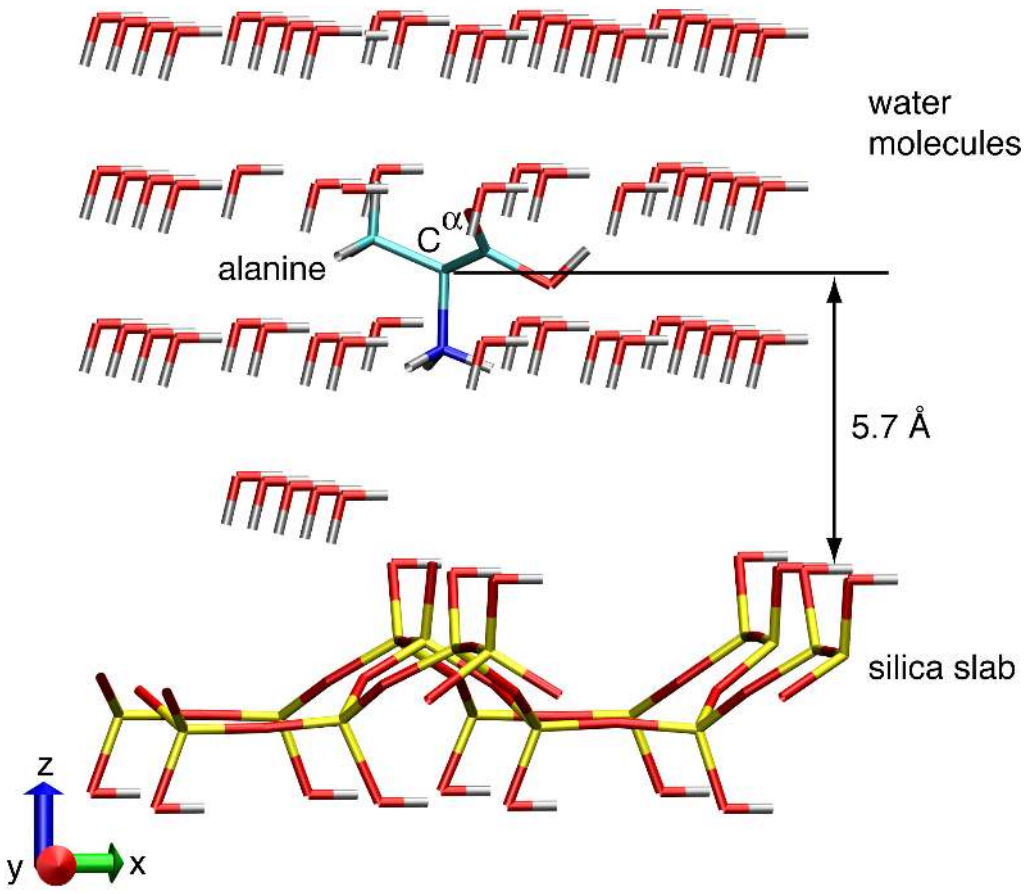

Figure 1: Start structure of the simulation system

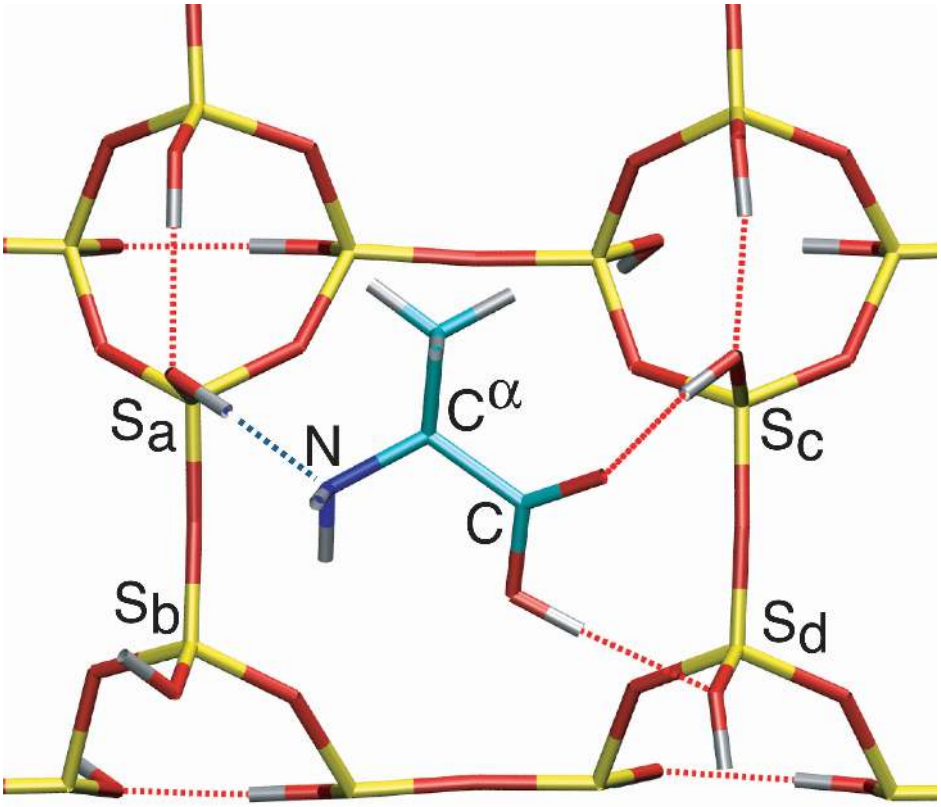

Figure 2: Dominating alanine - surface interactions found in the trajectory simulated at 100 K.

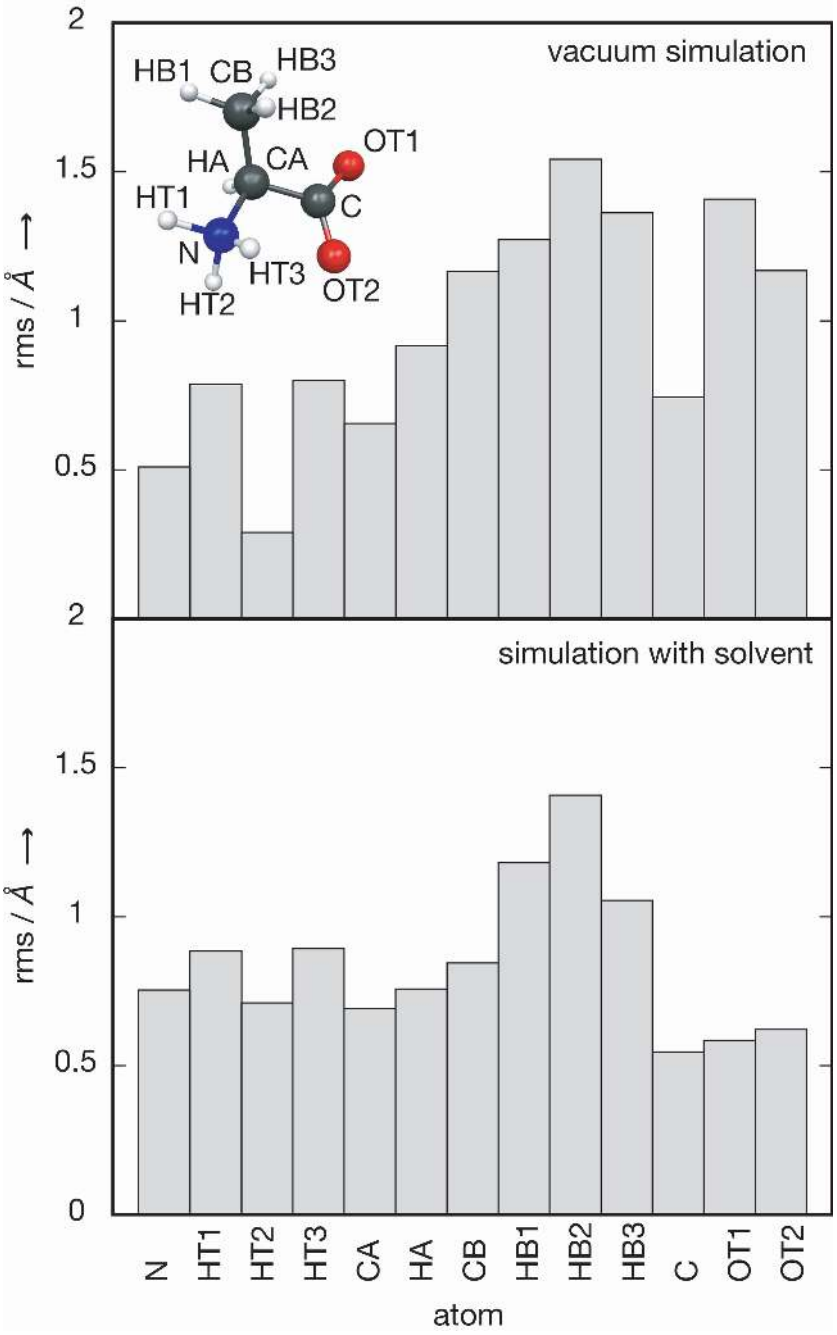

Figure 3: Mobilities of alanine atoms in terms of *rms* deviations from their average positions during the last 5 ps of simulations $\mathbf{A}^{Vac}$ (top) and $\mathbf{A}^{Sol}$ (bottom).

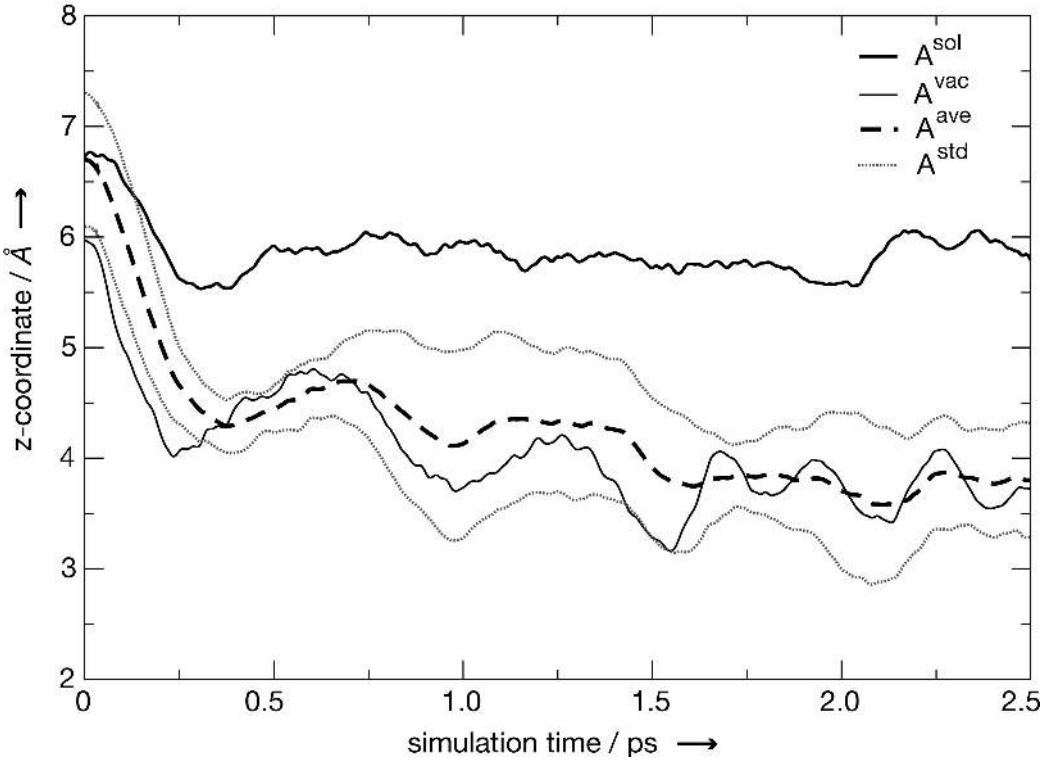

Figure 4: Comparison of the time development of the z coordinate of the amino group nitrogen in simulations at 100 K with and without explicit solvent molecules. The z coordinates of the surface oxygen atoms in these simulations are between 2.14 and 2.71 Å in the vacuum simulation (A^{vac}) and between 2.11 and 2.69 Å in the simulation with solvent molecules (A^{sol}). As well included is the averaged z coordinate of the nitrogen atom (A^{ave}, averaged over 7 trajectories) together with the standard deviation (A^{std}).

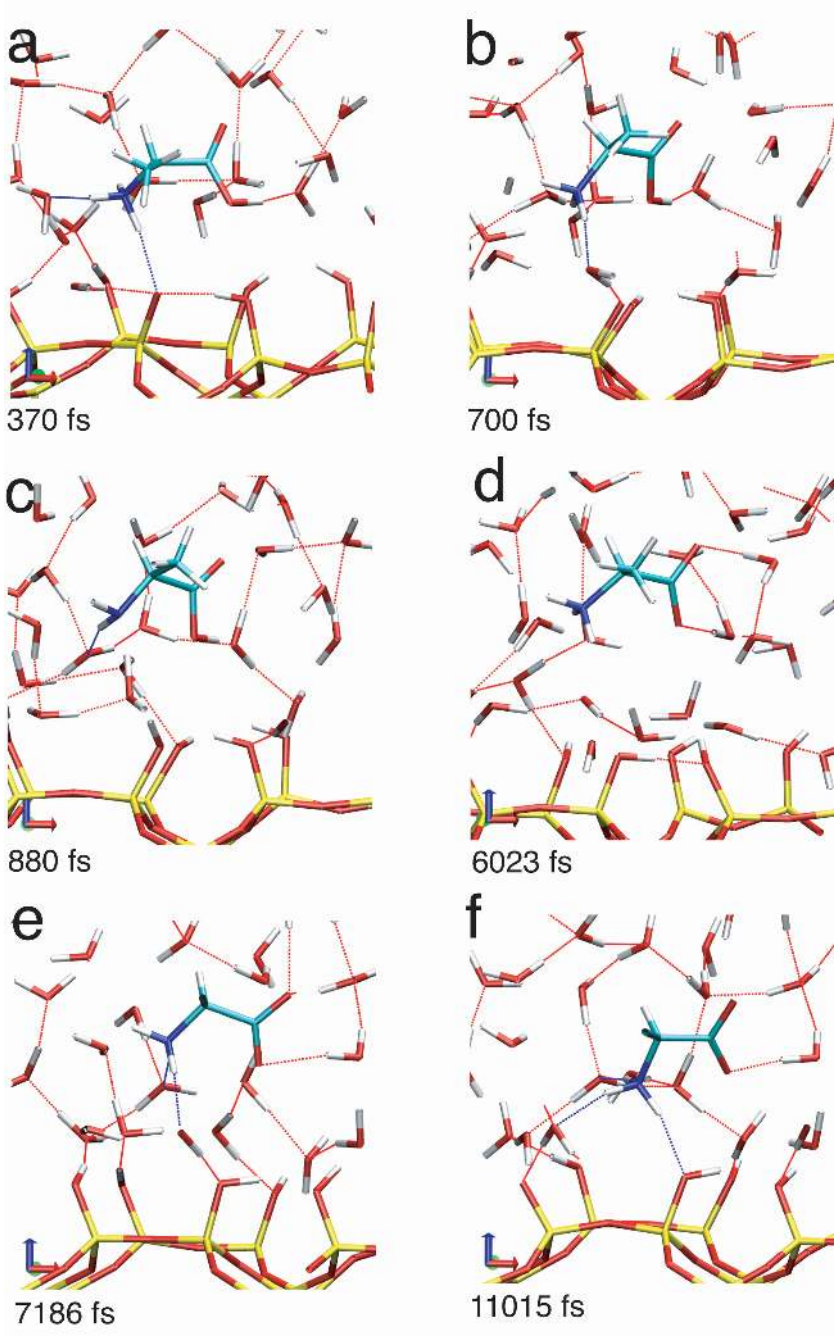

Figure 5: Snapshots during the simulation at 300 K.

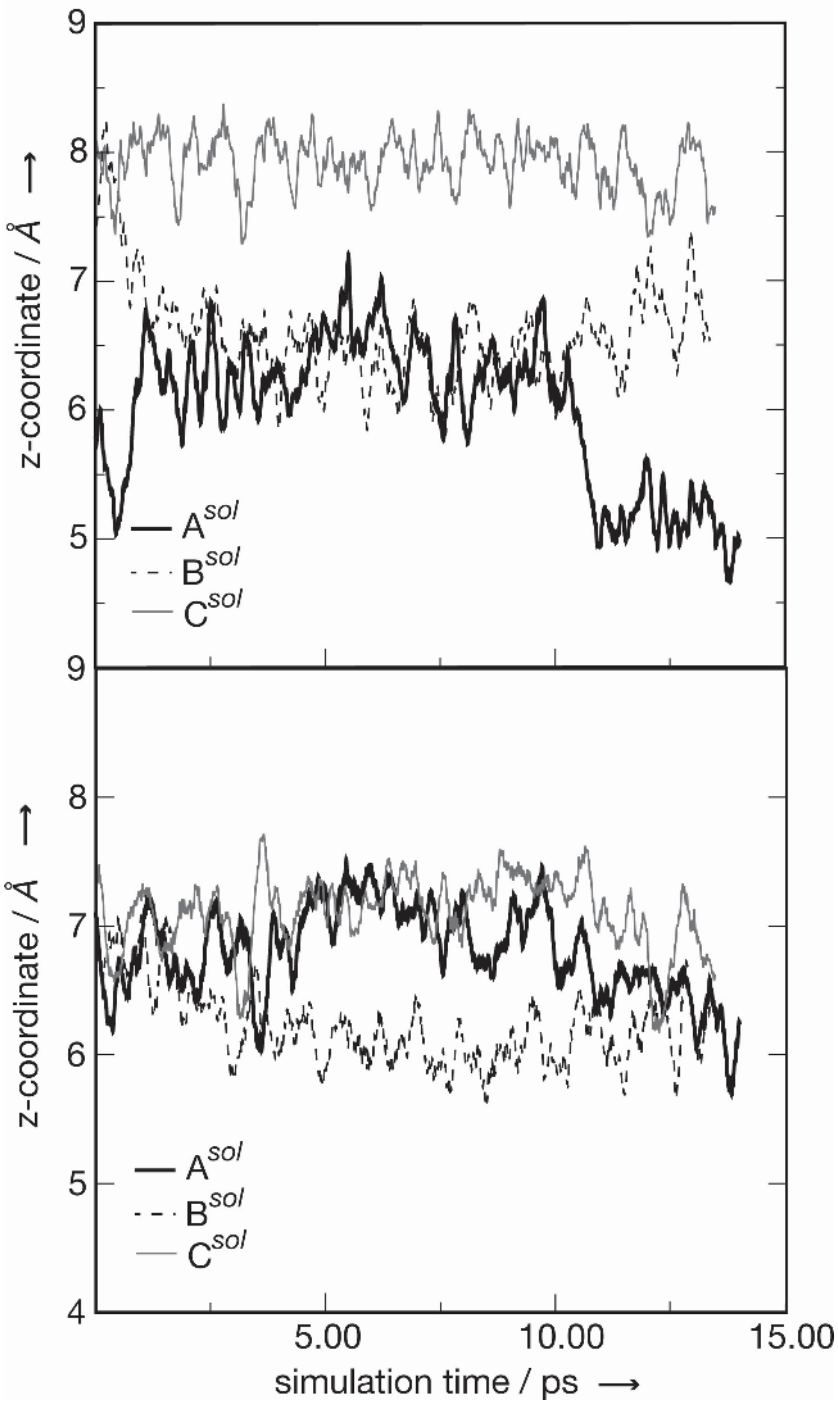

Figure 6: The z coordinates of the amino group nitrogens (top) and of the carboxylic carbons (bottom) in simulations $\mathbf{A}^{Sol}$, $\mathbf{B}^{Sol}$, and $\mathbf{C}^{Sol}$ at 300 K. The z coordinates of the surface oxygen atoms are between 1.91 and 2.74 Å.