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ORIGINAL PAPER

Adsorption of amino acids on the magnetite-(111)-surface: a force field study

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Abstract Magnetite (Fe_3O_4) is an important biomineral, e.g., used by magnetotactic bacteria. The connection between the inorganic magnetite-(111)-surface and the organic parts of the bacteria is the magnetosome membrane. The membrane is built by different magnetosome membrane proteins (MMPs), which are dominated by the four amino acids glycine (Gly), aspartic acid (Asp), leucine (Leu) and glutamic acid (Glu). Force field simulations of the interaction of the magnetite-(111)-surface and the main amino acid compounds offer the possibility to investigate if and how the membrane proteins could interact with the mineral surface thus providing an atomistic view on the respective binding sites. In a force field simulation the four amino acids were docked on the Fe-terminated magnetite-(111)-surface. The results show that it is energetically favorable for the amino acids to adsorb on the surface with Fe-O-distances between 2.6 Å and 4.1 Å. The involved O-atoms belong to the carboxyl-group (Asp and Glu) or to the carboxylate-group (Gly, Leu and Glu). Electrostatic interactions dominate the physisorption of the amino acids. During the simulations, according to the frequency of the best results, the global minimum for the docking interaction could be attained for all amino acids analyzed.

Keywords Adsorption · Amino acids · Force field simulations · Magnetite · Surface

Introduction

Magnetite (Fe_3O_4) is a well known oxide mineral of the spinel group which crystallizes in the inverse spinel structure. Its crystal and magnetic structure has been investigated many times by different methods such as X-ray diffraction [1] and neutron diffraction [2]. The structure of the magnetite-surface has been investigated with different experimental and numerical methods, e.g., LEED [3], STM [4], density functional studies [4] and spin-density functional theory [5] showing a good agreement in the atomic arrangement of the surface structure.

Because of its physical and chemical properties, magnetite is used for different applications such as, e.g., pigment, spintronic-components or as catalytic material [6]. In nature magnetite plays a very important role as a biomineral [7], e.g., bees, many birds and fishes use its permanent magnetic property in order to orientate themselves in the earth magnetic field.

In particular the reactivity and the atomic structure of the magnetite surface are very important for surface processes. They mainly influence the interaction between the inorganic magnetite surface and the organic parts of the cell called magnetosome membrane. Grünberg et al. [8] and Schüler [9] investigated the magnetosome membrane of the magnetotactic bacteria (MTB) *Magnetospirillum gryphiswaldense*. The membrane in *Magnetospirillum gryphiswaldense* is composed of many different magnetosome membrane proteins (MMPs). Two of these MMPs are the proteins MamJ and MamG. The structure of MamJ is dominated by the amino acids aspartic acid (Asp) and glutamic acid (Glu) [8], whereas in the structure of MamG glycine (Gly) and leucine (Leu) are dominating [9].

Repetitive motifs of amino acids with acidic groups are common in proteins involved in the crystal nucleation process of other biomineralization systems, e.g., mollusk shells and coccolithophorids [10, 11]. Their strong affinity for metal ions makes them probable binding partners for the interaction between membrane proteins and the growing crystal. Therefore Grünberg et al. speculate that MamJ and other acidic proteins are directly involved in the biomineralization process

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by providing iron binding sites through their acidic amino acid patterns [8]. The complex atomic structure of the proteins and their assembly in the magnetosome membrane is not known yet and it is both experimentally and theoretically difficult to obtain information about structure and function of the MMPs. To find out if the four acidic main constituents of the proteins MamJ and MamG provide a suitable binding site for magnetite crystals, molecular dynamic force field simulations of the interaction of the single amino acid molecules Asp, Glu, Gly and Leu with the magnetite-(111)-surface were carried out. By comparing the relative energies of the amino acids docked on the surface and analyzing the binding sites and bond distances, information about the physisorption process, the involved atoms, their binding modes and binding strengths are obtained.

Force field simulations provide a suitable tool for the investigation of adsorption processes between crystalline surfaces and amino acids, as shown, e.g., by Magdans et al. [12] and Pareek et al. [13, 14], since long range Coulomb interactions play a dominant role. In contrast to density functional studies [15–17] force field simulations also allow to calculate systems with a large number of atoms. Force field simulations carried out in this study consist of two phases. In the dynamical simulation phase, the most probable conformations of the entire system will be found and saved to a trajectory file. The second phase is the energy minimization. In this phase the energy of the conformations in the trajectory file is minimized, resulting in a local or the global minimum structures of the system. The energy minimization uses Newtonian mechanics to simulate molecular systems and to calculate interactions between the two systems. All atoms, bondings, torsions, movements around bondings or axes, van-der-Waals interactions and electrostatic interactions are defined as potentials. These potentials are saved in force fields. In order to describe the processes of docking and interaction with high enough precision it is very crucial for the system to use the appropriate force field for every simulation problem.

Methods

For the simulation studies, the morphologically most dominant (111)-surface of magnetite has been chosen. As study cases four isolated amino acids were selected which are most abundant in the magnetosome membrane proteins: glycine

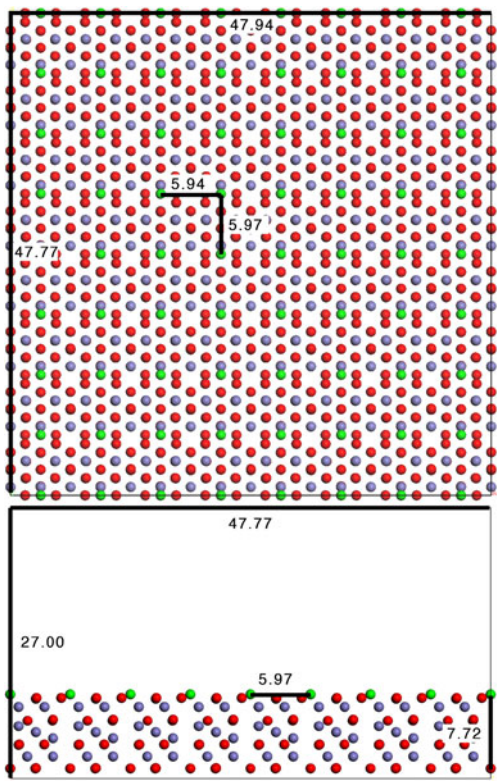

Fig. 1 Topview (upper part) and sideview (lower part) of the relaxed magnetite-(111)-surface slab build from the relaxed surface structure of Ritter and Weiss [3]. All distances in Å. *Green*: Fe-atoms of the topmost Fe-layer, *blue*: Fe-atoms and *red*: O-atoms

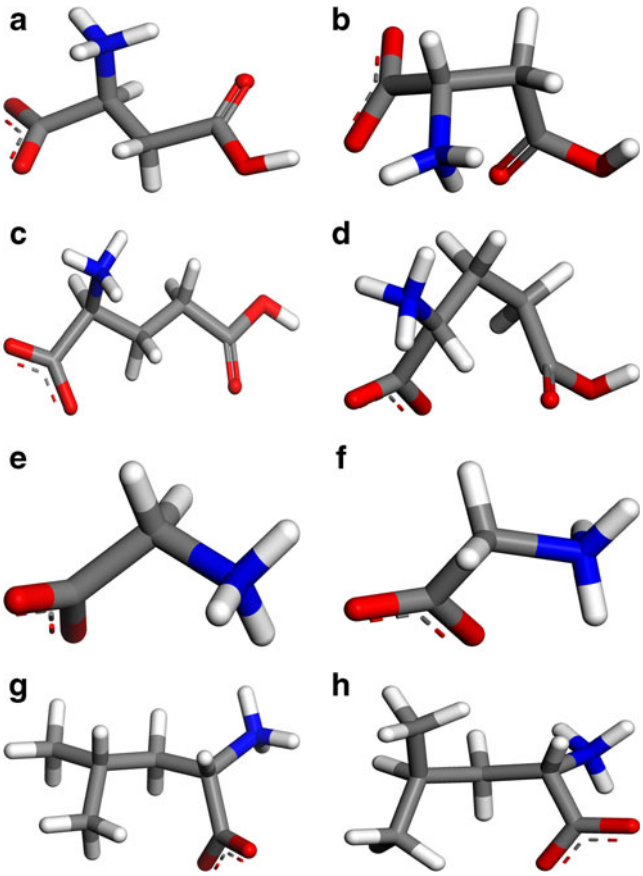

Fig. 2 Conformations of the amino acid molecules before and after the docking on the magnetite-(111)-surface. *Left column*: before simulation, *right column*: after simulation. **a**,**b** Asp **c**,**d** Glu **e**,**f** Gly and **g**,**h** Leu

Table 1 Distances, electrostatic interactions, van-der-Waals (vdW) interactions, calculated energies and resulting binding modes of the simulations of the amino acids on the magnetite-(111)-surface. All energies in this table are relative energies

Amino acids	E_{amino} [kcal/mol]	E_{total} [kcal/mol]	Electrostatic interaction [kcal/mol]	vdW interaction [kcal/mol]	ΔE [kcal/mol]	Fe-O distance [Å]	Binding mode
Gly	63.5	-216.5	-231.8	1.1	-280.1	2.7[a] 4.1[a]	bridging
Asp	12.6	-316.3	-343.8	2.4	-328.9	2.7[b] 3.9[b]	bidentate
Leu	37.3	-350.7	-367.2	0.8	-387.9	2.6[a] 4.1[a]	bridging
Glu	43.8	-448.2	-505.6	3.9	-492.0	2.6[a] 3.6[a]	bidentate
						3.7[b] 3.8[b]	bridging

[a] O-atoms of the carboxylate (COO^-)-group [b] O-atoms of the carboxyl (COOH)-group

(Gly), leucine (Leu), glutamic acid (Glu) and aspartic acid (Asp). Since their functional groups most likely determine the interaction with the mineral surface the case study should mimic the membrane-mineral surface interactions.

Amino acids in aqueous solution undergo protonation and deprotonation reactions dependent on the *pH*. This also varies the charge distribution in the molecule and influences the conformation state. In order to have a common basis for comparison, in this study the conformation of the amino acids at their isoelectric points were used, where the molecules are charge-neutral. The isoelectric point of Gly is at a *pH* of 5.97, for Asp at 2.77, for Leu at 5.98 and for Glu at 3.22 [18]. The single amino acid molecules were geometry optimized with Forcite [19], using the COMPASS force field. Here also the partial charges were determined.

The magnetite-(111)-surface is a polar surface when cut from the bulk structure and will stabilize through relaxation. In this study the relaxed surface structure of the magnetite-(111)-surface was built using the magnetite atom positions from the LEED analysis of the relaxed surface structure of magnetite from Ritter and Weiss [3]. During the simulation the surface structure was constrained. The docking box consisted of a 47.49 Å × 47.77 Å × 7.72 Å magnetite-(111)-surface slab with a vacuum slab of 19.28 Å high on top.

The simulations were carried out in Forcite [19], which is integrated in the software package Materials Studio 5.0 [20]. The COMPASS force field [21] was found to provide all necessary parameters for the potentials of the amino acids and of the magnetite surface. This force field has been used in many different simulations [22–24]. Initially the parameters of the COMPASS force field have been obtained from ab initio quantum mechanics calculations [21]. To obtain the global energy minimum conformation of the surface and amino acid system the quenching method was used with a pressure of 0.1 GPa working at a temperature of 298 K during the energy minimization step. During the dynamical phase of the quenching process the temperature was increased to

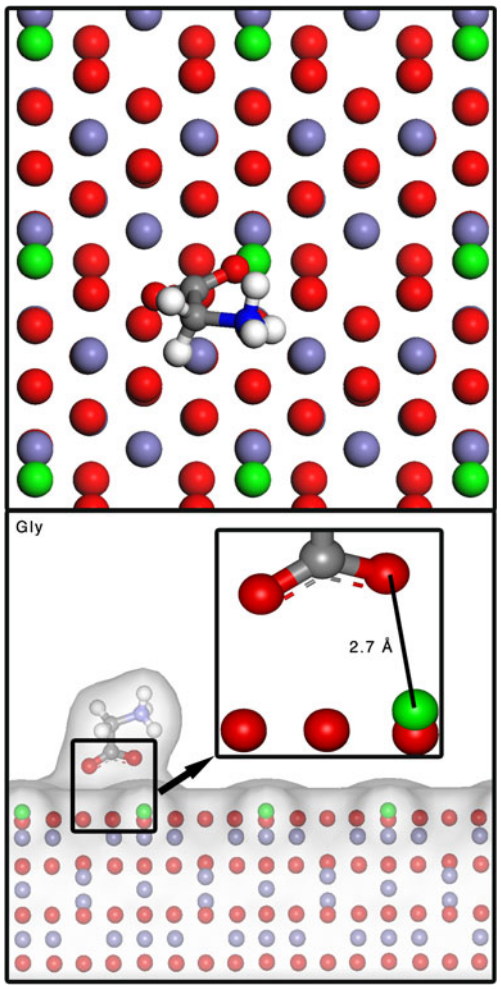

Fig. 3 Topview (*upper part*) and sideview (*lower part*) of the amino acid Gly docked on the magnetite-(111)-surface. Gly adsorbs above a Fe-atom of the topmost Fe-layer in bridging binding mode. The distance between the topmost Fe-atom and the O-atom of the carboxylate (COO^-)-group of Gly is 2.7 Å. *Cloudy white*: electrostatic potential, *green*: Fe-atoms of the topmost Fe-layer, *blue*: N-atoms, *purple*: other Fe-atoms, *red*: O-atoms, *white*: H-atoms and *gray*: C-atoms

2658 K and later cooled down to 298 K. The simulations were carried out in vacuum conditions without a solvent. The whole system was treated as NVE ensemble with constant N (number of atoms), V (volume) and E (energy). A cutoff radius of 10 Å, a time step of 1 fs, a total simulation time of 100 ps and 100,000 steps were chosen as simulation parameters. This resulted in 1000 system conformations (frames) per simulation. For each amino acid the simulations were repeated ten times resulting in 10,000 frames per amino acid for obtaining the energetically most favorable adsorption conformation of each amino acid on the (111)-magnetite surface.

For a better comparison between the results of all simulations the relative specific adsorption energy ΔE and the absolute value $|\Delta E|$ were calculated according to the following equation:

$$\Delta E = E_{total} - E_{amino} - E_{surface} \quad (1)$$

E_{total} is the relative energy of the whole system and was calculated after finishing the simulation. E_{amino} is the relative energy of the free amino acid molecule geometry optimized before it was docked on the surface. Due to the selection of the relaxed surface as a constraint (the relative energy of the magnetite-(111)-surface $E_{surface}$ remains constant for all of the four amino acids) the equation reduces to:

$$\Delta E = E_{total} - E_{amino} \quad (2)$$

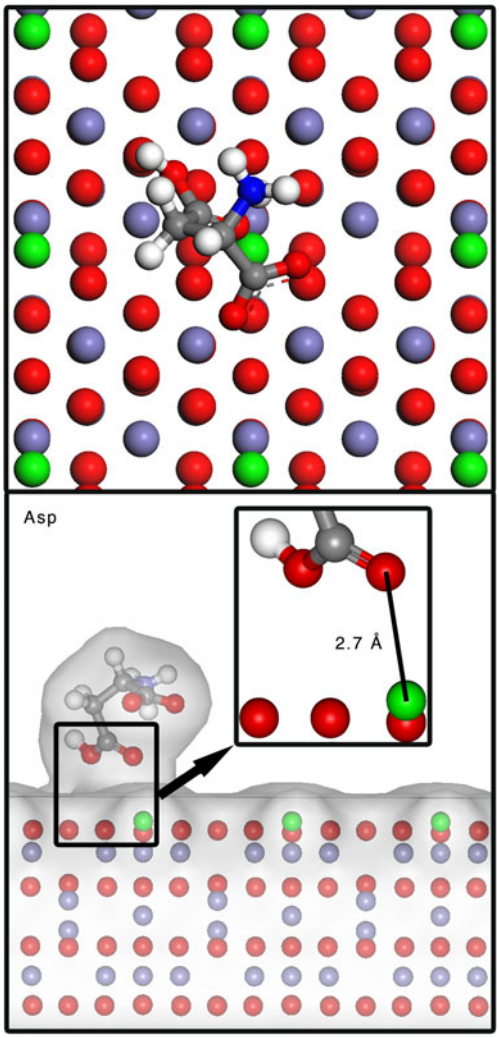

Fig. 4 Topview (*upper part*) and sideview (*lower part*) of the amino acid Asp docked on the magnetite-(111)-surface. Asp adsorbs above a Fe-atom of the topmost Fe-layer in bidentate binding mode. The distance between the topmost Fe-atom and the O-atom of the carboxyl (COOH)-group of Asp is 2.7 Å. *Cloudy white*: electrostatic potential, *green*: Fe-atoms of the topmost Fe-layer, *blue*: N-atoms, *purple*: other Fe-atoms, *red*: O-atoms, *white*: H-atoms and *gray*: C-atoms

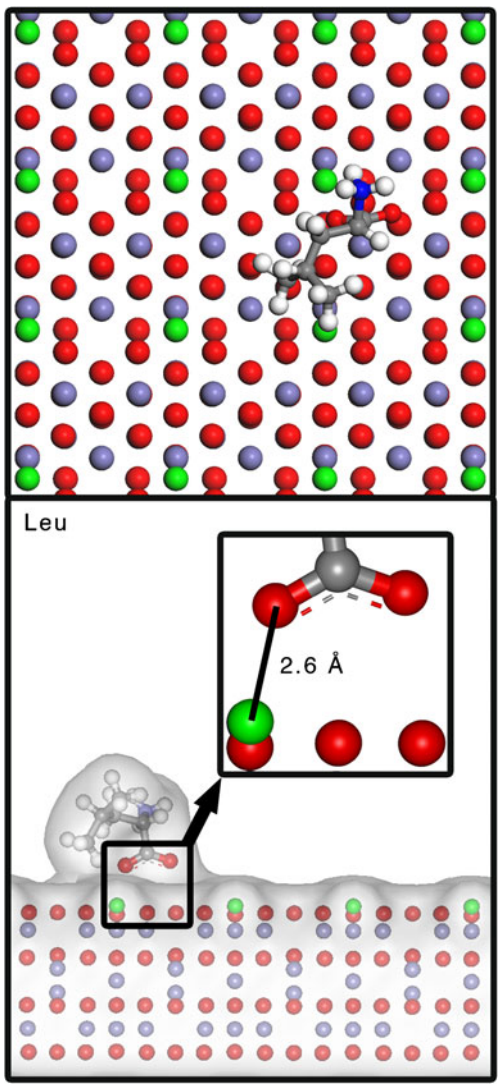

Fig. 5 Topview (*upper part*) and sideview (*lower part*) of the amino acid Leu docked on the magnetite-(111)-surface. Leu adsorbs between two Fe-atom of the topmost Fe-layer in bridging binding mode. The distance between the topmost Fe-atom and the O-atom of the carboxylate (COO^-)-group of Leu is 2.6 Å. *Cloudy white*: electrostatic potential, *green*: Fe-atoms of the topmost Fe-layer, *blue*: N-atoms, *purple*: other Fe-atoms, *red*: O-atoms, *white*: H-atoms and *gray*: C-atoms

with the already explained parameters. ΔE provides information about the relative physisorption strength of the amino acid-(111)-magnetite interaction. ΔE and $|\Delta E|$ have been calculated for the energetically most favorable amino acid conformation only.

Results and discussion

The surface structure of the magnetite-(111)-surface is described in detail with all coordinates of the atoms and with their differences to the magnetite bulk structure by Ritter and Weiss [3]. The relaxation process of the magnetite-(111)-surface itself is described in detail by Zhu et al. [25]. The surface consists of Fe^{3+}-atoms protruding from a hexagonal close-packed oxygen layer underneath [3]. Immediately below the topmost Fe-layer the first O-atom layer follows. The topmost Fe-atoms have almost equal distances to their next Fe-neighbors of 5.94 Å and 5.97 Å (see Fig. 1).

The start conformation of the amino acid molecules were energy minimized in vacuum. Due to the interactions between the amino acids and the magnetite-(111)-surface the amino acids alter their conformation (see Fig. 2) which is particularly obvious in the reorientation of the –COOH and CH_2 groups which move away from the $–COO^-$ groups building the surface connecting anchors of the molecules.

For all amino acids the global minimum energy docking sites on the magnetite-(111)-surface were determined. The resulting energies and the calculated relative values of ΔE are displayed in Table 1. The exothermic values of ΔE show that it is energetically favorable for the amino acid molecules to dock onto the magnetite surface. The molecule-surface interaction is dominated by electrostatic forces between the topmost Fe^{3+}-atoms and the negatively charged O-atoms of the carboxyl- and carboxylate-groups. Only very small proportions of the overall interaction can be attributed to the van-der-Waals interaction (see Table 1).

Comparing the absolute values $|\Delta E|$ reveals differences in the strength of adsorption for the amino acids studied. The

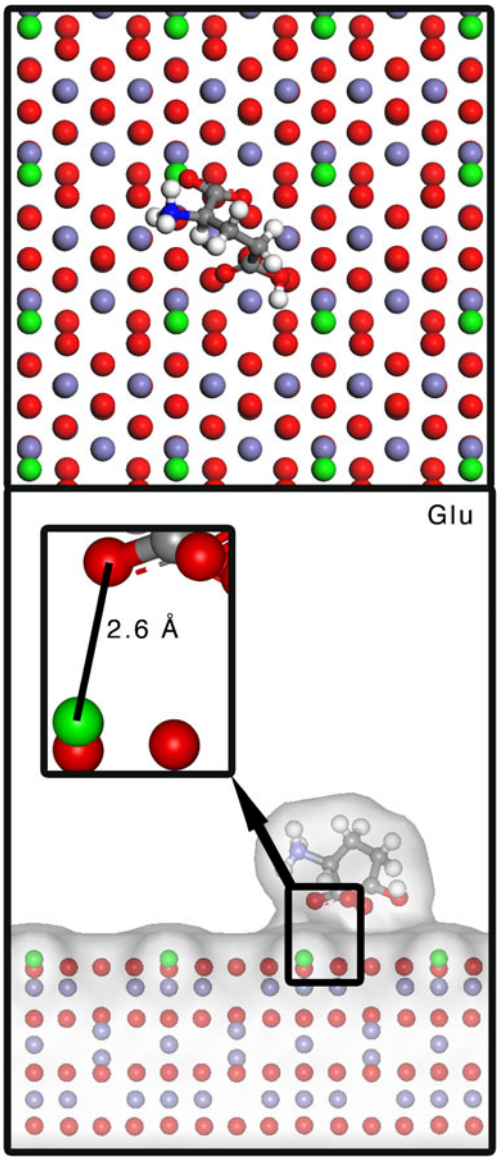

Fig. 6 Topview (*upper part*) and sideview (*lower part*) of the amino acid Glu docked on the magnetite-(111)-surface. Glu adsorbs between four Fe-atom of the topmost Fe-layer in bidentate binding mode. The distance between the topmost Fe-atom and the O-atom of the carboxylate (COO^-)-group of Glu is 2.6 Å. *Cloudy white*: electrostatic potential, *green*: Fe-atoms of the topmost Fe-layer, *blue*: N-atoms, *purple*: other Fe-atoms, *red*: O-atoms, *white*: H-atoms and *gray*: C-atoms

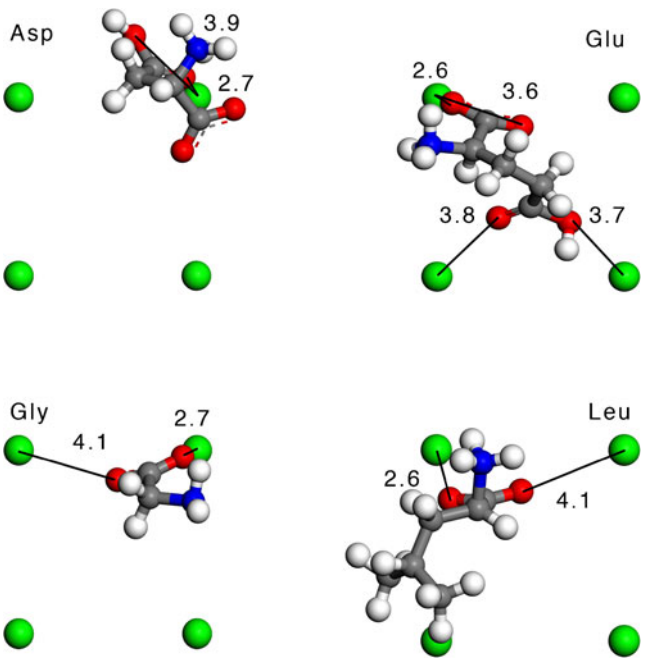

Fig. 7 Binding modes and Fe-O distances of the amino acids and the topmost Fe-layer of the magnetite-(111)-surface. All distances in Å. *Green*: Fe-atoms of the topmost Fe-layer, *blue*: N-atoms, *red*: O-atoms, *white*: H-atoms and *gray*: C-atoms

absolute values range from 280.1 kcal/mol for Gly to 492.0 kcal/mol for Glu, respectively. The absolute values of Asp (328.9 kcal/mol) and Leu (387.9 kcal/mol) are in between. Thus, in vacuum conditions, Glu with the four docking O-atoms adsorbs most strongly on the surface, followed by Leu and Asp, both have two docking O-atoms. Gly shows the least strong binding energy with two docking O-atoms.

The distances between the amino acids and the surface are in the range from 2.6 Å to 4.1 Å (see Table 1). The relevant distances building up the strongest interactions in all samples are the Fe-O-distances between the topmost Fe-layer of the mineral and the nearest O-atom of the carboxyl-group (Asp and Glu) or the carboxylate-group (Gly, Leu and Glu) (see Figs. 3, 4, 5 and 6).

Differences between the four amino acids can be found in the adsorption position on the surface. Each O-atom of the carboxylate (COO^-)-group of Gly and Leu adsorbs above one of the Fe-atoms of the topmost Fe-layer in bridging binding mode, whereas the O-atoms of the carboxyl (COOH)-group of Asp adsorb above one Fe-atom of the topmost Fe-layer in bidentate binding mode (see Fig. 7). For Glu the carboxylate-group adsorbs in bidentate binding mode and the carboxyl-group adsorbs in bridging binding mode above the topmost Fe-layer (see Fig. 7).

All measured distances between the topmost Fe-layer of the surface and the nearest O-atom of the amino acids are in good agreement with typical values of bonds dominated by electrostatic interactions. To the best of our knowledge there are no other studies of the interaction between the four amino acids and the relaxed magnetite-(111)-surface. Due to that we can only compare our results with results including the amino acids or the relaxed magnetite-(111)-surface on the one hand and results of other adsorption simulations or experiments on the other hand, e.g., Nyberg et al. describe the adsorption distances between the O-atom of the carboxylate-group of Gly and the Cu-(111)-surface simulated by DFT studies [26]. Their results are 2.02 Å, 2.07 Å and 2.11 Å surface distances for the different conformations of Gly. In addition to these results Guo et al. [27] report some adsorption distances of Asp on the pure rutile-(110)-surface of 2.648 Å between Ti- and O-atoms. Their results are based on DFT studies, too.

An experimental model of the adsorption of an aqueous film of Gly on the fluorapatite-(001)-surface is given by Pareek et al. [13]. They report a distance of 2.44 Å and 2.47 Å between the Ca-surface atoms and the nearest Gly O-atoms, measured with grazing incidence X-ray diffraction (GIXRD).

Another experimental and simulation model of the adsorption of aqueous Gly solution on the calcite-(104)-surface is given by Magdans et al. [12]. In their surface diffraction experiment they measured distances of 3.5 Å–4.9Å between the Ca-surface and the nearest O-atoms of Gly, in agreement with distances between 3.2 Å and 4.5 Å obtained from force field simulations. Information about the energy values were not given by the authors. The higher binding distances are due to the water environment, consisting of a water layer directly above and around the Gly molecules ($Ca\text{-}O_{H2O}$ distances of 2.45 Å).

The distances, measured in this study, are in good agreement with those given by the literature resulting from different simulation methods and experiments.

Conclusions

The molecular dynamics simulations of the interaction of single amino acids with the magnetite-(111)-surface prove the metal ion binding function of the acidic amino groups to the iron determined magnetite surface. The results of the study indicate that the membrane proteins MamJ and MamG are indeed involved in the biomineralization process by providing iron binding sites through their acidic amino patterns. As expected, the interaction is dominated by electrostatic forces between the Fe^{3+}-surface atoms and the O-atoms of the carboxyl- and carboxylate-groups of the molecules, respectively.

This study provides evidence for the affinity of acidic amino acid patterns mainly present in the membrane proteins MamJ and MamG, to bind on the Fe^{3+} ion determined magnetite surface, but as long as the atomic structure, position and orientation of the proteins in the magnetosome membrane are not yet determined, detailed information about the interactions and binding sites and function of the complex membrane proteins will remain a topic of investigation.

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