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Functionalized metal-organic frameworks interacting with Histidine amino acid: DFT study

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Abstract: The study of complexes between nanostructures and biomolecules has attracted the attention of many researchers in various fields because it can contribute to the coherent growth and widespread use of nanostructures in various technologies. One of the main goals is to fabricate structures with functional surfaces where proteins become immobilized without losing their biological activity. In this research, following a comprehensive approach, the interaction between different amino acids and metal-organic frameworks (MOFs) at atomic scale was evaluated using computational chemistry. For this purpose, density functional theory (DFT-D2) calculations was employed to afford a molecular description of the interaction properties of the amino acids and MOF-5 by examining the interaction energy and the electronic structure of the amino acid/MOF complexes. Strong interactions between the amino acids and MOF through their polar groups were reported as well as aromatic rings in the gas phase. However, findings were significantly different in solvent media, where water molecules prevent the amino acids from approaching the active sites of MOF, causing weak attractions between them. The accuracy of the DFT-PBE model of theory was validated against the comprehensive MP2 quantum level of theory. Comparing the present results with those obtained for perfect MOFs show that the binding energy of the Histidine amino acid is increased for physisorption on defected MOFs.

Keywords: MOFs, Amino acids, DFT, Functionalization, Nanotechnology.

Introduction

Drug delivery systems are one of the most promising applications for human health care and represent an ever-evolving field for biomedical materials science [1-4]. In the area of drug delivery, looking for appropriate non-toxic carriers which is efficient for drugs delivery to the body is a crucial challenge [5-7]. Until now a lot of different strategies have been studied for bio-applications, such as organic polymers [8] and inorganic porous materials [9, 10]. However, their applications are limited either by lower drug-loading capacity or by uncontrolled release. To circumvent these problems, a new avenue has recently been explored, that is employing metal-organic frameworks (MOFs) as carriers for biomedical applications.

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MOFs represent a new born family of hybrid inorganic--organic materials which are formed by the self-assembly of metals (single-metal ions, metal clusters, or metal chains) and organic linkers under mild conditions [11] and have already shown promise in a number of applications, including catalysis, nonlinear optics, luminescence, gas separation, and gas storage [12-19]. Compared to organic porous materials (e.g., carbons) or inorganic counterparts (e.g., zeolites, silica), MOFs as potential drug carriers have some unique advantages. Nucleo-bases are nitrogen containing biological compounds which are found in nucleotides, the basic building blocks of DNA and RNA and play a central role in all biological systems. Recently much attention has been devoted to the adsorption of bio-molecules such as proteins, DNA and nucleo-bases onto the surface of nano-materials for their potential therapeutic applications [5–11].

Several computational research studies have recently been used to apply various theoretical methods, including molecular mechanics, the theory of density of citizenship, and even the hierarchy of atomic orbitals, in addition to the Muller-Plast disorder theory. In another theoretical study of the binding of amino acids of collagen (eg glycine, proline, hydroxyproline) to graphene and graphene contaminated with calcium using calculations of the density of citizenship theory [8], which showed that glycine, proline and hydroxyproline binding is desirable, but depends on the direction of the acid. Simulation based on molecular mechanics shows that thermal room temperature stimulation for the separation of glycine and proline from graphene is enough and to isolate all three amino acids from calcium-doped graphene. Scientists have recently proven that the transfer and expression of the gene using carbon nanotubes and their guidance to produce target proteins results in coding in a double-stranded pDNA. For example, pDNA and the expression of β-galactosidase gene in the hamster ovary are five to ten times that of a single pDNA alone [9]. In another study, a gene release system consisting of carbon nanotubes carrying nickel particles presented that were placed inside the nano-tubes and pDNA adsorbed on the surface of the nanotubes. By applying a foreign magnetic field, the researchers showed that the combination of pDNA-CNT was introduced into the mammalian cells and the gene appeared in 80 to 100% of the infected cells [10]. Optical absorption of different gold isomers was investigated by DFT method at different frequencies from IR to UV to detect geometric structure. It was observed that there is a difference between the absorption spectrum of gold in a twenty-fold and isoamorphic state [11]. Gold nano-particles provide good material for the delivery of drug and gene drugs, which is a useful ingredient for the transport of information [12, 13]. A theoretical study has been presented on the interaction between various DNA, RNA and various Nanoparticles of ZnO, such as ZnO nano wires, nanotubes, surfaces and quantum dots (QD3). They used the DFTB quantum mechanics method to optimize the complex system. The specific nature of the site and the strength of absorbing these nucleic acids with different nanoparticles, ZnO, prefer to connect with a single pair through a high location of nucleic acids with nitrogen atoms of the ring [14]. The nano-silver nano-cluster (AgNC) used as a carrier for oligo-olothiots to illustrate and deactivate the targeted micro-RNA genes [15]. Exploiting multi-core magnetic nanoscale molecules has been developed for genes delivery, transmission and tracing of stem cells, and achieving desirable and targeted results. The results suggest that this new type of nano-composite can be found in stem cell research and is useful in the development of cell-based therapeutic agents [16]. Several groups focused on determining the type of interaction of DNA-CNT and attempted to investigate the nucleic acid binding of nucleo-bases and different pairs on carbon nanotubes and graphene, either in experimental or computational studies [17-21]. Laboratory studies show different degrees of energy transitions for various studies that may be due to different laboratory conditions. In computational studies, for most cases, G> A> T> C> U is an order of magnitude, and in some cases they could not detect nucleo-bases such as T, A, and C, and rank them as G ~ A ~ T ~ C> U.

In this study, nano-composites based on molecular scale nanostructures are investigated. Stability, absorption energy, absorption power as well as molecular, electron and geometric structure, atomic loads on nano-materials are investigated. The goal is to identify suitable nano-composites based on biological nano-structures and metal-organic frames for effective gene/drug delivery, which is of great biological significance. Investigations of the electronic structure of nano-structures studied in the design of suitable nano-sensors for biological compounds, and in particular the sequencing of DNA, can be applied. The purpose of the calculations is to lower the cost, speed, and acceptable accuracy in the design of the appropriate nano-composite for the gene/drug delivery.

Significant of the study

The use of nano-materials for drug delivery attracted many researchers. The potential benefits of this method are:

- Drug delivery, especially in long-term drug delivery at low doses
- Minimizing side effects of the drug. By investigating the interaction between biological molecules and organic carvings, the carriers can be used to make use of these Nano-structures in drug delivery and gene transfer.

With the advances made in computational chemistry, many scientists come up with simulation techniques to,

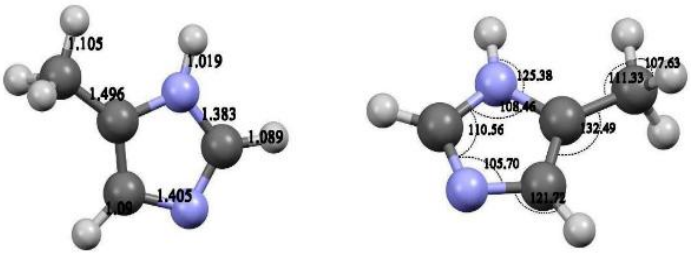
- Examine many processes, especially toxins that are not economically feasible in their laboratory tests.

▶ Also, studying the interactions between chemicals and nanostructures by using laboratory methods is very difficult, costly and time consuming

▶ Simulations of quantum mechanics and molecular dynamics can effectively evaluate these interactions, determine and predict the properties of materials, as well as the amount and power of interaction between different types of molecules with nanostructures.

Results and discussion

To evaluate the interaction between a Histidine molecule and MOF, at the first, the binding energy (Eb) of adsorbed systems was calculated. To this end, the stable adsorption geometry of Histidine on pristine was searched and functionalized MOF starting from different initial geometrical configurations. The structure of Histidine has been widely examined both experimentally and theoretically using quantum chemical calculations [20–22]. The geometric parameters of Histidine obtained in this work (Figure **1a**) are consistent with the literature [20–22].



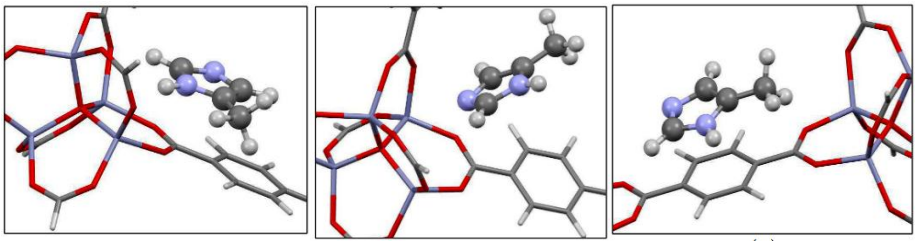


Figure 1. (a) Geometric parameters of the optimized structure of Histidine molecule. Model for different adsorption states for Histidine on the MOF above the center of a hexagon of carbon atoms approaching via its (b) CH2 , (c) CO, (d) NH2 and (e) OH groups. Atom colors: gray–carbon, white–hydrogen, blue–nitrogen and red–oxygen. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.

Histidine molecule is placed above the hollow site of the hexagon of tube surface via its four related active sites, i.e. amino nitrogen (N), hydroxyl oxygen (OH), methyl (CH_2) and carbonyl oxygen (O) groups. The graphical representations of the initial configurations of HIS–MOF systems are shown in Figure **1**. After full structural optimization of the selected complexes, Histidine molecule is found to be adsorbed onto the exterior side of the MOF through its CH_2 group. The calculated Eb value and equilibrium distance between two closest atoms of the considered molecules are 0.17 eV (3.92 kcal/mol) and 2.334 ˚A, respectively. Our calculated values of the binding energy and equilibrium distance are typical for physisorption [23–29], which are comparable with the other theoretical results [8–11]. Adsorption of Histidine on the functiona- lized MOF has been investigated. For this propose, MOF functionalized by COOH, OH and CHO groups has been considered. The orientation schemes employed in modeling Histidine interacting with F-MOF by CHO groups (F–MOF–CHO) are presented in Figure **2**.

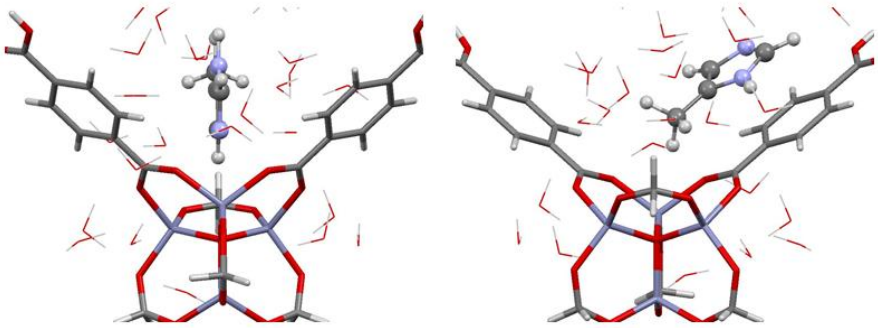


Figure 2. Schematic representation for different adsorption states of a Histidine molecule approaching the side of the functionalized MOF its various active sites

Figure **3** shows a Histidine molecule attached to the functionalized MOF by COOH and OH groups. The optimized F-MOFs and Histidine structures were used for the adsorption process. After optimization of the considered systems it found that Histidine adsorption on functionalized surfaces takes place preferentially on the COOH group with adsorption energy of about 0.69 eV (–15.91 kcal/mol). The average equilibrium distance between two closest atoms (O and H atoms) of the considered molecules is estimated to be 1.998 ˚A. The calculated adsorption energies for the energetically most favorable states of the OH and CHO functionalized systems are about 0.27 eV and 0.20 eV, respectively. Our first principles calculation results also show that the average bond lengths of the C–O and O–H in HIS extended to 1.390 and 0.986 ˚A, which is considerably larger than that in an isolated molecule (1.339 and 0.972 ˚A, respectively). Further information with respect to the bond lengths of the adsorbed molecule is presented in Fig. 4 and compared with those of the MOF–HIS system. One of the most outstanding results obtained here is that the interaction of Histidine with F-MOF is stronger than with pristine MOF. It is interesting that, the binding energy of Histidine at F-MOF–COOH is more than four times stronger than in pure MOFs.

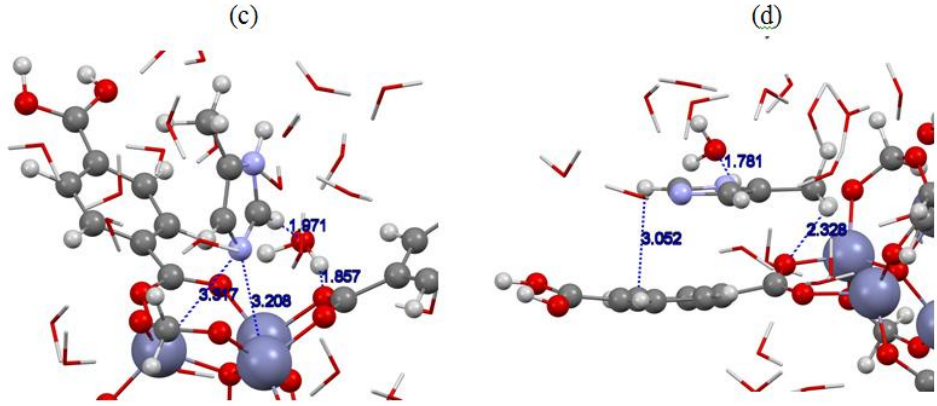


Figure 3. Model for a Histidine molecule approaching the sidewall of the functiona- lized MOF by (c) OH and (d) COOH groups

In order to understand the adsorption property of Histidine on the MOFs, the electronic structures and charge population for the considered complexes are analyzed. Fig. 5 depicts the highest occupied molecular orbital (HOMO) electron density of the optimized structures for the Histidine /F-MOF and Histidine /MOF complexes. They were obtained with the first-principles DFT code OpenMX [30]. As showed in Fig. 5, the HOMO is accommodated on both Histidine and F-MOF, indicating strong interaction between the two

entities. However, for the case of Histidine/MOF system, the HOMO is located only on MOF, which reveals that there exists a weak interaction between them. Further insight can be gained from the analysis of dipole moment, which can show the charge redistribution caused by adsorption. The calculated dipole moment for the MOF/Histidine system is determined to be 4.31D, smaller than 10.32D for the F-MOF–COOH/Histidine system, which reveals that introducing functionalized groups significantly affects the electronic properties of MOFs. To further elucidate these effects seen in nanotubes and Histidine complexes we have analyzed charge transfer between them. Mulliken charge analysis shows there is 0.90 ē transfer from F-MOF–COOH to Histidine molecule while for the Histidine /MOF complex the charge transfer from MOF to Histidine was determined to be about 0.01 ē. It is obvious from charge analysis that the interaction between functionalized MOFand Histidine is remarkably stronger than that of MOF and Histidine. Our results also indicate that Histidine is an acceptor here and can actually p-dope the host MOFs. The analysis of binding energies and electronic structures emphasizes that there exists a weak interaction between the Histidine and the exterior surface of intrinsic MOFs while the functionalized MOFs seem to be promising materials for strong physisorption of Histidine amino acid.

Conclusion

The interaction of Histidine with intrinsic and functionalized MOFs has been investigated by means of density functional theory calculations. Several possible configurations were selected for a Histidine molecule approaching the functional groups and exterior surface of the MOFs. The calcu-lated results reveal that Histidine is weakly physisorbed on the outer surface of intrinsic MOF, consistent with other theoretical investigations. The adsorption of Histidine on the functionalized MOF by OH, CHO and COOH groups indicated that the binding energy of Histidine is remarkably increased for adsorp-tion on the functionalized MOFs. It was found that the adsorption of Histidine on the functionalized MOF by COOH group is remarkably different, the binding energy of about 15.91 kcal/mol, indicating a strong physisoption process for the Histidine adsorption. The Mulliken population and dipole moment analysis supports that the electronic properties of functionalized MOFs change more significantly than those of intrinsic MOFs after the Histidine adsorption. In addition, the electronic structures (HOMO) result shows a larger orbital hybridization between Histidine and functionalized MOFs. Therefore, the functionalized nanotubes seem to be promising materials for strong physisorption with proteins.

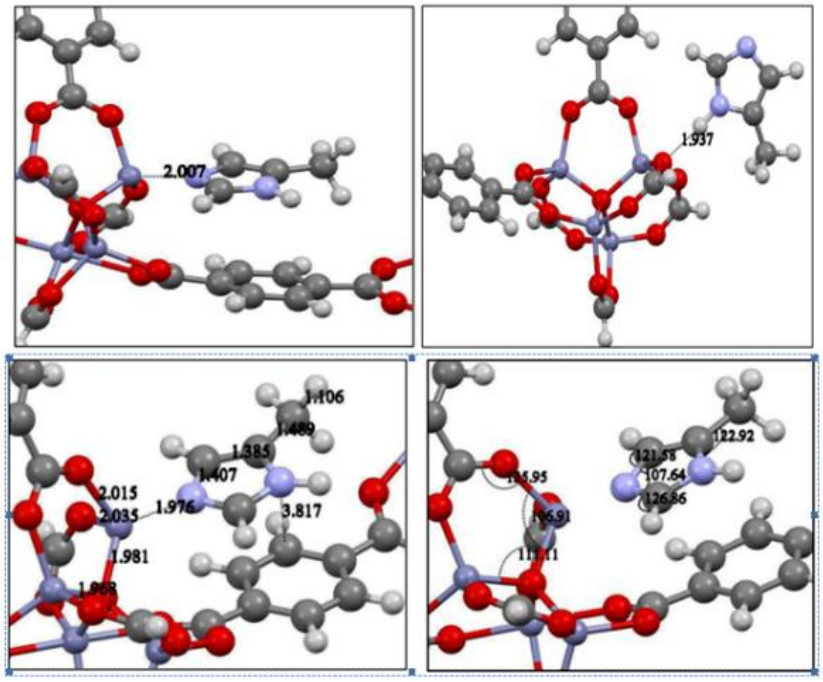


Figure 4. Geometric parameters of the optimized structure of (a) MOF/HIS and (b) F-MOF–COOH/HIS complex

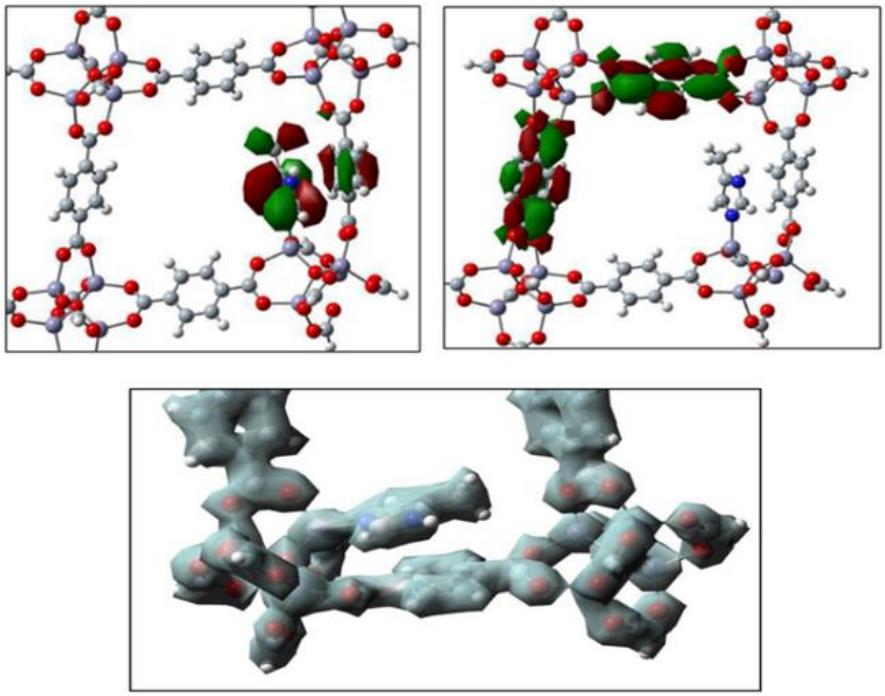


Figure 5. Calculated isosurface of orbitals localized at the top most valence band (HOMO) for (a) a Histidine molecule adsorbed on the side of bare MOF and (b) on thesidel of the functionalized MOF by COOH group (the selected absolute values of the isosurfaces of wavefunctions are 0.02).

Computational method

Structure optimizations and corresponding total energy calculations have been performed using the self-consistent charge–density-functional-based tight-binding (SCC–DFTB) method [14]. All calculations were performed utilizing the recently developed first-principle package DFTBþ [15], which uses a tabulated set of integrals derived from ab initio DFT calculations [16]. In this method it is possible to produce parameterizations capable of accuracy close to that of LDA/GGA with minimal adjustable parameters and also transferable between different systems. In addition, the basics functions are also available, allowing the reconstruction of actual wave functions from the calculations. Further details of the method have been fully reviewed in Refs [15–18]. In this work the Slater–Koster type parameter set [14] was utilized. We have also considered dispersion corrections for the vander Waals interaction using the Slater–Kirkwood type model [19]. From the well known expression for calculating the molecular binding energies, Eb is obtained for various cases of our study:

Eads = - (EMOF + EHis) - σ BSSE (1)

Where EMOF-His is the total energy of the adsorbed Histidine on the MOF, EMOF is the total energy of the pure MOF and E HIS is the total energy of the isolated Histidine.

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