Plane Wave Density Functional Theory Studies of the Structural and the Electronic Properties of Amino Acids Attached to Graphene Oxide via Peptide Bonding

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We studied via plane wave pseudopotential total-energy calculations within the local spin density approximation (LSDA) the electronic and the structural properties of amino acids (alanine, glycine, and histidine) attached to graphene oxide (GO) by peptide bonding. The HOMO-LUMO gap, the Hirshfeld charges, and the equilibrium geometrical structures exhibit distinctive variations that depend on the species of the attached amino acid. The GO-amino acid system appears to be a good candidate for a biosensor.

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I. INTRODUCTION

Immobilization of a protein on a graphene system is an exciting research topic that may lead to many important applications in biomedical technology [1–4]. This is due to the unique electronic properties of graphene as a two-dimensional zero-gap material. Its electronic structure exhibits linear dispersion near the Fermi level, making the system sensitive to charge transfer. Because the electronic structure of a graphene-amino acid system is likely to change sensitively as an amino acid is attached to graphene, we may hope to fabricate a biosensor that can be used in the diagnosis and the treatment of many diseases.

However, immobilization of a protein on pure graphene is a challenge because of the chemical inertness of graphene. The interaction between the protein and the graphene is mostly due to π-π interactions [5]. Because a stronger bonding is preferable for the fabrication of a robust biosensor, a protein attached to graphene oxide (GO) via peptide bonding has attracted interest [6].

GO may be considered as graphene decorated with functional groups, such as hydroxyl, epoxy, and carboxyl groups. The carboxyl group of GO is protonated at low pH, but as the pH increases, the carboxyl group dissociates, yielding a carboxylate ion. Forming a peptide bond between the carboxyl group of GO and the amino group of amino acid, with the release of a water molecule, becomes possible. Peptide bonds are higher in energy but very stable; thus, spontaneous hydrolysis takes an extremely long time.

We intend to investigate via plane wave density functional theory calculations the structural and the electronic properties of three selected amino acids, alanine (Ala), glycine (Gly), and histidine (His), covalently attached to GO. Because amino acids are the building blocks of proteins, we hope to provide theoretical insights that may be applicable to the much bigger problem of GO-protein systems. In addition, the GO-amino acid system in itself is an interesting topic from the basic science point of view and may even have its own applications.

II. CALCULATION

We constructed a cluster model of GO by assembling 36 carbon atoms in a graphene-like configuration, passivating the dangling bonds with 16 hydrogen atoms, and then adding an epoxy group and a hydroxyl group. The presence of an epoxy group and a hydroxyl group introduces a conspicuous curvature in the GO cluster, implying a fair amount of elastic energy. A carboxyl group is added at the edge of the GO cluster; then, an amino acid

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(Ala, Gly, or His) is connected to the cluster via peptide bonding.

The initial configuration is built by using the Avogadro package [7]. The functional groups and the amino acids are attached to the GO cluster group by group, its geometry being optimized under the universal force field (UFF) [8] at every stage as each functional group is added to the cluster. The GO cluster reacts quite sensitively as another group of atoms are attached, as can be expected from the linear dispersion of the electronic structure of graphene near the Fermi level.

The resulting configuration is used as the starting position in the ab-initio molecular dynamics simulation, performed by using the ABINIT package [9]. Periodic boundary conditions are imposed by assuming a cubic box of 18.52 Å for each dimension. Gamma point sampling is used. Norm-conserving pseudopotentials of a Troullier-Martins type [10] with Teter parameterization of the exchange-correlation functional [11] are used within the local spin density approximation (LSDA). A plane wave energy cutoff of 980 eV is used. Self-consistency cycles are repeated until the difference in the total energy become smaller than $2.72 \times 10^{-6}$ eV twice in a row. The system is relaxed until the average force on the atoms become smaller than $2.57 \times 10^{-3}$ eV/Å.

**III. RESULTS AND DISCUSSION**

The present GO model that has an epoxy group, a hydroxyl group, and a carboxyl group, together with the GO-alanine (GO-Ala), GO-glycine (GO-Gly), and GO-histidine (GO-His) structures determined from the present calculation, are shown in Fig. 1. We find a big change in the bond length of the carboxyl group in the amino acids (shown in black in Fig. 1) as the amino acid becomes attached to the GO. The bond length changes
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### Table 1. The bond lengths (in Å) of the carboxyl group of GO-Ala, GO-Gly, and GO-His compared to those of protonated and deprotonated amino acids.

|           | GO-attached | protonated amino acid | deprotonated amino acid |
|-----------|-------------|-----------------------|-------------------------|
| Ala       | 1.682       | 1.514                 | 1.531                   |
| Gly       | 1.625       | 1.498                 | 1.527                   |
| His       | 1.598       | 1.512                 | 1.729                   |

### Table 2. The Hirshfeld net charges (in units of e) of the amino acids, the carbon atoms, the epoxy group, and the hydroxyl group of GO.

| Amino acid | Carbon atoms | Epoxy group | Hydroxyl group |
|------------|--------------|-------------|----------------|
| GO+Ala     | −0.356       | −0.461      | −0.121         | −0.032         |
| GO+Gly     | −0.387       | −0.437      | −0.120         | −0.035         |
| GO+His     | −0.507       | −0.348      | −0.111         | −0.021         |

Fig. 2. (Color online) Side views of (a) GO-Ala, (b) GO-Gly, and (c) GO-His.

to 1.682 Å for GO-Ala, 1.625 Å for GO-Gly, and 1.598 Å for GO-His compared to 1.514 Å for Ala, 1.498 Å for Gly, and 1.512 Å for His. The bond length increases are 0.168 Å for Ala, 0.127 Å for Gly, and 0.086 Å for His. If we consider the bond length of the COO group in free-standing amino acids (with the H atom removed from the carboxyl), we observe an even more distinctive difference. The bond lengths in this case are 1.531 Å in Ala, in 1.527 Å in Gly, and 1.729 Å in His. Relative to the deprotonated amino acids, the bond length changes upon attachment to GO are 0.151 Å for Ala, 0.098 Å for Gly, and −0.131 Å for His. The results are summarized in Table 1. Despite the similarity between the amino acids, their structures change in drastically different manners when the H atom is removed from them and, more importantly, when they are attached to GO. Side views of the GO-amino acid systems are shown in Fig. 2. Ala appears to orient more in the direction perpendicular to the GO plane than the others.

Hirshfeld net charge analysis also shows distinct characteristics. The COO group in GO-Ala has a charge of −0.38e compared to −0.42e in GO-Gly and −0.45e in GO-His. To verify the amount of the charge transfer due to the attachment to GO, we calculated the Hirshfeld net charges of the free-standing amino acids with the H atom removed from the carboxyl group. The COO groups in Ala, Gly, and His turn out to have charges of −0.28e, −0.28e, and −0.29e, respectively. Then, with these values as the reference, the additional charge transfers are estimated as −0.10e in GO-Ala, −0.14e in GO-Gly, and −0.16e in GO-His.

The total charge transfer from the amino acids to the GO varies characteristically, too. The Hirshfeld net charges of the carbon atoms in the GO sheet, the hydroxyl group, the epoxy group, and the amino acids are summarized in Table 2 and Fig. 3. The Hirshfeld net charges of the amino acids are −0.507e for GO-His, −0.387e for GO-Gly, and −0.356e for GO-Ala. The carbon atoms in the GO sheet have net charges of −0.461e (GO-Ala), −0.437e (GO-Gly), and −0.45e (GO-His) compared to −0.690e for the carbon atoms in the original GO model. The net charge of the epoxy group is almost without variation. In contrast, the charge of the hydroxyl group has a smaller magnitude, but shows a larger variation. The net charges of the passivating H atoms are 0.971e (GO-Ala), 0.980e (GO-Gly), and 0.988e (GO-His), compared to 0.886e (GO model). The H atoms should represent the response from the larger GO sheet that cannot be treated explicitly within our present model system.

The HOMO-LUMO gaps of GO-Ala, GO-Gly, and GO-His are 0.533 eV, 0.496 eV, and 0.129 eV, respectively, compared to 4.221 eV, 4.275 eV, and 3.563 eV for Ala, Gly, and His alone (Table 3). Again, the HOMO-LUMO gaps of the free-standing amino acids become
more distinct as they are attached to GO. Especially, GO-His has a very small HOMO-LUMO gap, which is consistent with a previous experiment [12]. The density of states profiles are shown in Fig. 4. Even the deep-lying states near $-20$ eV below the Fermi level show discernible differences. The density of states near the Fermi level is shown in Fig. 5 for better visibility.

The energetics of GO-amino acid systems also depend sensitively on the species of the amino acids. The binding energy, as defined by

$$E_b = E(GO' + \text{Amino Acid}) - E(GO') - E(\text{Amino Acid}) + E(H_2O),$$

where $GO'$ denotes GO without the H atom in the carboxyl group, varies significantly. The values of $E_b$ are 0.32 eV for GO-Ala, 0.10 eV for GO-Gly, and $-0.02$ eV for GO-His. These are quite large deviations from the typical peptide bond energy of 0.16 eV. Our results suggest that GO - amino acid bonds are not the ordinary peptide bonds.

In a typical peptide bond, the C-N distance is approximately 1.32 Å [13], which is between the C-N single bond distance of 1.49 Å and the C-N double bond distance of 1.27 Å. In our calculation, the bond lengths are 1.472 Å for GO-Ala, 1.478 Å for GO-Gly, and 1.487 Å for GO-His. These values are close to the C-N single-bond length and in agreement with the deviation of the bond energy from the typical peptide bond energy.

Quite a pleasant surprise is that albeit all the outward appearances of similarity between these amino acids, their equilibrium structures and electronic properties show distinct differences. Our results are encouraging for the prospect of building a GO-based biosensor system.

**IV. CONCLUSION**

We studied via plane wave pseudopotential calculations the structural and electronic properties of amino acids.
acids, alanine, glycine, and histidine, attached to GO. The similarity of the equilibrium structures and the electronic properties of the amino acids disappear as they become attached to GO. The equilibrium structure and the electronic properties change in a quite distinct manner, depending on the species of the amino acids. Such sensitivity would be a welcome feature for applications in the field of biosensing.

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