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Insight into the interaction between DNA bases and defective graphenes: Covalent or non-covalent

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ABSTRACT

Although some metal clusters and molecules were found to more significantly bind to defective graphenes than to pristine graphenes, exhibiting chemisorptions on defective graphenes, the present investigation shows that the adsorption of DNA bases on mono- and di-vacant defective graphenes does not show much difference from that on pristine graphene, and is still dominantly driven by noncovalent interactions. In the present study the adsorptions of the nucleobases, adenine (A), cytosine (C), guanine, (G), and thymine (T) on pristine and defective graphenes, are fully optimized using a hybrid-meta GGA density functional theory (DFT), M06-2X/6-31G*, and the adsorption energies are then refined with both M06-2X and B97-D/6-311++G**. Graphene is modeled as nano-clusters of $C_{72}H_{24}$, $C_{71}H_{24}$, and $C_{70}H_{24}$ for pristine, mono- and di-vacant defective graphenes, respectively, supplemented by a few larger ones. The result shows that guanine has the maximum adsorption energy in all of the three adsorption systems; and the sequence of the adsorption strength is G > A > T > C on the pristine and di-vacant graphene and G > T > A > C on the mono-vacant graphene. In addition, the binding energies of the DNA bases with the pristine graphene are less than the corresponding ones with di-vacant defective graphene; however, they are greater than those of mono-vacant graphene with guanine and adenine, while it is dramatic that the binding energies of mono-vacant graphene with thymine and cytosine appear larger than those of pristine graphene.

1. Introduction

As one of the most recent interesting material due to its unique chemical and electronic properties [1], graphene has attracted wide attention to its promising applications in bio-medicine and micro-electronic devices. For example, nano-graphene has been proposed to make sensors for small molecules such as H_2, H_2O, NO, and NH_3 [2,3], and for biomolecules like carbohydrates, proteins, nucleic acids [4,5], and to convey drug and gene for cancer treatment [6]. Like carbon nanotubes [7,8], a major barrier for biomedical applications of nano-graphene is its low solubility in aqueous solutions. Strategic approaches toward solubilization of nanographene have been developed through non-covalent functionalization, which can not only enhance solubility of nanographene but also maintain its attractive geometric, electronic and mechanical properties. It is apparent that carbohydrates, proteins, and nucleic acids are very important species for functionalizing graphene in living systems.

With different models for pristine graphene, a variety of the first-principles based methods have been widely employed to investigate the binding of the nucleobases to pristine graphene, including local density approximation (LDA) type of density functional theory (DFT), GGA, meta-hybrid GGA, plane-wave GGA type of DFT, dispersion-corrected DFT (DFT-D) as well as second-ordor Møller–Plesset perturbation theory (MP2) [9–16]. Using B97-D, B2PLYP-D and SCS-MP2 methods, Antony et al. extensively investigated the adsorption of the DNA nucleobases on a variety of graphene clusters from 24 to 150 carbon atoms [10]. The interaction sequence after basis set superposition error correction (BSSE) at B2PLYP-D/TVZ(2df,2pd)//B97-D/TZV(d,p) level for DNA bases on $C_{54}H_{18}$ is, G (23.9 kcal/mol) > A (19.7) > T(18.5) > C(18.2), and they suggested the proper size of nano graphene with at least about 50 carbon atoms. MP2/6-311+G(d,p) results in the binding order of G(24.6 kcal/mol) > A(21.7 kcal/mol) ≈ *T*(21.4 kcal/mol) > C(18.4 kcal/mol) [9], parallel to the polarizability of the DNA bases. The plane-wave LDA method usually considerably underestimates the binding strength, like only 9.0 and 11.03 kcal/mol for cytosine [9,12]. Both the B3LYP-D/6-31G(d) with fifty five C_6 rings for graphene [14], and vdw-HF/6-31G(d,p) with twenty C_6 rings[11] reproduce the binding sequence, G > A > T > C, (17.5 > 15.0 > 14.3 > 13.3 kcal/mol; [14] 19.1 > 17.8 > 16.6 > 14.5 kcal/mol [11]); however, the absolute binding energies for the given base are a few kcal/mol lower than those predicted by the above B2PLYP-D method [10]. Van der Waals

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density functional (vdW-DF) [17–19] for adenine on graphene also yields a too low binding (16.4 kcal/mol) [1,13], as compared to the result of Antony and Grimme (19.7 kcal/mol [10]). The binding energies from the wB97XD/6-31G(d,p) with 8 × 8-ring graphene sheet [16] agree very well within 0.1–1.4 kcal/mol with those of Antony et al. [10], yet the relative strength for T and C are switched (G > A > C > T, 22.5 > 20.3 > 18.9 and 18.4 kcal/mol). Varghese et al. carried out an experimental investigation into the binding of DNA nucleobases with graphene using isothermal titration calorimetry (ITC) [11]. They indicated that the relative interaction energies of the nucleobases decrease in the order G > A > C > T, although the C and T seems to be interchangeable. Even before BSSE, the M06-2X/6-31G(d) in the scheme of ONIOM (M06-2X/6-31G*:AM1) results in a rather weak binding and different sequence (14.8, 14.1, 16.0 and 13.8 kcal/mol for G, A, T and C.) [14] Although B3LYP-D/6-31G(d)//M06-2X/6-31G(d) done by Umadevi et al. also brings about the sequence G > A > T > C [14], the BSSE correction (9.6 kcal/mol) for cytosine–graphene complex was predicted dramatically high, while others were regular in 3.1–6.2 kcal/mol. In spite of extensive theoretical investigations into the binding between DNA bases to pristine graphene, the above discussion indicates that there is still a controversial with respect to binding strength and binding sequence. In this present study, in order to assess its performance as well as to provide consistent result for a comparison with adsorptions on defective graphene the M06-2X will be further used to optimize the adsorptions of DNA on pristine graphene and then improve the binding energy with B97-D.

During production of graphene from the thermal expansion of graphite oxide (GO), some carbon atoms are missing to form defective graphene [20]. The most common defects of graphene include mono-vacancies, multivacancies, pentagon heptagon pairs, and adatoms [21–23]. Di-vacant defective graphene is energetically favored over the mono-vacant one because of its reconstruction without dangling bond [24]. Because of carbon vacancies the defective graphene may demonstrate significant influences on the chemical and physical characteristics of graphene, for example, chemisorptions on the defect sites [25–27]. Very recently, the adsorptions of metal clusters on the mono-vacant and di-vacant defective (5-8-5 defect) graphenes were investigated [28–32]. The structural and electronic properties of the nanoparticles adsorbed on the defective graphene usually show peculiarities. The defective sites sever as anchoring points for the nanoparticles, and under-coordinated neighboring carbons further strengthen the binding of the nanoparticles to graphene layer. Catalytic reactivity of the adsorbed nanoparticles may be also enhanced. Lim found that the most stable conformation of Pt_{13} on mono-vacant defective graphene has D_{4h} symmetry, rather than the isolated I_h symmetry, and the Pt_{13} donates electron to the defective graphene and the adsorbed O_2 [29]. The binding of Pt_4 to mono-vacant graphene was 3–4 times higher than to pristine graphene.[32] A variety of gas molecules (O_2, CO, N_2, B_2, H_2O) can be chemically adsorbed on the di-vacancy defective graphene, with a magnitude of 3–13 eV binding energy [3]. The DFT predicted chemisorption of H_2S on the mono-vacancy defective graphene by forming weak covalent bond (1.55 eV) [24]. However, in spite of many publications for the adsorptions of DNA nucleobases on pristine graphene as described above, to the best of our knowledge the adsorption of the defective graphene with DNA nucleobases has not been reported. Obviously, it is important to reveal the binding behavior (covalent or non-covalent) of the defective graphene with DNA nucleobases in biomedical science because the defect site of graphene could give rise to a local electronic structure change around it [33]. In the present work M06-2X and B97-D were employed to study the interaction of DNA nucleobases with mono- and di-vacant defective graphene.

2. Computational methods

Accurate description for noncovalent weak interaction systems like the π-stacked systems is still a challenge for density functional theory (DFT), a promising quantum mechanics method for large systems, although considerable improvements have been achieved over LDA and such conventional hybrid DFT as B3LYP in the recent years [34,35]. Recently, the novel hybrid meta-GGA functional, M06-2X, developed by Truhlar et al. [33], provides relatively reasonable results for π···π stacking systems [36]. Therefore, in this paper the geometric parameters of all nucleobase-graphene adsorption complexes are fully optimized in gas phase at M06-2X/6-31G(d) level. To obtain accurate binding energy, the bigger basis set of 6-311++G(d,p) was employed to refine the stationary point energy at both M06-2X and B97-D levels of theory with BSSE correction. Based on the suggestion of Antony and Grimme [10], the pristine graphene is modeled with $C_{72}H_{24}$, which is also compared with $C_{78}H_{24}$, $C_{86}H_{26}$, and $C_{106}H_{28}$. The defective graphenes are modeled with $C_{71}H_{24}$ for mono-vacancy and $C_{70}H_{24}$ for di-vacancy. All calculations were done using the Gaussian09 version B01 [37].

3. Results and discussion

3.1. Adsorptions of DNA nucleobases on pristine graphene

The structures of the adsorption complexes of DNA nucleobases on pristine graphene are shown in Fig. 1. The graphene sheet is modeled by $C_{72}H_{24}$, larger than the suggested minimum carbon cluster of C_{54} for graphene [10]. $C_{72}H_{24}$ keeps planar and basically parallel to the rings of nucleobases. Table 1 lists the distances between graphene and the nucleobase plane for the adsorption complexes optimized at the M06-2x/6-31G(d) level. For all of the four nucleobases, the distances from the graphene to the hexagon rings are in the range of 3.103–3.137 Å, and those to the pentagon rings of adenine and guanine are 3.156 and 3.163 Å, respectively. However, the electronegative O atom is closer to the graphene with vertical distances of 2.964, 2.943, and 2.968 Å for $C_{72}H_{24}$–guanine, $C_{72}H_{24}$–thymine, and $C_{72}H_{24}$–cytosine, respectively. There may be a stronger interaction of nucleobase oxygen with the graphene plane (C═O···π) than the rings of nucleobases (π···π). Although the distances of the N atoms of NH_2 group from graphene are nearly identical to those of hexagon rings of nucleobases, the H atoms of the NH_2 group have shorter distances of 2.864, 2.606, and 2.900 Å for $C_{72}H_{24}$–adenine, $C_{72}H_{24}$–guanine, and $C_{72}H_{24}$–cytosine, respectively. For the methyl group of connected in thymine there are the distances of 3.253 and 2.580 Å from the C atom and one of the H atoms, respectively, to graphene. Because of the short distances of both amine and methyl groups with graphene, there is also weak interaction of the H atom of amino (N—H···π) or methyl group (C—H···π) with graphene.

Table 2 lists the binding energies of nucleobases with graphene together with reference data. With the $C_{72}H_{24}$ model of graphene, the binding energies at the M06-2X/6-31G(d) level are 20.2, 16.6, 15.8, and 15.6 kcal/mol for G, A, T, and C, respectively. The predicted binding is much stronger than that with ONIOM (M06-2X/6-31G*:AM1) (14.8, 14.1, 16.0, and 13.8 kcal/mol for G, A, T, and C) [14], and also shows a different sequence. The basis set 6-311++G(d,p) including diffuse and polarization of H increases the binding energies by 3.0–4.0 kcal/mol; yet the BSSE decreases the binding energies by 4.5–6.0 kcal/mol. As a result, the binding energies of G, A, T and C with $C_{72}H_{24}$ at M06-2X/6-311++G(d,p)//M06-2X/6-31G(d) level are 18.2, 14.7, 14.2, and 14.1 kcal/mol, respectively, which agree very well with the