DFT analysis of Thymine adsorption on Ti doped graphene for biosensor applications

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Abstract. Density functional theory quantum chemical calculations have been performed to investigate the adsorption of thymine on pristine graphene (Gr) and Titanium doped graphene (GrTi) in order to explore the potential of doped graphene as adsorbent for biomolecule DNA nucleobase thymine. The various parameters including adsorption energy, mode of charge transfer, dipole moment, HOMO-LUMO gap and DOS confirms the Ti doped graphene can be good candidate as adsorbent for thymine in terms of biosensor applications.

1. Introduction
Deoxyribonucleic acid (DNA) is genetic material [1] which possessing complex biomolecular structure including four different nitrogenous bases. Two-dimensional nanomaterial (2D) particularly graphene [2] widely studied 2D nanomaterial with biomolecule DNA sequencing [3] Furthermore, diagnosis of diseases, forensic characterization, pharmaceuticals are the DNA based applications [4-9]. Rad et al [10] investigated that adsorption of guanine on surface of pristine and Al doped graphene. Furthermore, O-side of guanine interacts rigorously with Al doped atom of the graphene, it alters the electronic properties of the AIG and acts as good sensor for guanine. Using DFT method M. Mirazai et al found mode of hybridization of graphene layer by thymine, uracil nucleobases [11]. Saravanan et al [12] reported adsorption of DNA/RNA base pairs on defective, Stone-Wales, Boron and Si defect dopant graphene sheet can be exploited to design Bio-sensor or DNA/RNA sequencing devices. The quantum chemical calculations performed (DFT) on complex system of chloroform on pristine graphene, N-doped graphene, Al-doped graphene found that Al-doped graphene is more sensitive to adsorption of chloroform. It is good candidate for sensor [13]. Rad [14] used DFT method for the adsorption of cytosine on Ga and Al doped graphene. He found notable changes in its electrical conductivity. Recently, graphene utilized for building DNA based biosensors to detect metal ions, proteins, transmit drugs [15-18]. Fonseca et al [19] revealed the mechanism of Graphene-Ti using molecular dynamics gives new insights with and without substrate. Mudedla et al [20] investigated the doping of Si atom causes change in structural, optical and electronic properties of graphene which gives higher binding affinity towards modified nucleobases than pristine graphene. Furthermore, in this present investigation, the DFT based
quantum chemical calculation is performed to explore an interactions of nucleobase thymine with pristine and Ti doped graphene sheets.

2. Computational details

The molecular models of pristine graphene sheet (Gr) and DNA nucleobase thymine (Thy) generated using code Gauss View 5.0 [21]. We structured 4x4 pristine graphene (Gr) and Titanium (Ti) doped graphene sheet (GrTi). The Gr model constitutes 42 carbon atoms whereas GrTi model constitutes 41 carbon atoms with single Ti atom as shown in fig.2. We considered the concept of previously published graphene model [14]. The DFT based methods such as wB97XD [22] with basis set LanL2DZ [23] employed to study interaction of doped heavy atom Ti with Gr adsorbed by Thymine nucleobase. The evaluated an electronic property including natural bond analysis (NBO) [5], HOMO-LUMO, DOS of the complex system have been performed using Gaussian09 code [24]. The isolated and complex system, Gr and Ti-Gr defined at 1x1x3 Monkhorst-Packgrid fork point sampling of the Brillouin zone [25]. The K-point adjusted at 3x3x1 for integration of Brillouin zone. The optimization process continued till residual forces are normalized at 0.01eV/Å.

We can calculate adsorption energy $E_{\text{ads}}$ of the complex system as

$$E_{\text{ads}} = E_{\text{GrTi-Thy}} - (E_{\text{GrTi}} + E_{\text{Thy}})$$

Where $E_{\text{GrTi}}$ indicates energy of relaxed metal Ti doped graphene sheets, $E_{\text{Thy}}$ is the energies of the isolated thymine molecule and $E_{\text{GrTi-Thy}}$ represents energies of adsorbed thymine on Ti doped graphene sheets.

3. Result and Discussion

3.1. Structural Analysis

Figure 1 shows chemical (a) and molecular (b) structures of biomolecule DNA nucleobase thymine. We optimized the molecular geometries of complex system Ti doped Graphene (GrTi) sheet and Thymine. When a carbon atom was replaced by single Ti atom in graphene sheet. The bond length of Ti-C is 1.90 Å and C-C bond length is 1.43 Å.

![Figure 1](image_url)

**Figure 1.** (a) Schematic presentation of Chemical structures of DNA nucleobase Thymine; (b) molecular structure of biomolecule DNA nucleobase possible sides of Thymine interactions highlighted in numbering for adsorption sequence of atoms on surface of GrTi.

The hybridization of graphene sheet alters from sp2 to sp3 taking place at doped atom sites due to deformation process.
3.2. Adsorption of DNA nucleobase Thymine on Ti doped graphene surface

3.2.1. Mechanism of possible adsorption sites of Thymine molecule on GrTi

We considered four active sites of thymine (fig.1.b) molecule on GrTi surface. The mechanism of possible adsorption site of thymine molecule on surface of Ti doped graphene as shown in fig.3 (B1 to B4). The possible sites include =O, -NH, -N, =O of the DNA nucleobase thymine molecule. Our quantum chemical investigation on complex system (GrTi-Thy) suggests favourable an interaction (Fig.B1 & Fig.B4) of Thymine adsorption on Ti doped graphene interpreted by means of adsorption energy and bond lengths tabulated in table 1. The values of adsorption energy are -186.82, -56.80, -98.40, -182.21 kj/mol. The high value of adsorption energy at B4 owing to its nucleophilic property of -N as compared to =O functional. Furthermore; another factor responsible to of its high value of energy when thymine was closed in position B4 fig.3. In short it is due to low distance low distance to Ti doped atom as shown in fig.3 at position B4.

Figure 2. (a) Optimized structure of pristine Graphene (Gr); (b)Ti doped Graphene (Ti); optimized geometries pristine graphene sheet (Gr) on which thymine molecule adsorbed top (C) and side (d) views respectively.
**Figure (3).** Fully optimized complex system of Ti doped graphene adsorbed by Thymine at different positions.

The extracted values indicate that the adsorption of thymine nucleobase on Ti doped graphene favours optimized geometries at position B1 and B2 shown in fig.3. The reported values of adsorption energies are quite high as compared to [26-27]

| Complex system | E_{ads} (kJ/mol) | Q_{NBO} (e) | Binding distance (Å) | Mulliken charge transfer Q_{Mu} (e) |
|----------------|-----------------|-------------|----------------------|------------------------------------|
| GrTi-T-B1      | -186.82         | 0.166       | 1.84                 | 0.253                              |
| GrTi-T-B2      | -56.80          | 0.142       | 2.38                 | 0.234                              |
| GrTi-T-B3      | -98.40          | 0.158       | 2.21                 | 0.242                              |
| GrTi-T-B4      | -182.21         | 0.194       | 2.09                 | 0.278                              |

The optimized binding distances of thymine on surface of Ti doped graphene sheet are tabulated in table 1. The optimized distances of complex system GrTi-T-B1 calculated 1.84 Å and for the GrTi-T-B4 it is 2.09 Å. The results binding distances are consistence with adsorption energies. The lower distance implies higher binding energy. The large adsorption energy values and short binding distances at positions B1 and B4 (Fig.3) attributed to chemisorption phenomenon in the GrTi-Thy complex system.
3.2.2. Charge transfer in complex system GrTi-Thy
The charge transfer phenomenon numerically reported in the table 1 based on optimized extracted data. The adsorption of thymine molecule on surface of GrTi system is responsible to transfer charge (Mulliken) at different positions from B1 to B4. The highest value of Mulliken charge transfer in the order of B4, B1, B3 and B2 respectively.

3.3. HOMO-LUMO analysis of GrTi-thymine complex biosystem
The highest occupied molecular orbital (HOMO) and lowest occupied molecular orbital analysis of the GrTi-Thymine complex biosystem have been studied. We reported in our recent study [17] and [14] HOMO of pristine graphene is located on C-C bonds whereas LUMO is placed on doped site of graphene sheet.

Figure (4). HOMO-LUMO extracted data of complex system; Ti doped graphene (X), B1 complex system of Ti doped graphene(Y)and B4 complex system of Ti doped graphene (Z).

When Ti doped on graphene both HOMO-LUMO changes its orbital positions around doped atom (Fig.4. X.), this attributes to high reactivity of Ti doped graphene sheet as compared to pristine graphene. This validates charge analysis of complex biosystem GrTi-Thymine.
Table 2. Parameters of complex system GrTi adsorbed by Thymine at different positions.

| Complex system | $E_{\text{HOMO}}$ (eV) | $E_{\text{LUMO}}$ (eV) | $E_{\text{gap}}$ (eV) | $\mu$D (Debye) |
|----------------|------------------------|------------------------|------------------------|---------------|
| GrTi-T-B1      | -2.80934               | -1.72886               | 1.08048                | 10.465        |
| GrTi-T-B4      | -2.48365               | -1.73454               | 0.74911                | 11.091        |

In Table 2 summarized the HOMO-LUMO orbital parameters, its gap and dipole moment of the GrTi, GrTi-T-B1 and GrTi-T-B4 complex biosystem respectively. The HOMO-LUMO distributions are shown in Fig.4. The energies for HOMO and LUMO of GrTi system found -3.51928 eV and -1.98708 eV with its gap 1.53220 eV. The Complex biosystem GrTi-T-B1 HOMO-LUMO energies are -2.80934 and -1.72886 eV respectively. The system GrTi-T-B1 HOMO-LUMO gap found is 1.08048 eV. The complex system GrTi-T-B4 HOMO values -2.48365 eV and LUMO values -1.73454 eV by energy gap 0.74911 eV. We conclude that the hybridization is rigorously taking place in B4 instead of B1 (Fig.4).

3.4. Dipole moment significance in GrTi-Thy complex biosystem

Table 2 indicates change in dipole moment of system after complex system formation. We can observe that naturally the GrTi system dipole moment is low whereas the dipole moment increases for complex biosystem GrTi-T-B1 and GrTi-T-B4 successively (Table.2). The increase in dipole moment values of B1 and B4 complex system signifies the increase in polarity of the respective systems. Furthermore, more charge transfer attributes to more polarity of the system. When interaction is taking place in the complex system (B1, B4) dipole moment increases. The Ti doped graphene of B4 have higher dipole moment as compared to B1 of Gr-Ti-T system. This validates the results of charge analysis.
Figure (5). Density of states of complex systems; Ti doped graphene GrTi (a); Isolated Thymine (b); GrTi at B1(c) and B4 complex system of Ti doped graphene (d).

3.5. The role of Density of States (DOS) in GrTi-Thy complex biosystem

The densities of states of complex system shown in Fig.5. After successfully comparison of the Fig.5 (a-d), it confirms the adsorption of Thymine is responsible to cause significant shift of orbitals titanium doped graphene (GrTi) to high energy levels. The newly generated HOMO’s lies between HOMO-LUMO of Ti doped Graphene shown in Fig.5 for (a, c and d) complex biosystem. The $E_g$ and conductivity relation can be defined as [28]

$$\sigma \alpha \exp \left( \frac{E_g}{kT} \right)$$

(2)

Where $\sigma$ is electrical conductivity, $K$ -Boltzmann constant, $T$ - is the temperature. This equation signifies that smaller the $E_g$ value larger the conductivity. The above results show the adsorption of thymine on Ti doped graphene increase its electrical conductivity; it can be used as a good candidate for designing Thymine based biosensors in future.
4. Conclusion
In summary; the biosensor-based capabilities of Ti doped graphene complex biosystem for detection of thymine molecule were studied by using DFT method. The structural and electronic characterization of these complex systems were evaluated by using the adsorption energy, charge transfer, dipole moment, HOMO-LUMO, HOMO-LUMO gap and DOS of the complex biosystems. Our results reveal that the decrease in gap of HOMO-LUMO values increased an electrical conductivity values of Ti doped graphene by adsorption of thymine molecule. Furthermore; the higher electrical conductivity of GrTi-Thymine complex system makes it more sensitive which enables for designing Thymine based biosensors in future.

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