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Original scientific paper

Pre/post electron transfer regioselectivity at glycine modified graphene electrode interface for voltammetric sensing applications

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Abstract

In the last few years, glycine (GL) showed good experimental evidence as an electron transfer (ET) mediator at the carbon (in particular graphene (GR)) interface. However, ET properties of GL modified GR interface are still not known completely. These can be achieved using density functional theory-based models. Modelling of modified carbon electrode interfaces is essential in electroanalytical chemistry to get insights into their electronic and redox properties. Here we have modelled glycine modified graphene interface to find out its interfacial redox ET properties. Conceptual density functional theory concepts like frontier molecular orbital (FMO) theory and analytical Fukui functions were utilized to predict the ET sites on the modified graphene surface. It is shown that at the glycine-modified graphene interface, amine groups act as additional oxidation sites and carboxylic acid groups as additional reduction sites. Therefore, glycine acts as an ET mediator at the graphene-based electrode interface. The obtained results are well supported by previously published experimental reports.

Keywords
Redox reaction, density functional theory; frontier molecular orbitals (FMO); Fukui analysis

Introduction

Over the past few decades, the carbon paste electrode (CPE) has become a rising star in the electrochemical community, where it is used as a working electrode in voltammetric sensing technologies due to various reasons like easy fabrication, huge redox potential window, and low resistance with minor background current [1,2]. In voltammetry, the charge transfer interaction between the working electrode surface and the analyte is crucial for sensing applications. Therefore, the electroanalytical community engineers are using CPE surfaces with various mediators like metal derivatives [3,4], electrodeposited amino acids [5-7], or surfactants [8].

Polymer-modified electrodes have recently attracted a lot of attention due to biocompatibility and a broad range of applications in electrochemistry. Because of their excellent selectivity, sensitivity, and uniformity in electrochemical deposition, strong adhesion to the electrode surface, and chemical durability, polymer-modified electrodes have several advantages in the detection of analytes. Amino acid-based monomers can also be immobilized on the CPE surface using electrodeposition [9-12].

Glycine (GL) is an important non-essential amino acid that is essential for humans for the production of collagen and creatine and also for the protection of cells from free radicals. GL also acts as an inhibitory neurotransmitter and helps in processing sensory information. Owing to its biocompatibility and easiness of fabrication, GL has been utilized as an electrode modifier and has already been applied for sensing various electroactive compounds like catechol (CC) [9], hydroquinone (HQ) [9], dopamine (DA) [10], ascorbic acid (AA) [10], uric acid (UA) [11], glucose (GLU) [12,13], guanine (GN) [11], adenine (AN) [11], and indigo carmine (IC) [14]. Gilbert *et al*. [10] deposited GL on CPE using cyclic voltammetry, and the prepared GL-modified CPE (GL-MCPE) was later applied for the simultaneous detection of DA and AA, showing that GL-MCPE is able to detect DA in the presence of AA. Harish *et al*. [9] showed that GL-MCPE could detect CC in the presence of HQ, and detection limits for CC and HQ were determined as 0.16 and 0.20 µM, respectively. Manjunatha [14] showed that GL-MCPE can detect IC in injection samples with a recovery range of 98-105 %.

Nowadays, preparing composites (GL + graphene (GR)) is gaining attraction because of possible synergistic contributions, which could enable a wide range of prospective applications. Unfortunately, GL-GR composite research is still in its infancy, and only a few reports are available in the literature on this area. Thus He *et al*. [11] constructed GL-GR composite glassy carbon electrode for simultaneous detection of DA, UA, GN, and AA. The GL-GR composite showed excellent electrocatalytic activity for sensing all analytes in real samples of urine and fish sperm. The authors concluded that GL-GR composite increases electrode sensitivity, stability, and reliability.

GL is the simplest known amino acid comprising methylene, carboxylic acid, and an amine group. It will be interesting to know which group acts as an electrocatalyst during redox reactions. Understanding GL interaction and its electron transfer (ET) regioselectivity with GR will be very helpful in further improving the catalytic activity of this combination for sensing applications.

Quantum chemistry can be used to better understand electrochemical reactions on the electrode surface. In particular, conceptual density functional theory is more useful for understanding electron transfer regioselectivity of modified carbon surfaces [15,16]. At the atomic scale, quantum chemistry approaches like density functional theory (DFT) can be utilized to calculate the surface properties of electrodes. As a result, electroanalytical findings may be supported and explained using first principles and DFT [8].

Earlier, we used the DFT-based models to understand the effect of defects on the graphene surface [16] and regioselectivity at the lysine [5], cetyl pyridinium bromide [8], and TX-100 [3]. Ambrusi *et al*. [17] used the DFT model to understand the carbon dot surface-interaction with silver nanoparticles and found that carbon dots with the COOH group is beneficial for silver nanoparticle interactions. Pineda-Urbina *et al.* [18] utilized the carbon surface model to understand the 2-mercaptobenzothiazole-modified carbon paste electrode interface. Their theoretical results are useful to understand the selectivity of the modified surface for metal ions (Cu^{2+} > Pb^{2+} > Cd^{2+}) sensing. Saghravanian *et al*. [19] utilized the DFT to understand metronidazole non-covalent interaction with SWCNT. The authors calculated the binding energy between metronidazole (with different orientations) and SWCNT. The minimum binding energy is obtained when metronidazole interacts with SWCNT by its $–CH_2$-CH_2-OH moiety. Thus the earlier theoretical studies suggested that DFT-based modelling is helpful in understanding the electrode interface at a molecular level.

In the current article, we have studied the binding interaction between graphene and GL, and by using frontier molecular orbitals (FMO) with analytical Fukui interpretation, the electron transfer regioselectivity of graphene GL complexes is differentiated. The obtained theoretical results are found in good agreement with earlier experimental interpretations.

Theoretical methods

Geometries of GL, GR, and GLGR complexes are drawn using the Sinapsis tool [20]. Frontier molecular orbitals (FMO) and analytical Fukui plots are also plotted using Sinapsis [20]. Entire geometry optimization of all models and analytical Fukui calculations were performed using Auxiliary functions employed density functional theory (DFT) in vogue of the deMon2k program [21] with the VWN [22] correlation functional with DZVP [23] basis sets. Single point energies were calculated using PBE [24,25] correlation functionals with TZVP [23] basis sets. Auxiliary functions were automatically generated as previously described in the literature [26–29]. Graphene models were optimized as described in our previous work [16]. The graphene model consists of 96 carbon atoms and 24 hydrogen atoms. The geometries of the graphene model were optimized without freezing hydrogen positions.

Results and discussion

Electrochemical behaviour of potassium ferrocyanide at GL-MCPE (earlier experimental status)

The electrochemical behaviour of potassium ferrocyanide ($K_4[Fe(CN)_6]$) is commonly used as a standard redox probe to compare the bare carbon paste and modified carbon paste electrodes. Several experimental reports have been published to compare the $K_4[Fe(CN)_6$ ET activity of bare carbon paste electrode (BCPE) and GL-modified carbon paste electrode (GL-MCPE). Raril and Manjunatha [30] have compared the active surface area of BCPE and GL-MCPE. They found that GL-MCPE has a higher active surface area when compared to the BCPE. The performance of the CPE is dependent on the substrate and binder ratios, grinding time, and homogenous quality of the surface. Therefore, different electrodes will give different ΔE_p values. In Table 1, the redox ET behaviour of different GL-MCPE prepared by different authors is compared. It is seen from Table 1 that ΔE_p values of GL-MCPE are lower than the BCPE. Therefore, at the GL-MCPE surface, GL acts like an electron transfer mediator and electrocatalyst.

Table 1. *Redox ET behavior of GL-MCPE.*

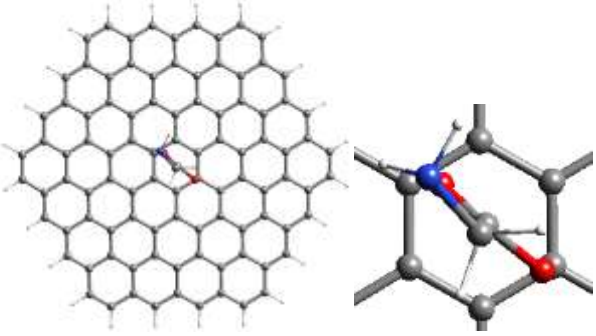
Reference	ΔE_p BCPE / V	ΔE_p GL-MCPE / V	Scan rate, V s^{-1}
[7]	0.056	0.048	0.050
[27]	0.248	0.148	0.100
[6]	0.101	0.093	0.100

Quantum modeling of GLGR complexes.

Density functional theory-based first principle calculations are helpful in predicting the interaction between GR and GL. Usually, several monomers (here GL) may deposit on the CPE surface as monomers, dimers, or polymers. For modelling purposes with the limited computational facility, we have placed a single GL (monomer) on the GR substrate as prescribed in previous literature [5]. GL comprises methylene, carboxylic acid, and an amino group. It is interesting to know which group has favourable interaction with the graphene surface. All possible modes of GL interaction with graphene are shown in Figure 1. GLGR complex formed by the interaction of the carboxylic acid group has minimum energy as shown in Table 2. Therefore, GL will horizontally interact with the GR surface as shown in Figure 1(a), and this model is considered for further analysis. GL interaction with GR surface by amine group (Figure 1(b)) and carboxylic group (Figure 1(c)) are not considered for further studies.

GLGRa; GL interacting with GR in a horizontal way

GLGRb; GL interacting with GR with an amine group



GLGRc; GL interacting with GR with a carboxylic acid group

***Figure 1**. Quantum chemical models of GLGR. Gray: carbon, blue: nitrogen, red: oxygen, white: hydrogen*

***Table 2.** Energies of GLGR complex*

Model	Energy, eV
GLGR-a	0.000
GLGR-b	0.124
GLGR-c	0.065

FMO and analytical Fukui analysis of GL

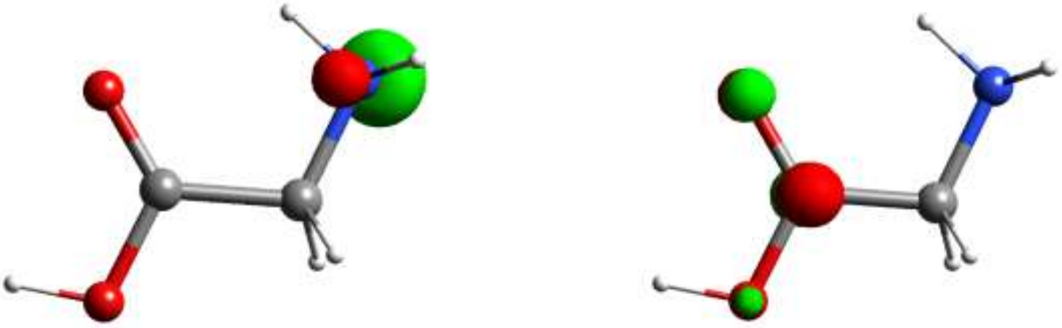
FMO theory was introduced by K. Fukui *et al.* [31-33], and it provides an intriguing method for predicting ET reactivity based on the locations of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). During redox electrochemical processes, HOMO undergoes oxidation and LUMO undergoes reduction. For identifying electron transfer sites, simulations based on the Fukui function can be used in chemical and electrochemical applications. Fukui function is defined by the following equation [34-36]:

$$f(\mathbf{r}) = \left[\frac{\partial \rho(\mathbf{r})}{\partial N}\right]^{+/-}_{v(r)} \tag{1}$$

Here, $\rho(\mathbf{r})$ is the electron density, N denotes the number of electrons in the system, and the + and - signs denote electron addition and removal, respectively.

In electrochemistry, the Fukui function is commonly employed to explain redox reaction processes [3-8,35]. However, analytical Fukui functions based on Auxiliary density perturbation theory (ADPT) have advantages like applicability to larger systems with reduced human errors [36]. It will also eliminate artifacts of the numerical method [36]. Therefore, we are using ADPT-based analytical Fukui functions in the current work.

FMO and analytical Fukui computational results of glycine are shown in Figure 2. The HOMO of glycine (Figure 2(a)) is situated in the amine group and LUMO is positioned in the carboxylic acid group (Figure 2(b)) results were further supported by simulation utilizing the Fukui function in this study. $f^{-}(\mathbf{r})$ in Figure 2(c) and $f^{+}(\mathbf{r})$ in Figure 2(d) show the results of simulations using the Fukui equation, which consistently demonstrates that the glycine oxidation site is situated at the amine group and the glycine reduction sites are placed on the carboxylic acid group. To say it in another way, the amine group of glycine will be easily oxidized, whereas the carboxylic acid group will be reduced easily.



HOMO [ISO=0.02; Grid=0.2] LUMO [ISO=0.05; Grid=0.2]

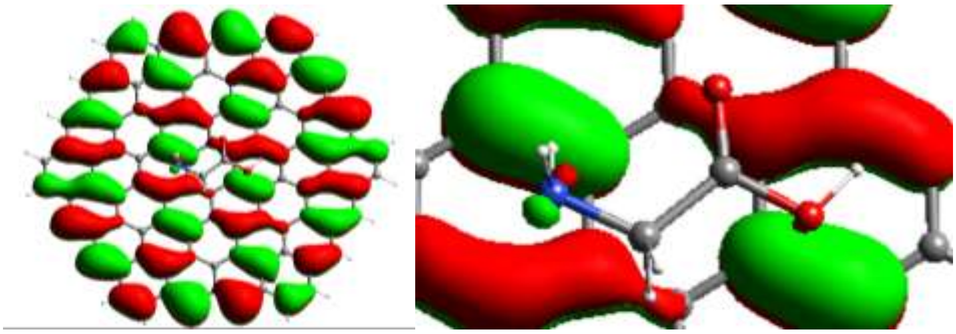
$f^{-}(\mathbf{r})$ [ISO=0.03; Grid=0.2] $f^{+}(\mathbf{r})$ [ISO=0.03; Grid=0.2]

Figure 2. *FMO and analytical Fukui analysis of glycine*

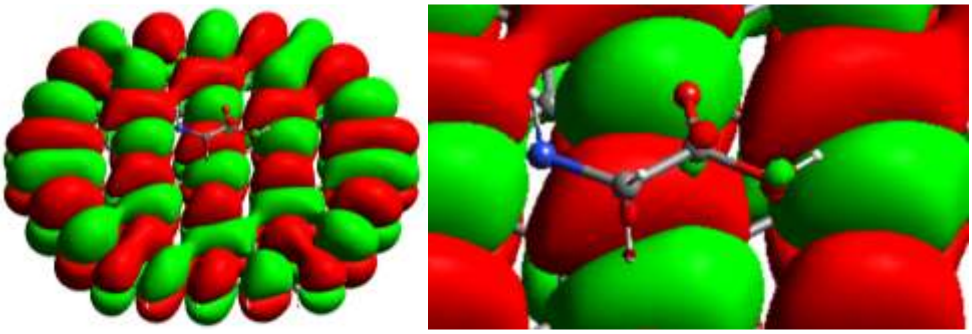
FMO and analytical Fukui analysis of GLGR

FMO and analytical Fukui computational results are shown in Figures 3 and 4, respectively. The highest occupied molecular orbital (HOMO) of GLGR is positioned on the terminal carbon atoms and amine group (Figure 3(a)), whereas the lowest occupied molecular orbital (LUMO) is placed on the terminal carbon atoms and a carboxylic acid group of glycine (Figure 3(b)). The results of this study show that the amine group in the glycine molecule is involved in oxidation, whereas the carboxylic acid group is involved in reduction.

As can be seen in Figure 4(a), the amine group is more probable for nucleophilic reactions (loss of electrons). In GL amino group has the N atom, which is comparatively less electronegative than the O atoms of the carboxylic acid group. Therefore, amine group of GL acts as an oxidation site on the electrode interface. Similarly, as can be seen in Figure 4(b), the carboxylic acid group is more probable for electrophilic reactions (gain of electrons). Carboxylic acid has two O atoms with comparatively higher electronegative than C and N. Therefore, the carboxylic group of GL acts as a reduction site on the electrode interface.

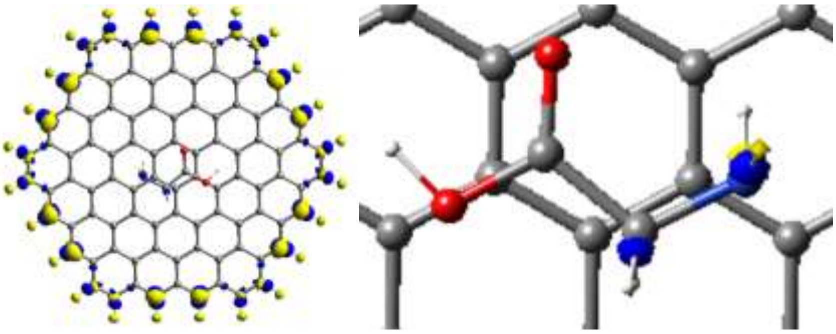


HOMO [ISO=0.01; Grid=0.2]

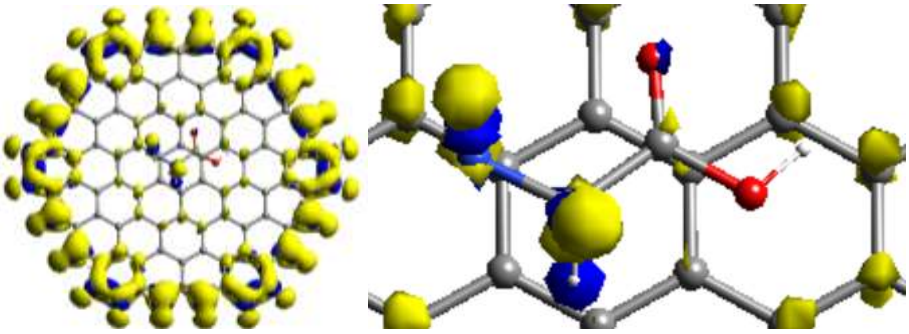


LUMO [ISO=0.03; Grid=0.2]

***Figure 3**. FMO of glycine graphene complex*



f⁻(**r**) [ISO=0.03; Grid=0.2]



f⁺(**r**) [ISO=0.03; Grid=0.2]

***Figure 4**. Analytical Fukui analysis of glycine graphene complex*

Conclusion

Previous reports proved that GL acts as an electrocatalyst on the GR surface and improves its ET activity. The ET properties of the GL-modified carbon surface can be understood using DFT-based quantum chemical models. Till now, GLGR ET properties were not verified by theoretical methods, but in the present work, FMO and analytical Fukui functions are utilized to observe ET sites at the GLGR interface. The obtained results propose that on the GL-modified graphene electrodes, the amine group increases oxidation ET sites, and the carboxylic acid group increases reduction sites. As a result, voltammetric signals will also increase, increasing the sensing ability. Thus, current work will give theoretical evidence to explain the catalytic activity of GL on the carbon surface.

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