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Graphene Nanoflakes as a New Nanobiosensor for Histidine Amino Acid in Fish with Gas, Ethanol, DMSO and Water Environment

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ABSTRACT

The interactions of biomolecules with nanomaterials are important topics to design new materials for nanobiosensors applications. In this study, we investigate graphene nanoflakes (GNFs) as a new nanobiosensor for histidine (His) amino acid with the gas, ethanol, DMSO and water environment by using results of the density functional theory (DFT) calculations. The polarizable continuum method was used to investigate solvent effects on the structural properties, energetic parameters, global reactivity indices. To investigate the applications of biosensor of the real physical cases, gas with low polarity, ethanol with modest polarity, and DMSO and water with high polar solvent were studied. by increasing the electric permittivity of solvents, the stabilization energies of different complexes of biosensor moves to a lower value as of the additional attractive interactions between nanobiosensor and solvent. The His/GNFs shows high stability with considerable values of stabilization energies, charge transfer and sensible energy gap in a polar medium which confirms both in the living and in glass biosensing application. The field of nanobiosensor was developed because to the same length order of the magnitude scale of many of the fundamental building blocks of life with nanoscale material. Nanomaterials that depend on the biosensors with high sensitivities, low detection limit and short response time are good candidates for biosensing applications.

Keywords: Biosensor; Histidine; Graphene nanoflakes; DFT; Adsorption.

1. INTRODUCTION

A biosensor is an analytical device, which is employed for the sensation of the chemical substance, which involves a biological component with a physicochemical sensor [1, 2]. Biosensors are devices used to sense the presence or concentration of a biological analyte, for example a biomolecule, a biological structure or a microorganism. Biosensors are very useful devices for evaluating a wide spectrum of analytes which contain gases, organic compounds, bacteria and ions [2]. A biosensor is employed for sensation of an analyte which includes biological molecules with a physicochemical sensor. Interaction of small biological molecules, cells, or protein to the sensor surface is a main part in a biosensor. The key requirements for

a biosensor technique to be useful in relations of research and medical, and commercial applications are the identification of the target element, the potential for disposable portable discovery systems, and availability of suitable biological recognition element to be chosen to detective laboratory-based methods in some states [3, 4].

Proteins are large bio molecules involving of one or more long chains of the amino acid residues. Proteins perform a large number of functions within the organisms, counting DNA replication, catalyzing metabolic reactions, providing structure to cells and organisms. Proteins are the main structural synthesis of all cells in the body that can be detected by a nanobiosensor. They involve of chains of amino acid subunits combined together via peptide bonds. Determination of the amino acids is significant in many applications, particularly in biotechnology and food [5, 6].

Histidine is the important amino acid in mammals and humans. It is an α-amino acid which is used in the bio synthesis of proteins. Histidine is an α-amino acid with imidazole functional group and it is one of the twenty three protein genic amino acids. It comprises α-amino group, a carboxylic acid group, and an imidazole side chain, which classify it as a positively charged amino acid at physiological pH. Histidine long has been known as a scavenger of the hydroxyl radical and of singlet oxygen, a biologically significant non radical toxic oxygen species which is greatly reactive because of an excited electron promoted to a higher energy orbital [3].

Histidinemia is a rare hereditary metabolic disorder described by a deficiency of the histidase, that is needed for the metabolism of the histidine. The concentration of histidine is raised in the blood. Extreme quantities of histidine, imidazole pyruvic acid, and other imidazole metabolism products are excreted in the urine. The majority of persons with histidinemia have no observable indications which would show that a person has this disorder [3, 7].

The purpose of the present study is to design a new nanobiosensor to histidine amino acid. Thus, we investigated graphene nanoflakes (GNFs) to gain this purpose by using results of the density functional theory (DFT) investigations. We employed orbital analyses to discovery possible hybridizing between adsorbent and adsorbates.

2. COMPUTATIONAL DETAILS

The complete geometric properties and energy calculations of the graphene nanoflakes were realized in the presence and absence of a Histidine molecule by using results of the density functional theory (DFT) at the level B3LYP functional and the 6-32G(d) basis set with Gaussian 09W software [8, 9]. The B3LYP density functional has been previously presented to reproduce experimental proprieties and has been usually used in nanostructures because of the accuracy associated with it [10-14]. The adsorption energy (E_{ads}) of Histidine on the pristine and the doped GNFs are calculated by the following equation [15, 16]:

$$E_{\mathrm{ads}}(\mathrm{PGNFs}) = E_{\mathrm{His/GNFs}} - (E_{\mathrm{PGNFs}} + E_{\mathrm{His}}) \qquad (1)$$

where the $E_{\mathrm{His/PGNFs}}$ represent the relaxed energies of the complexed form of pure GNFs; E_{PGNFs} is the total energy of the of the pristine GNFs; and then E_{His} refers to the energy of isolated Histidine molecule, respectively. The sign of the absorption energy is negative which indicates the exothermic nature of the adsorption.

The density of states (DOS), frontier molecular orbital (FMO), and all of the energetic properties were achieved with the same level of theory. DFT-based and with Koopmans theorem the descriptors of the stability and the reactivity for the sensor were defined [10, 17]:

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{V(\vec{r})} \quad (2)$$

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{V(\vec{r})} \quad (3)$$

$$S = \frac{1}{2\eta} = \left(\frac{\partial^2 N}{\partial E^2}\right)_{V(\vec{r})} \quad (4)$$

$$\omega = \frac{\mu^2}{2\eta} \quad (5)$$

where E is the total electron energy, N is the number of electrons at a constant external potential $V(\vec{r})$, μ is the chemical potential, S is global softness, η is the chemical hardness, and ω is the electrophilicity index. In the next section, we will present the results, which are calculated directly from DFT method with Gaussian 09W software and the equations 1-5.

3. RESULTS AND DISCUSSION

3.1. Geometric properties

We select GNFs as a model biosensor, that consists of 24 carbon atoms and 12 atoms of hydrogen, as seen in Fig. 1(a). After a full structure relaxation, the geometric properties and the bond lengths of GNFs and Histidine are given in Fig. 1, respectively. The results show that the bond lengths of the C-C bond (1.42 Å) are in good agreement other results in ref. [14, 18, 19]. To study the interactions between GNFs and Histidine, adsorption of Histidine molecule on the surface of GNFs were studied and shown in Fig. 2.

To relate the applications of the biosensor to the real physical cases, gas with low polarity (ε = 1), ethanol with modest polarity (ε =24.55), and DMSO (ε = 48.90) and water (ε = 78.39) with high polar solvent were considered [20]. The values of the total energies of complicated structure, adsor-ption energies and dipole moments that are calculated by DFT/ 6-31G (d) level, of His/GNFs in four environments for all complexes are shown in Table 1.

From Table 2, it is noted that by increasing the electric permittivity of solvent, there is a decrease in the total and adsorption energies, while it is seen an increase in the dipole moment, where the largest dipole moment value is (9.646 D) in water. The negative value of E_{ads} (-137.2 eV) indicates to the stable systems. Dipole moment (α) is another important factor in the molecular orbitals analysis. Higher α normally is associated with higher values of interaction energy that seems to be sensible for the reason that higher α means greater shifts in the probability distribution of electrons.

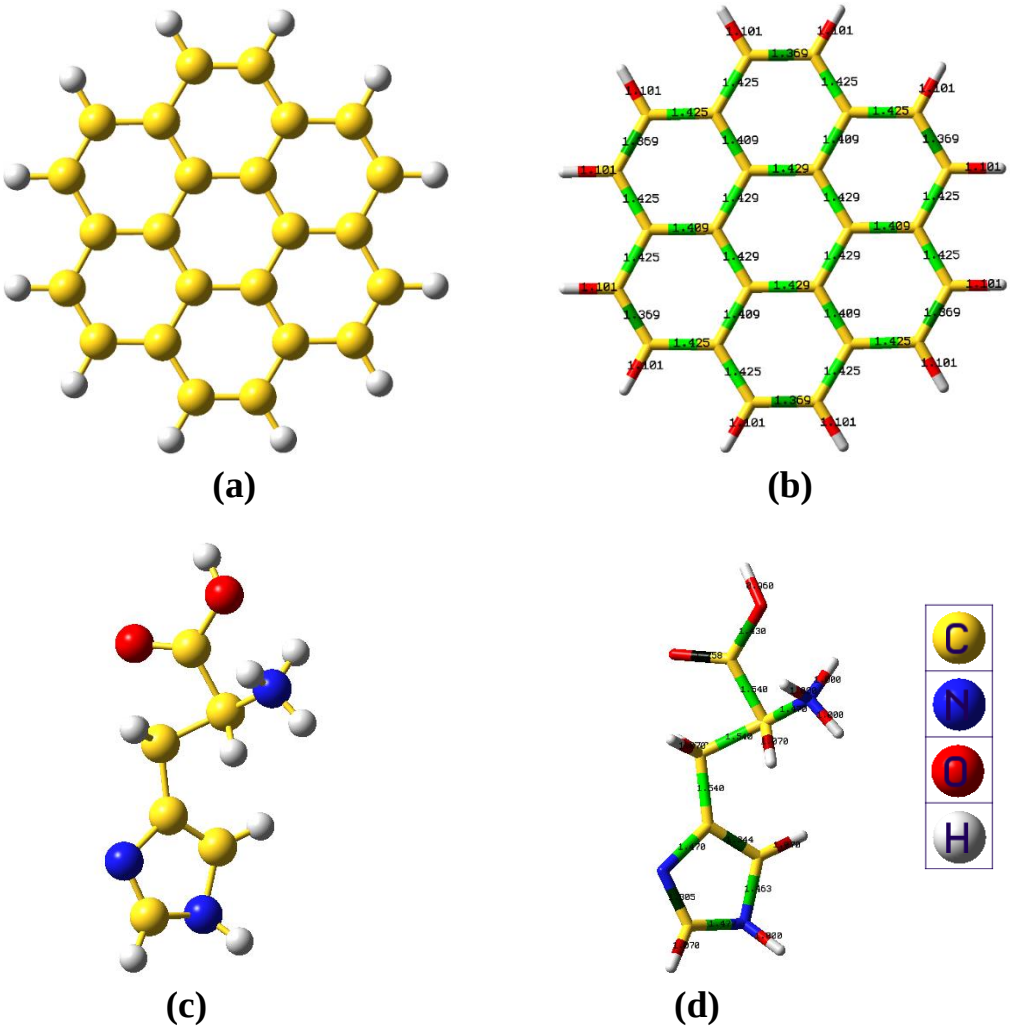

Fig. 1. *The structured geometries and the bond lengths (in angstrom unit) of graphene nanoflakes (a and b) and histidine amino acid (c and d) with the bond lengths in angstrom.*

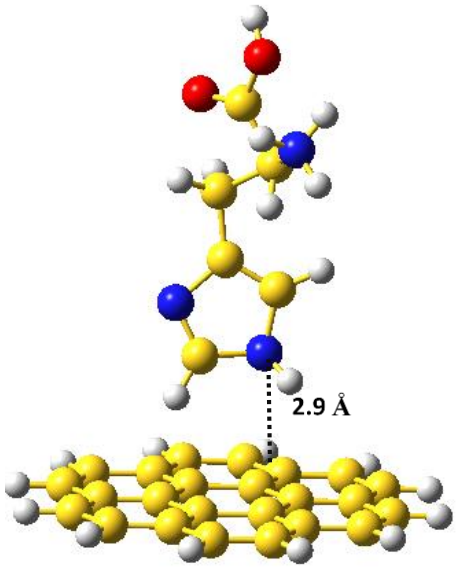

Fig. 2. *Adsorption of histidine amino acid on GNFs with the interatomic distances in angstrom.*

Table 1. *The total energy (E_{tot}), dipole moment (D_m/Debye), HOMO energies (E_{HOMO}), Fermi level energy (E_{FL}), LUMO energies (E_{LUMO}), and energy gap (E_{gap}) calculated in gas phase for graphene nanoflakes and histidine amino acid.*

	E_{tot}	D_{m}	E_{HOMO}	E_{FL}	E_{LUMO}	E_{gap}
GNFs	-24948.14	0.00002	-5.615	-3.548	-1.482	4.133
His	-14938.37	7.422	-5.673	-2.685	0.302	5.975

* All energies are in eV unit.

Table 2. *The total energy (E_{tot}), adsorption energies (E_{ads}), dipole moment (D_m/Debye), HOMO energies (E_{HOMO}), Fermi level energy (E_{FL}), LUMO energies (E_{LUMO}), and energy gap (E_{gap}), and change of E_{gap} calculated in the gas phase and three environments for His/ GNFs.*

Complex / **Solvent**	**His / GNFs**							
	E_{tot}	E_{ads}	D_{m}	E_{HOMO}	E_{FL}	E_{LUMO}	E_{gap}	$\Delta E_{\mathrm{gap}}\%$
Gas phase (ε = 1)	-40023.74	-137.237	6.597	-3.652	-2.546	-1.440	2.213	-46.454
Ethanol (ε =24.55)	-40024.58	-138.072	9.439	-3.765	-2.655	-1.546	2.219	-46.316
DMSO (ε = 48.90)	-40024.61	-138.102	9.579	-4.471	-3.011	-1.552	2.919	-29.367
Water (ε = 78.39)	-40024.62	-138.116	9.646	-3.770	-2.662	-1.554	2.215	-46.395

* All energies are in eV unit.

3.2. Energetic properties

The frontier molecular orbitals (FMOs) analysis was employed, to study the electronic behavior of the systems under study. Also, the determination of interaction between the biosensor and His molecule can be best described with the concept of FMOs analysis. The highest occupied molecular orbital (HOMO), the lowest unoccupied molecular orbital (LUMO), Fermi level, and energy gap that are important properties related to the FMO were seen in Table 2. The calculated energy gap displays that the GNFs in free mode has the value 4.133 eV, that is in good agreement with previous articles [14, 18, 21], but after the interaction of Histidine molecule with GNFs, the energy gap of GNFs is changed.

It can be observed that the order of energy gap for different solvents. The order of energy gap as important scale of stability in different solvents are in the order; Ethanol < DMSO < Water, see Table 2. These results display that the biosensor has a tendency to has lower reactivity and higher stability in lower the polarized medium.

3.3. The global reactivity descriptors

We used Koopmans' theorem to evaluate solvent effects on the reactivity descriptors, which that: the ionization potential, electron affinity, electronegativity, chemical hardness,

chemical softness, and electrophilicity have been studied in the homogeneous polar medium, and summarized in Table 3. Based on the Koopmans' theorem, the HOMO energy is a well approximation to negative experimental ionization potential and the negative electron affinity is equal to the LUMO energy [4, 22]. Table 3 displays that The chemical potential (μ) of studied biosensor in all solvents increases in the order of Ethanol > DMSO > Water. The chemical hardness (η) and softness (S) are one of the most important parameters to describe the stability and reactivity of the molecules. The molecule, which has the maximum values of chemical softness, is expected to be excellent corrosion inhibitors used for bulk metals in the acidic media. The electrophilicity index (ω) decreases with increasing solvent polarizability, thus, if it is desired to a raise the electrophilicity of nanobiosensor, so the ethanol is the best solvents.

Table 3: *The Global chemical indexes: the chemical potential, chemical hardness, softness and electrophilicity calculated in the gas and three environments for His/ GNFs.*

Complex	Solvent	I_P	E_A	μ	η	S	ω
His /GNFs	Gas phase	-3.652	-1.440	-2.546	-1.106	-0.553	-2.929
	Ethanol	-3.765	-1.546	-2.655	-1.109	-0.555	-3.178
	DMSO	-4.471	-1.552	-3.011	-1.460	-0.730	-3.107
	Water	-3.770	-1.554	-2.662	-1.108	-0.554	-3.199

* All energies are in eV unit.

3.4. The molecular electrostatic potential counter map

Finally, this section, the molecular electrostatic potential (MEP) counter map and the total electron density were constructed. Visualization of variable charge distributions provides deep insight into the chemical reactive position of molecules, intermolecular interactions, molecular properties and prediction of electrophilic and nucleophilic reactions at the specific site of nanobiosensor. The visualized results for energy surfaces of MEP of GNFs, Histidine amino acid, and their adsorbed systems are presented in Fig.s 3 and 4. The electronegativity difference is another important index to define the nature of a chemical bond. The electrostatic potential is designated by a colored spectrum.

These results support the fact that amino acids get physically adsorbed on the GNFs-surface and this works in favor of the suitability of the GNFs as it assures reusability of the GNFs as well as targeted delivery of the amino acid as desorption can be easily achieved. Our results designates that for adsorbing amino acids, the GNFs is a potential candidate than pure graphene and it should be discovered to further biomedical applications.

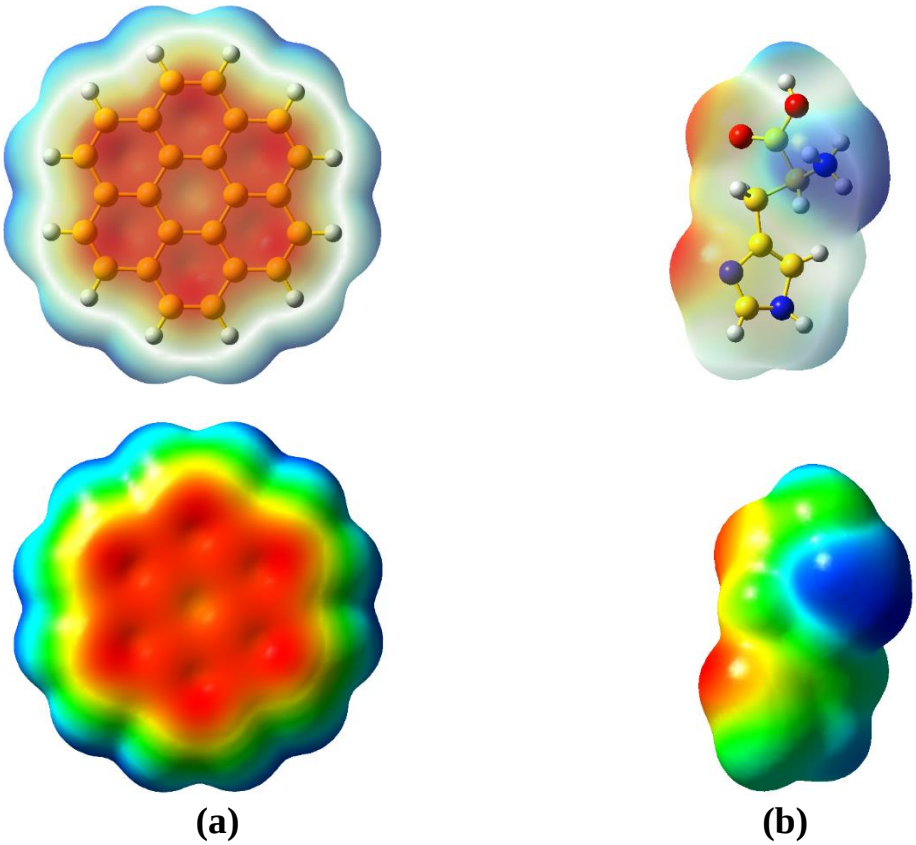

Fig. 3. *The molecular electrostatic potential graphic for (a) GNFs (b) His, a colored spectrum, with red as lowest and blue as the highest electrostatic potential energy values.*

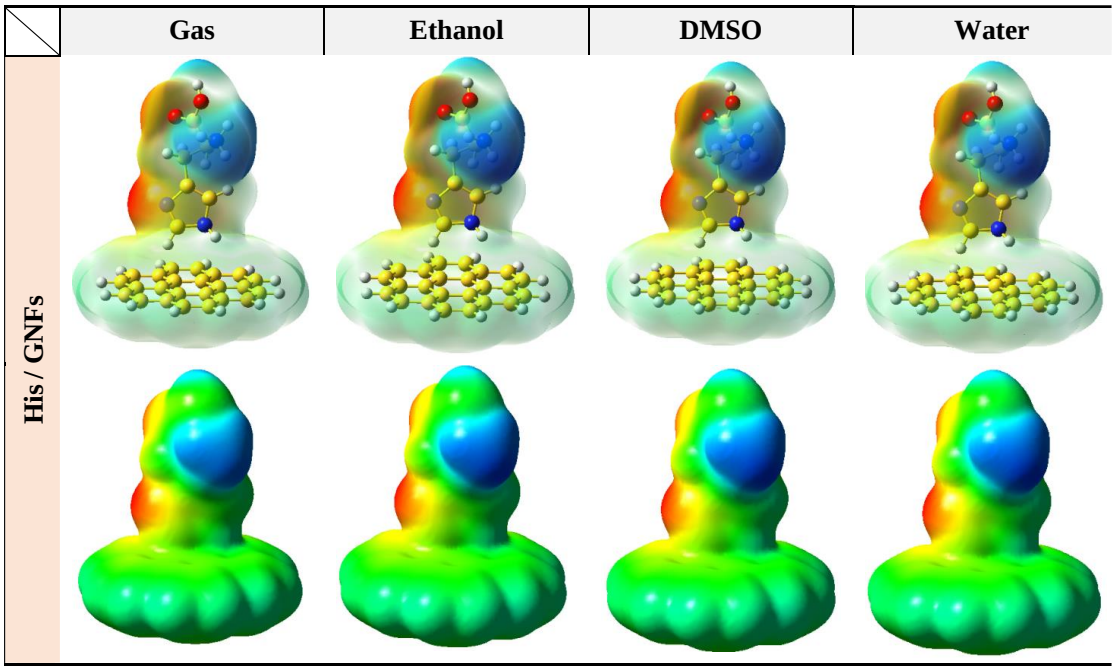

Fig. 4. *The molecular electrostatic potential graphic calculated in the gas and three environments for His/GNFs, a colored spectrum, with red as lowest and blue as the highest electrostatic potential energy values.*

4. Conclusion

The present study, which is - based on density functional theory, has been conducted to study the possibility of using the graphene nanoflakes (GNFs) as nanobiosensor for histidine amino acid depending on their chemical and physical properties. The sensing mechanism in this study indicates that histidine molecule can be adsorbed on the surface of GNFs with appreciable adsorption energies and charge transfer that would lead to important changes of the conductance with studing solvent effect for this nanobiosensor. Then, the lower energy gap displayed the more reactive and less chemical stable configuration of a biosensor in water. These changes might be useful to proposal novel generation of biosensors based on GNFs.

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الكرافين نانوفلكس كمستشعر نانوي بايلوجي جديد للحامض الأميني هيستيدين مع الوسط: غاز، ايثانول، DMSO، والماء

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الملخص: تعد تفاعلات الجزيئات البايلوجية مع المواد النانوية من المواضيع المهمة لتصميم مواد جديدة للتطبيقات النانوية. في هذه الدراسة، فحصنا الكرافين نانوفلكس (GNFs) باعتباره مستشعر نانوي بايلوجي جديد للحامض الأميني هيستيدين (His) مع الوسط: الغاز، الإيثانول، DMSO، والماء باستخدام نتائج حسابات نظرية الكثافة الدالية (DFT) . حيث تم استخدام طريقة الاستمرارية القطبية لفحص تأثيرات المذيبات على الخصائص التركيبية ، معاملات الطاقة، مؤشرات التفاعل الشاملة. ولفحص تطبيقات المستشعرات البايلوجية للحالة الفيزيائية المختبرية، تمت دراسة الغاز ذو القطبية المنخفضة ، والإيثانول ذو القطبية المتوسطة ، و DMSO والماء ذوات القطبية العالية. ووجد بان مع زيادة السماحية الكهربائية للمذيبات، فان طاقات الاستقرارية للتراكيب المختلفة تنتقل إلى أقل قيمة، بالاضافة الى التفاعلات الجذابة الإضافية بين المستشعرات النانوية البايلوجية والمذيب. ان النظام (His/GNFs) يقدم استقرارية عالية مع القيم المفروضة لطاقات الاستقرارية ونقل الشحنة وفجوة الطاقة المعقولة مع الوسط القطبي المتوافق مع تطبيقات الاختبار الحية والزجاجية. ان تطور مجال المستشعرات النانوية البايلوجية كان نتيجة ان مقياس طول الوحدات الأساسية للحياة هو تقريبا نفس طول المواد النانوية. ان أجهزة الاستشعار البايلوجية المستندة على المواد النانوية ذات الاستشعار العالي، الحد الأدنى للاكتشاف، ووقت الاستجابة القصير تجعلها مرشحات جيدة لتطبيقات الاستشعار البايلوجي.

الكلمات المفتاحية: مستشعر بايلوجي، هيستيدين، كرافين نانوفلكس، DFT ، الامتزاز.