

Applications of DNA bases, Graphene and Biosensors : A Critical Review

Shamsan Ali¹, Baliram G. Lone²

¹Department of Physics, Aden University, Aden, Yemen

^{1,2}Nanomaterials Research Laboratory, Department of Physics, Vinayakrao Patil Mahavidyalaya Vaijapur, Dist. Aurangabad, Maharashtra, India

ABSTRACT

Article Info

Volume 9, Issue 2

Page Number : 303-313

Publication Issue :

March-April-2022

Article History

Accepted : 10 April 2022

Published: 22 April 2022

The current research paper presents a theoretical exploration of the interaction between 2-D nanomaterials and the DNA bases that embody graphene properties and biosensors applications. Regarding its role as a conveyer of genetic information, Deoxyribonucleic acid (DNA) has been understood as a constructed substance for various components and structural collations with nanoparticle merits. It is counted as the bearer of genetic information in the human being's life, where it is a fundamental biomacromolecule in almost all living apparatuses. Because of DNA's self-recognition characteristics (based on the specific base pairing of G-C and T-A), more attention has been drawn to monolayer films of nucleic acids. It is seen that many doping techniques have been carefully investigated. Thus, this survey article provides a new and comprehensive outline of the modern strategies that include specifically immobilized DNA on Graphene. further, it is expected in the near future that there will be a designee of DNA nanodevices that are distinguished in smartness, accuracy, and sensitivity where they will contribute to the fields of biological analysis, clinical diagnosis, and biomedicine

Keywords : DNA Bases, Graphene (Go), Graphene Oxide (rGo), and Biosensing.

I. INTRODUCTION

The DNA sequence is the blueprint for life on Earth. [1] it encodes information about individuals' shape and physical appearance about how their bodies function. [2]. It can detect disease diagnosis and treatment, cancer detection, forensic sciences, evaluation, environmental monitoring, food safety, and agriculture. [3]. The DNA molecule is composed of a monosaccharide sugar (deoxyribose), a phosphate

group, and four different nitrogen-containing nucleobases. These include two purines, adenine (A) and guanine (G), and two pyrimidines, thymine (T) and cytosine (C). [4, 5]. C and T are frequently interchangeable; the same pattern holds for nucleosides, with A-T and G-C couples' interaction energies falling between the constituent bases. Calculations of the theorem, which take into account van der Waals interaction and solvation energy, indicate that the trend is G>A- T>C.

The interaction between various DNA sequences and the graphene surface, according to the signal detected by the device during the DNA tentacular, biosensors can also be classified as electrochemical DNA sensors [6-8], electronic sensors [9], and optical DNA sensors [10] and DNA biosensors. Increased sensitivity, extreme specificity, and rapid response have demonstrated potential for DNA tests.

Andre Geim and Konstantin discovered the nanomaterial Graphene in 2004 and were awarded the Noble prize in physics in 2010 due to their groundbreaking [11]. The significant advantage of using two-dimensional materials in molecule sensing is their high specific surface area to volume ratio [12]. Graphene is one of the most efficient nanomaterials, with a considerable surface area (2600 m²/g).

Two-dimensional nanomaterials are a large family with numerous groups of assemblies and crystalline structures collectively coating a wide range of electrochemical and physical properties, some of these family members as (Graphene (G), Graphene oxide (Go), and reduced Graphene oxide (rGo) as shown in Figure 1. Graphene is made out of carbon atoms [13, 14] Since the first produced in 2004. [15] it is a single layer of carbon atoms that are sp²-bonded together and arranged in a honeycomb structure [16], exhibiting extraordinary chemical, electrical, material, optical, and physical properties [17]. Because of the varieties in their chemical compositions, (G) and (rGo) have different chemical and structural properties. It is observed that the most significant dissimilarities in the electrical connection, hydrophilic activity, mechanical force, and dispensability of these materials [18].

Recently, various novel ideas for DNA sequencing have been proposed theoretically and experimentally using numerous graphene nanostructures. Go and rGo have multiple properties used in the bank of power implementations, sensors, supercapacitors, solar energy cells, and biomedical applications.

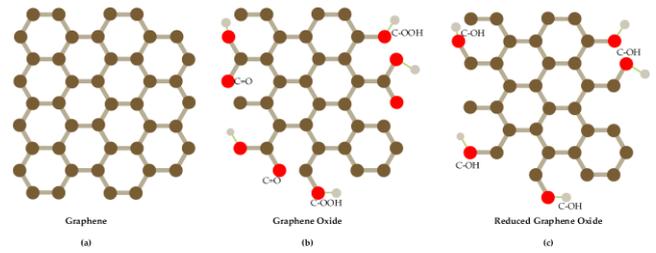


Figure 1: Structures of graphene-based materials show (a) pure Graphene, (b) (Go), and (c) (rGo).

This paper highlighted the state of graphene science and Technology, emphasizing its potential applications in biosensors, presenting several general properties and applications of (G), (GO), and describing the interaction between DNA sequences and graphene material for biosensors Applications. [3] They investigated the condensation of nucleobases on 2D Transition-metal Dichalcogenides and Graphene Sheets and the resulting shifts in the electronic structures due to adsorption and the observed optical absorption spectrum. They found all nucleobases are physisorbed on MoS₂ and WS₂ due to van der Waals interaction, which is similar to nucleobases on GRA [14] investigated the chemical reactions with Graphene – DNA interaction develop a new biosensor fabrication strategy. They drew plans to point out that a new technique to figment several forms of biosensors can be evolved by mixing this feature with successional chemical reflections.

Using the glucose sensor as an example, while the detection target can regulate the graphene DNA interaction via three cascade chemical reactions, electrochemical techniques are used to detect the target-regulated graphene DNA interaction.

II. PROPERTIES OF GRAPHENE

The Graphene-based material has some properties, such as superior mechanical properties, good conductivity, and ion-transport insulation. Graphene is a highly stiff substance with good thermal conductivity, no effective mass, impermeable to gases,

has a high charge carrier mobility, and is transparent optically [19].

Mechanical Properties

The hardness of Graphene has been determined to be greater than that of diamond and approximately 300 times that of steel. Graphene has a tensile strength greater than one terapascal. It can be stretched to a maximum of 20% of its original length, and no boundaries exist between crystals, pure single-layer sheet, and specific gravity - 0.77 mg / sq.m [20, 21]

Chemical Properties

Chemically, Graphene is the most reactive type of carbon (and, in general, all solid materials) because each atom is exposed to chemical reactions on both sides due to the 2D structure. The carbon atoms at the edges of graphene sheets have a distinct chemical reactivity.

The temperature at which graphene burns is shallow, less than 350 °C. Graphene has the highest ratio of edgy carbons (compared with similar materials such as carbon nanotubes).

Graphene is generally amended with oxygen- and nitrogen- including functional groups [22, 23]

Thermal Properties:

Graphene is an ideal thermal conductor; at room temperature, its thermal conductivity is significantly greater than all other carbon structures, including carbon nanotubes and diamonds ($> 5000 \text{ Wm}^{-1}\text{K}^{-1}$). Graphite, the three-dimensional version of Graphene, has a thermal conductivity of approximately five times lower ($1000 \text{ Wm}^{-1}\text{K}^{-1}$). The ballistic thermal conductance of Graphene is isotropic, which means it is the same in all directions [24]. The material's high electron mobility and thermal conductivity may result in faster and better chips at dissipating heat. Thermal Conductivity - $5000 \text{ Wm}^{-1} \cdot \text{K}^{-1}$ usual transmission rate, absorbs 2.3% white light, Thinnest 0.335 nm [25].

Optical Properties:

Graphene is transparent to the naked eye, nevertheless just one atom thick. Due to its unique electronic and optical properties, it absorbs a whopping 2.3 percent of

the light that passes through it. Graphene was photographed in transmitted light. The naked eye can see this one-atom-thick crystal.

Electrical Properties:

Because of its crystal and band structures, Graphene exhibits remarkable electrical properties.

Electrical Characteristics Graphene is a 2D semimetal with a zero-overlap structure with extremely high electrical conductivity (It contains charge carriers in the form of holes and electrons.). Electrons can pass more easily through Graphene than even copper. The electrons move at a hundredth of the speed of light through the graphene sheet. High charge carrier mobility, with values as high as $100 \times 10^{-3} \text{ cm}^2/\text{Vs}$., and in some cases as high as $200 \times 10^{-3} \text{ cm}^2/\text{Vs}$. [26, 27].

Recent nanotechnology-focused research has yielded a plethora of innovative material systems suitable for constructing biosensors (nanostructures, carbon nanotubes (CNT), Graphene, and 2D materials) 2D materials, on the other hand, have the most significant surface-to-volume ratio of any material. This property makes them particularly well suited for sensor applications. As a result, the number of publications devoted to biosensors utilizing 2D materials as a transducer has been steadily increasing since the discovery of Graphene, as seen by a simple PubMed search (Figure 2) using the keywords "graphene sensors" and "graphene biosensors,"

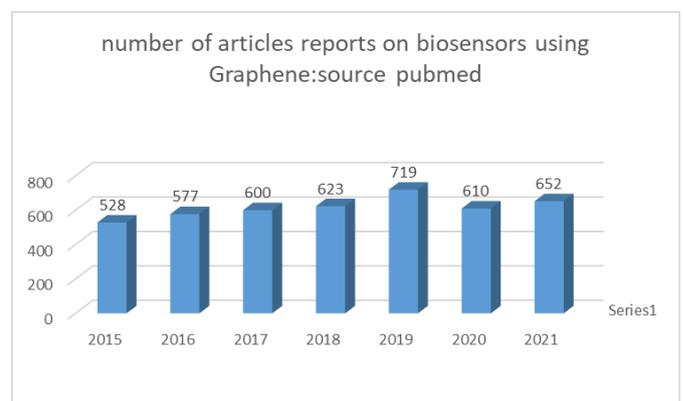


Figure 2: several articles report on biosensors used during 2015–2021. Source: PubMed research

III. BIOSENSOR OPERATION AND DEVELOPMENTS IN BIOSENSING TECHNOLOGY

In this regard, the Biosensors of operation designing and domains of A biosensor can be described as a system that converts a biorecognition event into another signal, such as an optical, electrical, physical, or chemical signal order to measure one or more analytes. [28]. Biomedical nanotechnology is a rapidly developing field with enormous science-technical potential [29]. A biosensor is a technologically advanced miniaturized device with a bio-sensitive layer linked to a signal detection transducing system. The bio-sensitive layer is formed by immobilizing a biological recognition component (antibody, oligonucleotide, enzyme, or the entire cell) on the biosensor's surface see Figure 2 [30].

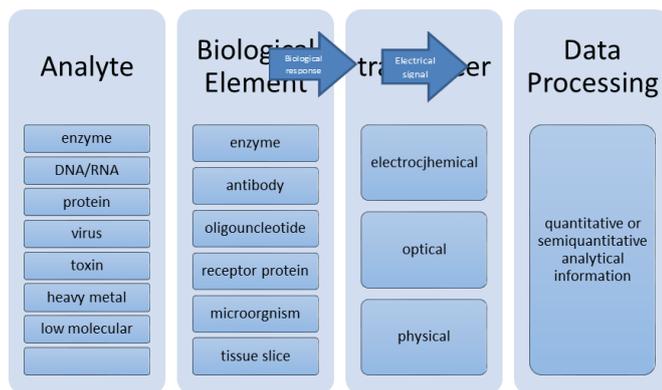


Figure 3 The operation of a biosensor and its main components are as follows: The transducer transforms the biological signal into an optical signal, electrochemical, or electrical signal, which is then processed to provide the information[31].

Biosensors are classified as electrochemical, physical, Thermal biosensors, Piezo-electric biosensors, or optically based on their transducer device and detection process.

Several chemical reflections in an electrochemical biosensor form absorb electrons or ions, resulting in a modification in the solution's electrical characteristics that might be sensed and employed as measurement parameters.

Electrochemical biosensors: are combined systems that utilize biological recognition components in conjunction with an electrochemical transduction element to supply precise analytical data that is quantitative or semi-quantitative. Amperometry, Conductimetric, and Potentiometry are commonly used in electrochemical biosensing. Since biosensor research began, amperometric biosensors have achieved the most significant commercial success, Among the various kinds of biosensors [32]. The latest developments in electrochemical biosensors have comprehensively been analyzed by [33, 34] Loh et al. [35] They covalently grafted or stacked the platform of Graphene epitaxially anodized with a high concentration of COOH groups and showed its ability to detect immobilized DNA. Covalent grafting of probe DNA onto anodized Graphene was discovered to provide a more comprehensive dynamic range and a more sensitive response than the π - π stacked DNA probe.

1-Amperometric Biosensors:

The amperometric biosensor has high sensitivity and can detect electroactive species present in biological test samples. Because biological test samples are not always intrinsically electroactive, enzymes are required to catalyze the radioactive species processing.

2-Conductimetric Biosensors:

The Conductometric biosensors have several significant advantages: they do not require a reference electrode; they operate at low-amplitude alternating voltage, which prevents Faraday processes on the electrodes; they are light-insensitive, and they can be easily miniaturized and integrated using a low-cost thin-film standard technology [36].

The electrical conductance resistance of the solution is being calculated; when electrochemical reactions generate ions or electrons, the solution's conductivity or resistivity varies. This adjustment is calculated and balanced on an appropriate scale.

3. Potentiometric Biosensors:

A potentiometric biosensor is an instrument that combines a biological sensorimotor component with a

potential electrochemical transducer. Typically, potentiometric biosensors rely on a biochemical reaction that produces a simpler chemical specie and then detects it electrochemically (NH_4OH , CO_2 , pH, H_2O_2 , etc.). A potentiometric biosensor generates an analytical signal in the form of an electrical potential [37].

The working theory is based on the fact that electrochemical reactions induce current flow when a ramp voltage is supplied to an electrode in a solution.

4-Optical detection biosensor:

Optical biosensors' fundamental concept is to generate an electrical signal proportionate in intensity or frequency to the amount of a particular analyte or collection of analytes bound by the biosensing component. [38]. The calculated output transducer signal for this type of biosensor is light [39, 40].

IV. BIOSENSORS DESIGN AND APPLICATION OF TWO-DIMENSIONAL NANOMATERIALS

Recent publications include several excellent reviews on biosensors based on Graphene. [41]. The field of graphene analogues, on the other hand, is largely unexplored and is not covered in any specific study. As a result, we concentrated our efforts on the most present publications on biosensors of based Graphene. Zhu et al. [42]. Showed a straightforward and homogeneous DNA and small molecule assay format. We have utilized single-layer assays. Fluorescent nanoprobe constructed with molybdenum disulphide (MoS_2). Narayanan et al. [43]. We classified the reported 2D- biosensors of Graphene into some groups based on the detected analyses.

[42] Huang et al. created a new MoS_2 nanosheet-based microfluidic biosensor for ultrasensitive DNA detection.

As illustrated in Table 1, various biological factors can be successfully absorbed on the surface of two-dimensional non-graphene materials, enabling sensors for a diverse array of biologically relevant targets.

V. DNA DETECTION USING GRAPHENE-NANOPARTICLE HYBRID COMPOSITES

Graphene-Nanostructured (G-NP) composites, in which Graphene, graphene oxide, or rGO layers are decorated with nanoparticles reaching from several nanometers to a to the several hundred nanometers [70] since any atom on the surface graphene sheet is molecular interaction. As a result, electron transport in Graphene can be particularly sensitive to adsorbed molecules. [71]. The electron transfer rate may significantly increase with the addition of metal nanoparticles to Graphene, leading to enhanced electrocution performance considerably. [72].

Numerous investigations have been conducted on Graphene- nanoparticle hybrid compounds' applications for DNA exposure, which can be broadly classified into three categories: electrical, electrochemical, and DNA biosensors with an optical component. Lin and her colleagues [73] combined graphene and gold nanoparticles conjugated with DNA, resulting in the development of an DNA biosensor electrochemical. The ssDNA was collected using the π - π stacking technique on a graphene-modified electrode. Du et al. [74] The authors described an DNA biosensor electrochemical comprised of multilayer graphene-AuNPs immobilized by a dual-labelled stem-loop DNA probe (50-SH and 30-biotin). Wang et al. [56] employed a methylene blue-labelled signal probe to identify sequence-specific DNA and single-base mismatched target DNA with extreme sensitivity. Neenu Varghese et al.

[75] Using isothermal titration calorimetry, they investigated the interaction of two different graphene samples with DNA nucleobases and nucleosides. They discovered that the magnitudes of the nucleobases' interactions with Graphene are comparable to those observed with single-walled carbon nanotubes. Hakkim Vovusha and Biplab Sanyal [3] investigated the adsorption of nucleobases on 2D Transition-metal Dichalcogenides and Graphene Sheets, analyzing changes in electronic structures caused by adsorption and the repercussions in the estimated optical

absorption spectra. They discovered that all nucleobases are physisorbed on MoS₂ and WS₂ due to van der Waals interaction, similar to nucleobases on GRA.

Baliram Lone [76] investigated the molecular bonds and angled calculated before and after the adsorption of adenine and thymine on SWNT; these findings

provide insight into the interaction of DNA with the surface of single-wall carbon nanotubes. The study demonstrates that the electrical structure of metallic nanotubes does not change significantly due to adsorption.

Table 1 Applications of graphene two-dimensional materials in various types of biosensors

Detection element	Sensing substance	Range of detection	Reference
Single-stranded DNA	Nanowalls of graphene	0.1pm to 10 mM	[44]
double-stranded DNA , Single-stranded DNA and single nucleotide polymorphism	(PAMAM) with graphene core	10×10^{-5} to 100×10^{-10} M Detection- limit 1 pM	[45]
DNA	AuNCs/GR	2×10^{-2} fM to 0.02×10^2 pM Detection -limit at 5.7×10^{-2} fM	[46]
Single-stranded DNA	GO	Detection- limit 200 nM	[47]
double-stranded DNA	Epitaxial Graphene	1 μ M	[48]
DNA and exonuclease activity	GO (EB)	0.5×10^2 to 25×10^2 nM	[49]
Single-stranded DNA	rGO (Thi-rGO)	10×10^{-18} to 10×10^{-13} M	[50]
Single-stranded DNA	Exonuclease III (ExoIII) and Graphene oxide	Detection -limit 5×10^{-2} pM	[51]
Single-stranded DNA	Graphene oxide	200nm	[52]
HIV-1 gene	AuNPs/GO nanocomposite	0.5×10^2 fM to 0.01×10^2 nM Detection- limit 15 fM	[53]
Single-stranded DNA	Graphene oxide and exonuclease III	Detection- limit 20 pM	[54]
Deoxyribonucleic Acid	Graphene oxide –Chitosan (CHI) nano-composite	0.01×10^2 fM to 0.5×10^2 nM Detection- limit $0,1 \times 10^2$ fM	[55]
Single-stranded DNA	reduced Graphene oxid (Au NPs/ reduced Graphene oxid)	0.1 μ M to 0.1fM	[56]
Deoxyribonucleic Acid	AuNPs/ERGNO/GCE	20×10^{-8} to 10×10^{-7} M Detection -limit at 100×10^{-8} M	[57]
Single-stranded DNA	(NG) and Fe ₃ O ₄ nanoparticles	10×10^{-15} to 100×10^{-8} M Detection -limit 36.3×10^{-16} M	[58]
Single-stranded DNA of human immunodeficiency virus	Graphene –Nafion composite film	Detection- limit 2.3×10^{-14} M	[59]
Survivin gene	(G-3D Au/GCE)	$50-5 \times 10^3$ fM detection limit 3.4 fM	[60]
Listeria monocytogenes	Au/GR/CILE	100×10^{-14} to 100×10^{-8} M Detection- limit 29×10^{-14} M	[61]

Hepatitis B virus (HBV)	(GO/PGE)	0.2×10^2 to 1.6×10^2 $\mu\text{g/mL}$ Detection- limit 202×10^{-2} μM	[62]
BRCA1 DNA	Graphene/Au	1 fM	[63]
Single-stranded DNA	rGO-graphene double-layer electrode	10×10^{-8} to 10×10^{-13} M Detection limit 158×10^{-15} M	[64]
field-effect transistor	Detection of proteinis	7.13×10^{-2} for a pH of one unit	[65]
fluorescent	Ag	0.25×10^{-2} mg/mL	[66]
electrochemical	$\text{C}_6\text{H}_{12}\text{O}_6$	28×10^{-1} M 3×10^{-2} M	[67]
electro-chemical	$\text{C}_6\text{H}_{12}\text{O}_6$	2.241×10^3 $\mu\text{A/mM/cm}$, 0.1^{-4} mM	[68]
fluorescent	Platform for biosensing Single-stranded DNA	$1-0.8 \times 10^2$ ng.mL ⁻¹	[69]

VI. CONCLUSION

This review article argued the investigation of Graphene interaction with DNA bases in different methods. This article revealed the use of DNA Nanodevices to detect a wide variety of biomolecules, such as nucleic acids, proteins, and cells. We found that due to the advantages of DNA nanotechnology, including its programmability, design capability, stability, and biocompatibility, it has been widely employed in a variety of biological sectors. With this feature with cascade chemical events, a new technique for fabricating an array of biosensors may be devised. With the dangerous growth of terrorism that threatens the lives of people and the deploying of viral diseases, such as the Corona outbreak, there is an essential need for an instrument or system that can identify critical parameters for viruses rapidly, efficiently, carefully, and accurately. In this regard, Biosensors can work basically as cheap, high-efficiency, and quality devices and can be utilized in various applications of the other daily life aspects. In the near future, it is expected that there will be a designee of DNA nanodevices distinguished in smartness, accuracy, and sensitivity where they will contribute to biology, clinical diagnosis, and biomedicine.

It is seen that the progression in nanotechnology impacted the progress of nanostructure biosensors that are distinguished by sensitivity and multitasking. The fundamental aim of Nano- biosensors is to examine any chemical or biophysical remark related to a particular

disease at the molecular or cellular level. These can facilitate molecular diagnostics such as lab-on-a-chip when combined with another technology. Thus, their uses include examining microbes in various specimens, monitoring metabolites in bodily liquids, and detecting pathological cells cancer. Their capability makes them appropriate not for cancer pathogenesis applications but also for laboratory use.

VII. ACKNOWLEDGMENTS

The authors are grateful for the high-performance computing facility available at Nanomaterials Research Laboratory, Department of Physics Vinayakrao Patil Mahavidyalaya, Vaijapur, District Aurangabad, MS, India.

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Cite this article as :

Shamsan Ali, Baliram G. Lone, "Applications of DNA bases, Graphene and Biosensors : A Critical Review", International Journal of Scientific Research in Science, Engineering and Technology (IJSRSET), Online ISSN : 2394-4099, Print ISSN : 2395-1990, Volume 9 Issue 2, pp. 303-313, March-April 2022. Available at doi : <https://doi.org/10.32628/IJSRSET229247>
Journal URL : <https://ijsrset.com/IJSRSET229247>