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Role of graphene in many innovative sensor materials

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Abstract
The objective of the present article is the Role of Graphene in many innovative sensor materials**.** Graphene is an ideal material for sensors. Every atom in graphene is exposed to its environment allowing it to sense changes in its surroundings. For chemical sensors, the goal is to be able to detect just one molecule of a potentially dangerous substance. Graphene now allows for the creation of micrometre-size sensors capable of detecting individual events on a molecular level. Graphene sensors could boost the effectiveness of monitoring vital crops in the agriculture industry. Farmers would be able to monitor the existence of any harmful gasses which could impact upon crop fields and take relevant action. As graphene sensors are so sensitive it is feasible that they could determine the ideal areas for growing certain crops depending on atmospheric conditions. Graphene detects. Ultra-sensitive sensors made from graphene could detect minute dangerous particles helping to protect potentially dangerous environments. Graphene has been making tremendous influences in several research areas due to its unique physical and chemical properties Graphene-based electrochemical biosensors are the most widely used devices which measure the changed electrical signals caused by the electrons produced by the chemical reactions between the target and biorecognition element. Graphene-based biosensors are expected to show great potential in biological analysis and clinical medicine too.

Keywords: Graphene, biosensor, innovative sensor, electrode surface, biological analysis and clinical medicine, engineering application of graphene

Introduction
A sensor is a device that detects events that occur in the physical environment (like light, heat, motion, moisture, pressure, and more), and responds with an output, usually an electrical, mechanical or optical signal. The household mercury thermometer is a simple example of a sensor - it detects temperature and reacts with a measurable expansion of liquid. Sensors are everywhere - they can be found in everyday applications like touch-sensitive elevator buttons and lamp dimmer surfaces that respond to touch, but there are also many kinds of sensors that go unnoticed by most - like sensors that are used in medicine, robotics, aerospace and more [1].
Traditional kinds of sensors include temperature, pressure (thermistors, thermocouples, and more), moisture, flow (electromagnetic, positional displacement and more), movement and proximity (capacitive, photoelectric, ultrasonic and more), though innumerable other versions exist. sensors are divided into two groups: active and passive sensors. Active sensors (such as photoconductive cells or light detection sensors) require a power supply while passive ones (radiometers, film photography) do not [2-3].
Graphene is the thinnest material known to man at one atom thick, and also incredibly strong - about 200 times stronger than steel. On top of that, graphene is an excellent conductor of heat and electricity and has interesting light absorption abilities. It is truly a material that could change the world, with unlimited potential for integration in almost any industry. Graphene is a single layer (monolayer) of carbon atoms, tightly bound in a hexagonal honeycomb lattice. It is an allotrope of carbon in the form of a plane of sp^2-bonded atoms with a molecular bond length of 0.142 nanometres [4]. Layers of graphene stacked on top of each other form graphite, with an interplanar spacing of 0.335 nanometres. The separate layers of graphene in graphite are held together by vanderWaals forces, which can be overcome during exfoliation of graphene from graphite. Due to the special structure of graphene, the obtained characteristics can meet the requirements of high-performance sensors [5]. Therefore, graphene materials have been applied in many innovative sensor materials in recent years. Sensitivity reflects the change in the response of a sensor to a small change in stimulus causing the response and

corresponds to the slope of the calibration curve. For example, graphene-based sensors afford a sensitivity of −0.15 in the detection of dimethyl-methylphosphonate (DMMP) [6].
Chemical warfare agents, particularly nerve agents such as sarin, are exceptionally harmful and incredibly perilous to people. Thus, the sensitive detection of these gases is indispensable for reducing the risk of chemical weapons. Herein, we fabricated a room-temperature chemiresistive gas sensor based on two-dimensional few-layer tungsten diselenide (WSe_2) nanosheets, which were prepared through a facile liquid-phase exfoliation method. The WSe_2-based sensor has demonstrated sensitive and selective detection of dimethyl methylphosphonate (DMMP), which is a well-known simulant of the nerve agent sarin [7]. The sensor based on WSe_2 nanosheets revealed a high response reaching 8.91% to 10 ppm DMMP with a fast response time of 100 s. Furthermore, the sensor displayed reliable stability, excellent selectivity, and a low theoretical limit of detection of about 122 ppb. The enhanced sensing performance of WSe_2 nanosheets can be ascribed to the increase of the specific surface area, which provides more active adsorption sites for DMMP molecules, thereby facilitating the charge transfer process between DMMP molecules and WSe_2 nanosheets. Overall, our results indicate that two-dimensional transition metal dichalcogenide materials have the potential for the design and fabrication of high-performance nerve agent sensing [8-10].
Graphene-based electrochemical biosensors are the most widely used devices which measure the changed electrical signals caused by the electrons produced by the chemical reactions between the target and biorecognition element. The development of biosensors with high sensitivity and low-detection limits provides a new direction for medical and personal care. Graphene and graphene derivatives have been used to prepare various types of biosensors due to their excellent sensing performance (e.g, high specific surface area, extraordinary electronic properties, electron transport capabilities and ultrahigh flexibility). This perspective review focuses on graphene-based biosensors for quantitative detection of cancer-related biomarkers such as DNA, miRNA, small molecules and proteins by integrating with different signal outputting approaches including fluorescent, electrochemistry, surface plasmon resonance, surface enhanced Raman scattering, etc. The article also discussed their challenges and potential solutions along with future prospects [11].
Recently, graphene has been drawing tremendous attraction owing to the outstanding feature of electrochemical, adsorption performance, mechanical strength and flexibility to serve as an attractive candidate for biosensors [12-15]. Graphene, formed by carbon atom hybridization with sp^2 electron orbital, has a high specific surface area, excellent electron transport capabilities and strong mechanical strength, which is essential for constructing biosensors. This review gives a detail of classification and characteristics of graphene, and a detail of the application of various types of graphene and graphene derivatives-based methods with diverse signals outputting approaches to achieve quantitative detection of different kinds of biomarkers including DNA, microRNA, small molecules and proteins. We also comprehensively summarized and compared the detection principle, target molecules, detection limits and detection range of graphene-based different sensors in recent years. Such graphene-based biosensors are expected to show great potential in biological analysis and clinical medicine [16].
Its superiority in terms of strength, electron mobility, surface area, and thermal conductivity are all major factors in the development of greener applications. These properties make graphene ideal for contaminant monitoring systems, water treatment and desalination as well as improving batteries and solar energy technology. These are technologies that could have a positive impact on agriculture and the shift away from petrochemicals [17]. Graphene implementation could even help reduce CO_2 emissions in construction and help produce biodegradable plastics because it has the right properties to replace more harmful materials." Although graphene-based sensors have received considerable attention in health monitoring and biomedical applications, it is crucial to consider the impact of graphene and its derivatives on human health such as its biocompatibility, toxicity, as well as its potential risks to the environment before graphene is integrated with human skin, particularly when implanted into the human body. Numerous studies have been devoted to graphene-based nanomaterials (GBNs) [18].

2. Flexible Sensors
Graphene-based materials have shown potential in flexible and stretchable strain and pressure sensors, photodetectors, Hall sensors, electrochemical sensors, and biosensors. Graphene's electrical properties do not degrade when mechanical strain is applied to it because of its inherent flexibility. As a result, graphene has been considered as an ideal material for making highly stretchable and flexible sensors and other electronic devices.
Investigating this area further, research has shown that flexible strain sensors can be made of piezoresistive graphene, microfluidic liquid metal, and stretchable 151 elastomers. In order to achieve flexible electrical contacts with graphene sensing elements, liquid metal was put into microfluidic channels as interconnect material. There could be an application for flexible strain sensors in wearable electronics, especially for monitoring purposes during sport and exercise. A flexible strain sensor of this type has already been developed by researchers using a graphene-based composite fiber with compression characteristics, which was integrated into wearable strain sensors. The sensor structure was made up of a highly elastic yarn consisting of polyurethane as the core fiber and polyester fibers as the scaffold [19].

3. Physical properties of graphene
Graphene is neither a metal nor a plastic. It's a form of carbon, like diamond or graphite. It is a single layer of carbon atoms arranged in a two-dimensional honeycomb lattice. However, it has properties that can seem metallic, such as high electrical and thermal conductivity. On the other hand, it can also be mixed with plastics to enhance their properties, but it remains distinct from both these categories of materials [20]. Graphene nanocomposite is an inorganic nanocomposite material, which has been widely used in the treatment of tumor at present due to its ability of drug loading, modifiability, photothermal effect, and photodynamic effect. However, the application of graphene nanocomposite is now limited due to the fact that the functions mentioned above are not well realized. This is mainly because people do not have a systematic understanding of the physical and chemical properties of GO (Graphene Oxide**)** nanomolecules, so that we cannot make full use of GO nanomolecules to make the most suitable materials for the use of medicine. Here, we are the first to discuss the influence of the physicochemical properties of graphene nanocomposite on the various

functions related to their antitumor effects. The relationship between some important physicochemical properties of graphene nanocomposite such as diameter, shape, and surface chemistry and their functions related to antitumor effects was obtained through analysis, which provides evidence for the application of related materials in the future [21].

It has a low density, high melting point, and it is a coefficient of thermal expansion. Unlike other non-metals, it has high thermal and electrical conductivity. Chemically, graphite is inert, resistant to heat, pressure, and does not react with water or air at standard temperature. Graphene is a two-dimensional carbon allotrope. It is composed of carbon atoms positioned in a hexagonal design, which can be said to resemble a chicken wire. Graphene has been making tremendous influences in several research areas due to its unique physical and chemical properties [22]. There are several advantages of such graphene-based sensors for sensing, including the following

i) A graphene-based sensor for detecting gas molecules works by measuring alterations in the electrical conductivity of the material. Graphene-based gas sensors operate by adsorbing a gas molecule on the graphene's surface, which acts as donors or acceptors of electrons are showing in Fig 1. (In the picture, the black spheres represent carbon atoms, the red spheres represent oxygen atoms, and the green spheres represent hydrogen atoms). Graphene oxide is a single atom carbon layer where both surfaces of the layer are modified by oxygen containing functional groups. Although it shares some characteristics with graphene, its properties are very different, including low electric conductance and significantly higher chemical activity. GO has found applications in many areas such as membranes, coatings, sensors, photocatalysis, and solar cells [23].

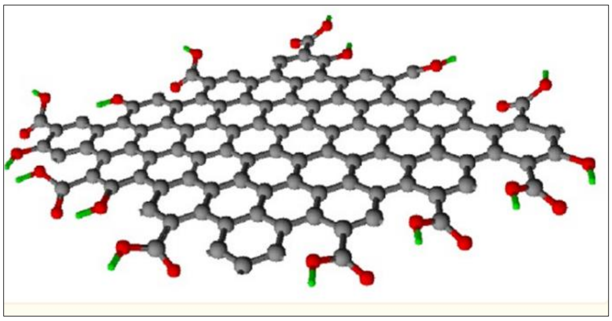


Fig 1: Graphene-based gas sensors

(ii) Strong mechanical strength and pliability

Single-layer graphene possesses a thickness of ~0.335 nm, the hardness of which is higher than diamond due to strong C=C bonding in the atom plane; while opposite to diamond, the interlayer bonding via Van der Waals forces makes it a soft material. This will greatly benefit the development of wearable sensor devices.

(iii) Excellent electronic properties and electron transport capabilities

The carbon atoms of graphene hybridized in the form of sp2 constitute a huge π–π conjugate system in which the electrons are freely moving. These properties make graphene a candidate in the field of electrochemical sensing.

(iv) High specific surface area

2630 m2/g for single-layer graphene theoretically, which gives rise to high densities of attached recognition component or analyte molecules. It contributes to high detection sensitivity and the miniaturization of the device.

3. Chemical properties of graphene

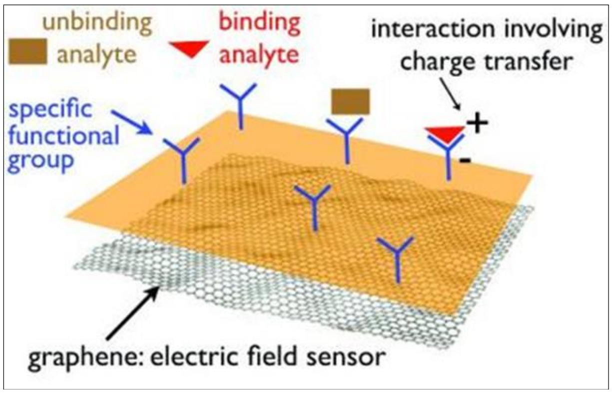
Researchers hope to synthesize a cell-targeted drug-loaded nanoparticles by biologically modifying GO nanoparticles to be specifically identified, phagocytosed, or absorbed by tumor cells to kill tumor cells. The use of folic acid as a solution to this problem has become a common idea because the folic acid receptors on tumor cells are often over expressed, which is much higher than in normal cells [24]. However, the direct linking of FA on GO often leads to physiological fluid aggregation, and the introduction of folic acid is often accompanied by the introduction of other stabilizers to stabilize the nanomolecules [24-26]. This functionalization is preferably noncovalent, as noncovalent functionalization has the advantages of reducing chemical reactions, reducing purification steps, and maintaining the original conjugated structure and physical properties of GO [27-28]. Therefore, it is very important to design a noncovalent functional molecule of GO that can be used as both a stabilizer to prevent the aggregation of GO and a target to tumor cells. At present, a new active targeted drug carrier FA-BSA/GO system has been successfully designed. This system adopts folic acid grafted bovine serum albumin (FA-BSA) as stabilizer and target agent to improve the stability and dispersion of GO in physiological fluid, and good results have been achieved [29]. The authors believe that this idea may provide a better direction for the design and manufacture of antitumor graphene oxide nanomolecules in the future. When designing the molecular carrier, the stability of the drug and the carrier function *in vivo* should be taken into account, while the inherent properties of the drug molecule and the carrier molecule should be retained to maximize the antitumor effect and make it precise.

The application of graphene oxide nanomolecules in antitumor effects is a representative achievement of the intersection of medicine, materials science, and chemistry. GO nanoparticles are modifiable and have good photo thermal and photodynamic effects, which provides a good idea for targeted killing of tumors. Nowadays, graphene oxide nanomolecules have been applied in many antitumor researches. Scientists have carried out various chemical modifications and physical properties control, loaded with different antitumor drugs to kill tumor cells, and achieved certain research results. In the process of application, we found that determining the chemical and physical properties of nanoparticles is a critical step. A lot of special properties of graphene oxide nanometer carrier, such as thermal effect and ability of carrying drugs, are all related to the physical and chemical properties of the nanoparticles, and a multitude of graphene oxide surface oxygen groups are left for us to modify, so as to enrich the nature of nanoparticles. It can be concluded that the development of graphene oxide nanomolecular applications will be based on the understanding, utilization, and expansion of its rich physical and chemical properties. The toxicity of graphene is a complex issue and is currently a subject of ongoing research. Preliminary studies indicate that it may pose some environmental or health risks, but more research is needed to fully understand its effects [30].

4. Graphene and sensors

Graphene and sensors are a natural combination; as graphene âs large surface-to-volume ratio, unique optical properties, excellent electrical conductivity, high carrier mobility and density, high thermal conductivity and many other attributes can be greatly beneficial for sensor functions. The large surface area of graphene is able to enhance the surface loading of desired biomolecules, and excellent conductivity and small band gap can be beneficial for conducting electrons between biomolecules and the electrode surface. Graphene is thought to become especially widespread in biosensors and diagnostics. The large surface area of graphene can enhance the surface loading of desired biomolecules, and excellent conductivity and small band gap can be beneficial for conducting electrons between biomolecules and the electrode surface. Biosensors can be used, among other things, for the detection of a range of analytes like glucose, glutamate, cholesterol, hemoglobin and more. Graphene also has significant potential for enabling the development of electrochemical biosensors, based on direct electron transfer between the enzyme and the electrode surface [31].

Graphene will enable sensors that are smaller and lighter - providing endless design possibilities. They will also be more sensitive and able to detect smaller changes in matter, work more quickly and eventually even be less expensive than traditional sensors. Some graphene-based sensor designs contain a Field Effect Transistor (FET) with a graphene channel. Upon detection of the targeted analyte âs binding showing in (Fig 2.) the current through the transistor changes, which sends a signal that, can be analyzed to determine several variables. Graphene-based nanoelectronic devices have also been researched for use in DNA sensors (for detecting nucleobases and nucleotides), Gas sensors (for detection of different gases), PH sensors, environmental contamination sensors, strain and pressure sensors, and more. Graphene-based magnetic sensor 100 times more sensitive than an equivalent device based on silicon [32].



5. Potential applications

Graphene is an extremely diverse material, and can be combined with other elements (including gases and metals) to produce different materials with various superior properties. Researchers all over the world continue to constantly investigate and patent graphene to learn its various properties and possible applications, which include: Batteries, Transistors, Computer chips, Energy generation, supercapacitors, DNA sequencing, water filters, Antennas, Touchscreens (for LCD or OLED displays), solar cells, spintronics-related products.

Graphene's interaction with the human body is still under active research, and definitive conclusions have yet to be drawn. Some studies suggest that graphene, especially in its nanoparticle form, could potentially have harmful effects if inhaled or ingested, as it could interact with biological systems in unpredictable ways. Conversely, other research indicates the potential of graphene in the biomedical field. Its strength, flexibility, and conductivity could be beneficial in areas like tissue engineering, drug delivery systems, and biomedical devices. As of now, though, the precise effects of graphene on the human body largely depend on its form, exposure level, and the route of exposure [33].

6. Applications of Different Types of Graphene-Based Biosensors

The discovery of graphene provided an immense boost up and new dimension to materials research and nanotechnology. The multidisciplinary characteristics of graphene have a wide range of applications from health to aerospace. Modern graphene research has been directed towards the exploration of new graphene derivatives and their utilizations for fabrication of products and devices. The enhancement of graphene properties by fictionalization or surface modification is another innovative approach. However, like other 2D materials, graphene research also needs amendments and up-gradation in the light of recent scientific output. In this contribution, we have reassessed the recent research output on graphene and graphene-based materials for applications in different fields [34].

A. Graphene and graphene derivatives with properties of a large specific surface area, high electron transport rate and high temperature resistance can be used as a signaling device or carrier of biometric components to achieve a quantitative detection of biomolecules, which is described in detail in the following sections. However, there are more than 10,000 publications about five types of graphene-based sensors (Fluorescence, FA (fluorescence anisotropy), Electrochemistry, SPR (surface plasmon resonance), SERS (surface enhanced Raman scattering). In this manuscript, we only focused on the recent graphene-based biosensors.
B. Fluorescence is the emission of light by a fluorescent tag with labeled targets that have absorbed external incident light, which is a commonly used detection technique in biological monitoring owing to the high sensitivity, low detection limit, good accuracy, etc. Graphene and its derivatives have high surface-to-volume ratio and highly distance-dependent fluorescence quenching ability based on fluorescence resonance energy transfer (FRET), making them universal carriers and quenchers for fluorescence recognition probes or targets [35-37].
C. Enzyme amplification technology can be applied to graphene-based fluorescent sensors.

This method used aptamer as an affinity element to identify ATP, as the amplification capability of Exo III and the adsorption characteristics of graphene contribute to sensitive detection of ATP with a detection limit of 31 nM. Xia *et al*. reported a GO-based fluorescent aptasensor for simultaneous detection of telomerase and miRNA in living cells and tissue samples. Template-strand primer and fluorophore-labeled telomerase/miRNA oligonucleotides were loaded onto GO. In the presence of targets, the double-stranded oligonucleotides would be away from the GO surface, leading to obvious fluorescence recovery. The current studies on biocompatibility of GBNs are still controversial on account of the high heterogeneity of GBNs on the market and various synthesis methods. It should be noted that GBNs may produce a varying extent of potential toxicity to cells associated with a direct interaction with the cell membrane. So far, GO is preferred to original graphene for biomedical application, due to its surface chemistry, better solubility and stability in biological fluids Hence, future studies should fine-tune the properties of functionalizing GBNs to acquire selected performance, while avoiding its potentially adverse effects if possible [38].

To overcome these limitations and to extend the biological applications of GBNs, many graphene-biomacromolecule hybrid materials, such as graphene-biopolymer nanohybrids (achieved by combining GBNs with biocompatible polymers), graphene-polysaccharide nanohybrids (achieved by combining GBNs with biocompatible polysaccharides), have been synthesized to meet the demands of biomedical and pharmaceutical application with enhanced biocompatibility, minimized toxicity, improved solubility as well as stability and even to promote cell proliferation. Moreover, a number of green routes have also been proposed to reduce the toxicity in the fabrication of rGO with the utilization of microbes, plant extracts and reducing sugars such as glucose instead of strong chemical reducing agents. Additionally, avoiding direct contact between GBNs and the human body and even biological fluids, is also a potential method [39].

In addition to the biological toxicity and biodegradability, material biodegradability should also be considered and ensured in the event of exfoliation or tear when designing implantable devices. Furthermore, the antibacterial activity of GBNs have also been highlighted in tissue engineering, which have certain antibacterial or antimicrobial properties and can decrease the threat of bacteria, as GO can be absorbed by the bacterial cells and its sharp edges can damage the cell membrane, which results in cell damage or death. The intracellular oxygen partial pressure is also altered by GO, which results in oxidative damage of the intracellular substances, destruction of the cell internal composition and ultimately cell death. As the most effective antibacterial agents among GBNs, GO and rGO are deemed as a superb material for the synthesis of innovative antibacterial agents [40].

The future of graphene is promising, with ongoing research in various fields exploring its potential applications. However, there are still challenges to overcome, particularly in terms of large-scale production and integration into existing manufacturing processes.

7. Conclusions

1. In conclusion, the recent progresses of graphene and its derivatives-based biosensors are reviewed including the design strategies and detection results. These biosensors always functioned with a DNA probe, antibody, aptamer, protein or small organic molecules for target recognition. Even though a large number of graphene-based sensors reported in the literature exhibited good stability and repeatability, performance of some sensors in actual biological samples (such as blood and urine) often failed to achieve the desired detection results, which was mainly due to some non-specificity of biological and chemical molecules during the interfacial reaction of graphene and targets. Although some sample preparations (e.g, separation or pre-concentration) are necessary before the final tests for biological samples, however, they always face the limits of complex procedures and are a time-consuming operation. One effective solution to such problems is to develop ultrasensitive and high-specific sensors. Those challenges remain to be overcome by continuous effort to achieve large-scale production of graphene-based sensors. Nowadays, graphene-based all-in-one sensors have received extensive attention, as described in which greatly expanded the application range of such sensors and provided new ideas for multiple target detection analytical methods. These multifunction sensors make a combination of multiple biomarkers recognition and different signal readouts. The future development direction of graphene-based biosensors should be more portable, reproducible, miniaturized and high-throughput in detection.
2. The focus of human healthcare has shifted gradually from hospitals to communities (families, individuals). Tremendous effort has therefore been devoted toward sensors and devices for health monitoring. Due to its unique features, including chemical and physical properties, graphene is extremely attractive for flexible electronics and sensors. In this review, recent achievements in graphene-based sensors for human health monitoring, including both non-invasive flexible wearable sensors and invasive devices have been reviewed. The graphene-based sensors have been explored to measure a wide range of vital signs and biomarkers of the human body, which are highly promising in the foreseeable future for applications in healthcare, personalized/preventive medicine, disease treatment, human-machine interaction, as well as brain computer interfaces. Novel structures have been employed to improve performance, while their sensing mechanisms and technological innovations were also thoroughly discussed.
3. Each material has its unique advantages and limitations, and the requirements in different applications are also different, thus trade-offs are required. Although graphene provides a variety of distinctive characteristics in one, limitations also exist. First, a zero-gap structure of graphene results in the relatively low on/off ratio as FETs, which hinders its usability in biomedical applications. A possible way to open its bandgap is with functionalized organic molecules. Other attempts such as strain engineered lattice distortions, spintronics have also been explored. In addition, graphene is absent of selectivity toward target analytes of interest, owing to its excessive sensitivity to external stimuli. One possible approach to improve selectivity is to modify its surface with specific functional groups, bioreceptors or to cover it with a thin selective layer such as metal-organic frameworks (MOFs). Furthermore, graphene has relatively low long-term stability induced by the moisture absorption and ultrathin nature. The solution may be to coat the surface with stable thin layer materials. Furthermore, the employment of graphene for functional devices in different applications requires a close integration with other functional materials; the intrinsic properties of graphene could be easily (usually negatively) impacted by these material integrations, device fabrication, and processing steps. Primary challenges including control, quality, scalability, and durability, should be resolved before commercially significant devices with graphene move forward.

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