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Review

Graphene-based nanoelectronic biosensors

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ABSTRACT

There is a great need for an accurate and rapid analytical technique to detect hazardous chemical/biological substances. Various detection methodologies, such as optical, electrochemical, surface plasmon resonance, and magnetic resonance techniques, have shown excellent sensing performance toward target molecules. The observation of signal changes based on nanoelectronics enables highly sensitive and selective recognition and real-time responses. Among the many functional materials used as signal transducers, graphene, a carbon allotrope with an atomic-scale two-dimensional planar structure, is of special interest. Graphene possesses excellent electrical and electronic properties, such as high carrier mobility and capacity, ambipolar field effect, and highly tunable conductance. It is used broadly in electronic, optoelectronic, energy, and environmental applications. In particular, because graphene has a large surface-to-volume ratio, extraordinary carrier mobility, and high compatibility, nanoscale graphene sensors are very promising. Herein, we introduce state-of-the-art biosensor technologies based on various types of graphene, especially field-effect-transistor-type and electrochemical biosensors.

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Introduction

Human health is threatened by many hazardous chemical/biological molecules, such as toxic gases, infectious viruses, and super-bacteria [1]. Various detection methodologies, including optical [2], magnetic [3], plasmonic [4], and acoustic [5] analyses, have been developed for the rapid and accurate discrimination of low concentrations of target molecules. Although such assays have attractive sensing mechanisms, they also have critical limitations, such as their time-consuming operation, high costs, low resolution, and noisy backgrounds. The observation of changes in electrical signals can provide more specific and precise information about target molecules [6], and electrical sensing devices also offer label-free and real-time measurements. Various conductive nanomaterials, including conducting polymer nanomaterials (e.g., polypyrrole, polyaniline, and polythiophene), carbon-based nanomaterials (e.g., fullerene, carbon nanotubes (CNTs), and carbon nanohybrids), and metal alloys (e.g., aluminum, copper, gold, and silver) have been used to construct electrical sensing devices for biological and medical applications. These devices have demonstrated high-performance with selectivity and sensitivity [7–9].

Two-dimensional (2D) nanomaterials, such as graphene, hexagonal boron nitride, and transition metal dichalcogenides (e.g., MoS_2, TiS_2, WS_2, $MoSe_2$, and WSe_2), have been investigated extensively. These nanomaterials have ultrathin nanostructures with a high degree of anisotropy and unique material characteristics, and their electronic, optical, mechanical, and chemical properties [10] are highly versatile, being dependent on their sizes [11], shapes [12], and degradabilities [13]. Based on their unique properties, 2D nanomaterials have proven suitable for a wide range of applications, such as flexible electronics, supercapacitors, tissue engineering, solar cells, and chemical sensors [12–16]. Additionally, they have been used to improve the performance of chemical/biomedical sensors because of their high surface-area-to-volume ratios and modulus [17,18]. These sensors have shown ultra-high sensitivity and selectivity toward target molecules, even at low concentrations.

One of the most attractive 2D nanomaterials is graphene, which consists of a 2D sheet of sp^2-hybridized carbon atoms. It has excellent electrical and electronic properties, such as extremely high charge carrier mobility and the ambipolar field and quantum Hall effects [19]. Its unique physical properties have been utilized in electrodes and transducers for electrochemical and field-effect-transistor (FET) sensors [20]. For example, graphene electrodes have been reported to have a large theoretical surface area ($2630\ m^2\ g^{-1}$), large potential window (approximately 2.5 V in 0.1 mM phosphate-buffered saline), low charge-transfer resistance, excellent electrochemical activity, and a fast electron transfer rate, and graphene transistors have demonstrated high carrier mobilities ($200{,}000\ cm^2\ V^{-1}\ s^{-1}$) [20]. Due to these properties, graphene-based nanoelectronics can pave the way for rapid, accurate, and portable sensing technologies for chemical/bio-hazardous substances, such as cancers, infectious diseases, super-bacteria, and hormones. This review of graphene covers its fabrication and applications, particularly in nanoelectronic sensors.

Fabrication of graphene

There are two types of graphene synthesis methodologies: (i) top-down and (ii) bottom-up. Each approach has different advantages (Fig. 1) [21]. In the top-down methods, stacked graphite layers are exfoliated via chemical, physical, and thermal treatments to overcome the van der Waals forces caused by physical adsorption, electrostatic interactions among ions, etc. [21,22]. One of the greatest advantages of top-down approaches is the ease with which large quantities of graphene can be prepared. However, these methods have a serious drawback: it is almost impossible to produce single-layer graphene with controlled size in a top-down manner. Therefore, the development of effective separating technologies remains a key challenge. Bottom-up approaches are very simple, but the graphene must be treated at high temperatures and pressures [23–26]. Compared with the top-down methods, the bottom-up approaches can produce graphene sheets of better quality and, more importantly, larger surface areas via growth on certain substrates.

Top-down approaches

Micromechanical exfoliation is one of the most widespread processes for preparing graphene. The standard micromechanical exfoliation method uses Scotch® tape. This was the method first used to experimentally isolate graphene by Andre Geim and Konstantin Novoselov, who shared the 2010 Nobel Prize in Physics (Fig. 2a) [27]. Graphene was prepared by a simple technique in which sticky tape with graphite adhered is repeatedly folded and peeled to create progressively thinner layers [28]. This process detaches the graphene from the graphite crystal, and multi-layer graphene remains on the tape after peeling. To make few-layer graphene, after repeated peeling, the tape is attached to a substrate, and the glue is removed by dissolution in acetone. Single-layer graphene on a SiO_2/Si substrate can be observed by light microscopy because of interference effects [29]. However, the critical limitation of this method is its restriction to the production of only small amounts of graphene. The graphene prepared by the Scotch® tape method is of high quality, without any defects, but the method is extremely labor-intensive. Therefore, various alternative methods have been developed to overcome this drawback of micromechanical exfoliation. Versatile intercalants for graphite exfoliation have been designed (e.g., small molecules [30], supramolecular assemblies [31], conducting polymers [32], and water-soluble polymers [33]), and their ability to physically separate graphene from graphite has been examined. Even nanoparticles have been used as intercalants for graphite exfoliation [34,35].

Graphene oxide (GO) has been used as a precursor to produce graphene. This chemical approach is the most popular method for preparing graphene in large quantities. GO is usually obtained by the Hummers and Offeman method, which utilizes concentrated

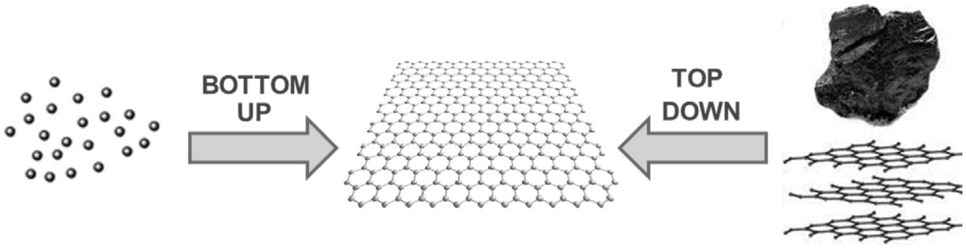

Fig. 1. Schematic diagram of graphene preparation strategies: top-down and bottom-up.