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Preface

Coronavirus disease 2019 (COVID-19) is an emerging human infectious disease associated with severe respiratory distress. Since a series of unexplained pneumonia cases were reported in Wuhan City, Hubei Province, China in December 2019, the number of infections has increased rapidly with human-to-human transmission. As of October 13, 2020, more than 37745,000 COVID-19 cases have been confirmed worldwide, and a conservative estimate has caused 1079963 deaths. As there is currently no specific drug for COVID-19, large-scale and rapid early diagnosis will often play a vital role in controlling the epidemic for this rapidly spreading epidemic.

Currently, the main detection methods include Nucleic Acid Detection (NAT), which is a technique used to detect specific nucleic acid sequences, so it is usually used to detect and identify specific viruses or bacteria. NAT needs to collect blood, tissue, urine, etc., and detect whether it contains pathogens. The difference between NAT and other tests is that it detects the genetic material (RNA or DNA) instead of antigens or antibodies. The detection of genetic material can diagnose diseases early because the detection of antigens and/or antibodies takes a while to begin to appear in the blood or body fluids. Since the amount of genetic material collected is usually small, many NATs include steps that can amplify genetic material, that is, copy a large amount of genetic material. This NAT is called a Nucleic Acid Amplification Test (NAAT). However, because the amplification step is necessary for the NATs, it always takes several hours then gets the result. Thus the nucleic acid test is usually unable to achieve large-scale rapid testing, which makes epidemic control a very difficult problem. Therefore, there is an urgent need to develop a new type of sensor that can perform large-scale rapid detection while having a certain sensitivity and specificity, especially for large-scale epidemic diseases like COVID-19.

Graphene is a type of carbon. As the first two-dimensional material discovered in the world, it is almost completely transparent. It is not only the thinnest but also the strongest. It has excellent electrical and thermal conductivity. Initially, Profs. Geim and Novoselov extracted graphene from graphite. They used tape to mechanically peel off the graphite to obtain graphene. Although many people believed that this two-dimensional crystal material could not exist stably at that time. Now, using the two-dimensional material graphene, physicists can study the strange properties of matter in the two-dimensional world. Graphene makes a series of new experimental ideas

and designs possible, which brings many surprising new experimental phenomena and exciting new application areas. Currently, graphene has already many novel practical applications. Especially, graphene-based field-effect transistors biosensors, due to their excellent electrical properties and two-dimensional size, are expected to become ultra-sensitive biological and chemical-sensing platforms.

At present, various biological technologies such as avidin-biotin technology have been diffusely applied in different types of ELISA (enzyme-linked immunosorbent assay) kits, polymer-based detection, and labeled immunosensors for detecting distinct biomarkers related to different kinds of diseases (such as cancer and influenza). Here we demonstrated these Graphene Field-Effect Transistors (GFET) based on different biological technologies and illustrated its ultrasensitive detection capability for the specific target biomolecule (such as virus, microbes, cells) in the sub-pico molar (pM) range. Although the invention and development of the graphene FET biosensor have only gone through 10 years, this novel rapid detection platform has shown great potential for ultra-sensitive rapid detection, which is difficult to achieve by traditional detection methods. Especially for large-scale epidemic detection and point-of-care testing, this new type of sensor platform is expected to exert its unique advantages.

Generally speaking, this monograph is divided into 11 chapters. As the upper part, Chaps. 1–4 mainly state the basic knowledge of graphene FET biosensors, including graphene-related applications, graphene preparation, mathematical principles about the graphene FET, fundamental of graphene FET biosensing, etc. Chapters 5–11, as the lower part, mainly state the application of graphene FET biosensor combined with various biotechnologies. In the lower part, not only previously existed technologies are introduced but also inserted some of my personal ideas and conceives for the first time. In addition, it discusses some related problems existing in graphene FET biosensor and then introduces some improve methods about these problems. Finally, it states the future application prospects.

Chapter 1 extensively introduces recent research related to the application of graphene and its potential applications in various fields. Chapter 2 introduces the electrical properties of graphene and provides the relevant electrical theoretical basis for graphene FET sensors. Based on the above theoretical, I proposed two important inferences in the field of graphene FET sensing. At the end of this chapter, the low-temperature characteristics of graphene are also briefly introduced. Chapter 3 systematically introduces the preparation method for graphene. At the same time, some of my personal experiences with graphene preparation are also inserted in this chapter. Chapter 4 introduces the fundamental of the biosensor based on graphene FET and briefly demonstrates its current application in biological detection. Chapter 5 describes the graphene FET biosensor based on the avidin-biotin interaction and systematically explains its preparation method and the expected detection effect. Chapter 6 introduces the graphene FET biosensor based on antigen-antibody interaction, focusing on its application in biomarker detection. Chapter 7 discusses the graphene FET biosensor based on base complementary pairing technology and discusses the possibility of applying this technology to large-scale population detection of COVID-19. Chapter 8 introduces the graphene FET biosensor based on

aptamer technology and compares its difference with the biosensor based on antigen–antibody technology. Chapter 9 introduces the graphene biosensor based on ConA technology, and based on the technical characteristics of ConA, two different detection methods are proposed: adsorption detection method and dissociation detection method. Chapter 10 summarizes the current problems in the field of graphene FET biosensing and briefly states some of the improved methods for these problems. Chapter 11 summarizes and outlooks the research on graphene FET biosensors based on various biotechnologies. Moreover, some aspects have been proposed, which need to be improved and noted in the future.

Currently, the most direct problem facing clinical detection is that most of the existing testing methods cannot achieve rapid testing, including PCR and ELISA, especially in the context of the current COVID-19 pandemic. Based on the above considerations, the GFET biosensor as a new type of biosensor that can achieve rapid quantitative detection of specific biological molecules with ultra-high sensitivity and specificity compared with traditional detection methods. To quickly provide a potentially reliable basis for clinical diagnosis, it is expected to achieve rapid screening for large-scale epidemics.

Therefore, the GFET biosensor, as an emerging sensing platform that has only been invented for a decade, I hope that readers can grasp the basic knowledge and future directions of graphene FET biosensors in general through this monograph. At the same time, enjoying the fun of research.

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Chapter 1
Fundamental of Graphene

Abstract Graphene is the first two-dimensional material discovered in the world. It has many excellent properties that traditional bulk-materials cannot match, such as ultra-high mechanical strength, high thermal conductivity, electrical conductivity, ultra-high specific surface area, stable chemical properties, etc. This makes graphene have great application potential in many fields such as composite materials, conductive inks, nano power generation, anti-corrosion coatings, and biological applications. Although it has been less than 20 years since Andre Geim and Konstantin Novoselov discovered graphene in 2004, a series of remarkable results have been achieved in the related theories and practical applications of graphene around this new two-dimensional material. This also indicates that scientists have paid great attention to two-dimensional materials including graphene. This chapter introduces the discovery history of graphene and the main application directions of graphene in recent years.

Keywords Graphene · Supercapacitor · Conductive ink · Microbial fuel cells · Flexible sensing · Nanogenerator · Thermal applications · Biomedical applications

Graphene is the first two-dimensional material discovered in the world. It is an allotrope of carbon and consists of single atomic layers arranged in a two-dimensional honeycomb lattice [1, 2]. The name is the suffix of "graphite", the suffix is -ene, reflecting that the graphite allotrope of carbon is composed of stacked graphene layers [3, 4].

Each carbon atom is connected to the three neighboring atoms through a σ bond and contributes an electron to the conduction band in the entire graphene film. This is the same type of bonding seen in carbon nanotubes and polycyclic aromatic hydrocarbons, and (partially) in fullerenes and glassy carbon [5, 6]. These conduction bands make graphene a semimetal with unusual electronic properties that are best described by theories for massless relativistic particles [1]. Charge carriers in graphene show linear, rather than quadratic, dependence of energy on momentum, and field-effect transistor s with graphene can be made that show bipolar conduction. Charge transport is ballistic over long distances; the material exhibits large quantum oscillations and large and non-linear diamagnetism [7]. Graphene conducts heat and electricity

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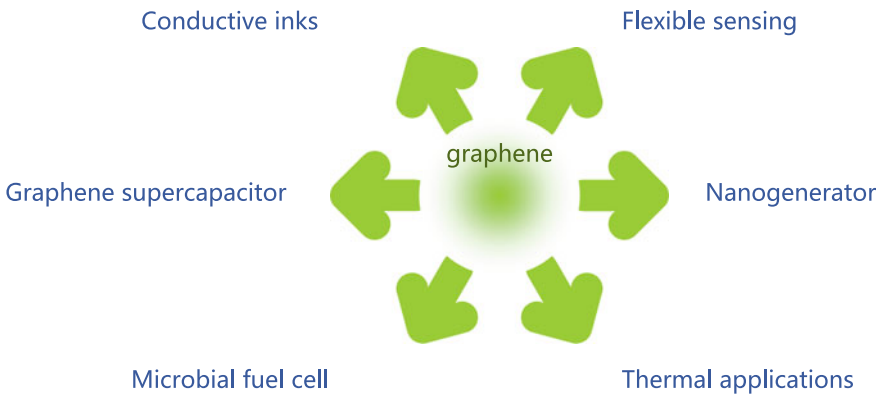

Fig. 1.1 The main application directions of graphene since its discovery

very efficiently along its plane. The material strongly absorbs light of all visible wavelengths [8, 9], which accounts for the black color of graphite; yet a single graphene sheet is nearly transparent because of its extreme thinness. The material is also about 100 times stronger than would be the strongest steel of the same thickness [10, 11].

For decades, scientists have been working on graphene and graphene-related applications. In fact, pencils and other graphite-related applications may have been unknowingly produced in small quantities for hundreds of years. It was first observed in an electron microscope in 1962, but it was only studied under the support of a metal surface [3]. But graphene was rediscovered, separated, and identified by Andre Geim and Konstantin Novoselov of the University of Manchester in 2004, [12] due to their research they obtained the 2010 Nobel Prize in Physics. During the PhD research, my major work is to focus on the research of the biological applications based on the graphene FET. Developing a kind of ultrasensitive rapid detection method for specific biomolecules, besides, we should also mention that graphene composite materials have received more attention in recent years, such as graphene composite rubber and graphene composite coatings.

The global market for graphene was $9 million in 2012 [13], with most of the demand from research and development in semiconductor, electronics, electric batteries, and composites. In 2019, it was predicted to reach over $150 million by 2021 [14]. Figure 1.1 lists the main application directions of graphene since its discovery, and brief introduction about these main application directions is also followed below this section.

1.1 Graphene Conductive Ink

Series of applications in the emerging field of printed electronics require a new set of functional materials for development including flexible and large-area displays [15], radio frequency identification tags, portable energy harvesting and storage [16,