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Graphene-based field effect transistor (GFET) as nanobiosensors

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12.1 Introduction

In the first stage, we provide a minireview about FET-based biosensors and models with graphene. Also, considering the extraordinary electrical, chemical, and optical properties of graphene, this material is introduced as a good candidate for transistor-based biosensors.

In this ever-changing world the new kind of coronavirus (CoV) has undoubtedly become a serious issue due to its rapid transmission from one human to another in a matter of minutes. COVID-19 has faster transfer capability compared to the other coronaviruses like SARS and MERS. The name corona is derived from the Latin word omeaning crown due to its similarity in shape under the electron microscope. CoVs have high adjustability in the host in terms of their mutation rate (Sheikhzadeh et al., 2020). The genetic structure of the coronavirus includes three parts. Two-thirds of it includes RNA synthesis materials for encoding polymerase and the open reading frame which are nonstructural polyprotein. The remaining part consists of four protein parts: nucleocapsid, spike, membrane, envelope, and other proteins. It has been found that the coding part of COVID-19 has a 92.67% and 96.92% similarity to nucleotides in pangolin and has a 97.82% and 98.67% similarity to amino acid in bat CoV genome. There is a wide range of experiments that have been done that have showed the most validated identification of this worldwide pandemic belongs to beta CoVs. In December 2019 the first signs of coronaviruses were discovered in Hubei province. The World Health Organization
WHO announced COVID-19 was of international concern. Early symptoms of this disease commonly include fever, shortness of breath, fatigue, and cough (Akinwande et al., 2019; Sheikhzadeh et al., 2020). In some patients symptoms like diarrhea, headache, and dyspnea have been observed. It is believed that males are more at risk than females, perhaps this because of their hormones and immune system which are more resistant. Most importantly this infection can spread quickly via respiratory droplets during talking, sneezing, and coughing. The recovery period of this disease is estimated to be 1 to 14 days. On the other hand the transmission of the disease is dependent on R0 (basic reproduction) and the range of R0 estimated for COVID-19 is between 3.3 and 5.5. This range of R leads to fast transmission from animals to human and humans to humans. To note the biggest concern is that patients may have the disease but with no symptoms but they can transmit virus to other people. Moreover, the number of infected and deaths have been dramatically increasing daily. Hence early diagnosis is very important to prevent it from spreading from one person to another and to cut the transmission chain and isolate the infected person. The WHO proposed a guideline as ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment free, and Deliverable to end-users) for the diagnosis of patients. There are several current methods shown below, such as immunological assays, amplification method, and biosensors (Fig. 12.1).

12.1.1 Immunological assays

This method involves immunological assays [e.g., lateral flow immunoassay (LFIA), enzyme-linked immunosorbent assay (ELISA)].

![Figure 12.1](https://example.com/figure12.1.png)
This method is based on the detection of antigen/antibody interactions. Some improved examples of immunoassays include peptide-based luminescent, automated chemiluminescent immunoassay, enzyme-linked immunosorbent assay, and immunochromatographic assay. This method requires the complex production routes of recombinant proteins and antibodies.

### 12.1.2 Amplification method

This method involves amplification-based techniques [e.g., reverse transcription polymerase chain reaction (RT-PCR), nanopore target sequencing (NTS)]. This technique was classified into groups: firstly, reverse transcription polymerase reaction which is based on amplification of RNA and genes extracted from biological samples; secondly, amplifying of nucleic acids at a steady temperature, called the isothermal nucleic acids technique. This method is divided into four advanced techniques including (1) loop-mediated isothermal amplification, (2) clustered regularly interspaced short palindromic, and (3) rolling circle amplification (Hess, Seifert, & Garrido, 2013).

All of these techniques are expensive, require skilled personnel, are difficult to work, and offer slow detection. This is the reason why biosensors have received great attention in the early detection of different samples with various concentrations.

### 12.1.3 Nanobiosensors

Biosensors can offer fast, inexpensive, time-efficient, highly stable, quick response, simultaneous detection, and multisample detection measurements. Localized surface plasmon resonance is one of the promising candidates for the early detection of real samples of coronavirus. LSPR biosensors have exponential sensitivity to detect any surrounding changes like the variation in refractive index RI with low limit of detection.

Applying nanoparticles in biosensors brought a revolution in biological detection due to their unique optical and physical properties. Due to their remarkable properties like high surface to area ratio, high conductivity, high biocompatibility with sample, and high bioaffinity, they are widely used in biosensors. One of the most significant nanoparticles is graphene. In 2004 graphene flakes were isolated by Andre Giem and Konstantin Novoselove (Farmani & Mir, 2020; Farmani et al., 2020; Farmani, Farmani, & Biglari, 2020; Ghodrati, Mir, & Farmani, 2020; Hamzavi-Zarghani et al., 2019; Han et al., 2020). The lightest
known material with a two-dimensional structure has improved biosensors application in terms of its outstanding properties like high mobility, strong structure, high conductivity, transparency, and high capability to drug delivery and loading.

### 12.2 Graphene-based field effect transistor (FET) as biosensors

A field effect transistor (FET) is based on applying an electronic field to control the flow of modulated carrier (Amoosoltani, Zarifkar, & Farmani, 2019; Baqir et al., 2019; Farmani & Mir, 2019; Farmani, 2019a, 2019b; Sadeghi et al., 2019). In a graphene-based FET, graphene is employed as a channel of the structure that leads to a quick response and detection of different kind of viruses and bacteria. It was reported that graphene was suitable when used in the Si MOS FETs for highly sensitive biosensors. In graphene, its two-dimensional electron gas was bare and exposed directly to the liquid, whereas in the Si MOS FETs, its two-dimensional electron gas was covered by a thick SiO$_2$ layer (Matsumoto, Kenzo, Ohno, & Inoue, 2014).

Some GFET application have been reported for the detection of both human and avian influenza. Additionally, a graphene-based FET device was used in identifying Ebolavirus with a low detection limit. Furthermore, a graphene oxide nanogrid in a FET structure showed high ability to detect Hepatitis B virus. Fig. 12.2 presents the optical microscope image of a GFET and a schematic image of biosensing by the GFET (Matsumoto et al., 2014).

Much work has been done to detect HIV virus by applying amine-functionalized graphene-based FET devices. Research groups has found that using a flexible kapton substrate improved the detection performance of norovirus. Likewise, a small amount of zika virus was detectable with the FET device. Recently scientists proposed graphene-FET in the detection of SARS-CoV-2 (COVID-19). In this case, 1-pyrenebutyanoic acid succinimidyl ester was applied as a reporter in functionalization of GFET with a COVID-19 spike antibody for identification (Farmani, 2019a; Farmani et al., 2017; Mozaffari and Farmani, 2019).

Table 12.1 shows some types of virus that could be detected using graphene-FET.
12.3 Conclusion

For the next-generation of biosensors, graphene plays an important role, especially in the field of COVID-19. Several recent advances in graphene-based materials for biosensors have been carefully reviewed, and advanced applications have been highlighted. The GFET biosensor is introduced as a reliable and selective method which shows a low limit of detection for the detection of COVID-19. GFET can play an important role in identifying SARS-CoV-2 at an early-stage and aid in

| Virus sample          | Basic material | Limit of detection |
|-----------------------|----------------|--------------------|
| Human influenza       | Graphene       | 1 nm/mL            |
| Hepatitis B virus     | Graphene       | 0.1 fm             |
| Papilloma virus       | Graphene oxide | 1.75 nm            |
| Rotavirus             | Graphene oxide | 100 pfu            |
| Rotavirus             | Graphene oxide | Na                 |
| Covid-19 virus        | Graphene       | 1 fg/mL            |
| Covid-19 virus        | Graphene       | 0.2 pm             |

Figure 12.2 Optical microscope image of a GFET (left) and a schematic image of biosensing by the GFET (right) (Matsumoto et al., 2014). Reproduced with permission of Kazuhiko Matsumoto, et al., Recent advances in functional graphene biosensors, J. Phys. D Appl. Phys., 47, (9) (2014), Article 094005. Licensed under creative commons Attribution 4.0 International (CC BY 4.0).
protecting other people with no symptoms of COVID-19. Although GFET has paved the way for the detection of COVID-19, there are still problems like the preparation of samples and sometimes it is difficult to control immobilization and binding between virus and antibody.

References

Akinwande, D., et al. (2019). Graphene and two-dimensional materials for silicon technology. Nature, 573(7775), 507–518.

Amoozoltani, N., Zarifkar, A., & Farmani, A. (2019). Particle swarm optimization and finite-difference time-domain (PSO/FDTD) algorithms for a surface plasmon resonance-based gas sensor. Journal of Computational Electronics, 18(4), 1354–1364.

Baqir, M. A., et al. (2019). Tunable plasmon induced transparency in graphene and hyperbolic metamaterial-based structure. IEEE Photonics Journal, 11(4), 1–10.

Farmani, A. (2019a). Graphene plasmonic: Switching applications. Handbook of Graphene: Physics, Chemistry, and Biology, 455.

Farmani, A. (2019b). Three-dimensional FDTD analysis of a nanostructured plasmonic sensor in the near-infrared range. JOSA B, 36(2), 401–407.

Farmani, A., & Mir, A. (2019). Graphene sensor based on surface plasmon resonance for optical scanning. IEEE Photonics Technology Letters, 31(8), 643–646.

Farmani, A., & Mir, A. (2020). Nanosensors for street-lighting system. Nanosensors for Smart Cities (pp. 209–225). Elsevier.

Farmani, A., et al. (2017). Design of a tunable graphene plasmonic-on-white graphene switch at infrared range. Superlattices and Microstructures, 112, 404–414.

Farmani, A., et al. (2020). Optical nanosensors for cancer and virus detections. Nanosensors for Smart Cities (pp. 419–432). Elsevier.

Farmani, H., Farmani, A., & Biglari, Z. (2020). A label-free graphene-based nanosensor using surface plasmon resonance for biomaterials detection. Physica E: Low-dimensional Systems and Nanostructures, 116, 113730.

Ghodrati, M., Mir, A., & Farmani, A. (2020). Carbon nanotube field effect transistors–based gas sensors. Nanosensors for Smart Cities (pp. 171–183). Elsevier.

Hamzavi-Zarghani, Z., et al. (2019). Tunable mantle cloaking utilizing graphene metasurface for terahertz sensing applications. Optics Express, 27(24), 34824–34837.

Han, B., et al. (Eds.), (2020). Nanosensors for Smart Cities. Elsevier.

Hess, L. H., Seifert, M., & Garrido, J. A. (2013). Graphene transistors for bioelectronics. Proceedings of the IEEE, 101(7), 1780–1792.

Matsumoto, K., Kenzo, M., Ohno, Y., & Inoue, K. (2014). Recent advances in functional graphene biosensors. Journal of Physics D: Applied Physics, 47(9), Article 094005.

Mozaffari, M. H., & Farmani, A. (2019). On-chip single-mode optofluidic microresonator dye laser sensor. IEEE Sensors Journal.
Sadeghi, T., et al. (2019). Improving the performance of nanostructure multifunctional graphene plasmonic logic gates utilizing coupled-mode theory. *Applied Physics B*, 125(10), 189.

Sengupta, J., & Hussain, C. M. (2021). Graphene-based field-effect transistor biosensors for the rapid detection and analysis of viruses: A perspective in view of COVID-19. *Carbon Trends*, 2, 100011.

Sheikhzadeh, E., et al. (2020). Diagnostic techniques for COVID-19 and new developments. *Talanta*, 121392.