Laser-induced graphene (LIG)-driven medical sensors for health monitoring and diseases diagnosis

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Abstract
Laser-induced graphene (LIG) is a class of three-dimensional (3D) porous carbon nanomaterial. It can be prepared by direct laser writing on some polymer materials in the air. Because of its features of simplicity, fast production, and excellent physicochemical properties, it was widely used in medical sensing devices. This minireview gives an overview of the characteristics of LIG and LIG-driven sensors. Various methods for preparing graphene were compared and discussed. The applications of the LIG in biochemical sensors for ions, small molecules, microRNA, protein, and cell detection were highlighted. LIG-based physical physiological sensors and wearable electronics for medical applications were also included. Finally, our insights into current challenges and prospects for LIG-based medical sensing devices were presented.

Keywords Laser-induced graphene (LIG) · Medical sensors · Electric/electrochemical sensors · Wearable electronics · Diseases diagnosis · POCT

Introduction
Sensors are a type of promising diagnostic tools for laboratory medicine [1]. Sensors-driven point-of-care testing (POCT) plays a unique role in the personalized health monitoring, diseases diagnosis, and global public health events warning [2]. It enables home testing, community testing, and large-scale preliminary screening without the support of large medical instruments. It is worth mentioning that the COVID-19 epidemic has attracted more attention to medical sensors which have potentials to timely track symptomatic infection or asymptomatic infection and remotely monitor isolated patients [3]. Hence, developing ultrasensitive and low-cost medical sensors is extremely important.

The development of medical sensors strongly depends on the advances of nanomaterials [4, 5]. Graphene has excellent physical and chemical properties, such as high carrier mobility rate, high thermal conductivity, excellent mechanical properties, and larger specific surface area [6–9]. These performances enable it widely applied in sensors, optics, biology, medicine, energy storage, and other fields. Graphene has been extensively applied in medical sensors such as field-effect transistors (FETs) biosensor [10], artificial throat [11], artificial skin [12], wearable human–machine interface [12, 13], and artificial muscle [14]. Laser-induced graphene (LIG), which was introduced in 2014 by Lin and
coworkers, has attracted widespread attention in recent years [15, 16]. It is a type of three-dimensional (3D) porous carbon nanomaterial fabricated by direct laser writing with carbon dioxide (CO₂) lasers on polymer materials in the air. It was also named laser-ablated graphene (LAG), laser-scribed graphene (LSG), or laser-derived graphene (LDG) [17]. The morphology of the LIG can be easily controlled by a computer, which is of great significance to the development of highly sensitive electric/electrochemical sensors and wearable electronics for medical biomarkers detection. Polyimide (PI) and its complexes are commonly employed for preparing the LIG. Polyetherimide (PEI), potato skin wood, cork, coconut, cloth, and polysulfone (PSU) are also reported as the base polymer materials for engraving 3D porous graphene [18–20]. In the process of LIG preparation, infrared CO₂ laser (commonly, the wavelength of the excitation light is 10.6 μm) [21] is commonly used. The main principle is that during the laser scanning of the base polymer material, the nitrogen-carbon bonds, carbon–oxygen bonds, and carbon–oxygen bonds of the base material are broken, and then rearranged to form a 3D porous graphene structure [22]. In addition to the infrared CO₂ laser, ultraviolet (UV) laser [23] and visible laser [24] have been confirmed to prepare the LIG.

With worldwide research efforts, LIG-driven sensors have been successfully applied in different fields, including clinical diagnostics, food safety, and environmental monitoring [25]. It was also applied in energy storage micro-supercapacitors (MSCs) [24, 26], cell culture [27], and fuel cell [28]. Meanwhile, LIG possesses characteristics such as flexibility, chemical resistance, and porosity, which makes useful as a porous channel or electrode material in microfluidic devices [29]. The various applications of LIG are shown in Fig. 1. It is foreseeable that this advanced material will soon bring a new generation of medical sensing device, which will have exciting characteristics and applications [30].

Several LIG-related review articles have been published. Ye and coworkers told a comprehensive story about LIG from its discovery to wide range of applications, including sensors, electrocatalysts, and microfluidics [31]. You and coworkers summarized and discussed the LIG-based flexible electronics [32]. However, this review is mainly focusing on the LIG-driven medical sensors for health monitoring and diseases diagnosis. Applications of the LIG-driven sensors for POCT and in vitro diagnosis (IVD) are emphasized.

**Various preparation methods and characteristics of graphene**

The existing methods for preparing graphene include mechanical stripping [33], thermal decomposition [34], epitaxial growth [35], chemical vapor precipitation (CVD) [36, 37], and wet chemical methods [38]. Heat-intensive processing techniques such as silicon carbide thermal decomposition and CVD can be used to grow graphene with almost no defects and high crystal quality [39]. However, the high-temperature conditions limit the types of substrates that can be used for directly growing graphene. Hence, additional processes are usually required to transfer graphene on substrates that are not resistant to high temperatures (such as plastics). The wet chemical method is time-consuming and it requires series of oxidation and reduction steps, extensive washings, and centrifugations. The prepared graphene is less control over the number of sheets and amount of oxygen functionalities. What’s more, aqueous solutions of graphene tend to restack to yield the graphite. These existing methods are often plagued by cumbersome manufacturing processes, high energy consumption, and/or low productivity. In addition, the inability to achieve large-area graphene on divers substrates associated with these traditional methods inevitably limits graphene’s widespread adoption.

In 2014, Lin and coworkers successfully prepared 3D porous graphene (also known as LIG) by direct writing of a commonly accessible CO₂ infrared laser system on the commercial PI [15]. The 3D porous graphene has a high specific surface area (≈ 340 m²·g⁻¹), high thermal stability (> 900 °C), and excellent electrical conductivity (5~25 S·cm⁻¹). The whole process can be carried out in the air, without any solvent, expensive machine, and costly materials. The method of engraving PI by laser avoids complicated wet chemical methods, and can directly prepare patterned...
structures, laying a good foundation for the wider application of graphene.

For the laser writing or engraving, various process parameters, such as laser wavelength, power, frequency, time, pulse width, and scanning speed, are all of great significance. A satisfactory LIG-based device is often the result of the synergy of multiple laser parameters. As shown in Figs. 2 and 3, by adjusting the laser parameters, different processing effects can be obtained [40].

Doping heteroatom in the LIG is an effective way to improve its sensing properties. Nitrogen [41] and boron [42] have been utilized as doping heteroatoms to tailor the electrochemical performance of the LIG and to enhance its surface wettability and electrical conductivity. Chen’s group proposed a method for preparing phosphorus-doped (P-doped) LIG electrodes on the H₃PO₄-doped polyimide (PI)/polyvinyl alcohol (PVA) composite flexible film [43]. Figure 4A presents the schematic diagram of the production process of the P-doped LIG interdigitated array electrodes. It was demonstrated that P-doped LIG has enhanced affinity to electrolyte ions on the electrode surface. As a result, the electrode possesses an improved electrochemical performance. The study provides a convenient and potentially efficient method for preparing free-standing heteroatom-doped porous graphene electrodes, which would have broad application in various flexible/wearable electronic devices.

A facile method for the in situ preparation of metal sulfide (MS)-graphene (G) nanocomposite, PbS-G and CdS-G, on indium-tin oxide (ITO) glass was demonstrated by scalable direct laser writing in ambient atmosphere [44]. Through the CO₂ laser irradiation of a metal-complex containing polyethersulfone layer on ITO glass, both the formation of LIG and crystallization of laser-induced MS (LIMS) were achieved within one step (Fig. 4B). The fabricated LI-MS-G@ITO possesses the porous architecture of the polyethersulfone-derived LIG, in which the LIMS nanocrystals were achieved. B Raman spectra of LIG under different laser conditions. C The correlation between the length of the laser power and the LIG crystal width. D The surface resistance of LIG and the ratio of $I_D/I_G$ dependence on laser energy density. Reprinted with permission from ref. [40], Copyright 2020 Elsevier Ltd.
uniformly decorate the 3D porous graphene sheets with excellent dispersion, showing a stable and fast photocurrent response and good reproducibility.

Through the modification or functionalization of the LIG, the detection of analytes can be achieved sensitively and selectively. The adsorption of analytes on the LIG electrode surface will change the electrode impedance, surface area, and other parameters, and the electrical signals will respond to the variety of parameters [45, 46].

**LIG-based sensors**

The LIG has been more and more prevalent for developing sensors. It shows great potential in biochemical sensors and physical physiological sensors. These sensors have great potential in monitoring the normal life activities of the human body. Some of them can be used as wearable devices to monitor human biomarkers continuously. In this section, the wearable devices were listed independently.

An biochemical sensor is an analytical device that can convert biological or chemical reactions into measurable physical signals, and can provide quantitative assessment of analyte concentration [47]. The basic principle of the biochemical sensor is to combine the identification of analytes and the signal that can be detected [48]. In past years, due to its extraordinary electrical and optical properties, the graphene has been employed in the field of biochemical sensor such as ionic species detection [49], glucose monitoring [50], microRNA detection [51], DNA detection [52], and folic acid detection [37]. However, reliable and scalable biochemical sensor manufacturing and transformation methods are in high demand to fill the existing gap between laboratory research and commercialization [53]. Direct laser writing will be an ideal fabrication technology and the LIG can be an alternative sensing material or device.

**Sensors for ions and small molecules**

Potentiometric ion sensing is one of the oldest and most well-known forms of chemical sensing that is useful for a variety of applications including clinical diagnostics. Kucherenko et al. reported LIG electrodes functionalized with ion-selective membranes for monitoring the concentrations of $\text{NH}_4^+$ and $\text{K}^+$ in urine samples. This electrochemical LIG sensor exhibits a broad sensing range (0.1–150 mM for $\text{NH}_4^+$ and 0.3–150 mM for $\text{K}^+$) with high stability across a wide range of pH (3.5 to 9.0) in aqueous solutions [54].
Dopamine (DA) is an important information transmitter in the mammalian central nervous system. The continuous overproduction of DA can cause irritability, uncontrollable emotion, extreme hyperactivity, and rapid nerve reflex. Even very low levels can lead to Huntington’s chorea or Parkinson’s disease [55, 56]. Hence, it is necessary to develop rapid, low-cost, and accurate detection devices for the DA. A Pt-Au nanoparticles (NPs) functionalized LIG/PDMS (polydimethylsiloxane) electrode was reported for detecting the DA in a neutral solution and in human urine [57]. The LIG-based sensor exhibited an excellent sensitivity of approximately 865.80 mA/mM cm\(^{-2}\) and a limit of detection (LOD) 75 nM. Meanwhile, it was demonstrated that it showed acceptable selectivity for interfering substances such as uric acid (UA) and ascorbic acid (AA).

The determination of urea is closely related to the human body’s kidney function [58], cardiovascular function [59], and environment [60]. Sharma et al. [61] developed a LIG-based pH sensor for urea detection. The sensor is flexible and compatible with catheters. It can successfully detect urea concentrations as low as 10\(^{-4}\) M and with the response time of less than 1 min. By comparing the direct connection of urease on the surface of LIG and the electrodeposition of chitosan hydrogel film on the surface of LIG, it was found that the electrostatic and covalent immobilization strategy of chitosan can increase the amount of immobilized urease. These ureases can catalyze the hydrolysis of urea into CO\(_2\) and ammonia [62], which can be easily detected with the LIG-based pH sensor. This makes the large-scale usage of the urea sensor possible.

Diabetes is a major health concern in the modern society. The monitoring of the blood glucose is crucial to provide treatment and control plans for patients. Tehrani et al. reported an enzyme-free and sensitive glucose sensor based on Cu NCs (copper nanocubes)-decorated LIG [63]. In the glucose concentration range of 0.25 μM to 4 mM, the sensor showed a linear response with a LOD of 250 nM and an excellent sensitivity of 4532.2 μA mM\(^{-1}\) cm\(^{-2}\). The amperometric readout time was within 3 s. The sensor was demonstrated to have a great potential for glucose detection in sweat, saliva, tears, and urine. The porous LIG with an abundance of crystallographic defects and large surface area enhances the electroplating process of the Cu NCs (as the catalyst for oxidation of glucose) and increases loading of the highly reactive Cu NCs as well as accessibility of glucose molecules. N-doped LSG electrodes decorated with MXene/Prussian blue (Ti\(_3\)C\(_2\)Tx/PB) composite via a simple spray-coating process were designed for sensitive detection of three analytes including glucose, lactate, and ethanol [64]. The Ti\(_3\)C\(_2\)Tx/PB-modified N-LSG electrodes were functionalized with corresponding catalytic enzymes. The enzyme/Ti\(_3\)C\(_2\)Tx/PB/N-LSG electrodes exhibited
remarkably enhanced electrochemical activity toward the
detection of these analytes with a performance on par with
previously reported on-chip carbon-based biosensors.
The detection of other small molecules, macromolecules,
and cells based on LIG is summarized in Table 1.

**Sensors for nucleic acids**

MicroRNAs (miRNAs) are a class of small noncoding RNAs (about 21–23 nucleotides in length) which regulate gene expression at translational or posttranslational levels. They were demonstrated as a type of significant biomarkers for various diseases [65]. Recently, a LIG-based biosensor for preeclampsia specific miRNA detection was reported [40]. The authors demonstrated that the nitrogen (N) atoms in the precursor PI have been partially incorporated into the LIG in the form of polyrolic N (1.6 to 4.4%) and graphitic N (from 2.4 to 4.5%). The self-N-doped porous LIG possesses enhanced conductivity as an electrochemical sensor and improved sensitivity to nucleic acids. Combining with the miRNA extraction and magnetic isolation procedures, the limit of detection (LOD) of the miRNA was down to 10 fM and it showed an excellent reproducibility. The study suggested that the self-N-doped LIG has great potential as a simple and low-cost biosensor platform for the detection and analysis of nucleic acids.

**Sensors for protein**

Thrombin is a vital therapeutic biomarker for diseases associated with coagulation abnormalities. It is a serine protease which can convert soluble fibrinogen into insoluble strands of fibrin [66]. Recently, a reliable and sensitive LIG biosensor functionalized by aptamer was demonstrated to thrombin in serum [67]. The LIG electrodes with enhanced electrochemically active area were manufactured by a laser direct-write process on PI foils. A universal immobilization approach is established by anchoring 1-pyrenebutyric acid to the LIG and subsequently

| Table 1 Overview of various biochemical sensors based on the LIG |
|-------------------|------------------|------------------|------------------|-----------------|-----------------|-----------------|-----------------|
| Sensor configuration | Functionalization method | Matrix | Analyte | Sensitivity | Concentration range | LOD | Ref |
| LIG-ISEs | Ionophores | Urine | NH4+ K+ | 51 mV dec−1 | 0.1–150 mM | 30 μM | [54] |
| Pt-LIG | Enzyme | DMEM | H2O2 | 248.4 mA mM−1 cm−2 | 0.5–5 mM | 0.1 μM | [74] |
| Pt-LIG/PDMS electrode | Pt-Au NPs | Human urine | Dopamine | 865.80 mA mM−1 cm−2 | 0.95–3.45 mM | 75 nM | [57] |
| PEDOT-LIG | NA | NA | Dopamine | 0.220±0.011 μA μM−1 | 1–150 μM | 0.33 μM | [75] |
| LIG/chitosan | Urease enzyme | NA | Urea | NA | NA | 0.1 μM | [61] |
| LIG | Cu NCs | NA | Glucose | 4532.2 μA mM−1 cm−2 | 0.25 μM–4 mM | 250 nM | [63] |
| LIG fibers (PEDOT-PSS)-LIG | Pt@Ni | Sweat | Glucose | 3500 μA mM−1 cm−2 | 0–30 mM | 1.5 μM | [76] |
| T3C2Tx/PB/N-LSG | Enzyme | Sweat | Glucose | 49.2 μA mM−1 cm−2 | 10 μM–5.3 mM | 0.3 μM | [64] |
| LIG | Antibody-PPA | Sweat | Cortisol | NA | 0.43–50.2 ng/mL | 0.22 μM | [78] |
| LIG | MIP | Aquaculture | Cortisol | NA | 1 nm–10 mM | 0.62 μM | [22] |
| LIG | Cu-DAO | Food | Biogenic amines | 23.3 μA mM−1 | NA | 11.6 μM | [79] |
| N-doped LIG | NA | NA | MicroRNA | NA | NA | 10 fM | [40] |
| LSG | Aptamer | Serum | Thrombin | −2.41 ± 0.16 μA cm−2 | 1–100 pM | 1 pM | [67] |
| PtNPs/PAAm-LIG | Antibody | Serum | IgG | 0.012–15 and 15–352 ng mL−1 | 6 pg mL−1 | [69] |
| Au NS-LIG | Antibody | Serum | SARS-CoV-2 S protein | NA | 5.0–500 ng mL−1 | 2.9 ng mL−1 | [70] |
| LIG | Antibody | Chicken broth | Salmonella | NA | 25 to 10^3 CFU mL−1 | 13±7 CFU mL−1 | [80] |

Au NSs gold nanostructure; CAP chloramphenicol; DAO diamine oxidase; DMEM Dulbecco’s Modified Eagle’s Medium; EBT eriochrome black T; LAG laser-ablated graphene; LSG laser-scribed graphene; MIP molecular imprinted polymers; NA not available; NCs nanocubes; NPs nanoparticles; PAAm polyelectrolyte polyallylamine; PEDOT-PSS poly(3,4-ethylenedioxythiophene)-poly(styrene sulfonate); PPA 1H-pyrrolo propionic acid; PVC polyvinyl chloride; ISEs ion-selective electrodes
covalently attaching an aptamer against the thrombin as a specific bioreceptor to the carboxyl groups (Fig. 5). The incubation time of the aptamer and the thrombin is just 30 min. The developed LIG biosensor showed relatively low LOD of 1 pM in buffer and 5 pM in the serum. The resulting sensitivity was $-2.41 \pm 0.16 \mu A \cdot cm^{-2}$ per logarithmic concentration unit.

Immunoglobulin (IgG) plays a critical role in certain disease. The abnormal of the IgG concentration may affect the function of organs and cause a failure to prevent infections [68]. Park’s group reported an electrochemical immunosensor using cationic polyelectrolyte polyallylamine (PAAMI)–anchored LAG as the electrode [69]. The addition of the PAAMI gave abundant clipping sites for fixing antibodies through introducing the amino group. Meanwhile, it increases the stability of the LAG flakes by electrostatic adsorption. Then, Pt nanoparticles were employed to decorate the PAAMI@LAG by the electrodeposition method and thus offered a fast electron transfer rate. The developed immunosensor was utilized to detect the IgG as a proof of concept. Under optimized conditions, the immunosensor showed a linear range of 0.012–15 and 15–352 ng mL$^{-1}$ with a LOD of 6 pg mL$^{-1}$.

The global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues. Instant detection and timely isolation are still the most effective management and control strategy. Hence, there is the urgent need for developing rapid, accurate, and low-cost diagnostic devices. An electrochemical immunosensor based on three-dimensional (3D) gold nanostructures decorated LSG was reported for the coronavirus disease 2019 (COVID-19) diagnosis [70]. This electrode was functionalized with antibodies to the SARS-CoV-2 spike (S) antigen following a proper surface modification step (Fig. 6). The analytical performance of the electrochemical immunosensor was evaluated applying the standard solution of S protein in the range of 5.0–500 ng/mL with a LOD of 2.9 ng/mL. The LSG-based electrochemical immunosensor can offer faster readout time compared to commercial diagnostic tools and provide a promising alternative method for affordable and rapid POCT devices.

**Sensors for cells**

Graphene has a relatively large surface area and can provide a stable interface for eucaryotic cells and microorganisms [71, 72]. A study reported the usage of LSG as a novel electrode material for cell monitoring based on the impedance measurement [73]. The prepared LSG electrodes showed 25 times larger interface capacitance than standard flat gold electrodes because of their foam-like 3D topography. The LSG electrodes can be prepared in customized sizes from micrometer to centimeter with tunable surface topography and they can be easily integrated to by roll-to-roll manufacturing lines. Furthermore, the LSG electrodes were demonstrated to have excellent compatibility for cell attachment.

A LIG-based electrochemical immunosensor was developed for the detection of *Salmonella typhimurium*. The LIG electrodes were fabricated by laser induction on the polyimide film in ambient conditions, which circumvents the need for high-temperature, vacuum environment, and metal seed catalysts commonly associated with graphene-based electrodes fabricated via chemical vapor deposition processes. After functionalization with *Salmonella* antibodies, the LIG biosensors were able to detect live *Salmonella*.

![Fig. 5](image.png)

*Fig. 5* Schematic diagram of preparing LIG-based aptamer interdigitated array electrodes. Reprinted with permission from ref. [67], Copyright 2017 American Chemical Society.
in chicken broth across a wide linear range of 25 to 10^5 CFU mL^{-1} and with a low LOD of 13 ± 7 CFU mL^{-1}. These results were acquired with an average response time of 22 min without the need for sample preconcentration or redox labeling techniques.

**Sensors for physical physiological markers**

The monitoring of physical physiological signals (such as the human humidity and breathing rhythm) has a critical role in chronic disease management (CCM), elderly care management, and personalized medicine. Interdigitated array electrodes are mostly used transducers of electrical/electrochemical sensors [81]. Recently, LIG-based interdigitated array electrodes (IDEA) were developed by laser direct writing technology [82]. The graphene oxide (GO)–coated IDEA was applied to develop a humidity sensor with low hysteresis, high sensitivity (3215.25 pF/% RH), and long-term stability (variation less than 1%). The IDEA images shown in Fig. 7A–C are cross-sectional images of electrodes without and with graphene oxide layer, respectively. GO was introduced as a sensitive material because of its unique 2D structure and super-permeability to H_2O molecules. Under low humidity conditions, H_2O molecules bond to active sites of GO by forming double hydrogen bonds, and with the humidity increasing, H_2O molecules bond to active sites of GO in the single hydrogen bond. Hence, it greatly increases the mobility of H_2O molecules. The increased activity induced H_2O molecules to move, and the moving H_2O molecules are ionized into hydrogen ions in an electric field, which can act as charge carriers. Then, they move on the GO layer, resulting in a significant increase in capacitance under high humidity conditions. Thanks to its flexibility, the LIG-IDEA-based humidity sensor could be easily employed as a wearable device for the in situ monitoring of the human breath humidity (the real object is shown in Fig. 7D). The results of human humidity and breathing rhythm are shown in Fig. 7E and F, which shows that the LIG-IDEA humidity sensor can detect breathing rhythm very well.

A temperature sensor and a flow sensor were developed by Marengo and coworkers based on the LIG [83]. The resistance of the temperature sensor reduces with the temperature increase. Thanks to the piezoresistive properties of the LIG, a flow sensor was fabricated. After a patterned LIG was engraved on the PI film, the copper tape was pasted on both contact points and conductive silver glue was used to connect the copper and the LIG, which can improve the stability of the contact points. Then, polydimethylsiloxane (PDMS) was evenly coated on the electrode to prevent the LIG electrode from being interfered by ions. The results revealed that the LIG-based flow sensor has an excellent performance to response the flow rates (0, 1500, 2500, 3500, 4500 rpm).

**Wearable devices**

In recent years, wearable sensing devices have attracted more attention, such as sweat biosensors [84] and electronic skin [85]. Graphene holds great promise for developing soft and flexible electronic products. The LIG artificial physical
A physiological device has the advantages of one-step molding, high efficiency, brilliant flexibility, and low cost, and has a broad and unexceptionable application. Multi-functional instruments based on LIG show great potential in medical monitoring and timely warning. Based on the excellent mechanical and thermal effects of graphene, scholars have proposed an integrated multi-functional device for sensing and alarm on the basis of double-layer asymmetric structure. When the detectable signal reaches the threshold conditions for real-time measurement by the ultrasensitive strain sensor, it can generate enough heat to warn the body. Advances in laser processing technology will definitely drive the rapid development of graphene electronic skin and wearable devices.

Tao and coworkers demonstrated that LIG has a high thermal conductivity and a low heat capacity, which makes it an ideal material for thermal sound sources [86]. Moreover, the porous structure of the LIG is sensitive to weak vibration and is suitable for sound detection. When working as a sound source, the LIG artificial throat can produce broadband sound in frequencies ranging from 100 Hz to 40 kHz. A thinner LIG will produce a higher sound pressure level (SPL). As a sound detector, the LIG artificial throat exhibits unique responses to different sounds and throat vibration modes. LIG can identify buzzes, screams, and coughs with different pitch and volume. When the device applies a low bias voltage, the vibration of the throat will cause changes in the device resistance, resulting in current fluctuations. The artificial throat also can produce sound. When an alternating voltage was applied to the device, the periodic joule heat causes the air to expand, resulting in sound waves. Therefore, the device can act as both sound source and detector. Cough, buzzing, or screeching can cause vibrations in the larynx, which can be detected by the LIG artificial throat, and the LIG artificial throat produces a controlled sound accordingly (Fig. 8A and B). When graphene is deformed, its resistance will also change [87, 88]. Drawing lessons from the principle of the above sound sensor, we can design some equipment according to some deformations that must occur in the daily life activities of the human body, such as heart pulse, breathing rhythm, and finger movement. Different gestures can cause different deformations in different positions of the hand. Placing multiple sensors on the hand may enable communication between aphasia and normal people. Park et al. improved the stretchability of LIG and made wearable devices for monitoring glucose in sweat, pH value, and electrocardiogram [89]. Wearable electrochemical-physiological sensors

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**Fig. 7** A The image of the LIG interdigitated array electrodes. B Side view of the LIG electrodes. C SEM image of the cross-section of the electrodes with GO coated. D The application of the LIG-based sensor in face masks. E The capacitive response of the sensor to human breathing. F Capacitance response based on different distances between face and the sensor. Reprinted with permission from ref. [82], Copyright 2020 Elsevier B.V.
are integrated, pointing out the direction for future integrated devices.

Interestingly, LIG-based masks were developed which can be used for sterilization. Scholars processed the graphene inside the mask to achieve a super-hydrophobic state, which can kill virus under the sunlight [90]. The schematic diagram and production process of the antibacterial LIG-based mask are shown in the Fig. 8C and D. Another research group reported LIG-based face masks which can kill bacteria by its photothermal effect [91]. By comparing with conventional masks on the market, the bacteria on conventional masks are still alive after 8 h, while the sterilization rate of the LIG-based mask reached an amazing number 99.998% within 10 min. The antibacterial abilities of LIG, activated carbon fiber (ACF), and melt-blown fabrics (MBF) are shown in the Fig. 8E. The LIG-based mask can block and kill germs more effectively, making the mask safer and more beneficial to the natural environment.

In daily life, wearable devices with timely alarm functions are expected to help people avoid potential dangers. At present, various types of flexible wearable sensor devices are widely studied and applied to different physiological signal monitoring. However, to achieve the early warning function, they usually need to integrate additional early warning devices, such as light-emitting diodes and buzzers, which will increase the complexity of the system. Scholars have proposed a method based on a two-layer asymmetric pattern structure by combining the mechanical and thermal properties of porous graphene [92]. The porous graphene of different patterns is transferred to a flexible and stretchable PDMS substrate, and the device is lifted by patterning. At the same time, it is proposed to use device heating for direct warning, and finally realize the application of integrated sensing and alarm multi-functional flexible devices. Figure 9A presents schematic diagram of integrated device synthesis, Fig. 9B shows a schematic diagram of principle, Fig. 9C, D, and E describe the mechanical performance, pulse monitoring performance, and thermal performance of the developed sensor, respectively. This research provided a novel method for developing multi-functional wearable devices which would be beneficial for health monitoring and timely warning. Figure 9F shows the device has good performance for the temperature warning.

Conclusions and perspectives

This review mainly discusses the application of LIG in medical sensors. There is no doubt that the LIG has drawn a great attention from biomedical sensor field and it is making
great strides forward. However, the study in this field still stays in the beginning stage. It still faces challenges. The interactions between lasers and polymer materials are a non-equilibrium, nonlinear, and multi-scale process. At present, the mechanism of the interaction between laser and polymer materials is still not fully explored. It is necessary to reveal the interaction mechanism between photons and lattices or electrons. Besides, the LIG is not robust enough as a substrate for electrophoretic coating or surface-enhanced Raman spectroscopy (SERS) because of the porous graphene that may be peeled off or scorched under a relatively high voltage or laser.

There are plenty of ways to extend this research area. The performance of LIG, such as stability, conductivity, and electrocatalytic activity, can be further improved by controlling the morphology, porosity, and surface functionalization. Optimizing its composition through doping heteroatom is an imaginative approach for developing more robust LIG-based medical sensors. In addition, current readout method using LIG as transducer is limited, and it mainly relies on the electrochemical measurement. Other readout methods, such as SERS, fluorescence, and quartz crystal microbalance (QCM), should be explored and demonstrated. Further development of LIG-based biosensors, especially wearable biomedical sensors, for detecting biomarkers (including RNAs, DNAs, proteins, virus, and whole cells) is highly encouraged. In all, it can be concluded that continued efforts in graphene laser direct manufacturing will drive rapid advances in the biomedical fields.

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Declarations

Conflict of interest The authors declare no competing interests.

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