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Graphene based sensors

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1. Introduction

Sensors are analytical devices that detect any change or reaction and responds to some type of input from the physical environment. The first biosensor for detection of glucose in blood was invented by Leland C. Clark who is also referred to as the “Father of Biosensors” [1]. In recent times, the use of biosensors has increased owing to their advantages such as high specificity and sensitivity, rapid results, reliability, easy handling and PoC diagnostics [1–3]. Due to these advantages over older conventional

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diagnostic methods [4,5], biosensors have paved their way into medical diagnostics [6], environmental impact analysis [7–9], food industry, marine sector etc. [3,10].

Each biosensor device comprises of three parts, namely, a biological recognition element, a transducer, and a signal processor. The recognition element may be an organic or inorganic substance that specifically binds to the target analyte, in this case, a biomolecule [11]. The transducer converts the chemical reaction into a detectable signal, which may be an electrical or optical or piezoelectric signal. The signal processor amplifies and records the signal for data representation [1,12,13].

Biosensors are classified based on the different type of recognition element, transducer or amplifier used. On the basis of the type of recognition element [12], biosensors are often classified into enzymatic sensors [14–16], immunosensors [13,17–19], DNA based sensors [20–22], aptamer based sensors [23,24] or whole cell microbial biosensors [25–28]. Based on the type of transducer, biosensors can be categorized into four types– Electrochemical biosensors [29,30], Optical biosensors [31–33], Piezoelectric biosensors [34–36], and Thermal biosensors [37–39]. Another mode of classification is based on the amplifying material, mainly nanomaterial [40,41], used such as gold nanoparticles [42,43], graphene [13,17,19], etc.

It is a well-established fact that graphene based biosensors are one of the most sensitive. Graphene is honey comb like structure formed with single thick planer carbon sheet [44]. It is a two-dimensional (2D) nanomaterial that has made a major contribution in the sensor and electronic industries. Its properties are similar to those of semimetals and is found to be stable under suitable conditions [45]. Graphene has been utilized in biosensors because of its numerous advantages which include a high electron transfer rate, large surface area, its ability to immobilize molecules and increased electrical conductivity [46]. The larger surface area promotes active sites for charge-biomolecular interaction which assists in proper functionalization/immobilization [47] that leads to enhanced sensing of the target molecule for increased sensitivity. Moreover graphene is easily available and also cost-effective as compared to other material such as metallic nanoparticles.

Nanomaterials made up of graphene and its derivatives have contributed to the fabrication of different types of advanced biosensors as demonstrated in Fig. 1. In recent years, novel sensing platforms are in high demand for immobilizing biomolecules, such as DNA, antibodies, antigen, etc. for creating highly sensitive and selective biosensors. Different strategies were

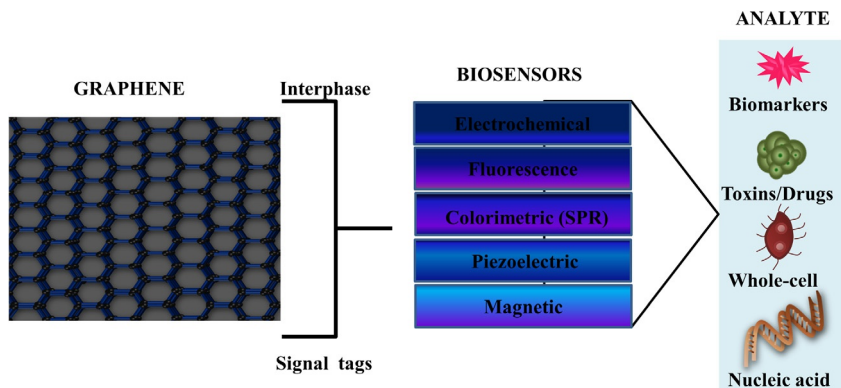


Fig. 1 Flow chart representing the types of graphene biosensors based on principles of detection such as electrochemical, fluorescence, colorimetric (SPR), piezoelectric and magnetic and target analytes such as disease biomarkers, whole-cells, toxins/drugs and nucleic acids.

used for the attachment of analyte on the surface of graphene based nanoparticles such as covalent coupling method via polyethylene glycol (PEG) [48,49] coating, EDC-NHS [50–53] or physisorption [19]. There are numerous graphene based sensors which have been developed for detection of cancer markers [19], pathogen detection [54–56], and early diagnosis of various other deadly diseases [13]. Several implantable devices have also been reported for the real time measurement of glucose levels in diabetic patient, respiration rate, heart rate, body temperature, electrocardiogram signals, etc. [57] using graphene and its derivatives as well as analytical lab on chip platforms [58–60].



2. Characteristics and classification of graphene and its derivatives

In recent years, different forms of graphene and its derivatives have been utilized in the fabrication and development of sensors and biosensors in various field such as, detection of narcotic drugs and toxins [61], medical theranostics, food science research, environmental and clinical sectors. Majority of the sensors are electrochemical, optical, or piezoelectric principle based. Highly cross-linked graphene has also been used to develop molecularly imprinted polymers (MIPs) which show high selectivity and affinity towards a target analyte [62]. Schematic of a graphene based biosensor has been depicted in Fig. 2.

Graphene in its pristine form and its functionalized derivatives such as graphene quantum dots (GQDs), graphene oxide (GO), and reduced graphene oxide (rGO) are some of the significant forms of graphene based nanomaterials [46]. Depending on the synthetic method, different derivatives of graphene can be synthesized. Different types of graphene based nanomaterials have been used in biosensor research and development which includes graphene in its pure form and its functionalized derivatives such as graphene quantum dots (GQDs), graphene oxide (GO), reduced graphene oxide (rGO), etc. [45]. Numerous strategies and techniques have been carried out to make different types of graphene based nanomaterials.

Different methods of synthesis methods result in different functional properties of the graphene based nanomaterials as shown in Fig. 3. Different number of layers, functional group addition and oxidation states causes the impact on the bonding between the bio receptor and transducer, and also causes the difference in the sensing performances among sensors. In comparison with graphene, GO consists of various oxygen functional groups such as $-OH$, $C-O-C$, $C=O$, and $-COON$ [63] which have relatively good dispersibility, strong reactivity, and multiple binding sites

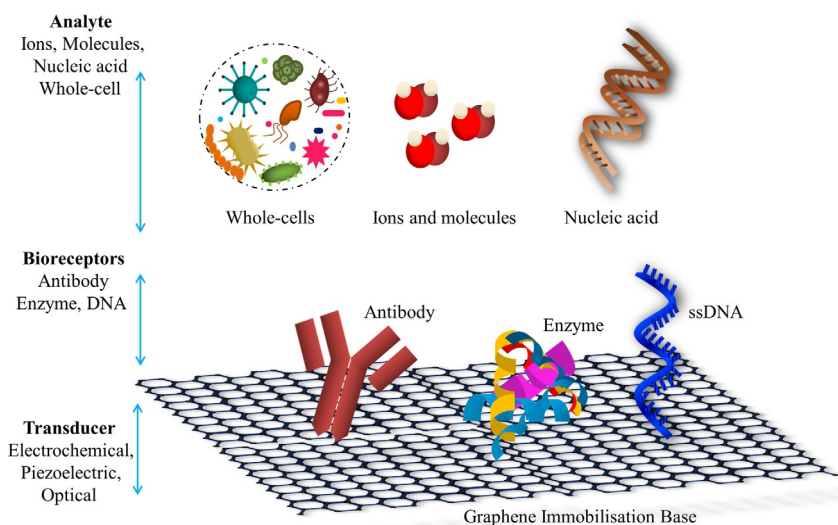


Fig. 2 Schematic of graphene based biosensors where antibody, enzymes and ssDNA (aptamer) are immobilized on the surface of the graphene which act as bioreceptors for target analytes like whole-cells, ions/molecules and nucleic acid.

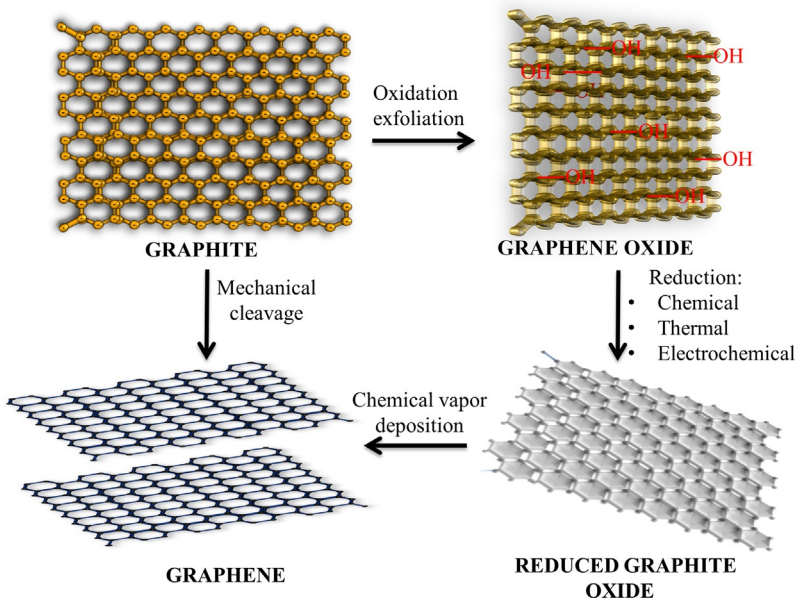


Fig. 3 Different types of methods for the synthesis of pure form of graphene, graphene oxide and reduced graphene oxide from graphite using oxidation exfoliation, chemical, electrochemical and thermal reduction, mechanical cleavage and chemical vapour deposition.

for further functionalization. When the oxygen containing groups are removed by chemical, electrochemical or thermal methods, rGO is obtained which has good thermal conductivity, chemical stability and a large surface area.

2.1 Graphene

Graphene is made up of a sp^2 bonded carbon atoms, arranged in a single layer, existing as a 2-D honeycomb structure. It shows properties which are unique such as quantum Hall effect, very high electron mobility, excellent electrical conductivity, large surface to volume ratio so it can absorb a large amount of aromatic biomolecules by π - π stacking [64], tuneable optical properties, and high mechanical strength, which make it an ideal nano-material [65,66] for potential application in medical and biological fields as a biosensor [11]. It has been used for the detection of different varieties of biomolecules such as Deoxyribonucleic Acid (DNA), antibodies, enzymes, aptamers, etc. [67–70].

2.2 Graphene oxide (GO)

Graphene oxide (GO), a nanomaterial also known as graphitic acid, belongs to the graphene superfamily, containing several reactive oxygen functional group such as epoxy group, hydroxyl group and carboxyl group which result in bulking of the plane [71–73]. Modification of GO with different functional groups set an impact on the properties of the material which lead to its application in theranostics field. It has been reported that spacing between the layers is almost twice as that of normal graphene (7\AA^0) [72,74], and thus due to this increase in interplanar space, water layers can be seen in between the GO layers and it gets hydrated immediately on immersion into water. Apart from water, polar solvents like alcohol are also easily incorporated between the layers. In terms of electrical conductivity, GO acts as an insulator due to the sp^2 network disruption [71]. However, the presence of oxygen containing groups makes it thermally unstable. GO, due to their unique properties, such as dispersion ability in aqueous medium and large surface area, have been used in different bio-application. They have been utilized in early stage diagnosis and treatment of various diseases as they can be used for detection of different target analytes such as proteins, DNA, pesticides and microbes.

2.3 Reduced graphene oxide (rGO)

Reduced graphene oxide (rGO) is an alternative form of GO which has been processed by various methods which include chemical, thermal, etc. in order to minimize the amount of oxygen as the oxygen content makes GO more unstable [75]. In its usual oxidized state, GO shows reduced sensitivity due to the oxygen functional groups, making it electrically insulating and not ideal for fabrication of a sensor based on conductance. However, reduction of GO using chemical or thermal methods such as hydrazine hydrate vapour [76], hydrogen sulphide [77], hydroquinone [78], dimethylhydrazine [79], NaBH_4 [80], and aluminium powder [81] can restore the conductivity by multiple times by removing oxygen and restoring the double-bonded aromatic carbon atoms. This method does not convert GO back to graphene in its pure form since at least few oxygen groups are present even after chemical and thermal exposure. Hence, rGO shows high conductivity, stability, and the presence of defective sites which are chemically active making it a potential candidate in the application as an active material in biosensors [82].

2.4 Graphene quantum dots (GQDs)

Graphene quantum dots are a relatively new class of material, which are derived from both carbon dots (CD) and graphene. It has extraordinary chemical, structural, electrical and tunable optical properties of photoluminescence and electrochemiluminescence [83]. Due to their noble properties, GQDs are used for the fabrication of highly sensitive sensors. GQDs are synthesized by various methods such as nanolithography [84–86], acidic oxidation, hydrothermal or solvothermal [87,88], sonication-assisted [89,90], selective plasma oxidation [91] and photo-Fenton reaction [92] technique. Unlike graphene, which is used in field-effect transistor (FET), GQDs are being utilized in charge sensors made up of single electron transistor (SET) [93,94]. It is also used for the detection of pressure and humidity. GQDs have also been used for the development of photoluminescence based sensor. Blue and green are the common photoluminescence colours observed in the GQDs. Optical biosensors are one of the best established sensors for the detection of biomolecules. Kermani et al. introduced a biosensing method for the detection of DNA methyltransferase which is crucial for the biological activities [95] as abnormal expression of this enzyme may lead to cancer. As shown in the Fig. 4, double stranded-DNA (ds-DNA) acts as a

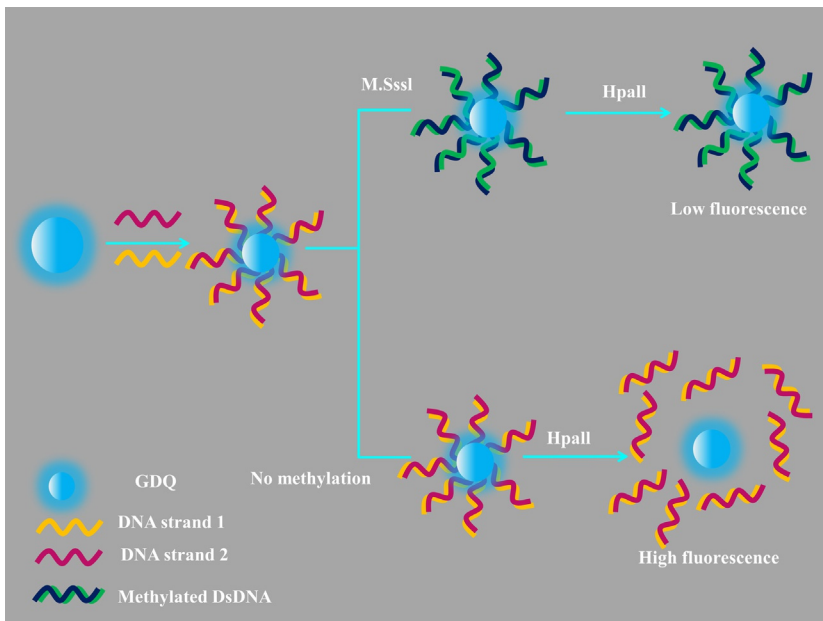


Fig. 4 Detection of methyl transferase enzyme activity using graphene quantum dots based on fluorescence anisotropy.

recognition site for both methyltransferase I (M.SssI) as well as endonuclease *HpaII*. When ds-DNA combine with GQDs, there is a 45% significant reduction in fluorescence intensity. But when ds-DNA conjugates with M.SssI, it gets methylated and develops resistance to cleavage by *HpaII* and no change in fluorescence is observed. But in the absence of M.SssI enzyme, *HpaII* cleaves the unmethylated ds-DNA resulting in an increased fluorescence.



3. Application of different types of graphene based sensors

Desirable and superior properties of graphene and its derivatives are what make it useful as a signalling device for the quantitative detection of biomolecules, antigen, antibody, antibiotics, chemicals, narcotics, toxins, DNA, whole cell virus/bacteria, etc. In the environmental sector, it is also used for the detection of pesticides, e.g. Chloropyrifos, along with the detection of antibiotics such as, Chloramphenicol, Tetracycline, Streptomycin, Kanamycin, etc. In the field of diagnostics, graphene based sensors are being researched into for diagnosis of various ailments by detecting viruses, bacteria, disease biomarkers, immune bodies, etc. Sensitivity, limit of detection (LOD) [96,97] and reproducibility of the biosensor can be improved when graphene sheets are used in combination with nanoparticles [98]. A few examples of biosensors fabricated using graphene have been compared and discussed in Table 1.

3.1 Graphene-based fluorescence biosensors

Nanoparticles like gold nanoparticles, carbon-nanotubes and graphene can efficiently be used as fluorescence quenchers and are widely used as bio sensing platforms [57,112]. Graphene and GO both exhibit fluorescence quenching properties which has sparked an interest in their potential application in the field of the clinical and environmental research. Graphene is used in fluorescent detection due to its extraordinary potential of Fluorescence Resonance Energy Transfer (FRET) [107]. A FRET based graphene aptasensor has been developed to detect thrombin in blood serum and buffers. By choosing appropriate aptamers, this sensor may be modified and alternatively be used to detect narcotics, toxins, pesticides and proteins, identify cancer cells, etc. Graphene oxide, due to its high photoluminescence has been used as a fluorophore to detect label free

Table 1 Development of the graphene based sensors and detection of different analyte.

Analyte detected	Sensor design	Sensing material/electrode	Limit of detection (LOD)	References
Glucose	Electrochemical sensor	Graphene–copper NP	0.5 μ M	[99]
Cancer uPAR biomarker	Electrochemical sensor	FTO-Graphene nanosheets	4.8 fM	[19]
HIV, arthritis, cardiovascular disease	Electrochemical sensor	Graphene-FET	10 fg/mL	[13]
Dopamine	Electrochemical sensor	Graphene and PVP	0.2 nM	[100]
DNA	Magnetic field (Hall effect)	Graphene–PMMA	10 pM	[101]
b-Amyloid	Magnetic/plasmonic GO	SERS	100 fg/ mL	[1]
Lysozyme	Au/PDDA–GO–Micrococcus lysodeikticus	Surface plasmon based sensing	3.4 nM	[102]
Glucose	GQDs–bipyridine boronic acid	Fluorescence graphene quantum dots	1 mM	[103]
DNA	GO nanowalls	DPV	9.6 zM	[104]
α -Fetoprotein	Electrochemical immunosensor	Graphene–gold NP–carboxyl groups	5.4 pg/mL	[105]
Thrombin	Optical biosensor	Aptamer and graphene nanocomposite	0.45 fM	[106]
Thrombin	Optical aptasensor	Graphene	31.3 pM	[107]

Continued

Table 1 Development of the graphene based sensors and detection of different analyte.—cont'd

Analyte detected	Sensor design	Sensing material/electrode	Limit of detection (LOD)	References
Chlorpyrifos	Electrochemical biosensor	Graphene-FET	1.8 fM	[17]
Chlorpyrifos	Electrochemical biosensor	Carboxylic graphene-NiO NP-Nafion	5×10^{-14} M	[108]
Chloramphenicol	CV, amperometry	GCE/MoS ₂ /MWCNTsCOOH	0.015 mM	[109]
Tetracycline	DPV	SPCE/graphene	0.08 mM	[63]
Streptomycin	DPV	GCE/PCNR/graphene Fe ₃ O ₄ -AuNPs	28 pg/mL	[110]
Kanamycin	Graphene oxide based fluorescent aptasensor	rGO	1.0×10^{-12} M	[111]

mercury by allowing graphene to undergo fluorescence quenching with a detection limit of 0.92 nM. When compared to nanomaterials like gold nanoparticles and carbon nanotubes, it was revealed that GO has the highest quenching ability, quick binding with DNA molecules, repeatability, and specificity to different DNA structures [112]. Graphene oxide displays amphiphilicity, which allows biomolecules to get adsorbed onto its planar surface. It has the potential to undergo proper energy transfer leading to fluorescence quenching with a minimum background signal if the adsorbed molecule is coupled with a fluorescent dye [113,114]. Graphene oxide has also been used for screening of Hepatitis C Virus (HCV) NS3 helicase inhibitors and Severe Acute Respiratory Syndrome coronavirus (SARS CoV) helicase using a GO-helicase based assay which can be further applied for screening of other essential enzymes too [115]. GO has also been used to detect Circulating Cancer Cells (CTCs) by using dye conjugated aptamers. When the aptamers are in close proximity, GO readily quenches its fluorescence. In the presence of CTCs, due to specificity, the aptamers bind to the cells. This leads to an increased gap between the aptamer and GO as a result of which the fluorescence remains unquenched [116]. A GO-based immunosensor was developed to detect pathogens, where the antibodies against the pathogen were immobilized on the GO sheet. When the target pathogenic cells bound to the antibodies, fluorescence quenching by GO was detected [56].

3.2 Graphene-based electrochemical biosensors

There are several electrochemical based sensors for the detection of biological analyte. These electrochemical sensors are based on the change in the current, voltage and impedance due to the presence of analyte on the electrode surface. In recent research, they have gained immense popularity due to high specificity, sensitivity, stability, low cost and lower limit of detection [117]. Varieties of electrochemical based graphene biosensors are constantly being developed with ultra-high sensitivity as the 2 dimensional lattice comb structured graphene demonstrates excellent conductivity and is biocompatible for easy conjugation. Adding a graphene base to electrochemical sensors improves sensitivity of the sensor. Islam et al. [17] fabricated an electrochemical based sensor by exfoliating graphene onto a Field-Effect Transistor (FET) electrode for chlorpyrifos pesticide detection. In this study, the graphene channel acts as a transducer which converts the chemical signal from the biomolecule interaction into an electrical signal that can be

measured by a lock-in amplifier. Drude conductivity equation demonstrates this diffusive motion of channel carriers, which is shown as $\sigma = ne\mu$, where σ is the conductivity, n is the carrier density, and μ is the carrier mobility. Doping of graphene channel occurs due to the heterogenous electron transfer caused by the Ag–Ab interaction, which shows a change in the resistance of the graphene channel which can be measured. Anti-chlorpyrifos antibody was conjugated onto the graphene using carbodiimide chemistry and this device was successfully able to detect chlorpyrifos in spiked samples. Similar work has been carried out using graphene coated FETs for the detection of Human Immunodeficiency Virus (HIV), Cardio Vascular Disorders (CVDs) and Rheumatoid Arthritis (RA) [13]. Another example of enhancing an electrochemical sensor using graphene has been demonstrated by Roberts et al. [19] where graphene nanosheets were coated on a Fluorine Doped Tin Oxide (FTO) glass electrode. Reduced graphene oxide was modified and converted to graphene nanosheets which were then fabricated onto the electrode. A cancer biomarker antibody was allowed to conjugate with the graphene nanosheets using carbodiimide chemistry and this fabricated electrode was then used to detect a cancer biomarker.

3.3 Graphene-based SPR biosensors

In SPR Biosensors, the interaction between the biorecognition element and the sensor surface is analysed using surface plasmon polariton waves. In a study, graphene as a biorecognition element was adsorbed onto the surface of a gold film. This combination showed that biomolecules with carbon-based ring structures, like ssDNA, were firmly adsorbed onto the surface and increased the adsorption efficiency as shown in Fig. 5. This led to a local increase in the refractive index (RI) along the surface of the metal, causing a deviation in the propagation constant of the surface plasmon polariton, hence increasing the sensitivity of the optical measurement [118,119]. A GO based SPR biosensor was developed where graphene oxide was adsorbed onto the surface of a gold film for highly sensitive Human (Immunoglobulin G) IgG detection. Due to the increased surface area of GO, a larger number of goat anti-human IgG could get immobilized, leading to more antigen being detected [120]. In a study comparing the characteristics of graphene and GO, it was seen that GO provided a greater number of binding sites (3.25 times) than a monolayer graphene surface, hence presenting enhanced sensitivity [121]. In another study, it was seen that sandwiching a silicon layer between a gold film and graphene layer also led to a

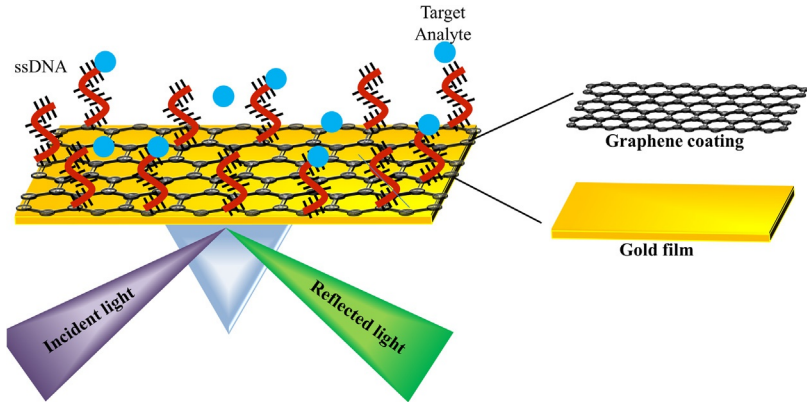


Fig. 5 SPR based sensor where graphene is adsorbed onto gold film and the biorecognition element such as ssDNA is immobilized onto it for the detection of a specific target analyte.

significant increase in sensitivity. Highest sensitivity was exhibited when the sensor was made of gold 40 nm thickness, silicon 7 nm thickness and two layers of graphene [122]. An SPR based biosensor made of carboxyl modified graphene oxide exhibited high biocompatibility and outstanding detection sensitivity as low as 0.01 pg/mL of BSA exceeding traditional chip detections [123]. Another SPR biosensor was developed where the graphene oxide sheets were coated with gold nanorods-antibody conjugates. The high sensitivity of gold nanorods and high loading capacity of graphene oxide led to highly sensitive detection of transferrin, indicating that various other proteins can be detected with the used of appropriate antibodies and nanorods on graphene oxide sheets [124]. Another graphene SPR biosensor was developed where NTA (nitrilotriacetic acid) functional groups were attached onto graphene. NTA controlled the adsorption of the bioreceptor, in this case cholera toxin on the surface. When compared to SPR sensors without graphene, it was observed that the NTA-functionalized graphene biosensor increased the performance of the sensor by 80% with a highly sensitive LOD of 4 pg/mL [125].

3.4 Graphene-based SERS biosensors

Raman spectroscopy or Surface Enhanced Raman Spectroscopy (SERS) is a method to determine the vibration, rotation and low mode frequency of the molecules. Graphene based SERS sensors are considered as a promising tool for quantitative and repeatable detection of the target molecules due to their

ultra-sensitive detection and relative insensitivity to external factors. Graphene can be used as Raman enhancement substrate due to its flat surface along with strong chemical interaction with target molecules. SERS has become an interesting field of research after Fleischmann et al. first reported the SERS phenomenon at roughened silver electrodes [126]. This tool is mostly used for the quantitative detection of biomolecules. For e.g. Feliu et al. has checked the protein expression level, which may be used to indicate genomic mutation [127]. Demeritte et al. worked on the development of a SERS-GO based plasmonic-magnetic multifunctional immunosensor for and label-free identification and selective separation of β -amyloid which is a biomarker for Alzheimer's disease [128]. DNA biosensing was developed using GO and AuNPs based SERS platform. Khalil et al., developed a PCR free SERS based DNA to be able to identify the endangered species-Malayan box turtle (MBT) (*Cuora amboinensis*) [129]. In this research work, one of the two capture probes was GO-AuNPs functionalized and the other was modified using AuNPs and Raman dye. Hybridization was induced by the target DNA between capture probe 1, capture probe 2 and the target. A locally enhanced electromagnetic field was generated by coupling of the two capture probes, which significantly amplified the SERS signal. Hence, coupling of two SERS active substrates in the presence of short-length probe DNA sequences has resulted in improvement of biosensor sensitivity to obtain an LOD as low as 10 fM. Moreover, the biosensor also displayed high specificity towards a particular target DNA as it was able to successfully discriminate between six non-target DNA sequences which were closely related and sensitivity for a base-mismatch comprising of a single nucleotide in the target DNA. In this research work, the fabricated SERS based biosensor could act as a potential platform for the authenticated identification of a Malayan box turtle from multiple archaeological and/or forensic samples. This sensor can further be applied in various other diagnostic fields, e.g. detection of cancer biomarkers.

3.5 Graphene based gas sensors

2D structure with extreme high surface area makes graphene compatible for the development of gas sensors. Gas sensing involves absorption and desorption of small gaseous molecules by the thin layer of graphene, resulting in change in the conductance of graphene. Now days, breath analysis for non-invasive diagnosis of diseases is attracting widespread attention. Human breath contains biomarkers that can be used for the diagnosis of

several disease like lung cancer, diabetes, etc. [130]. According to the research carried out by Clemens et al., compounds like isoprene, acetone and methanol are expelled in the normal exhalation of breath. However in the case of certain disorders, these three main components show abnormally high or low concentration as compared to healthy volunteers [130,131]. Therefore high sensitivity of graphene towards gaseous molecules led to the fabrication of a gas based sensor, which can be utilized for the detection of ethanol, NH_3 , NO_2 , and O_2 [132]. Engineer et al. have developed high-quality MNPs-rGO nanocomposites based gas sensor platforms for the detection of NH_3 gas. Graphene oxide nanosheets were synthesized and further decorated with metal nanoparticles (MNPs) like Ag, Pd, Cu, and Au to improve the charge transfer [133] as shown in the Fig. 6. Gas sensing principle is based on the electrical and ionic conductivity at low and high availability of gas molecules respectively. The sensor was fixed onto the non-conductive surface to negate the effect of ambient humidity. MNP-rGO nanocomposite was exposed to different concentrations of the analyte (NH_3) and electrical resistance was measured at different exposure concentrations. It was reported that the electrical resistance increases upon increase in the concentration of NH_3 and returns to initial value after removal of the analyte. Sensing response increases with increase in the concentration of gas

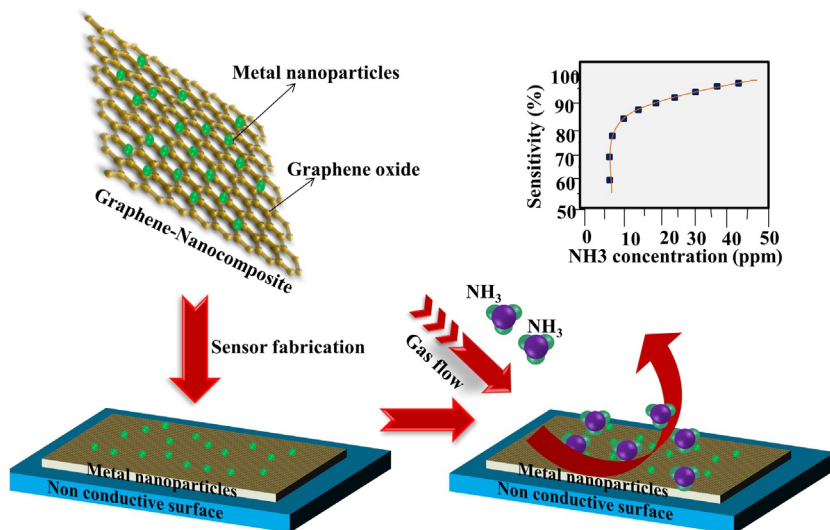


Fig. 6 Fabrication of graphene based gas sensor for detection of ammonia. Graphene oxide was synthesized directly using graphite powder. Metal-nanoparticles (MNPs) were fabricated by single step reduction process and electrical resistance was measured.

because of increase in gas molecule adsorption at the active sites of the graphene-based nanocomposites.

3.6 Graphene-based multifunction detection sensor

In recent times, there is a huge focus to develop miniaturized diagnostic devices which are portable and can be used on-site without the need of an elaborate laboratory set up. Graphene enables us to develop such devices for detection of various parameters as well as health-monitoring devices due to its robustness, added sensitivity and low cost. Xu et al. [134] developed a health monitoring device which can be mounted onto a person's neck (detection of laryngeal prominence motions) for simultaneous in-situ detection of various human movements and ion concentration in sweat. The sensor was made by applying an rGO film on top of a porous inverse opal acetylcellulose (IOAC) film. The rGO film due to its resistance change acted as a layer for strain-sensing to be able to monitor human motion, while the porous IOAC acted as a flexible microstructured substrate which enabled collection and analysis of sweat ion concentration using colorimetric principle/reflection peak shifts besides high sensitive motion sensing. Similarly, another rGO/single-wall carbon nanotubes (SWCNTs) hybrid fabric-based strain-pressure sensor was developed by Kim et al. In this study, GO was coated on cotton fabric with subsequent chemical reduction to rGO and later coated with SWCNTs to improve durability and electrical conductivity. The fabric showed water resistant properties (crucial for applicability of wearable electronics) and was used to make a wearable glove which could detect motion signals when it was bent, gripped, pressed, and wrist-turned [135].



4. Conclusion

In this book chapter, we have described recent advances made in graphene based sensors and have discussed about different types of graphite based material such as graphene in its pure form, graphene quantum dots, graphene oxide, and reduced graphene oxide along with their properties for the development of advanced sensors. Besides the different forms of graphene used, there are also various types of sensors developed based on different principals such as optical, electrochemical, etc. which have also been elaborated in this chapter. It is clear that graphene and its derivatives are a major advantage in the development of biosensors and graphene shows a lot of promise in the field of theranostics due to its unique properties such

as excellent electrical conductivity, high electron mobility, tunable optical properties, room temperature quantum Hall effect, large surface to volume ratio, high mechanical strength, and ease of functionalization. Graphene based sensors are cost effective and have the potential to be developed into miniaturized devices for on-field point of care diagnostic testing. Being one of the most sensitive tool for detection, it is vital for future research needs to focus on making this graphene based devices small, portable and cost effective without compromising on the sensitivity.

References

- [1] S. Szunerits, R. Boukherroub, Graphene-based biosensors, *Interface Focus* 8 (2018) 20160132–20160140. <https://doi.org/10.1098/rsfs.2016.0132>.
- [2] E.V. Korotkaya, Biosensors: design, classification, and applications in the food industry, *Foods Raw Mater.* 2 (2014) 161–171. <https://doi.org/10.12737/5476>.
- [3] E. Morales-Narváez, L. Baptista-Pires, A. Zamora-Gálvez, A. Merkoçi, Graphene-based biosensors: going simple, *Adv. Mater.* 29 (2017) 1604905. <https://doi.org/10.1002/adma.201604905>.
- [4] A. Roberts, S. Gandhi, Japanese encephalitis virus: a review on emerging diagnostic techniques, *Front. Biosci. (Landmark Ed.)* 25 (2020) 1872–1890. <https://doi.org/10.2741/4882>.
- [5] S. Nandi, A. Mondal, A. Roberts, S. Gandhi, Biosensor platforms for rapid HIV detection, *Adv. Clin. Chem.* 98 (2020) 1–34. <https://doi.org/10.1016/bs.acc.2020.02.001>.
- [6] D. Sharma, C.M. Hussain, Smart nanomaterials in pharmaceutical analysis, *Arab. J. Chem.* 13 (2020) 3319–3343. <https://doi.org/10.1016/j.arabjc.2018.11.007>.
- [7] C.M. Hussain, Magnetic nanomaterials for environmental analysis, *RSC Detect. Sci.* 2017 (2017) 3–13. <https://doi.org/10.1039/9781782629139-00001>.
- [8] S. Büyüktiryaki, Y. Sümbelli, R. Keçili, C.M. Hussain, Lab-on-chip platforms for environmental analysis, *Encycl. Anal. Sci.* (2019) 267–273, third ed. <https://doi.org/10.1016/B978-0-12-409547-2.14489-0>.
- [9] C.M. Hussain, R. Keçili, *Modern Environmental Analysis Techniques for Pollutants*, Elsevier, 2019. <https://doi.org/10.1016/C2018-0-01639-4>.
- [10] P. Mehrotra, Biosensors and their applications—a review, *J. Oral Biol. Craniofac. Res.* 6 (2016) 153–159. <https://doi.org/10.1016/j.jobocr.2015.12.002>.
- [11] M. Pumera, Graphene in biosensing, *Mater. Today* 14 (2011) 308–315. [https://doi.org/10.1016/S1369-7021\(11\)70160-2](https://doi.org/10.1016/S1369-7021(11)70160-2).
- [12] I. Banga, R. Tyagi, D. Shahdeo, S. Gandhi, Biosensors and their application for the detection of avian influenza virus, in: P.K. Maurya, S. Singh (Eds.), *Nanotechnology in Modern Animal Biotechnology*, Elsevier, 2019, pp. 1–16. <https://doi.org/10.1016/b978-0-12-818823-1.00001-6>.
- [13] S. Islam, S. Shukla, V.K. Bajpai, Y.-K. Han, Y.S. Huh, A. Kumar, et al., A smart nanosensor for the detection of human immunodeficiency virus and associated cardiovascular and arthritis diseases using functionalized graphene-based transistors, *Biosens. Bioelectron.* 126 (2019) 792–799. <https://doi.org/10.1016/j.bios.2018.11.041>.
- [14] S. Viswanathan, H. Radecka, J. Radecki, Electrochemical biosensor for pesticides based on acetylcholinesterase immobilized on polyaniline deposited on vertically assembled carbon nanotubes wrapped with ssDNA, *Biosens. Bioelectron.* 24 (2009) 2772–2777. <https://doi.org/10.1016/J.BIOS.2009.01.044>.
- [15] Y. Wei, Y. Li, Y. Qu, F. Xiao, G. Shi, L. Jin, A novel biosensor based on photoelectro-synergistic catalysis for flow-injection analysis system/ampereometric detection of

- organophosphorous pesticides, *Anal. Chim. Acta* 643 (2009) 13–18. <https://doi.org/10.1016/J.ACA.2009.03.045>.
- [16] D. Du, J. Ding, J. Cai, A. Zhang, Determination of carbaryl pesticide using amperometric acetylcholinesterase sensor formed by electrochemically deposited chitosan, *Colloids Surf. B: Biointerfaces* 58 (2007) 145–150. <https://doi.org/10.1016/J.COLSURFB.2007.03.006>.
- [17] S. Islam, S. Shukla, V.K. Bajpai, Y.K. Han, Y.S. Huh, A. Ghosh, et al., Microfluidic-based graphene field effect transistor for femtomolar detection of chlorpyrifos, *Sci. Rep.* 9 (2019) 276. <https://doi.org/10.1038/s41598-018-36746-w>.
- [18] A. Talan, A. Mishra, S.A. Eremin, J. Narang, A. Kumar, S. Gandhi, Ultrasensitive electrochemical immuno-sensing platform based on gold nanoparticles triggering chlorpyrifos detection in fruits and vegetables, *Biosens. Bioelectron.* 105 (2018) 14–21. <https://doi.org/10.1016/j.bios.2018.01.013>.
- [19] A. Roberts, P.P. Tripathi, S. Gandhi, Graphene nanosheets as an electric mediator for ultrafast sensing of urokinase plasminogen activator receptor—a biomarker of cancer, *Biosens. Bioelectron.* 141 (2019) 111398–111406. <https://doi.org/10.1016/J.BIOS.2019.111398>.
- [20] N. Dai, E.T. Kool, Fluorescent DNA-based enzyme sensors, *Chem. Soc. Rev.* 40 (2011) 5756–5770. <https://doi.org/10.1039/c0cs00162g>.
- [21] L. Gao, C. Lian, Y. Zhou, L. Yan, Q. Li, C. Zhang, et al., Graphene oxide-DNA based sensors, *Biosens. Bioelectron.* 60 (2014) 22–29. <https://doi.org/10.1016/j.bios.2014.03.039>.
- [22] T.G. Drummond, M.G. Hill, J.K. Barton, Electrochemical DNA sensors, *Nat. Biotechnol.* 21 (2003) 1192–1199. <https://doi.org/10.1038/nbt873>.
- [23] A. Kasoju, D. Shahdeo, A.A. Khan, N.S. Shrikrishna, S. Mahari, A.M. Alanazi, et al., Fabrication of microfluidic device for aflatoxin M1 detection in milk samples with specific aptamers, *Sci. Rep.* 10 (2020) 1–8. <https://doi.org/10.1038/s41598-020-60926-2>.
- [24] A. Kasoju, N.S. Shrikrishna, D. Shahdeo, A.A. Khan, A.M. Alanazi, S. Gandhi, Microfluidic paper device for rapid detection of aflatoxin B1 using an aptamer based colorimetric assay, *RSC Adv.* 10 (2020) 11843–11850. <https://doi.org/10.1039/d0ra00062k>.
- [25] J.C. Gutiérrez, F. Amaro, A. Martín-González, Heavy metal whole-cell biosensors using eukaryotic microorganisms: an updated critical review, *Front. Microbiol.* 6 (2015) 48. <https://doi.org/10.3389/fmicb.2015.00048>.
- [26] P. Riangrunroj, C.S. Bever, B.D. Hammock, K.M. Polizzi, A label-free optical whole-cell *Escherichia coli* biosensor for the detection of pyrethroid insecticide exposure, *Sci. Rep.* 9 (2019) 1–9. <https://doi.org/10.1038/s41598-019-48907-6>.
- [27] L.T. Bereza-Malcolm, G. Mann, A.E. Franks, Environmental sensing of heavy metals through whole cell microbial biosensors: a synthetic biology approach, *ACS Synth. Biol.* 4 (2015) 535–546. <https://doi.org/10.1021/sb500286r>.
- [28] L. Bousse, Whole cell biosensors, *Sensors Actuators B Chem.* 34 (1996) 270–275. [https://doi.org/10.1016/S0925-4005\(96\)01906-5](https://doi.org/10.1016/S0925-4005(96)01906-5).
- [29] E. Bakker, Electrochemical sensors, *Anal. Chem.* 76 (2004) 3285–3298. <https://doi.org/10.1021/AC049580Z>.
- [30] D.R. Thévenot, K. Toth, R.A. Durst, G.S. Wilson, Electrochemical biosensors: recommended definitions and classification, *Biosens. Bioelectron.* 16 (2001) 121–131. [https://doi.org/10.1016/S0956-5663\(01\)00115-4](https://doi.org/10.1016/S0956-5663(01)00115-4).
- [31] P. Damborský, J. Švitel, J. Katrlík, Optical biosensors, *Essays Biochem.* 60 (2016) 91–100. <https://doi.org/10.1042/EBC20150010>.
- [32] M.A. Cooper, Optical biosensors in drug discovery, *Nat. Rev. Drug Discov.* 1 (2002) 515–528. <https://doi.org/10.1038/nrd838>.

- [33] C. Chen, J. Wang, Optical biosensors: an exhaustive and comprehensive review, *Analyst* 145 (2020) 1605–1628. <https://doi.org/10.1039/c9an01998g>.
- [34] P. Skládal, Piezoelectric biosensors, *TrAC Trends Anal. Chem.* 79 (2016) 127–133. <https://doi.org/10.1016/j.trac.2015.12.009>.
- [35] M. Pohanka, The piezoelectric biosensors: principles and applications, a review, *Int. J. Electrochem. Sci.* 12 (2017) 496–506. <https://doi.org/10.20964/2017.01.44>.
- [36] M. Pohanka, Overview of piezoelectric biosensors, immunosensors and DNA sensors and their applications, *Materials (Basel)* 11 (2018) 448. <https://doi.org/10.3390/ma11030448>.
- [37] F. Lammers, T. Scheper, Thermal biosensors in biotechnology, *Adv. Biochem. Eng. Biotechnol.* 64 (1999) 35–67. https://doi.org/10.1007/3-540-49811-7_2.
- [38] K. Mosbach, Thermal biosensors, *Biosens. Bioelectron.* 6 (1991) 179–182. [https://doi.org/10.1016/0956-5663\(91\)80002-F](https://doi.org/10.1016/0956-5663(91)80002-F).
- [39] K. Ramanathan, B. Danielsson, Principles and applications of thermal biosensors, *Biosens. Bioelectron.* 16 (2001) 417–423. [https://doi.org/10.1016/S0956-5663\(01\)00124-5](https://doi.org/10.1016/S0956-5663(01)00124-5).
- [40] R. Keçili, S. Büyüktiryaki, C.M. Hussain, Advancement in bioanalytical science through nanotechnology: past, present and future, *TrAC Trends Anal. Chem.* 110 (2019) 259–276. <https://doi.org/10.1016/j.trac.2018.11.012>.
- [41] S. Büyüktiryaki, R. Keçili, C.M. Hussain, Functionalized nanomaterials in dispersive solid phase extraction: advances & prospects, *TrAC Trends Anal. Chem.* 127 (2020) 115893. <https://doi.org/10.1016/j.trac.2020.115893>.
- [42] S. Gandhi, N. Caplash, P. Sharma, S.C. Raman, Strip-based immunochromatographic assay using specific egg yolk antibodies for rapid detection of morphine in urine samples, *Biosens. Bioelectron.* 25 (2009) 502–505. <https://doi.org/10.1016/j.bios.2009.07.018>.
- [43] P. Mishra, I. Banga, R. Tyagi, T. Munjal, A. Goel, N. Capalash, et al., An immunochromatographic dipstick as an alternate for monitoring of heroin metabolites in urine samples, *RSC Adv.* 8 (2018) 23163–23170. <https://doi.org/10.1039/C8RA02018C>.
- [44] Y. Huang, X. Dong, Y. Liu, L.J. Li, P. Chen, Graphene-based biosensors for detection of bacteria and their metabolic activities, *J. Mater. Chem.* 21 (2011) 12358–12362. <https://doi.org/10.1039/c1jm11436k>.
- [45] P. Suvamaphaet, S. Pechprasarn, Graphene-based materials for biosensors: a review, *Sensors* 17 (2017) 2161. <https://doi.org/10.3390/s17102161>.
- [46] J. Peña-Bahamonde, H.N. Nguyen, S.K. Fanourakis, D.F. Rodrigues, Recent advances in graphene-based biosensor technology with applications in life sciences, *J. Nanobiotechnol.* 16 (2018) 1–17. <https://doi.org/10.1186/s12951-018-0400-z>.
- [47] C.M. Hussain, *Nanomaterials in Chromatography: Current Trends in Chromatographic Research Technology and Techniques*, Elsevier, 2018. <https://doi.org/10.1016/C2016-0-04157-8>.
- [48] J. Wang, M. Cheng, Z. Zhang, L. Guo, Q. Liu, G. Jiang, An antibody-graphene oxide nanoribbon conjugate as a surface enhanced laser desorption/ionization probe with high sensitivity and selectivity, *Chem. Commun.* 51 (2015) 4619–4622. <https://doi.org/10.1039/c4cc10401c>.
- [49] A. Shirai, T.G. Henares, K. Sueyoshi, T. Endo, H. Hisamoto, Fast and single-step immunoassay based on fluorescence quenching within a square glass capillary immobilizing graphene oxide-antibody conjugate and fluorescently labelled antibody, *Analyst* 141 (2016) 3389–3394. <https://doi.org/10.1039/c5an02637g>.
- [50] J. Zhang, Y. Sun, B. Xu, H. Zhang, Y. Gao, H. Zhang, et al., A novel surface plasmon resonance biosensor based on graphene oxide decorated with gold nanorod-antibody conjugates for determination of transferrin, *Biosens. Bioelectron.* 45 (2013) 230–236. <https://doi.org/10.1016/j.bios.2013.02.008>.

- [51] A. Huang, L. Zhang, W. Li, Z. Ma, S. Shuo, T. Yao, Controlled fluorescence quenching by antibody-conjugated graphene oxide to measure tau protein, *R. Soc. Open Sci.* 5 (2018) 171808. <https://doi.org/10.1098/rsos.171808>.
- [52] T. Soukka, H. Härmä, J. Paukkunen, T. Lövgren, Utilization of kinetically enhanced monovalent binding affinity by immunoassays based on multivalent nanoparticle-antibody bioconjugates, *Anal. Chem.* 73 (2001) 2254–2260. <https://doi.org/10.1021/ac001287l>.
- [53] J.S. Lee, H.A. Joung, M.G. Kim, C.B. Park, Graphene-based chemiluminescence resonance energy transfer for homogeneous immunoassay, *ACS Nano* 6 (2012) 2978–2983. <https://doi.org/10.1021/nn300684d>.
- [54] F. Liu, K.S. Choi, T.J. Park, S.Y. Lee, T.S. Seo, Graphene-based electrochemical biosensor for pathogenic virus detection, *Biochip J.* 5 (2011) 123–128. <https://doi.org/10.1007/s13206-011-5204-2>.
- [55] P. Zuo, X. Li, D.C. Dominguez, B.C. Ye, A PDMS/paper/glass hybrid microfluidic biochip integrated with aptamer-functionalized graphene oxide nano-biosensors for one-step multiplexed pathogen detection, *Lab Chip* 13 (2013) 3921–3928. <https://doi.org/10.1039/c3lc50654a>.
- [56] J.H. Jung, D.S. Cheon, F. Liu, K.B. Lee, T.S. Seo, A graphene oxide based immuno-biosensor for pathogen detection, *Angew. Chem. Int. Ed.* 49 (2010) 5708–5711. <https://doi.org/10.1002/anie.201001428>.
- [57] H. Huang, S. Su, N. Wu, H. Wan, S. Wan, H. Bi, et al., Graphene-based sensors for human health monitoring, *Front. Chem.* 7 (2019) 399. <https://doi.org/10.3389/fchem.2019.00399>.
- [58] J. Sengupta, C.M. Hussain, Graphene and its derivatives for analytical lab on chip platforms, *TrAC Trends Anal. Chem.* 114 (2019) 326–337. <https://doi.org/10.1016/j.trac.2019.03.015>.
- [59] C.M. Hussain, *Handbook of Nanomaterials in Analytical Chemistry: Modern Trends in Analysis*, Elsevier, 2019. <https://doi.org/10.1016/C2018-0-00945-7>.
- [60] C.M. Hussain, *Handbook on Miniaturization in Analytical Chemistry: Application of Nanotechnology*, Elsevier, 2020. <https://www.elsevier.com/books/handbook-on-miniaturization-in-analytical-chemistry/hussain/978-0-12-819763-9>.
- [61] S. Mahari, A. Roberts, D. Shahdeo, S. Gandhi, eCovSens-Ultrasensitive Novel In-House Built Printed Circuit Board Based Electrochemical Device for Rapid Detection of nCovid-19, 2020, *BioRxiv*, 2020. 04.24.059204. <https://doi.org/10.1101/2020.04.24.059204>.
- [62] R. Keçili, C.M. Hussain, Recent progress of imprinted nanomaterials in analytical chemistry, *Int. J. Anal. Chem.* 18 (2018) 1–18. <https://doi.org/10.1155/2018/8503853>.
- [63] L. Xu, Y. Wen, S. Pandit, V.R.S.S. Mokkapati, I. Mijakovic, Y. Li, et al., Graphene-based biosensors for the detection of prostate cancer protein biomarkers: a review, *BMC Chem.* 13 (2019) 1–12. <https://doi.org/10.1186/s13065-019-0611-x>.
- [64] A.K. Geim, K.S. Novoselov, The rise of graphene, *Nat. Mater.* 6 (2007) 183–191. <https://doi.org/10.1038/nmat1849>.
- [65] T. Arun, S.K. Verma, P.K. Panda, R.J. Joseyphus, E. Jha, A. Akbari-Fakhrabadi, et al., Facile synthesized novel hybrid graphene oxide/cobalt ferrite magnetic nanoparticles based surface coating material inhibit bacterial secretion pathway for antibacterial effect, *Mater. Sci. Eng. C* 104 (2019) 109932. <https://doi.org/10.1016/j.msec.2019.109932>.
- [66] S. De, S. Mohanty, S.K. Nayak, S.K. Verma, M. Suar, Nanotoxicity of rare earth metal oxide anchored graphene nanohybrid: a facile synthesis and in vitro cellular response studies, *Nano* 10 (2015) 1550091. <https://doi.org/10.1142/S1793292015500915>.

- [67] H. Wang, G. Zhao, D. Chen, Z. Wang, G. Liu, A sensitive acetylcholinesterase biosensor based on screen printed electrode modified with Fe₃O₄ nanoparticle and graphene for chlorpyrifos determination, *Int. J. Electrochem. Sci.* 11 (2016) 10906–10918. <https://doi.org/10.20964/2016.12.90>.
- [68] I.P. Mahendra Wijaya, S. Gandhi, T. Ju Nie, N. Wangoo, I. Rodriguez, G. Shekhawat, et al., Protein/carbon nanotubes interaction: the effect of carboxylic groups on conformational and conductance changes, *Appl. Phys. Lett.* 95 (2009) 073704. <https://doi.org/10.1063/1.3211328>.
- [69] N. Gao, T. Gao, X. Yang, X. Dai, W. Zhou, A. Zhang, et al., Specific detection of biomolecules in physiological solutions using graphene transistor biosensors, *Proc. Natl. Acad. Sci. U. S. A.* 113 (2016) 14633–14638. <https://doi.org/10.1073/pnas.1625010114>.
- [70] C. Wang, X. Cui, Y. Li, H. Li, L. Huang, J. Bi, et al., A label-free and portable graphene FET aptasensor for children blood lead detection, *Sci. Rep.* 6 (2016) 21711. <https://doi.org/10.1038/srep21711>.
- [71] D. Sharma, S. Kanchi, M.I. Sabela, K. Bisetty, Insight into the biosensing of graphene oxide: present and future prospects, *Arab. J. Chem.* 9 (2016) 238–261. <https://doi.org/10.1016/j.arabjc.2015.07.015>.
- [72] A.V. Talyzin, V.L. Solozhenko, O.O. Kurakevych, T. Szabó, I. Dékány, A. Kurnosov, et al., Colossal pressure-induced lattice expansion of graphite oxide in the presence of water, *Angew. Chem. Int. Ed.* 47 (2008) 8268–8271. <https://doi.org/10.1002/anie.200802860>.
- [73] D. Krishnan, F. Kim, J. Luo, R. Cruz-Silva, L.J. Cote, H.D. Jang, et al., Energetic graphene oxide: challenges and opportunities, *Nano Today* 7 (2012) 137–152. <https://doi.org/10.1016/j.nantod.2012.02.003>.
- [74] C.N.R. Rao, A.K. Sood, K.S. Subrahmanyam, A. Govindaraj, Graphene: the new two-dimensional nanomaterial, *Angew. Chem. Int. Ed.* 48 (2009) 7752–7777. <https://doi.org/10.1002/anie.200901678>.
- [75] D.G. Papageorgiou, I.A. Kinloch, R.J. Young, Graphene/elastomer nanocomposites, *Carbon* 95 (2015) 460–484. <https://doi.org/10.1016/j.carbon.2015.08.055>.
- [76] S. Park, R.S. Ruoff, Chemical methods for the production of graphenes, *Nat. Nanotechnol.* 4 (2009) 217–224. <https://doi.org/10.1038/nnano.2009.58>.
- [77] U. Hofmann, A. Frenzel, Die Reduktion von Graphitoxyd mit Schwefelwasserstoff, *Kolloid Z.* 68 (1934) 149–151. <https://doi.org/10.1007/BF01451376>.
- [78] W. Guoxiu, Y. Juan, P. Jinsoo, G. Xinglong, W. Bei, L. Hao, et al., Facile synthesis and characterization of graphene nanosheets, *J. Phys. Chem. C* 112 (2008) 8192–8195. <https://doi.org/10.1021/jp710931h>.
- [79] S. Stankovich, D.A. Dikin, G.H.B. Dommett, K.M. Kohlhaas, E.J. Zimney, E.A. Stach, et al., Graphene-based composite materials, *Nature* 442 (2006) 282–286. <https://doi.org/10.1038/nature04969>.
- [80] R. Muszynski, B. Seger, P.V. Kamat, Decorating graphene sheets with gold nanoparticles, *J. Phys. Chem. C* 112 (2008) 5263–5266. <https://doi.org/10.1021/jp800977b>.
- [81] Z. Fan, K. Wang, T. Wei, J. Yan, L. Song, B. Shao, An environmentally friendly and efficient route for the reduction of graphene oxide by aluminum powder, *Carbon N Y* 48 (2010) 1686–1689. <https://doi.org/10.1016/j.carbon.2009.12.063>.
- [82] J.T. Robinson, F.K. Perkins, E.S. Snow, Z. Wei, P.E. Sheehan, Reduced graphene oxide molecular sensors, *Nano Lett.* 8 (2008) 3137–3140. <https://doi.org/10.1021/nl8013007>.
- [83] P. Elvati, E. Baumeister, A. Violi, Graphene quantum dots: effect of size, composition and curvature on their assembly, *RSC Adv.* 7 (2017) 17704–17710. <https://doi.org/10.1039/c7ra01029j>.

- [84] H. Sun, L. Wu, W. Wei, X. Qu, Recent advances in graphene quantum dots for sensing, *Mater. Today* 16 (2013) 433–442. <https://doi.org/10.1016/j.mattod.2013.10.020>.
- [85] J. Shen, Y. Zhu, X. Yang, C. Li, Graphene quantum dots: emergent nanolights for bioimaging, sensors, catalysis and photovoltaic devices, *Chem. Commun.* 48 (2012) 3686–3699. <https://doi.org/10.1039/c2cc00110a>.
- [86] S. Zhu, S. Tang, J. Zhang, B. Yang, Control the size and surface chemistry of graphene for the rising fluorescent materials, *Chem. Commun.* 48 (2012) 4527–4539. <https://doi.org/10.1039/c2cc31201h>.
- [87] D. Pan, J. Zhang, Z. Li, M. Wu, Hydrothermal route for cutting graphene sheets into blue-luminescent graphene quantum dots, *Adv. Mater.* 22 (2010) 734–738. <https://doi.org/10.1002/adma.200902825>.
- [88] Q.Y. Tong, U.M. Gösele, Wafer bonding and layer splitting for microsystems, *Adv. Mater.* 11 (1999) 1409–1425. [https://doi.org/10.1002/\(SICI\)1521-4095\(199912\)11:17<1409::AID-ADMA1409>3.0.CO;2-W](https://doi.org/10.1002/(SICI)1521-4095(199912)11:17<1409::AID-ADMA1409>3.0.CO;2-W).
- [89] S. Zhuo, M. Shao, S.T. Lee, Upconversion and downconversion fluorescent graphene quantum dots: ultrasonic preparation and photocatalysis, *ACS Nano* 6 (2012) 1059–1064. <https://doi.org/10.1021/nn2040395>.
- [90] L. David, R. Bhandavat, G. Singh, MoS₂/graphene composite paper for sodium-ion battery electrodes, *ACS Nano* 8 (2014) 1759–1770. <https://doi.org/10.1021/nn406156b>.
- [91] T. Gokus, R.R. Nair, A. Bonetti, M. Böhmeler, A. Lombardo, K.S. Novoselov, et al., Making graphene luminescent by oxygen plasma treatment, *ACS Nano* 3 (2009) 3963–3968. <https://doi.org/10.1021/nn9012753>.
- [92] X. Zhou, Y. Zhang, C. Wang, X. Wu, Y. Yang, B. Zheng, et al., Photo-Fenton reaction of graphene oxide: a new strategy to prepare graphene quantum dots for DNA cleavage, *ACS Nano* 6 (2012) 6592–6599. <https://doi.org/10.1021/nn301629v>.
- [93] S. Mao, Graphene field-effect transistor sensors, *Graphene Bioelectron.* (2018) 113–132. Elsevier Inc. <https://doi.org/10.1016/B978-0-12-813349-1.00005-6>.
- [94] T. Ihn, J. Güttinger, F. Molitor, S. Schnez, E. Schurtenberger, A. Jacobsen, et al., Graphene single-electron transistors, *Mater. Today* 13 (2010) 44–50. [https://doi.org/10.1016/S1369-7021\(10\)70033-X](https://doi.org/10.1016/S1369-7021(10)70033-X).
- [95] H.A. Kermani, M. Hosseini, M. Dadmehr, S. Hosseinkhani, M.R. Ganjali, DNA methyltransferase activity detection based on graphene quantum dots using fluorescence and fluorescence anisotropy, *Sensors Actuators B Chem.* 241 (2017) 217–223. <https://doi.org/10.1016/j.snb.2016.10.078>.
- [96] L. Wu, D. Deng, J. Jin, X. Lu, J. Chen, Nanographene-based tyrosinase biosensor for rapid detection of bisphenol A, *Biosens. Bioelectron.* 35 (2012) 193–199. <https://doi.org/10.1016/j.bios.2012.02.045>.
- [97] Q. He, S. Wu, Z. Yin, H. Zhang, Graphene-based electronic sensors, *Chem. Sci.* 3 (2012) 1764–1772. <https://doi.org/10.1039/c2sc20205k>.
- [98] S. Singal, A.K. Srivastava, A.M. Biradar, A. Mulchandani, Rajesh, Pt nanoparticles-chemical vapor deposited graphene composite based immunosensor for the detection of human cardiac troponin i, *Sensors Actuators B Chem.* 205 (2014) 363–370. <https://doi.org/10.1016/j.snb.2014.08.088>.
- [99] C.I.L. Justino, A.R. Gomes, A.C. Duarte, T.A.P. Rocha-Santos, Graphene based sensors and biosensors, *TrAC Trends Anal. Chem.* 91 (2017) 53–66. <https://doi.org/10.1016/j.trac.2017.04.003>.
- [100] Q. Liu, X. Zhu, Z. Huo, X. He, Y. Liang, M. Xu, Electrochemical detection of dopamine in the presence of ascorbic acid using PVP/graphene modified electrodes, *Talanta* 97 (2012) 557–562. <https://doi.org/10.1016/j.talanta.2012.05.013>.

- [101] C.-T. Lin, P.T.K. Loan, T.-Y. Chen, K.-K. Liu, C.-H. Chen, K.-H. Wei, et al., Label-free electrical detection of DNA hybridization on graphene using hall effect measurements: revisiting the sensing mechanism, *Adv. Funct. Mater.* 23 (2013) 2301–2307. <https://doi.org/10.1002/adfm.201202672>.
- [102] A. Vasilescu, S. Gáspár, M. Gheorghiu, S. David, V. Dinca, S. Peteu, et al., Surface plasmon resonance based sensing of lysozyme in serum on *Micrococcus lysodeikticus*-modified graphene oxide surfaces, *Biosens. Bioelectron.* 89 (2017) 525–531. <https://doi.org/10.1016/j.bios.2016.03.040>.
- [103] Y.H. Li, L. Zhang, J. Huang, R.P. Liang, J.D. Qiu, Fluorescent graphene quantum dots with a boronic acid appended bipyridinium salt to sense monosaccharides in aqueous solution, *Chem. Commun.* 49 (2013) 5180–5182. <https://doi.org/10.1039/c3cc40652k>.
- [104] O. Akhavan, E. Ghaderi, R. Rahighi, Toward single-DNA electrochemical biosensing by graphene nanowalls, *ACS Nano* 6 (2012) 2904–2916. <https://doi.org/10.1021/nn300261t>.
- [105] Q. Zhu, Y. Chai, R. Yuan, Y. Zhuo, J. Han, Y. Li, et al., Amperometric immunosensor for simultaneous detection of three analytes in one interface using dual functionalized graphene sheets integrated with redox-probes as tracer matrixes, *Biosens. Bioelectron.* 43 (2013) 440–445. <https://doi.org/10.1016/j.bios.2012.12.030>.
- [106] Y. Wang, Y. Xiao, X. Ma, N. Li, X. Yang, Label-free and sensitive thrombin sensing on a molecularly grafted aptamer on graphene, *Chem. Commun.* 48 (2012) 738–740. <https://doi.org/10.1039/c1cc15429j>.
- [107] H. Chang, L. Tang, Y. Wang, J. Jiang, J. Li, Graphene fluorescence resonance energy transfer aptasensor for the thrombin detection, *Anal. Chem.* 82 (2010) 2341–2346. <https://doi.org/10.1021/ac9025384>.
- [108] N. Chauhan, J. Narang, C.S. Pundir, Immobilization of rat brain acetylcholinesterase on ZnS and poly(indole-5-carboxylic acid) modified au electrode for detection of organophosphorus insecticides, *Biosens. Bioelectron.* 29 (2011) 82–88. <https://doi.org/10.1016/j.bios.2011.07.070>.
- [109] M. Govindasamy, S.-M. Chen, V. Mani, R. Devasenathipathy, R. Umamaheswari, K. Joseph Santharaj, et al., Molybdenum disulfide nanosheets coated multiwalled carbon nanotubes composite for highly sensitive determination of chloramphenicol in food samples milk, honey and powdered milk, *J. Colloid Interface Sci.* 485 (2017) 129–136. <https://doi.org/10.1016/j.jcis.2016.09.029>.
- [110] Y. Feng, Q. Li, J. Chen, P. Yi, X. Xu, Y. Fan, et al., Salivary protease spectrum biomarkers of oral cancer, *Int. J. Oral Sci.* 11 (2019) 7. <https://doi.org/10.1038/s41368-018-0032-z>.
- [111] N.R. Ha, I.P. Jung, I.J. La, H.S. Jung, M.Y. Yoon, Ultra-sensitive detection of kanamycin for food safety using a reduced graphene oxide-based fluorescent aptasensor, *Sci. Rep.* 7 (2017) 1–10. <https://doi.org/10.1038/srep40305>.
- [112] H. Zhang, H. Zhang, A. Aldalbahi, X. Zuo, C. Fan, X. Mi, Fluorescent biosensors enabled by graphene and graphene oxide, *Biosens. Bioelectron.* 89 (2017) 96–106. <https://doi.org/10.1016/j.bios.2016.07.030>.
- [113] Z. Xue, Y. Zhang, W. Yu, J. Zhang, J. Wang, F. Wan, et al., Recent advances in aflatoxin B1 detection based on nanotechnology and nanomaterials—a review, *Anal. Chim. Acta* 1069 (2019) 1–27. <https://doi.org/10.1016/j.aca.2019.04.032>.
- [114] J. Kim, S.J. Park, D.H. Min, Emerging approaches for graphene oxide biosensor, *Anal. Chem.* 89 (2017) 232–248. <https://doi.org/10.1021/acs.analchem.6b04248>.
- [115] H. Jang, S.R. Ryoo, Y.K. Kim, S. Yoon, H. Kim, S.W. Han, et al., Discovery of hepatitis C virus NS3 helicase inhibitors by a multiplexed, high-throughput helicase activity assay based on graphene oxide, *Angew. Chem. Int. Ed.* 52 (2013) 2340–2344. <https://doi.org/10.1002/anie.201209222>.

- [116] B.P. Viraka Nellore, R. Kanchanapally, A. Pramanik, S.S. Sinha, S.R. Chavva, A. Hamme, et al., Aptamer-conjugated graphene oxide membranes for highly efficient capture and accurate identification of multiple types of circulating tumor cells, *Bioconjug. Chem.* 26 (2015) 235–242. <https://doi.org/10.1021/bc500503e>.
- [117] N.F. Atta, A. Galal, E.H. El-Ads, Graphene—a platform for sensor and biosensor applications, in: T. Rinken (Ed.), *Biosensors Micro and Nanoscale Applications*, InTech, 2015. <https://doi.org/10.5772/60676>.
- [118] J. Homola, Present and future of surface plasmon resonance biosensors, *Anal. Bioanal. Chem.* 377 (2003) 528–539. <https://doi.org/10.1007/s00216-003-2101-0>.
- [119] J. Homola, S.S. Yee, G. Gauglitz, Surface plasmon resonance sensors: review, *Sensors Actuators B Chem.* 54 (1999) 3–15. [https://doi.org/10.1016/S0925-4005\(98\)00321-9](https://doi.org/10.1016/S0925-4005(98)00321-9).
- [120] H. Zhang, Y. Sun, S. Gao, J. Zhang, H. Zhang, D. Song, A novel graphene oxide-based surface plasmon resonance biosensor for immunoassay, *Small* 9 (2013) 2537–2540. <https://doi.org/10.1002/smll.201202958>.
- [121] I. Jung, M. Vaupel, M. Pelton, R. Pinery, D.A. Dikin, S. Stankovich, et al., Characterization of thermally reduced graphene oxide by imaging ellipsometry, *J. Phys. Chem. C* 112 (2008) 8499–8506. <https://doi.org/10.1021/jp802173m>.
- [122] H. Xu, L. Wu, X. Dai, Y. Gao, Y. Xiang, An ultra-high sensitivity surface plasmon resonance sensor based on graphene-aluminum-graphene sandwich-like structure, *J. Appl. Phys.* 120 (2016) 053101. <https://doi.org/10.1063/1.4959982>.
- [123] D. Zhang, Q. Liu, Biosensors and bioelectronics on smartphone for portable biochemical detection, *Biosens. Bioelectron.* 75 (2016) 273–284. <https://doi.org/10.1016/j.bios.2015.08.037>.
- [124] J. Zhang, J. Zhang, F. Zhang, H. Yang, X. Huang, H. Liu, et al., Graphene oxide as a matrix for enzyme immobilization, *Langmuir* 26 (2010) 6083–6085. <https://doi.org/10.1021/la904014z>.
- [125] M. Singh, M. Holzinger, M. Tabrizian, S. Winters, N.C. Berner, S. Cosnier, et al., Noncovalently functionalized monolayer graphene for sensitivity enhancement of surface plasmon resonance immunosensors, *J. Am. Chem. Soc.* 137 (2015) 2800–2803. <https://doi.org/10.1021/ja511512m>.
- [126] M. Fleischmann, P.J. Hendra, A.J. McQuillan, Raman spectra of pyridine adsorbed at a silver electrode, *Chem. Phys. Lett.* 26 (1974) 163–166. [https://doi.org/10.1016/0009-2614\(74\)85388-1](https://doi.org/10.1016/0009-2614(74)85388-1).
- [127] N. Feliu, M. Hassan, E. Garcia Rico, D. Cui, W. Parak, R. Alvarez-Puebla, SERS quantification and characterization of proteins and other biomolecules, *Langmuir* 33 (2017) 9711–9730. <https://doi.org/10.1021/acs.langmuir.7b01567>.
- [128] T. Demeritte, B.P. Viraka Nellore, R. Kanchanapally, S.S. Sinha, A. Pramanik, S.R. Chavva, et al., Hybrid graphene oxide based plasmonic-magnetic multifunctional nanoplatform for selective separation and label-free identification of Alzheimer's disease biomarkers, *ACS Appl. Mater. Interfaces* 7 (2015) 13693–13700. <https://doi.org/10.1021/acsami.5b03619>.
- [129] I. Khalil, W.A. Yehye, N.M. Julkapli, S. Rahmati, A.A.I. Sina, W.J. Basirun, et al., Graphene oxide and gold nanoparticle based dual platform with short DNA probe for the PCR free DNA biosensing using surface-enhanced Raman scattering, *Biosens. Bioelectron.* 131 (2019) 214–223. <https://doi.org/10.1016/j.bios.2019.02.028>.
- [130] A. Bajtarevic, C. Ager, M. Pienz, M. Klieber, K. Schwarz, M. Ligor, et al., Noninvasive detection of lung cancer by analysis of exhaled breath, *BMC Cancer* 9 (2009) 348. <https://doi.org/10.1186/1471-2407-9-348>.
- [131] X. Zhou, Z. Xue, X. Chen, C. Huang, W. Bai, Z. Lu, et al., Nanomaterial-based gas sensors used for breath diagnosis, *J. Mater. Chem. B* 8 (2020) 3231–3248. <https://doi.org/10.1039/c9tb02518a>.

- [132] T. Kuretake, S. Kawahara, M. Motooka, S. Uno, An electrochemical gas biosensor based on enzymes immobilized on chromatography paper for ethanol vapor detection, *Sensors (Switzerland)* 17 (2017) 281. <https://doi.org/10.3390/s17020281>.
- [133] I. Karaduman, E. Er, H. Çelikkan, N. Erk, S. Acar, Room-temperature ammonia gas sensor based on reduced graphene oxide nanocomposites decorated by Ag, Au and Pt nanoparticles, *J. Alloys Compd.* 722 (2017) 569–578. <https://doi.org/10.1016/j.jallcom.2017.06.152>.
- [134] H. Xu, Y.F. Lu, J.X. Xiang, M.K. Zhang, Y.J. Zhao, Z.Y. Xie, et al., A multifunctional wearable sensor based on a graphene/inverse opal cellulose film for simultaneous: in situ monitoring of human motion and sweat, *Nanoscale* 10 (2018) 2090–2098. <https://doi.org/10.1039/c7nr07225b>.
- [135] S.J. Kim, W. Song, Y. Yi, B.K. Min, S. Mondal, K.S. An, et al., High durability and waterproofing rGO/SWCNT-fabric-based multifunctional sensors for human-motion detection, *ACS Appl. Mater. Interfaces* 10 (2018) 3921–3928. <https://doi.org/10.1021/acsami.7b15386>.