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TOPICAL REVIEW

Recent advances on application of gold nanorods in detection field

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Abstract

The development of new methods for applications of detection in the biological field is a topic of intense and growing interest. The currently practiced methods for biological detection have many defects, such as time-consuming, low accuracy, and cumbersome for operators. Gold nanorods (AuNRs) have received tremendous attention recently in the fields of biological detection owing to the unique characteristics of surface plasmon resonance (SPR), which provides a remarkable ability to absorb and scatter light. Furthermore, AuNRs can be functionalized with a wide variety of biomolecules for targeted detection. Moreover, their versatility and unique properties have generated more applications in medical areas. In this review, we briefly outline the synthesis and surface modification of AuNRs, and focus on the recent advances of the application of AuNRs in detection field. Finally, the outlook and future prospect on the development of AuNRs are provided.

1. Introduction

Biological testing has become one of the hottest topics in the world. Food contains a large number of microorganisms. Among them, harmful microorganisms such as E. coli [1], Staphylococcus aureus [2], Salmonella [3], Pseudomonas aeruginosa [4], etc, are serious threat to human health. On the other hand, due to the increase in heavy industry, heavy metal ions enter the soil through atmospheric deposition, causing heavy metal pollution to food and vegetables, which have led to increasing concerns in terms of human health, environmental preservation and economic challenges. In medicine, the early-stage tumor diagnosis is vital, which prevents about one third of cancers occur. Traditional detection methods include atomic absorption spectrometry [5, 6], atomic fluorescence spectrometry [7], and inductively coupled plasma [8] method et al. Although these methods can accurately detect biological parameters, they are time-consuming, cumbersome and expensive, making them unable to be widely used. Taking into consideration the health hazards posed, the novel biological detection methods need to be developed. In recent years, biological detection methods based on Gold nanorods (AuNRs) have received increasing attention.

AuNRs, one of the precious metals (gold, silver, platinum) nanomaterials, have been widely investigated for various biological detection applications due to their biocompatibility, simple synthesis, and facile surface modification [9, 10]. AuNRs possess two plasmonic peaks, one around 520 nm (transverse surface plasmon resonance) and the other one at 800 nm (longitudinal surface plasmon resonance). The latter one can be tuned by different synthesis conditions, which have been widely utilized for biological detection and imaging.

Owing to their superior optical response, facile surface modification and biocompatibility, AuNR has been considered as one of the most suitable materials for biological probe. This review presents a comprehensive summary of synthetic methods, surface modification and optical properties of AuNRs, aiming to highlight the progress of AuNRs in detection field.
2. Progress in the synthesis of AuNRs

2.1. Progress in the synthesis of AuNRs

The most primitive method to synthesize AuNRs was the electrochemical method, which later became the pioneer of seed growth. In the 1990s, the synthesis of electrochemical method of AuNRs reported by Wang et al [11]. Martin et al [12] and Evans et al [13] also utilized electrochemical deposition to fabricate AuNRs. Then Huang et al [14] and Yu et al [15] successfully fabricated high yield of suspended AuNRs via template methods. Although these early electrochemical methods can successfully prepare AuNRs, these strategies still have many disadvantages, such as energy consumption, small yield, and inhomogeneous structure.

With the development of technology, seed-mediated growth approach has emerged. The seed crystal growth method is the most common method for synthesizing AuNRs. The method is simple in process and can synthesize high-quality and high-yield AuNRs with easy shape control. Murphy et al [16] initially start to synthesize seeds by seed-mediated growth approach. The basic principle for this method involves two steps: first, the preparation of small size spherical gold nanoparticles, and second, growth of the prepared spherical particle in rod-like micellar environment. During the experiment, Chloroauric acid which replaces the gold plate in the electrochemical process serves as a gold source, and the weaker reducing agent ascorbic acid (AA) and silver nitrate replace the redox reaction in the electrochemical. Only CTAB is used as a surfactant. The initial seed-mediated growth approach that Murphy developed was able to successfully synthesize AuNRs, but the yield was not high enough and would produce more spherical particles.

Later, in 2003, many researchers improved previous method and developed a novel method for synthesizing smaller aspect ratio AuNRs with high yield [17]. This method greatly improved the yield of the rod structure employing CTAB-protected gold nanoparticles as seeds and silver nitrate as an adjuvant. This method can conveniently control the addition amount of silver nitrate to regulate the aspect ratio of AuNRs. Meanwhile, the yield of AuNRs synthesized by this method can reach more than 95%. This silver ion-assisted seed growth method is currently the most popular method for preparing AuNRs.

In 2010, Jana et al [18] improved the silver ion-assisted seed growth method. They added a small amount of sodium borohydride reducing agent directly to the growth solution without preparing the seed solution in advance. The aspect ratio of AuNRs is controlled by changing the concentration of sodium borohydride and have nothing to do with the amount of silver nitrate added. The AuNRs prepared by this seedless method are much smaller than the AuNRs prepared using seeds.

In 2012, Murray et al [19] reported an improved seed-mediated growth of AuNRs by using aromatic additives that reduce the concentration of hexadecyltrimethylammonium bromide surfactant to ~0.05 M. This method could obtain high aspect ratio AuNRs with longitudinal surface plasmon resonance tunable from 627 to 1246 nm and generate fewer impurities.

In 2013, Vigderman et al [20] described the use of a novel reducing agent, hydroquinone, to replace ascorbic acid in the seed-mediated growth of AuNRs to produce AuNRs with LSPR up to 1230 nm. Meanwhile, they modified the hydroquinone, silver, gold, and seed concentration in the growth solution. The same year, Kozek et al [21] utilized a secondary (seeded) growth procedure, in which continuous addition of ascorbic acid (AA) to a stirring solution of AuNRs was performed to synthesize large-scale AuNRs. The key to this method is that they deposit the remaining (~70%) of the Au precursor onto the AuNRs. However, the addition of a large amount of reducing agent will deform the AuNRs.

In 2014, Xu et al [22] reported that they used H2O2 as the reducing agent in the process of synthesis of AuNRs. It is found that the high-quality, high purity and monodispersity AuNRs with different sizes can be obtained through changing the experimental parameters, including the added amounts of NaOH, the H2O2/Au+ ratio, and the concentration of AgNO3. Moreover, the longitudinal localized surface plasmon resonance peak of AuNRs can be easily tuned and the maximum of 981 nm can be achieved when the H2O2/Au+ ratio is adjusted to 300:1. In 2015, Liopo and co-workers [23] used dopamine as a reducing agent to replace sodium borohydride (AA) in the process of seedless synthesis of AuNRs. But the yield of AuNRs is between 80% and 95%.

In the previous traditional seed growth method, the scale synthesis of AuNRs requires increasing the concentration of seeds and reducing agents. The growth of AuNRs results in deterioration of product quality such as dumbbell shaped rods and increased byproducts if the concentration of reducing agent is increased [24]. In 2017, Park et al [25] achieved the gram-scale synthesis of AuNRs with prescribed aspect ratio and volume, which is more than 100-times that of the conventional concentration by the two-step method. Firstly, the concentrated ‘seed rods’ solution of the high concentration was added into a relative dilute growth solution. Afterward, the ‘seed rod’ was added to the concentrated growth solution to produce a high concentration final product and the hydroquinone and dopamine were used as weaker reducing agents during the period.

In 2018, Chang et al [26] reported that they synthesized AuNRs by the seed-mediated growth method, for which the longitudinal LSPR can be tuned beyond 1300 nm. They controlled the dimensions of those mini...
AuNRs by changing the concentration of gold, silver nitrate and sodium borohydride in the growth solution at the optimal pH and using two reducing agents, ascorbic acid and hydroquinone. As is showed in figure 1, the average width of the mini AuNR is less than 10 nm, and the average length is significantly increased from 19 nm to 93 nm. The yield of mini AuNR in this method is above 96%.

Later, many groups have improved the method of seed synthesis of AuNRs. Although seed growth methods can produce higher yields of AuNRs, many parameters such as seed solution concentration, aging time, temperature, pH and CTAB could significantly affect the shape, length to diameter ratio, yield and position of the absorption peak of the AuNRs [27, 28]. Despite these exciting progresses, there is still a need to develop new techniques to obtain higher purity AuNRs.

2.2. Functionalization of AuNRs

The seed-mediated synthesis is the most widely used method for AuNRs preparation. In the process of seed synthesis of AuNRs, cetyltrimethylammonium bromide (CTAB) is used as a surfactant. AuNRs prepared by this method are coated with the structure-directing surfactant of cetyltrimethylammonium bromide (CTAB) and CTAB is known to lead to aggregation and toxicity [29]. Centrifugation cannot completely remove CTAB after the synthesis of AuNRs, which makes they have low biocompatibility. Therefore, surface modification and functionalization of AuNRs to remove or overcoat the residual CTAB is very essential to its stability. After appropriate functionalization, AuNRs will have better biocompatibility and improved detection ability in biosystems. Three general surface modification and functionalization methods for AuNRs are illustrated in schematic 1.

The first generally useful strategy is grafting polyethylene glycol (PEG) onto the nanorods. Due to the strong affinity between thiol and Au, the surface modification of AuNRs coated with PEG could form stable gold-sulfur ligand bond [30]. Li et al [31] reported an mPEG-SH/Tween 20-assisted method to load thiolated DNA on AuNRs and the procedure took about 1 h for fine functionalization. The CTAB on the surface of AuNRs were removed with Tween 20 and mPEG-SH by repeated centrifugation and resuspension processes. The functionalized AuNRs by this method can be used for a variety of applications such as drug delivery, self-assembly, and detection. In the same year, a novel, facile, one-step surface functionalization method was developed by Liu et al [32]. They used Tween 20 to stabilize AuNRs and then stimulated the AuNR surface by bis(p-sulfonatophenyl)phosphine (BSPP) for the subsequent PEGylation. The surface-bound CTAB of
AuNRs can be completely removed. The resultant sample has demonstrated to be no apparent toxicity with a concentration of 5 \( \mu g \) \( m^{-1} \). AuNRs are very suitable for cancer photothermal therapy due to their strong absorption of near-infrared (NIR) light. Therefore, for cancer treatment, PEG is modified on the surface of AuNRs so as to reduce toxicity to normal cells. For example, Niidome et al.\[33\] developed a method to modify AuNRs with PEG and found that PEG-modified AuNRs can be kept in the blood for 0.5 h, whereas AuNRs without PEG decoration quickly flow into the liver. Ji et al.\[34\] grafted a polythiol PEG-based copolymer on the AuNRs, which showed excellent stabilities. The result displayed that the multideterminate PEG coated AuNRs (AuNR-PTPEGm950) had very low cytotoxicity and the tumors injected with AuNR-PTPEGm950 were completely cured.

Layer-by-layer polyelectrolyte absorption is another commonly-used method to functionalize AuNRs and this method mainly relies on the sequential deposition of anionic, then cationic polyelectrolytes to the AuNRs surface\[35, 36\]. The outer layer of AuNRs is negatively charged in most cases. The positively charged polyelectrolytes that could be adsorbed on the surface of AuNRs by layer-by-layer polyelectrolyte absorption have lower toxicity than CTAB. For example, Tian et al.\[37\] designed a comprehensive platform that a Fuel Improved microRNA Explorer (FIRE) probe were loaded on polyethylenimine (PEI)-modified AuNRs (AuNR-PEI) via electrostatic interaction. This comprehensive platform could enhance 7-fold fluorescence signals in MCF-7 breast carcinoma and 4.5-fold fluorescence signals in HeLa cervical carcinoma cells, respectively. The efficiency of tumor detection was improved. Liu et al.\[38\] found that AuNRs modified by polyethyleneimine (PEI) showed specific cytotoxicity to A549 cells while little cytotoxicity to 16HBE cells.

The last and most promising surface modification approach is to form mesoporous silicon layer on the surface of AuNRs. Later, a stable bioagent that AuNRs were entrapped into multicompartment mesoporous silica nanoparticles (MMSNs) were fabricated. It is found that this nanocomposites improved stability and enhanced sufficient energy to kill tumor cells during the irradiation process\[39\]. AuNRs that coated with silica (SiO\(_2\)) capped by Aliphatic poly(urethane-amine) (PUA) increased distinguished pH-, thermal-, and NIR-dependent release properties, more than CTAB-AuNRs\[40\].

3. Optical properties of AuNRs

AuNRs have been receiving extensive attention owing to their outstanding surface plasmon resonance properties. This particular property is derived from the interaction of incident light and the free electron of gold nanoparticles. When the wavelength of incident light is resonantly coupled with the vibrational frequency of free electrons, surface plasmon occurs resonance which is called surface plasmon resonance (SPR)\[41\]. Meanwhile, AuNRs show two plasmonic peaks on the UV–vis spectrum. The transverse surface plasmon resonance is around 520 nm and the longitudinal surface plasmon resonance which can be tuned is around 800 nm\[9\].
unique property enables AuNRs to have a wide application in biological imaging, detection and photothermal therapy. For example, Wang et al. [42] found that the TPL signal produced by AuNRs irradiated on a far-field laser-scanning microscope with a wavelength of 830 nm femtosecond pulse laser was 58 times higher than that of the two-photon fluorescence signal produced by rhodamine. El Sayed et al. [43] utilized the strongly scattered red light from the AuNRs in dark field to distinguish and diagnose between the normal cells and malignant cells. As shown in figure 2, it is found that HSC and HOC malignant cells are easily distinguished from HaCaT nonmalignant cells. The intensities of light scattering from single AuNRs is especially bright. The AuNRs strongly scatter orange to red light due to their strong longitudinal surface plasmon oscillation with a frequency in the NIR region. Du and co-workers [44] also used the optical properties of the AuNRs to improve the signal intensity in tumor cells treated with D-AuNR that by self-assembling AuNRs on the surface of a DNA-origami structure. A novel nanocomposite comprising AuNRs and CdSe/ZnS quantum dots (QDs) with silica (SiO₂) as a bridge were fabricated, the AuNRs act as imaging agents owing to its optical properties, not only retains and even highly improves the optical properties of the AuNRs and another material, but also possesses excellent imaging performance compared with fluorescence dyes and other material [45]. On the other hand, AuNR has been regarded as one of the most popular ultra-sensitive bio-sensor in the field of detection because of its optical properties. For instance, AuNRs had been applied to colorimetric optical sensing of copper ions based on Cu²⁺ induced gold nanorod shortening in the presence of Na₂S₂O₃ and NH₃ [46]. This sensor with a detection limit of 1.6 nM, compared with conventional methods, has very high sensitivity and large dynamic range for Cu²⁺ covering 5 nM to 500 mM. A aggregation-based AuNRs probe that Cysteine (Cys) molecules were conjugated on AuNR surfaces had been developed for the detection of Pb²⁺ in aqueous solution [47]. The formation of aggregation of AuNRs significantly enhanced detection signals and had a linear detection range from 0.1 nM to 1.0 nM. Xing et al. [48] utilized the spillover effects between AuNRs and In₂O₃ to fabricate In₂O₃/AuNRs gas sensor which can clearly distinguish the acetone and ethanol biomarkers in human breath with a detection limit at 0.1 ppm to acetone and 0.05 ppm to ethanol, respectively. This gas sensor has a promising prospect in monitoring and detecting diabetes and safe driving area. Furthermore, AuNRs were decorated on the graphene oxide (GO) sheet on the surface of the glassy carbon electrode (GCE) to detect circulating miRNAs which is a novel reliable biomarkers for early detection of cancer diseases [49]. The conclusion indicated that this nanobiosensor demonstrated high specificity and could obviously discriminate between complementary target miRNA, single-, three-base mismatch, and non-complementary miRNA, respectively. The AuNRs have attracted much interest in the applications of cancer therapy due to their photothermal effect (the conversion of light to local heat under irradiation). Hong et al. [50] verified that the degree of cell death area could be modulated by GNR concentration by irradiating the MDA-MB-231 breast cancer cells containing AuNRs. Meanwhile, it was found that the cancer cells were successfully ablated by GNR-induced photothermal with different power densities near-infrared (NIR) laser. A new kind of ultrasmall dissociable AuNR vesicles were synthesized by assembling small AuNRs (dimension: approximate to 8 nm × 2 nm) [51]. This kind of AuNR vesicles could accumulate and prolong circulation in tumor prominently, which exhibited high photothermal cancer therapy efficacy. With the development of nanotechnology, the combination of AuNRs with chemotherapy, gene therapy and PDT is admired, where other materials may be involved. For instance, a multifunctional phototheranostic agent were developed by incorporating carbon dots (CDs) with AuNRs, using SiO₂ as a scaffold [52]. The combination of AuNRs and CDs has been proved to be more efficient in killing cancer cells compared to AuNRs alone under a low dose of laser irradiation. Another multifunctional nanocomposite based on mesoporous silica-coated gold nanorod for high-performance oncotherapy were reported [53]. AuNRs is used as the hyperthermal agent and mesoporous silica shell is used as the reservoir of photosensitizer, respectively. The studies in vitro and in vivo indicated that
and AuPb2 alloys in the presence of lead ions decreased significantly, resulting in the sodium thiosulfate
reactions that triggered the remarkable tumor cell death in vitro and inhibited tumor growth in vivo.

4. Application of AuNRs in detection field

The potential applications of AuNRs probes have received great attention for detection field, including chemical sensing and imaging applications. In general, the color changes associated with AuNRs aggregation, local refractive index change, and with different modifications or coatings have been validated as optical sensing methods for the detection of heavy metals, toxins, biomolecules and tumor or cancer biomarkers, as shown in table 1.

4.1. AuNRs for heavy metals detection

In recent years, heavy metal pollution has become increasingly serious due to human factors such as mining, waste discharge, sewage irrigation, and use of excessive heavy metal products. Heavy metals settle into the soil and enter the human body through the food chain, which has a great impact on human health. Therefore, the detection of heavy metal is particularly important. Traditional detection methods include atomic absorption spectrometry [5, 6], atomic fluorescence spectrometry [7], and inductively coupled plasma [8] method et al. Although these methods can accurately detect heavy metal, they are time-consuming, cumbersome, expensive, and other shortcomings, making them unable to be widely used. A fast, simple, and highly sensitive detection method needs to be established in order to overcome these shortcomings. The methods for heavy metal detection based on AuNRs have high selectivity and sensitivity.

Potential applications of AuNRs probes in heavy metal analysis include the application of etching reaction, functionalization of AuNRs probes, and aggregation reaction. There is a strong etching reaction between AuNRs and some heavy metal, which causes the morphological changes of AuNRs. In 2011, Li et al. [55] used Cr (VI) strong oxidation to etch AuNRs selectively at tips. They found the concentration of Cr (VI) in the range of 0.1–20 M was linear to the degree of reduction in aspect ratio of AuNRs, which was a simple, sensitive and selective colorimetric sensor. The detection limit is 88 nM. Zhang et al. [56] developed a novel approach to achieve rapid visual detection of Cu2+ in natural samples based on AuNRs coated with hexadecyltrimethylammonium bromide, which were catalytically etched by Cu2+ preferentially along the longitudinal direction. This method had high specificity, detecting Cu2+ directly in a complex matrix and especially in seawater, and sensitivity with a detection limit of 0.5 nM. In 2016, another etching method to detect lead ions was proposed [58]. With this method, the surface electrode potential of AuNRs covered a monolayer of AuPb2+ and AuPb3 alloys in the presence of lead ions decreased significantly, resulting in the sodium thiosulfate
accelerate dissolution rate of AuNRs. During the shape of AuNRs degenerating gold nanosphere rapidly, the lowest limit of detection for lead ions is 0.1 μM observed by the naked eye and 20 nM as measured by UV–vis spectroscopy. In 2018, Lu et al. [59] detected ferrous ion with high sensitivity and selectivity, because Fe2+ reacts with H2O2 in the acid condition, to produce superoxide radical which etches AuNRs along the longitudinal direction preferentially, resulting in morphology transition of AuNRs. AuNRs with high aspect ratio gradually

| Detection target | Sensor type | Sensitivity | References |
|------------------|-------------|-------------|------------|
| Cu2+             | Etching colorimetric sensor | 8.8 × 10⁻⁸ M | [55] |
| Pb2+             | AuNRs-based functionalized sensor | 0.5 nM | [56] |
| Hg2+             | AuNRs-based functionalized sensor | 0.1 μM | [57] |
| Fe2+             | AuNRs-based etching colorimetric sensor | 13.5 nM | [58] |
| As3+             | AuNRs-based functionalized sensor | 48 nM | [59] |
| Sn2+             | AuNRs-based functionalized sensor | 38 nM | [60] |
| E. coli O157:H7   | AuNRs-based functionalized sensor | 0.16 ng ml⁻¹ | [61] |
| AFB1             | AuNRs-based aggregation colorimetric sensor | 0.22 ng ml⁻¹ | [62] |
| Ota              | AuNRs-based colorimetric sensor | 6.5 × 10⁻⁶ U/L | [63] |
| endonuclease activity | AuNRs-based colorimetric sensor | 100 pg ml⁻¹ | [64] |
| ALP              | AuNRs-based colorimetric sensor | 100 pg ml⁻¹ | [65] |
| Ovarian cancer    | Photoacoustic Imaging | 100 cells/ml | [66] |
| MCF-7 breast cancer cells | Optical sensor | 100 cells/ml | [67] |
| CA15-3           | Optical sensor | Rapid detection | [68] |
| AFP              | Optical sensor | 9.2 pg ml⁻¹ | [69] |

Table 1. The detection effect achieved by AuNRs-based sensor platform.
became AuNRs with low aspect ratio, the assay has a 13.5 nM detection limit and a linear response in a concentration range of 75 to 1 μM.

The second simple detection strategy is the development of the nanoplasmonic biosensor based on functionalizing AuNRs. A study [60] demonstrated that the AuNRs functionalized with an N-alkylaminopyrazole ligand had a limit of detection of 3 ppt for Hg²⁺, illustrating that the functional of AuNRs plays a vital role in detecting heavy metal. Hong et al [57] fabricated the nanoplasmonics that the surface of AuNRs was conjugated with D-penicillamine (DPA) - a chelating agent of copper II ions. DPA is expected to bind to copper ions when copper ions are present in the environment, which localized surface plasmon resonance (LSPR) effect enable to identify copper II ions sensitively and selectively. Furthermore, the limit of detection of the DPA-conjugated nanoplasmonics was 100 pM, which has great potential for detecting copper II ions even in human blood conditions.

The color changes associated with AuNRs aggregation have been exploited as optical sensing methods for the detection of heavy metal. AuNRs were found to aggregate by forming a covalent Au-S bond in the presence of 6-mercaptopurine (6-MP). Then, a rapid, sensitive strategy for determination of mercury(II) ion was developed [61]. First, AuNRs aggregated after they modified 6-MP onto the surface of it. However, the 6-MP induced aggregation is inhibited when addition of Hg(II) by forming a more stable Hg-S bond. The different degree of aggregation of the AuNRs is linearly related to the Mercury ion content and the limit of detection is 0.48 nM. Ge et al [62] synthesized a colorimetric probe for determination of As (III) ions on basis of AuNRs that coated by dithiothreitol, which would be aggregated with the adding of As (III) ions. Under optimum conditions, (III) ions detected by this colorimetric probe has a low detection limit of 38 nM. An emerging photoacoustic probe for determination of Hg²⁺ on basis of photoacoustic signals was synthesized [72]. In this study, AuNRs modified with (11-mercapto-undecyl)-trimethylammonium (MTA) molecules containing sulfydryl groups were aggregated due to the loss of ligand protection on their surface in the present of Hg²⁺ and photoacoustic signals enhanced, which detected Hg²⁺ in the concentrations of 0–10 μM.

4.2. AuNRs for toxins detection

The wide applications of AuNRs in toxin detection, such as pesticides [73], virus [74], and bacterial et al [75] have been focused since the optical properties of AuNRs was discovered. Before, the parameters of toxic compounds require conventional and sophisticated instrumentation used by professionals. Now, an AuNR-based probe offers a feasible and easy-to-use solution for toxin detection with efficient response. For instance, AuNR assisted method that was developed to detect Escherichia coli O157:H7 enhanced the sensitivity of the biosensor [63]. The sensitivity of this AuNR assisted biosensor increased by almost 3.8 times compared with non-conjugated AuNR biosensor. An investigation into the detection of foodborne disease was studied by Wang [76]. It was found that amine groups modified AuNRs with antibodies could identify two major species of foodborne pathogenic bacteria, E. coli O157: H7 and Salmonella Typhimurium, in one assay. When pathogens in one solution simultaneously at concentrations are lower than 10⁷ cfu/ml, the E. coli O157: H7 and Salmonella Typhimurium could also be detected less than 30 min. In 2016, Chen and coworkers [75] also developed a novel enzyme-induced metallization colorimetric assay for detection of Escherichia coli. AuNR assisted optical biosensor, which have also been developed to detect aflatoxin B1 (AFB1) [64]. The AuNRs modified with AFB1-BSA (bovine serum albumin) conjugates aggregated after mixing with free antibodies, which are employed as a sensing platform. There is a result of competitive immune-reaction with antibodies with the existence of AFB1 molecules in environment, which led to dispersion of AuNRs and an absorption intensity response that was quantitatively correlated to the concentration of AFB1. With this approach, the linear range of detection for AFB1 from 0.5 to 20 ng ml⁻¹ and the limit of detection was 0.16 ng ml⁻¹ were realized. A simple and highly sensitive assay of AFB1 can be achieved, which can be potentially used for rapid monitoring of agriculture products and foods. Similarly, a new optical apta sensor based on AuNRs was designed for one-step determination of ochratoxin A (OTA). Xu et al [65] decorated thiol-modified DNA that could hybridize with Linker DNA containing aptamer sequences against OTA on the side sites of AuNRs. Thus, AuNRs assembled side by side oriented due to DNA hybridization. On the other hand, AuNRs dispersed in the presence of OTA due to specific aptamer-OTA recognition. It was found that the limit of detection obtained was 0.22 ng ml⁻¹ and the concentration of detection range of OTA from 0.5 to 20 ng ml⁻¹. Recently, AuNRs have been found to successfully apply for the detection of AFB1 in blood serum samples [77]. Simultaneously, AuNRs that coated with Glycoconjugates have also been found to develop for swift and sensitive detection of foodborne bacteria (Escherichia coli) [78]. The growing field of biosensor diagnostic probes is an exciting area that could produce more easy-to-use, cost-effective, rapid and accurate detection methods for biotoxins compared to conventional and sophisticated instrumentation.
4.3. AuNRs for biomolecules detection

Molecular biology is the study of life phenomena at the molecular level. Therefore, the development of rapid, simple and selective methods for biomolecules detecting are essential in the fields of modern molecular biology. The traditional detection approaches for biomolecules are based on gel electrophoresis [79], high-performance liquid chromatography (HPLC) [80], enzyme-linked immunosorbent assay (ELISA) [81], etc. However, these methods have the disadvantages of tedious operation, time-consuming or laborious and expensive. The novel detection strategies based on AuNRs have been proposed.

In 2005, Sudeep et al [82] exploited the interplasmon coupling in AuNRs for the selective detection of micromolar concentrations of cysteine and glutathione. Distinguish cysteine small biomolecules based on the end-to-end assembly of AuNRs [83]. The AuNRs could form chain by the end-to-end assembly in the presence of cysteine under acidic aqueous solution. Therefore, it can provide a quantitative measure of the cysteine concentration because the sharp absorption peak changes as the chain formed. This methodology is a simple, rapid, selective, and ultra-sensitive assay to detect cysteine. Similarly, selective detection of nucleic acid activity was achieved based on efficient fluorescence resonance energy transfer (FRET) between AuNRs and fluorescence-tagged single-stranded DNA (FDNA) [66]. In this research, the FRET between AuNRs and FDNA caused a decrease in fluorescence of FDNA when FDNA mixed with AuNRs. However, fluorescence is restored when FDNA1/cDNA1 hybrid was cleaved into small fragments by endonucleases, which determined endonuclease activity by monitoring changes in fluorescence. This feature enabled the detection limit of endonuclease to reach 6.5 × 10⁻¹⁶ U/ul. Zhang et al [67] also proposed a highly sensitive colorimetric detection of alkaline phosphatase (ALP) assay, which was achieved by iodine-mediated etching of AuNRs. The presence of ALP hydrolyzed ascorbic acid 2-phosphate into ascorbic acid which reduced the iodate into iodine. The shape of AuNRs was etched by iodine from rod to sphere and its solution color will also change. As a result, benefiting from the highly-sensitive detection of ALP, this proposed assay has achieved an ultra-low detection limit (100 pg ml⁻¹) for human immunoglobulin G (IgG). Recently, to enhance the sensing properties, different nanomaterials including graphene oxide [84], micro-quartz pieces [85], fluorophore ensemble [86], etc were incorporated onto AuNR surface as hybrid nanocomposites for biomolecules detecting. For example, AuNRs and GO were fabricated as nanocomposites by electrostatic attraction, which possess high determination stability for ALP activity by monitoring changes in fluorescence. This methodology is a simple, rapid, selective, and ultra-sensitive assay to detect cysteine. Similarly, selective detection of nucleic acid activity was achieved based on efficient fluorescence resonance energy transfer (FRET) between AuNRs and fluorescence-tagged single-stranded DNA (FDNA) [66]. In this research, the FRET between AuNRs and FDNA caused a decrease in fluorescence of FDNA when FDNA mixed with AuNRs. However, fluorescence is restored when FDNA1/cDNA1 hybrid was cleaved into small fragments by endonucleases, which determined endonuclease activity by monitoring changes in fluorescence. This feature enabled the detection limit of endonuclease to reach 6.5 × 10⁻¹⁶ U/ul. Zhang et al [67] also proposed a highly sensitive colorimetric detection of alkaline phosphatase (ALP) assay, which was achieved by iodine-mediated etching of AuNRs. The presence of ALP hydrolyzed ascorbic acid 2-phosphate into ascorbic acid which reduced the iodate into iodine. The shape of AuNRs was etched by iodine from rod to sphere and its solution color will also change. As a result, benefiting from the highly-sensitive detection of ALP, this proposed assay has achieved an ultra-low detection limit (100 pg ml⁻¹) for human immunoglobulin G (IgG). Recently, to enhance the sensing properties, different nanomaterials including graphene oxide [84], micro-quartz pieces [85], fluorophore ensemble [86], etc were incorporated onto AuNR surface as hybrid nanocomposites for biomolecules detecting. For example, AuNRs and GO were fabricated as nanocomposites by electrostatic attraction, which possess high determination stability for protamine and the lowest limit is 6.3 ng ml⁻¹ [87]. Similarly, a report on a simple visual colorimetric sensing system based on self-assembly of AuNRs and GO for heparin detection using polydiallyldimethylammonium chloride (PDADMAC) as a polycationic polymer molecular probe [88]. Under the optimized conditions, this hybrid nanprobe has the range of 20–140 ng ml⁻¹ for detection of heparin and the lowest limit is 10.4 ng μl⁻¹.

4.4. AuNRs for tumor or cancer biomarkers detection

Cancer is one of the leading diseases that cause worldwide human deaths. In 2018, it is estimated that there are 18 million new cancer cases worldwide, including 9.6 million deaths [89]. The early-stage tumor diagnosis is vital, which prevents about one third of cancers occur. In addition, cancer biomarkers like alpha fetoprotein (AFP) [90], prostate-specific antigen (PSA) [91], and circulating microRNAs [92] could be detected for early-stage tumor diagnosis. For example, the tumor that larger than 0.5 cm could be found by Computed Tomography (CT) and other tests. But it cannot be found when the tumor is 2–3 mm.

Earlier, the targeted AuNRs was successfully employed as contrast agent by photoacoustic imaging for prostate cancer [93] and ovarian cancer [68] detection. In addition, a new method has been proposed to detect selectively squamous cell carcinoma head and neck cancer cells based on diffusion reflection measurements of AuNRs [94]. Another diffusion reflection method based on AuNRs as absorbing contrast agents is also a simple, non-invasive imaging technique which has been validated useful detection for mice bearing human HNC tumor [95]. Li et al [69] described a novel strategy for the rapid diagnosis of human breast carcinoma MCF-7 cells with a detection limit of 100 cells ml⁻¹ by the AuNRs functionalized with Mucin 1 protein (MUC-1) aptamer.

Although these noninvasive and nonionizing optical detection methods provide a highly sensitive, simple, and inexpensive tool for cancer detection, they can only enable discrimination larger cancerous tissues based on the intense light absorption of AuNRs. Early diagnosis of cancer biomarkers is the key to guiding treatments and improving the survival rate of patients. Thus, the methods to detect cancer biomarkers with the help of AuNRs have been proposed. For instance, Hong et al [96] developed a sensitive nanobiosensor for invasive cancer biomarkers based on localized surface plasmon resonance of AuNRs that enables recognition for proteolytic activity of membrane type 1 matrix metalloproteinase (MT1-MMP) anchored on invasive cancer cells. Another AuNRs-based plasmonic detection sensor for determination of cancer antigen 15-3 (CA15-3) was developed [70]. Recently, Lu et al [71] reported a lateral flow immunoassay (LFIA), in which the AuNRs were modified with 5, 5′-dithiobis (2-nitrobenzoicacid), bovine serum albumin (BSA), and AFP detection antibody, for quantitative and ultra-sensitive analysis of alpha-fetoprotein (AFP). This detection assay showed a low detection limit of 9.2 pg ml⁻¹ and a broad detection range from 10 pg ml⁻¹ to 500 ng ml⁻¹ for AFP, which was about 10 times...
lower than conventional enzyme-linked immunosorbent assay. The early diagnosis of cancer biomarkers provides valuable time for treatments and improves the survival rate of patients.

The past one or two years, there are some innovative approaches for tumor or cancer biomarkers detection. Chen et al[54] used antibody-conjugated AuNPs as probes under darkfield tracking microscopy to introduce a single-particle mobility analysis based ratiometric strategy for quantitative detection of carcinoembryonic antigen (CEA) (figure 3). They demonstrated ratiometric detection of CEA by analyzing the diffusion mobility of nanoprobes in the presence of CEA at different concentrations, the aggregate-to-monomer ratio of nanoprobes as a function of CEA concentration was obtained. This ratiometric detection technique exhibited a linear dynamic range from 50 pM to 750 pM for the quantitative detection of CEA. Another advantage of this ratiometric detection technique is that it showed excellent anti-interference ability in the presence of non-specific proteins or complex protein mixtures, which is competent for clinic diagnostic analysis of CEA in tumor patients. The mechanism of this robust technique can not only accurately detect disease biomarkers and other biomolecules in the future, but also can be used in biochemical and diagnostic applications. In this experiment, the researchers used AuNPs as a reference. AuNRs are rod-shaped and have directionality. Although experiments on the mobility and rotation of AuNRs were described by literatures [97, 98], the detection of cancer markers using the mobility and rotation of AuNRs had not been reported. Future researchers can use the relationship between the mobility and rotation of AuNRs and the concentration of cancer markers for later research. Recently, on the other hand, the use of current responses of different nanocomposite to detect tumor markers has attracted the attention of a large number of researchers. For example, Jia et al[99] used MoS2/CuS-Au as sensing platform and mulberry-like Au@PtPd porous nanorods as signal amplifiers to successfully construct a sandwich-type electrochemical immunosensor for the detection of CEA. Among them, the AuNRs being wrapped by Platinum Palladium had a large specific surface area and a large number of catalytically active sites showed excellent electrocatalytic performance for hydrogen peroxide reduction. That amperometric response of immunosensor for different concentrations of CEA detection exhibited a wide linear detection range from 50 fg ml$^{-1}$ to 100 ng ml$^{-1}$ and a low detection limit of 16.7 fg ml$^{-1}$. A novel AuNR-based immunochromatographic strip for quantitative and sensitive analysis of prostate specific antigen (PSA) were reported by Lu et al[100] AuNRs coated with sodium polycrylate and the anti-PSA monoclonal antibody can maximize the good specificity, high stability and high sensitivity of AuNR-based immunochromatographic strip and the proposed AuNR-based immunochromatographic strip for PSA detection showed a broad detection range from 0.1 ng ml$^{-1}$ to 50 ng ml$^{-1}$. The detection limit of the AuNR-based immunochromatographic strip which showed a low detection limit of 0.1 ng ml$^{-1}$ could be successfully applied for PSA detection in serum.

4.5. AuNRs for volatile organic compounds (VOCs) detection

VOCs are related to different disease. In particular, high concentration of VOCs in air exceeding a certain threshold can cause severely human health [101], respiration dysfunctions and allergic disease [102], and even
sudden death \cite{103}. Therefore, it is particularly expected to construct a sensitive and selective method allowing for real-time detection of VOCs in a sample. Conventional methods for VOCs detection include fluorescence spectrometry \cite{104}, electrochemistry \cite{105}, chemiluminescence \cite{106}, etc. Although these methods are sensitive and effective, most of them require sophisticated and expensive instrumentation and well-trained operators. In recent years, a number of sensors based on functionalized AuNRs for the detection of VOCs had attracted a lot of attention. A few years ago, Li et al \cite{107} assembled graphene onto AuNRs through electrostatic interaction. Due to the synergistic effect between AuNRs and graphene and used alcohol dehydrogenase (ADH) as a model system, the functionalized AuNRs exhibited excellent toward ethanol assay, with a good linear range from 5 to 377 mM. The low detection limit is 1.5 μM. The synthesis of graphene-AuNRs hybrid nanosheets is a simple and effective sensing platform for the detection of ethanol. Furthermore, through this kind of strategy, we can assemble other substances onto AuNR to detect another volatile organic chemical. Recently, the colorimetric detection of VOCs had become more popular. Most of their detection mechanism was through replacing the surface material on AuNRs, leading to the variation in the dielectric constant of the material attached to the AuNRs, thereby changing their LSPR effect. Simultaneously, the color of the solution changed. For example, Lin et al \cite{108} developed a responsive, simple, sensitive and selective AuNRs colorimetric sensor for the determination of formaldehyde, which based on formaldehyde could reduce Ag\(^+\) to Ag on the surface of AuNRs to form Au core-Ag shell nanorods (Au@AgNRs), which caused the dielectric constant of AuNRs to change, and the color of the solution to change obviously. The limit of detection of this sensor for formaldehyde was 6.3 × 10\(^{-11}\) g ml\(^{-1}\). Liu et al \cite{109} also developed a rapid and sensitive method for colorimetric detection of formaldehyde in aqueous solutions and leather based on the color of AuNRs solution. The detection mechanism depend on formaldehyde would reduce Hg\(^{2+}\) to Hg-0 in an alkaline environment, which results in amalgamation between elemental mercury (Hg-0) and AuNRs to generate significant color change and the color of AuNRs from blue-green to purple. The proposed colorimetric approach had a linear correlation for formaldehyde detection from 0.1 to 10 mg l\(^{-1}\).

A recent study caught my attention \cite{110}. Zeng et al constructed Au/Ag dimeric nanoparticles(NPs) or highly selective colorimetric detection of hydrogen sulfide (H\(_2\)S) by taking advantage of the chemical transformation of AgI to Ag\(_2\)S upon reacting with sulfide, which accompanied by a color change of the solution from purplish red to blue depending on the concentration of sulfide. There are two points that attract me in this research. First, Ag shells were first deposited onto Au nanoparticles by the Tollens reaction, followed by the addition of I\(_2\) to oxidize the Ag shell to form AgI. It’s weird to form Au/AgI dimeric NPs instead of regular Au/AgI sphere after the reaction, as shown in figure 4. Second, Researcher immobilized Au/AgI dimeric NPs in agarose gels to produce test strips. Furthermore, the color changes were much more significant when the agarose gels were completely dried. As shown in figure 5, the color changes of the agarose gels were much more significant than commercially available Pb(Ac)\(_2\) test papers, indicting the agarose gel strip has superior performance for detecting sulfide in terms of sensitivity, selectivity, stability, and fidelity. Although gold nanoparticles were used in this experiment, Au core-Ag shell nanorods were synthesized in the previous experiment \cite{108}. The inspiration of this experiment is that we can synthesize Au core-Ag shell nanorods, followed by the addition of I\(_2\) to oxidize the Ag shell to form AgI and observe the structural changes. The newly synthesized material is immobilized in agarose gel as a test strip to detect H\(_2\)S whether has better sensitivity, selectivity, stability, and fidelity.
AuNRs was a sensitivity and stability electronic nose for H2S detection. Currently, certain gas sensors cannot be used for the detection of ethanol based on using alcohol dehydrogenase (ADH) as a model system, which had a detection limit 1.5 μM, indicted that functionalized AuNRs could be used as a good sensor of the electronic nose in the field of drunk driving detection. A study that fluorosurfactant functionalized AuNRs had been proposed to act as a selective colorimetric nanoprobe for H2S detection in human and mouse serum samples, indicating that fluorosurfactant functionalized AuNRs was a sensitivity and stability electronic nose for H2S detection. Currently, certain gas sensors cannot be placed in high temperature environment because of the gas sensors are not stable when the temperature is too high, and therefore those sensitive and selective gas sensors cannot take measurements of combustion parameters. Near-infrared (NIR) thermal energy harvesting has been demonstrated for AuNRs, which allowed to obtain temperature thermal imaging spectra at sample temperatures ranging from 275 °C–500 °C. Part-per-million detection capabilities of the AuNRs were demonstrated with a factor of 11 reduction in collection times in the NIR for H2, CO, and NO2 as compared to measurements made in the visible light region. The AuNRs as electronic nose are promising in the area of gas sensing technology and gas turbines. With the improvement of living standards, the electronic noses combined with AuNRs have very broad application prospects, not only for detecting the odors components in air, but also for identifying the freshness and quality of food, and detecting whether food is moldy or spoiled. For example, Chen et al. developed a method using glucose oxidase induced redox reaction to etch AuNRs for qualitative and quantitative detection of aflatoxins and zearalenones in maize. Fang et al. developed a method using glucose oxidase in duced redox reaction to etch AuNRs for qualitative and quantitative detection of aflatoxin M1 in milk. The above researchers used AuNRs to detect toxic substances in food, indicating that AuNRs have good performance as sensors in electronic noses. Besides, Wu et al. fabricated a new type of three-dimensional SERS sensors by loading AuNR@AgNCs on bacterial cellulose aerogels for the detection of 2, 4, 6-trinitrotoluene (TNT), indicating that AuNRs can be used as sensors in the electronic nose to detect explosives and become a good helper for the police. AuNRs are used for medical diagnosis, biomolecules and chemical material detection, also indicating AuNRs are an outstanding, sensitive and stable sensor in the electronic nose.

4.6. AuNRs is used in electronic nose

The electronic nose that could recognize simple and complex odors is mainly composed of gas sensor array, signal preprocessing and pattern recognition. That the gas sensor of the electronic nose responds to complex gases can be used as various gas sensors in a good electronic nose. Li et al. synthesized graphene-Au nanorods hybrid nanosheets (GN-AuNRs) through electrostatic interaction for the detection of ethanol based on using alcohol dehydrogenase (ADH) as a model system, which had a detection limit 1.5 μM, indicated that functionalized AuNRs could be used as a good sensor of the electronic nose in the field of drunk driving detection. A study that fluorosurfactant functionalized AuNRs had been proposed to act as a selective colorimetric nanoprobe for H2S detection in human and mouse serum samples, indicating that fluorosurfactant functionalized AuNRs was a sensitivity and stability electronic nose for H2S detection. Currently, certain gas sensors cannot be placed in high temperature environment because of the gas sensors are not stable when the temperature is too high, and therefore those sensitive and selective gas sensors cannot take measurements of combustion parameters. Near-infrared (NIR) thermal energy harvesting has been demonstrated for AuNRs, which allowed to obtain temperature thermal imaging spectra at sample temperatures ranging from 275 °C–500 °C. Part-per-million detection capabilities of the AuNRs were demonstrated with a factor of 11 reduction in collection times in the NIR for H2, CO, and NO2 as compared to measurements made in the visible light region. The AuNRs as electronic nose are promising in the area of gas sensing technology and gas turbines. With the improvement of living standards, the electronic noses combined with AuNRs have very broad application prospects, not only for detecting the odors components in air, but also for identifying the freshness and quality of food, and detecting whether food is moldy or spoiled. For example, Chen et al. developed a method using glucose oxidase induced redox reaction to etch AuNRs for qualitative and quantitative detection of aflatoxins and zearalenones in maize. Fang et al. developed a method using glucose oxidase in duced redox reaction to etch AuNRs for qualitative and quantitative detection of aflatoxin M1 in milk. The above researchers used AuNRs to detect toxic substances in food, indicating that AuNRs have good performance as sensors in electronic noses. Besides, Wu et al. fabricated a new type of three-dimensional SERS sensors by loading AuNR@AgNCs on bacterial cellulose aerogels for the detection of 2, 4, 6-trinitrotoluene (TNT), indicating that AuNRs can be used as sensors in the electronic nose to detect explosives and become a good helper for the police. AuNRs are used for medical diagnosis, biomolecules and chemical material detection, also indicating AuNRs are an outstanding, sensitive and stable sensor in the electronic nose.

5. Conclusions and perspectives

Over the past decade, advances in AuNRs synthesis and fabrication, unique optical properties, adjustable aspect ratios and good biocompatibility have led to an explosion of both efforts and reports on the emerging field of AuNRs-sensors. In this review, we summarized the recent progress in AuNRs synthesis, surface modification, and the applications of AuNRs in the field of biological detection. Although new advances in producing AuNRs with longer LSPR, higher yields and purity, and smaller sizes have been obtained by means of altering the amount of Ag+, Au3+, and the reducing agent, the progress of their fabrication and the regulation of the size, morphology, and LSPR, some issues are still unaddressed. For example, during synthesis, the growth mechanism of AuNRs is not fully understood, and AuNRs with specific LSPR reproducibly is still difficult to obtain. Rapid and accurate synthesis of AuNRs with longer LSPR, higher yields and purity, and smaller sizes is one of the key tasks for the future research. The rapid synthesis, unique optical properties, and of good biocompatibility AuNRs play a key role in a broad range of detection application. AuNRs-based sensors provide promising approaches for selective and sensitive analyses, and have advantages over traditional instrumental...
analyses, as they are more convenient and low-cost effectiveness. With the proposed of AuNRs-based sensors, this kind of sensors can be developed for multiplexed, quantitative and rapid analysis of heavy metals, toxins, biomolecules and tumor or cancer biomarkers.

Nevertheless, it is still desirable to obtain more tiny AuNRs because AuNRs as sensor that have more sensitive, efficient, specific and stable are size-dependent. But the optimum sizes for detection have not been investigated systematically, which is a new perspectives and new directions. Prior to their biomedical applications, the surface of AuNRs must be dealt with, because the CTAB in the synthesis affects the stability for tumor marker detection and biomolecules detection. The modification through Au-S bond or wrapping by deposition of polyelectrolytes is the common route. It is still necessary to resolve the contradictions and theoretical defects between theory and comprehensive methods for AuNRs for heavy metals and toxins detection. The detection of VOCs by AuNRs can be combined with electronic noses. In summary, our work should help the community gain new insights into AuNRs and the multidisciplinary research into their synthesis and safe use in detection field.

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Data availability statement

No new data were created or analysed in this study.

Conflicts of interest

No author has a financial/commercial Conflict of Interest.

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References

[1] Naganandhini S et al 2015 Persistence of pathogenic and non-pathogenic Escherichia coli strains in various tropical agricultural soils of India PLoS One 10 e0130038
[2] Kart D et al 2014 Activity of disinfectants against multispecies biofilms formed by Staphylococcus aureus, Candida albicans and Pseudomonas aeruginosa Biofouling 30 377–83
[3] Marathe S A et al 2012 Curcumin reduces the antimicrobial activity of ciprofloxacin against Salmonella Typhimurium and Salmonella Typhi J. Antimicrob. Chemother. 1 1
[4] Neznamysky A and Opatsky Y 2014 Expression, purification and crystallization of the phosphate-binding PstS protein from Pseudomonas aeruginosa Acta Crystallogr. 70 906–10
[5] Soyak M et al 2003 Column preconcentration/separation and atomic absorption spectrometric determinations of some heavy metals in table salt samples using amberlite XAD-1180 Turk. J. Chem. 27 235–42
[6] Bagheri H et al 2012 Preparation and characterization of magnetic nanocomposite of Schiff base/silica/magnetite as a preconcentration phase for the trace determination of heavy metal ions in water, food and biological samples using atomic absorption spectrometry Talanta 97 87–95
[7] Zhou Q, Zhao N and Xie G 2011 Determination of lead in environmental waters with dispersive liquid–liquid microextraction prior to atomic fluorescence spectrometry J. Hazard. Mater. 189 48–53
[8] Uysal K, Emre Y and KSE E 2008 The determination of heavy metal accumulation ratios in muscle, skin and gills of some migratory fish species by inductively coupled plasma-optical emission spectrometry (ICP-OES) in Beymlek Lagoon (Antalya/Turkey) Microchem. J. 90 67–70
[9] Chen H et al 2013 Gold nanorods and their plasmonic properties Chem. Soc. Rev. 42 2679–724
[10] Rez-Juste J P et al 2005 Gold Nanorods: Synthesis, Characterization and Applications 249 1870–901
[11] Chang S 1999 The shape transition of gold nanorods Langmuir 15 701–709
[12] Martin R C 1994 Nanomaterials: a membrane-based synthetic approach Science 266 1961–6
[13] Evans P et al 2006 Growth and properties of gold and nickel nanorods in thin film alumina Nanotechnology 17 5746–53
[14] Huang C J et al 2006 Synthesis of the gold nanodumbbells by electrochemical method J. Colloid Interface Sci. 303 430–6
[15] Yu-Ying Y U S S, Chang C L and LEE C R C 1997 Gold nanorods: electrochemical synthesis and optical properties Jphyschemb 101 6661–4
[16] Jana N R, Gearheart L A and Murphy C J 2001 Seed-mediated growth approach for shape-controlled synthesis of spheroidal and rod-like gold nanoparticles using a surfactant template Adv. Mater. 13 1389–93
[17] Nikoobakhht B and El-Sayed M A 2003 Preparation and growth mechanism of gold nanorods (NRs) using seed-mediated growth method Chem. Mater. 15 1937–62
[62] Ge K et al 2018 A colorimetric probe based on functionalized gold nanorods for sensitive and selective detection of as (III) ions Sensors 18 2372

[63] Eum N-S et al 2010 Enhancement of sensitivity using gold nanorods—antibody conjugator for detection of E. coli O157: H7 Sensors and Actuators B 143 784–8

[64] Xu X et al 2013 A simple and rapid optical biosensor for detection of aflatoxin B1 based on competitive dispersion of gold nanorods Biosens. Bioelectron. 47 361–7

[65] Xu X, Xu C and Ying Y 2016 Aptsensor for the simple detection of ochratoxin A based on side-by-side assembly of gold nanorods RSC Adv. 6 50437–43

[66] Deng J et al 2012 Sensitive detection of endonuclease activity and inhibition using gold nanorods Biosens. Bioelectron. 34 144–50

[67] Zhang Z et al 2015 Iodine-mediated etching of gold nanorods for plasmonic ELISA based on colorimetric detection of alkaline phosphatase ACS Appl. Mater. Interfaces 7 27639–45

[68] Jekerst J V et al 2012 Gold nanorods for ovarian cancer detection with photoacoustic imaging and resection guidance via Raman imaging in living mice ACS Nano 6 10366–77

[69] Li Y et al 2016 A simple aptamer-functionalized gold nanorods based biosensor for the sensitive detection of MCF-7 breast cancer cells Chem. Commun. 52 3959–61

[70] S C et al 2015 Combined detection of breast cancer biomarkers based on plasmonic sensor of gold nanorods Sensors & Actuators B Chemical 221 1391–7

[71] Luchun L U et al 2020 Rapid, quantitative and ultra-sensitive detection of cancer biomarker by a SERRS-based lateral flow immunoassay using bovine serum albumin coated Au nanorods RSC Adv. 10 271–81

[72] Huang Y et al 2018 Aggregation induced surface enhanced plasmonic detection of mercury (II) ions using quaternary ammonium group-capped gold nanorods Talanta 187 65–72

[73] Saute B et al 2012 Gold nanorods as surface enhanced Raman spectroscopy substrates for sensitive and selective detection of ultra-low levels of dithiocarbamate pesticides Analyst 137 5082–7

[74] Alvarez-Puebla R A et al 2011 Gold nanorods 3D supercrystals as surface enhanced Raman scattering spectroscopy substrates for the rapid detection of scrambled prions Proc. Natl. Acad. Sci. 108 8157–61

[75] Chen J et al 2016 Colorimetric detection of Escherichia coli based on the enzyme-induced metallization of gold nanorods Small 12 2469–75

[76] Wang C and Irudayaraj J 2008 Gold nanorods probe for the detection of multiple pathogens Small 4 2204–8

[77] Roushani M et al 2019 Development of electrochemical aptasensor based on gold nanorod and its application for detection of aflatoxin B1 in rice and blood serum sample Nanochemistry Research 4 35–42

[78] Kaushal S et al 2019 Glycoconjugates coated gold nanorods based novel biosensor for optical detection and photothermal ablation of food borne bacteria Sensors & Actuators B 289 207–15

[79] Castellanos-Serra L and Hardy E 2006 Negative detection of biomolecules separated in polyacrylamide electrophoresis gels Nat. Protoc. 1 1544–51

[80] Srupnar J et al 1998 Speciation analysis for biomolecular complexes of lead in wine by size-exclusion high-performance liquid chromatography–inductively coupled plasma mass spectrometry J. Anal. At. Spectrom. 13 749–54

[81] Lakshmipriya T, Gopinath S C and Tang T-H 2016 Biotin-streptavidin competition mediates sensitive detection of biomolecules in enzyme linked immunosorbent assay PLoS One 11 e0151153

[82] Sudeep P, Joseph B S and Thomas K G 2005 Selective detection of cysteine and glutathione using gold nanorods JACS 127 6516–7

[83] Huang H et al 2010 Ultra-sensitive detection of cysteine by gold nanorod assembly Biosens. Bioelectron. 25 2078–83

[84] Li Y et al 2019 Gold nanorods and graphene oxide enhanced BSA-AgInS2 quantum dot-based photoelectrochemical sensors for detection of dopamine Electrochem. Acta 295 1006–16

[85] Wang B et al 2019 Gold-nanorod-enhanced Raman spectroscopy encoded micro–quartz pieces for the multiplex detection of biomolecules Anal. Bioanal. Chem. 411 5509–18

[86] Liu J et al 2018 Rapid detection of heparin by gold nanorods and near-infrared fluorophore ensemble based platform via nanometal surface energy transfer Sensors and Actuators B 274 118–23

[87] Wiriyachairumph N et al 2019 A colorimetric sensor for protamine detection based on the self-assembly of gold nanorods on graphene oxide New J. Chem. 43 8502–7

[88] Barragán-Sparray N et al 2019 Visual colorimetric sensing system based on the self-assembly of gold nanorods and graphene oxide for heparin detection using a polycrystalline polymer as a molecular probe Anal. Methods 11 1387–92

[89] Guzman R D E and Malik M 2019 Global cancer burden and natural disasters: a focus on Asia Journal of Global Oncology 5 1–8

[90] Yamashita T et al 2008 EpCAM and α-fetoprotein expression defines novel prognostic subtypes of hepatocellular carcinoma Cancer Res. 68 1451–61

[91] Zheng G et al 2005 Multiplexed electrical detection of cancer markers with nanowire sensor arrays Nat. Biotechnol. 23 1294–301

[92] Mitchell P S et al 2008 Circulating microRNAs as stable blood-based markers for cancer detection Proc. Natl. Acad. Sci. 105 10513–8

[93] Agarwal A et al 2007 Targeted gold nanorod contrast agent for prostate cancer detection by photoacoustic imaging J. Appl. Phys. 102 064701

[94] Ankri R et al 2012 A new method for cancer detection based on diffusion reflection measurements of targeted gold nanorods Int. J. Nanomed. 7 449

[95] Ankri R et al 2012 In-vivo tumor detection using diffusion reflection measurements of targeted gold nanorods—a quantitative study J. Biophotonics 5 263–73

[96] Hong Y et al 2014 Localized surface plasmon resonance based nanobiosensor for biomarker detection of invasive cancer cells J. Biomed. Opt. 19 51202

[97] Ge F et al 2019 Real-time observation of dynamic heterogeneity of gold nanorods on plasma membrane with darkfield microscopy Science China-Chemistry 62 1072–81

[98] Sun H, Wang Z and He Y 2019 Direct observation of spatiotemporal heterogeneous gelation by rotational tracking of a single anisotropic nanoprobe ACS Nano 13 11334–42

[99] Jia Y et al 2020 Mulberry-like Au@PtPd porous nanorods composites as signal amplifiers for sensitive detection of CEA Biosens. Bioelectron. 149

[100] Lu L et al 2019 Rapid, quantitative and ultra-sensitive detection of cancer biomarker by a SERRS-based lateral flow immunoassay using bovine serum albumin coated Au nanorods RSC Adv. 10 271–281
[101] Cassagnes L-E et al 2020 Online monitoring of volatile organic compounds emitted from human bronchial epithelial cells as markers for oxidative stress J. Breath Res. 15 55

[102] Macedo G E et al 2020 Fungal compound 1-octen-3-ol induces mitochondrial morphological alterations and respiration dysfunctions in Drosophila melanogaster Ecotoxicology and Environmental Safety 206 111232

[103] Fielding D et al 2020 Volatile organic compound breath testing detects-situsquamous cell carcinoma of bronchial and laryngeal regions and shows distinct profiles of each tumour J. Breath Res. 14 111232

[104] Feng L et al 2020 Terbium-based metal-organic frameworks: highly selective and fast respond sensor for styrene detection and construction of molecular logic gate J. Hazard. Mater. 388 121816

[105] Bhattacharjee M, Vilouras A and Dahiya R S 2020 Microdroplet-based organic vapour sensor on a disposable GO-chitosan flexible substrate IEEE Sensors J. 20 7494–502

[106] Zhang J et al 2020 A polythiophene/UiO-66 composite coating for extraction of volatile organic compounds migrated from ion-exchange resins prior to their determination by gas chromatography Journal of Chromatography A 1633 461627–461627

[107] Li L, Lu H and Deng L 2013 A sensitive NADH and ethanol biosensor based on graphene-Au nanorods Nanoscale 113 1–6

[108] Lin J-M et al 2015 Design of an ultra-sensitive gold nanorod colorimetric sensor and its application based on formaldehyde reducing Ag+ RSC Adv. 5 99944–50

[109] Liu Q et al 2020 Development of gold nanorods-based colorimetric method for the determination of formaldehyde in leather J. Soc. Leather Technol. Chem. 104 227–34

[110] Zeng J et al 2018 Au/Agl dimeric nanoparticles for highly selective and sensitive colorimetric detection of hydrogen sulfide Adv. Funct. Mater. 28 1800515

[111] Zhang X et al 2015 Colorimetric detection of biological hydrogen sulfide using fluorosurfactant functionalized gold nanorods Analyst 140 7443–50

[112] Karker N A, Dharmlingam G and Carpenter M A 2015 Thermal energy harvesting near-infrared radiation and accessing low temperatures with plasmonic sensors Nanoscale 7 17796–804

[113] Chen C et al 2020 Non-CTAB synthesized gold nanorods-based immunochromatographic assay for dual color and on-site detection of aflatoxins and zearalenones in maize Food Control 118 106720

[114] Fang B et al 2020 Gold nanorods etching-based plasmonic immunoassay for qualitative and quantitative detection of aflatoxin M1 in milk Food Chem. 329 127160

[115] Wu J et al 2020 Nanocellulose-based surface-enhanced Raman spectroscopy sensor for highly sensitive detection of TNT Carbohydrate Polym. 248 116768

[116] Liu J et al 2020 The synergistic effect enhanced chemical etching of gold nanorods for the rapid and sensitive detection of biomarks Talanta 219 121203

[117] Zhang H et al 2020 Label-free fluorescent sensor for one-step lysozyme detection via positively charged gold nanorods Anal. Bioanal. Chem. (https://doi.org/10.1007/s00216-020-02814-2)

[118] Xu T et al 2019 Rapid detection of trace methylene blue and malachite green in four fish tissues by ultra-sensitive surface-enhanced Raman spectroscopy coated with gold nanorods Food Control 106 106720