

Aptamer Functionalized Gold Nanoparticles for the Detection of Heavy Metal Ions

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Date of publication (dd/mm/yyyy): 13/09/2019

Abstract – Gold nanoparticles are widely used in various fields including bioassay, biomarker and surface enhanced Raman due to their superior optical properties, catalytic properties and biocompatibility. Due to the nature of surface plasmon resonance, gold nanoparticles can be used as visual sensors and attract the attention of many researchers. Today, gold nanoparticles have been widely used by researchers for the detection of metal ions. The gold nanoparticles can be combined with the magnetic nano materials, and the formed magnetic materials are combined with the excellent properties of the gold nanoparticles and the magnetic nanoparticles, and can be visually analyzed in combination with the color reaction substance. There are also small atomic clusters of precious metal quantum dots with strong fluorescence properties that are also the focus of researchers. Fluorescent precious metal nanoparticles have the property of continuous luminescence, adjustable electronic transitions in the ultraviolet and visible regions, and thus can be used as photoelectron sources for biomarkers, biosensors, and nanoscale luminescence. This paper reviews the research literature on the use of aptamer-functionalized gold nanoparticles for the detection of heavy metal ions in recent years.

Keywords – Gold Nanoparticles, Heavy Metal Ions, Aptamer, Detection.

I. INTRODUCTION

Heavy metal pollution is highly toxic, low in toxic dose, long incubation period, easy to accumulate, difficult to degrade, difficult to treat, etc., causing great harm to the environment and humans. Heavy metal ions are easily complexed with other substances, especially biomolecules containing nitrogen, sulfur, oxygen, etc., which cause changes in their molecular structure, or damage to hydrogen bonds, or lead to protein inactivation and inhibition of enzyme production. Influencing the central nervous system (such as Hg^{2+} , Pb^{2+} , As^{3+} , etc.), kidney or liver (such as Cu^{2+} , Cd^{2+} , Hg^{2+} , Pb^{2+} , etc.), damage to skin, bones or teeth (such as Ni^{2+} , Cu^{2+} , Cd^{2+} , Cr^{3+} , etc.), and even it affects the human reproductive system (such as Cu^{2+} , Pb^{2+} , Cr^{3+} , etc.), and the heavy metal pollution is sudden and strong, and can spread and spread rapidly in a very short time. Therefore, under the standard of human health, rapid, real-time and trace analysis of heavy metals has always been the focus of human attention. The detection of heavy metal ions by gold nanoparticles has the advantages of simple operation, convenience and speed, and is very suitable for on-site monitoring, field survey, etc., and has attracted the attention of scientists.

1. Methods Heavy Metal Ion Detection

With the development of modern society and economy, environmental pollution has become increasingly serious. Most of the pollutants are present in environmental media for a long time. Methods for detecting Hg^{2+} in water samples have been reported to include atomic absorption spectroscopy (AAS), atomic fluorescence spectrometry (AFS), inductively coupled plasma mass spectrometry (ICP-MS) fluorescence and electrochemical analysis (Zhou, et al.2008). However, most of these methods are limited in their wide range of applications due to the use of expensive and cumbersome instruments, complex sample pretreatment processes or poor sensitivity

and selectivity (Murphy, et al. 2008).

Fluorescence analysis is considered to be an important analytical tool due to its high sensitivity, simplicity, low cost, and ease of miniaturization (Bhatt, et al. 2014). Optical materials or probes are an integral part of fluorescence analysis, and the choice of optical probes is the key to determining the performance of fluorescence analysis (Liang, et al. 2011). In the past few decades, several types of optical probes have been used in the construction of fluorescent sensors, including organic dye polymer dots, quantum dots, up converting nanoparticles, carbon dots, and metal nanoclusters (NCs). Among these optical probes, since the metal nanoclusters are ultra-thin, strong in fluorescence, and good in light stability, they are particularly considered to be a rising star, and in recent years, considerable attention has been paid to environmental monitoring (Torabi S F, 2015).

1.1 *Organic Fluorescent Dyes for the Detection of Heavy Metal Ions*

Organic fluorescent dyes have good photo stability and high fluorescence quantum yield. Fluorescent dyes and rhodamine dyes are commonly used as fluorescent dye markers (Kouassi, et al. 2007). It can also be used for cell imaging and fluorescence sensing, such as the detection of heavy metal ions and DNA. It is described in detail in the literature that the structure of stable T-Hg²⁺-T is formed by the mismatch of Hg²⁺ ions and thymus gland, and various labeled and unlabeled fluorescent probes are used for the detection of Hg²⁺ ions. A common mechanism for label-free detection of Hg²⁺ relies on Hg²⁺- induced conversion of thymidine-rich single-stranded oligonucleotides into double-stranded or hairpin structures, which can be detected by inserting fluorescent dyes to construct fluorescent probes (Barbosa, et al. 2014).

Chang and Liu's group used organic dyes such as TOTO-3 and SYBR Green I for Hg²⁺ ion detection. Hg²⁺ can destroy the fluorescence of the fluorophore by the spin-orbital scorching effect. When a fluorophore is used as a probe, the rhodamine-based dye has a large molar extinction coefficient, excellent spectral properties, and high fluorescence quantum yield. Rhodamine dyes have cationic properties, and these dyes generally have good water solubility and cell membrane permeability have been widely used as fluorescent probes (Lee, et al. 2012). In 2013, Feng et al. used this unique structure of rhodamine dye as a fluorescent probe to construct "open" Hg²⁺. Organic dyes have many disadvantages, such as fast photo bleaching, poor photochemical stability, and narrow wavelength range of excitation light.

1.2 *Quantum dot probe for Detection of Heavy Metal Ions*

Due to its superior performance, quantum dots have been used to detect heavy metal ions with high sensitivity. Since the pioneering work of Mr. Chen and Rosenzweig in 2002, the luminescent CdS quantum dots have been used as probes for Cu²⁺, Zn²⁺ and Fe³⁺, and metal ion detection has made great progress. In 2016, Tao et al. demonstrated that 3-mercapto-acid-stabilized CdTe/CdS quantum dots can be used as copper (II) ion sensors based on their near-infrared fluorescence caused by a competitive combination between 3-mercaptopropionic acid and Cu²⁺. Quantum dots are aggregated and quenched (Aghanejad A, Babamiri H, Adibkia K, et al. 2018). Chao et al. established a CdTe quantum dot coated with 1-(2-thiazolylazo)-2-naphthol as a copper (I) ion sensor. Ding et al. successfully used glutathione-functionalized ZnSe quantum dots (Shahat, et al. 2018). A simple and accurate method for the detection of Cu²⁺ fluorescence has been developed. In the presence of Hg²⁺ ions, the photoelectron transfer between QD and Hg²⁺ reduces the photoluminescence intensity of quantum dots (Sener, et al. 2014). These methods illustrate the quantum dot-based ion sensor in chemistry (Vinod Kumar V, Anbarasan S, Christena

L R, et al. 2014). And biological aspects have great potential for application (Wang, et al. 2012). However, quantum dots mostly contain heavy metal elements that are toxic, so the application of quantum dots is limited.

1.3 Graphene Oxide (GO) for the Detection of Heavy Metal Ions

In 1859, Brodie treated graphite with strong acid to obtain exfoliated graphene oxide (GO). Although it has excellent fluorescence quenching ability, the original graphene is highly hydrophobic and difficult to detect (Liu J, Lu Y. 2006). Since the discovery of graphene in 2004, GO has attracted more and more attention in the research of DNA sensors because of its good sensing capability. The main functional group of GO is the fumaric acid group on the periphery of the carbon sheet, which is soluble in water and various solvents, and is widely used for detecting metal ions (Bindhu M R, Umadevi M. 2014). Graphene oxide (GO) can effectively annihilate fluorescent probes because the large conjugated structure of GO makes it an excellent electron or energy acceptor during possible electron transfer or energy transfer. It has been reported that dye-labeled aptamers may adsorb on the GO surface, and aptamer fluorescence can be efficiently quenched by fluorescence resonance energy (Akolekar et al. 2005). After recognition of the target, the aptamer can switch its conformation to release from the GO surface, resulting in fluorescence recovery of the aptamer. Li et al. used molecular beacons (MBs) and graphene oxide (GO) to directly detect Cu^{2+} in solution. Molecular beacons are special single-stranded DNAs that carry a fluorescent source. When the molecular beacon is adsorbed on GO, it is used as a high-efficiency fluorescent fragmenter, which reduces the background signal and makes the detection method more sensitive. In the presence of Cu^{2+} and H_2O_2 , the molecular beacon is cut into short pieces and released by GO, resulting in fluorescence recovery. The detection limit of this method is about 50 nM (Slocik J M, Jr Z J, Phillips D M, et al. 2010). Although most researchers use simple physical adsorption of fluorescently labeled DNA, covalent bond sensors are less susceptible to non-specific probe replacement, reducing the occurrence of false positive results. Liu's group proposed three probes of different lengths of thymus-stained DNA and labeled with fluorophores at their 3 ends with amino modifications for covalent attachment to GO. When Hg^{2+} is present, the T-rich DNA binds to Hg^{2+} to form a double-stranded structure, and the fluorescence is restored by dissociation from graphene oxide. The detection limits of Hg^{2+} in this method are 16.3 and 20.6 nM, respectively.

In summary, although many methods for detecting heavy metal ions have been established, they have been limited in complex environmental systems and biological systems. Rapid development, low cost, simple and reliable technology, sensitive and real-time measurement of heavy metal ion concentrations are still an ongoing research area.

2. Sensing metal Ions with Au Nanoparticles

Certain metal ions in food have a positive effect on human health. Once lacked, it will cause the corresponding mineral deficiency symptoms. For example, the lack of iron will cause anemia, and the lack of calcium will cause osteoporosis and other symptoms. Therefore, metal ions play an important role in the diet of daily life. However, some heavy metal ions have a harmful effect on the human body. For example, heavy metal ions such as lead, cadmium, and mercury remaining in soil and water will accumulate in the liver, kidney, and other organs of the body after entering the human body, causing great harm to the bone hematopoietic system, nervous system, and digestive system. Therefore, it is very urgent to establish a sensitive and efficient sensor to accurately detect metal ions. Among them, the gold nanoparticle colorimetric detection and the detection of metal ions by fluorescent

nano-gold particles have achieved good results, opening up new ideas for the establishment of metal ion detection methods.

2.1 Gold Nanoparticle Colorimetric Detection of Metal Ions

The characteristic plasmon absorption peak of the nano gold particles is at 510-550 nm, and the position of the absorption peak is red-shifted as the particle size increases or the distance between the particles decreases. The size range of the gold particles and the degree of aggregation between the particles were determined by the absorption peak of the gold particles in the ultraviolet-visible spectrum, and the morphology and state of the gold particles were determined. When the gold nanoparticles were aggregated to a certain extent, the distance between the two particles was smaller than the particle size. Two times, the color of the solution changes significantly, from the original red color of the colloid to purple. This property has become the rationale for designing colorimetric devices. The colorimetric method only needs to be observed with the naked eye in judging the monitoring results. It is easy to operate in many applications and does not require other advanced instruments, thus attracting the attention of many researchers. The functionalized groups on the surface of the designed gold nanoparticles can coordinate with the target of detection, which leads to the aggregation of the originally monodisperse gold nanoparticles. The aggregation of the gold nanoparticles causes the broadening and displacement of the surface plasmon resonance absorption peak. And produced a colorimetric response, the color of the solution changed from red to blue-violet.

According to this nature, the Mirkin group of Northwestern University, USA, used direct color detection to analyze the hybridization characteristics of oligonucleotides. In 1997, Science reported that the Mirkin team applied gold particle-labeled oligonucleotides and detected target oligonucleotides, creating a new era of colorimetric detection using gold nanoparticles. Since then, researchers have used this principle to design various colorimetric detection devices based on gold and silver nanoparticles for the detection of DNA, enzymes, cancer cells, heavy metal ions, proteins, amino acids, TNT and other explosives, viruses, etc. Simple, flexible design, no need for large instruments, and high sensitivity and selectivity.

Recently, surface-functionalized gold nanoparticles have been used as colorimetric devices to detect materials Hg^{2+} , Pb^{2+} , Cu^{2+} and other heavy metal ions, and good results have been obtained. A group that can be coordinated with a heavy metal ion on the surface of a nano gold particle. When it is coordinated with a heavy metal ion in the water or solution to be tested, the gold nanoparticle will aggregate and the color changes from red to purple to achieve rapid detection. The purpose, the method is simple, the result is intuitive, and can be judged by the naked eye. For the detection of Hg^{2+} , the gold nanoparticle colorimetric device is used to detect Hg^{2+} by using the mismatch of thymus sputum in the DNA strand. The mismatched pair of thymus sputum uses its N atom to coordinate with a Hg^{2+} to generate the firm coordination structure allows the gold nanoparticles to aggregate. The macroscopically, the color of the solution changes from red to purple, and the color change of the solution is monitored to achieve the detection purpose. For example, Professor Mirkin uses DNA to functionalize nanogold particles. The mismatched thymus sputum and Hg^{2+} coordination are structurally stable, which increases the temperature of the double-stranded DNA chain, and the color of the gold gel changes to achieve the purpose of detection.

In 2003, Professor Lu Yi first used DNAzyme functionalized gold nanoparticles, specific DNase 17E colorime-

-tric detection of Pb^{2+} based on lead ions, and nanogold particles functionalized by DNase 17E and nano gold particles modified by the substrate. Assembled into double-stranded aggregates, the solution is blue. When Pb^{2+} is present in the solution, the substrate is cut into two segments, then the hybridized double strands are decomposed again, and the solution turns red, indicating Pb^{2+} presence. The method achieves high sensitivity and selectivity with a detection limit of 500 nM. Since then, a series of studies have been carried out based on this principle.

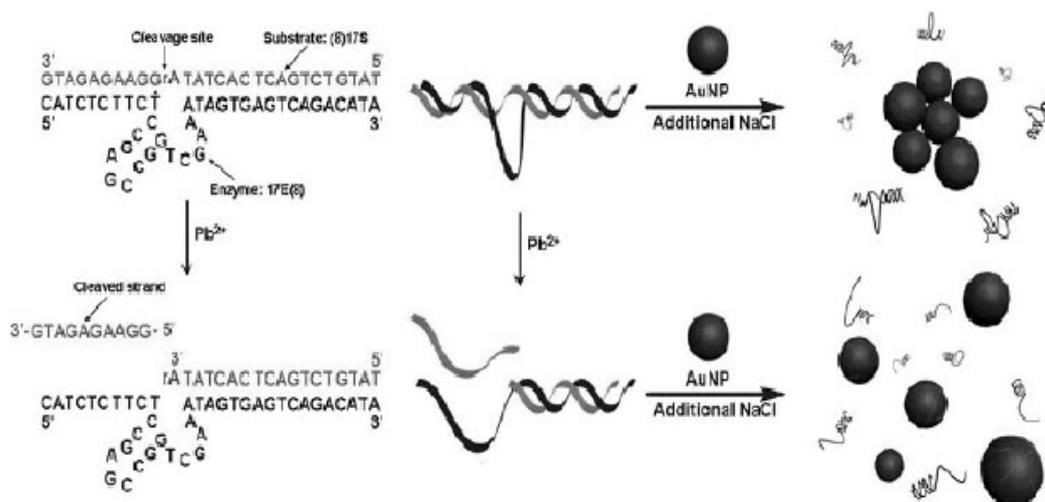


Fig. 1. The detection of Pb^{2+} ions using 8-17 DNAzyme.

In 2008, researcher Jiang Xingyu separately modified nano-gold particles with organic molecules containing alkyne and tri-nitrogen bonds, respectively. The monovalent Cu^+ can catalyze the reaction of carbon-carbon triple bonds and tri-nitrogen-containing bonds to aggregate gold nanoparticles. Thus, the color of the solution changes, indicating the presence of monovalent Cu^+ , and the reacted catalyst Cu^+ can be easily reduced by Cu^+ , and finally a Cu^{2+} detection system is detected, the detection limit is 50 μM , and the purpose of detecting Cu^{2+} is achieved, and Has very good selectivity. In 2009, J. S. Kim et al. used thiol erythritol as a functional reagent to prepare gold nanoprobe, and gold-based probes rich in carboxyl groups and sulfhydryl groups to detect Hg^{2+} , and obtained highly sensitive detection results. The above studies show that surface-functionalized gold nanoparticles can achieve rapid, real-time, on-site quantitative detection of heavy metal ions by colorimetry. Therefore, the colorimetric detection method using functionalized gold nanoparticles has unique advantages and broad advantages. Application prospects.

Lee's research group used the surface plasmon scattering properties of gold nanoparticles to assemble a 50 nm nano gold particle on a substrate, and designed a new method for selective plasmon resonance energy transfer with amino groups on the surface to detect Cu^{2+} . Probe. The light emitted by surface plasmon scattering is used to judge the detected concentration of Cu^{2+} . When the concentration of Cu^{2+} is high, the light emitted by the gold nanoprobe will be quenched. It can be clearly observed from the fluorescence imaging image that the method is also it is applied to detect Cu^{2+} in HeLa cells. The method has good selectivity and the lowest detection limit can reach 1nM.

Reynolds et al. used the gold nanoparticle colorimetric method to quantitatively detect calcium ions. First, lactose-stabilized gold nanoparticles are prepared, and then the target calcium ions are added, and the calcium ions can cause agglomeration of the gold nanoparticles. The concentration of calcium ions can be accurately determined by characterizing the degree of agglomeration of gold nanoparticles. Kim et al. established a sensor

using thiol undecanoic acid (MUA) modified gold nanoparticles as a colorimetric probe to measure lead, cadmium and mercury ions in water. Dang Yongqiang et al. used 5, 5-dimercapto (2-nitrobenzoic acid) modified gold nanoparticles to develop a colorimetric sensor that can detect chromium ions in water with high specificity. The detection limit of this method is as low as 93.6 ppb. And it can resist the interference of 15 kinds of ions such as zinc, lead and magnesium in water, and the selectivity and sensitivity meet the requirements.

E. Priyadarshini and N. Pradhan (2017) pointed out that gold nanoparticles play a key role in the development of high sensitive analytical GNP based bio-sensing tools with high surface to volume ratio and unique optical property. They reviewed the use of GNPs and its functionalization for colorimetric detection of metal ions and proved that colorimetric detection enables cost effective and simple monitoring of toxic ions accompanied with the advantages of on-site applicability, avoids complex instrumentation, ease of analysis and usage.

There are also many researchers who combine a variety of properties, based on precious metal nanoparticles to prepare colorimetric detection of heavy metal ion sensors. The sensor is further divided into heavy metal ions based on noble metal nanoparticle agglomeration colorimetric method and heavy metal ions based on anti-precious metal nanoparticle agglomeration colorimetric method.

1. Detection of Heavy Metal Ions based on Noble Metal Nanoparticle Agglomeration Colorimetry

The method utilizes heavy metal ions to specifically bind to groups modified on the surface of noble metal nanoparticles, resulting in agglomeration of noble metal nanoparticles, and the color of the system is changed due to the surface plasmon resonance absorption effect, thereby realizing the characterization of heavy metal ions., quantitative testing. Zhang et al. prepared α -alkyl acid (TGA) functionalized gold nanoparticles with cetyltrimethylammonium bromide as a protective agent. TGA can specifically bind to Co^{2+} , resulting in gold nanoparticles. Agglomeration, using Transmission Electron Microscope (TEM), X-ray energy spectrum (EDS) and ultraviolet-visible spectroscopy (UV-vis) to characterize the system. The detection of Co^{2+} is achieved with a detection limit as low as 3.0×10^{-7} M. Bhatt et al. synthesized pyrrole gold nanoparticles with pyrrole hexanoyl hydrazide as reducing agent and stabilizer. Many metal ions such as Pb^{2+} , Cd^{2+} , Mn^{2+} , Fe^{3+} , Ni^{2+} , Zn^{2+} , Hg^{2+} , Co^{2+} and Cu^{2+} are added to the gold sol, and only Co^{2+} can change the color of the sol from red to blue, achieving high sensitivity and high sensitivity to Co^{2+} . Selective detection. Jin et al. prepared 5-sulfosalicylic acid functionalized silver nanoparticles, which can specifically bind to Cd^{2+} , resulting in the agglomeration of silver nanoparticles and rapid detection of Cd^{2+} . Xu et al. prepared an organic-modified gold nanoparticle containing an alkyne and an azide group. The Cu^{2+} in the click chemistry can catalyze the azido-alkynyl Huisgen-Click cycloaddition reaction to agglomerate the gold nanoparticles. Specific detection of Cu^{2+} is achieved.

2. Detection of heavy Metal Ions based on Anti-precious metal Nanoparticle Agglomeration Colorimetry

The method utilizes specific binding of certain specific intermediate substances and groups modified by surface of precious metal nanoparticles, resulting in agglomeration of noble metal nanoparticles, and the color of the system changes due to surface plasmon resonance absorption effect, etc., when heavy metal ions exist. When heavy metal ions can compete with noble metal nanoparticles for intermediate substances, the noble metal nanoparticles are deagglomerated, and the color of the system changes accordingly, thereby realizing qualitative and quantitative detection of heavy metal ions. Duan et al. introduced a method for inhibiting the aggregation of

silver nanoparticles to detect Hg^{2+} . In the absence of Hg^{2+} , 6-thioguanine (an analogue of guanine) binds to the surface of the silver nanoparticles, causing the silver nanoparticles to agglomerate, the color of the solution shifting from yellow to brown, and the corresponding absorption spectrum is red-shifted. When Hg^{2+} is present, Hg^{2+} preferentially binds to 6-thioguanine, inhibiting the agglomeration of silver nanoparticles, thereby achieving detection of Hg^{2+} . Li uses gold citrate to reduce chloroauric acid to prepare gold nanoparticles. O-phenylenediamine and gold nanoparticles combine to make gold nanoparticles agglomerate. When Hg^{2+} is present, o-phenylenediamine preferentially binds to Hg^{2+} . The agglomeration of gold nanoparticles, combined with the color of the solution and the UV-visible absorption spectrum, enables the visual detection of Hg^{2+} . Hormozi-Nezhad et al. used D-penicillamine (D-PC) to induce gold nanoparticle agglomeration, while Cu^{2+} can chelate with D-PC, reducing the amount of D-PC bound to gold colloid, making gold sol from Blue changes to a red state, etc., to achieve detection of Cu^{2+} .

2.2 Fluorescent Nano Gold Particles for Detecting Metal Ions

Chang et al. used tetramethylphosphine chloride (THPC) as a reducing agent to prepare fluorinated gold clusters with different carbon chain length thiols or carboxylic acids as protective agents. Experiments were carried out with different carbon chain lengths of carboxylic acids or Thiol is used as a protective agent to prepare gold nanoclusters, and the fluorescent gold clusters obtained by protecting agents with different carbon chain lengths are compared. It is concluded that a longer carbon chain as a protective agent has a higher fluorescence intensity and a smaller six carbons. The protection of the chain length does not result in a fluorescent gold cluster. Nano-gold clusters protected by thiol-undecylcarboxylic acid (11-MUA) with a carboxyl group as a carboxyl group were also used as fluorescent detection probes for experimental studies on the detection of mercury ions in aqueous solution, 11-MUA-protected nano-gold clusters Mercury ion detection sensitivity is high but does not have high selectivity, but when 2,6-pyridinedicarboxylic acid is added, the ruthenium cooperation of the two carboxylic acids improves the selectivity of the detection probe sensitivity. The limit can reach 5 nM.

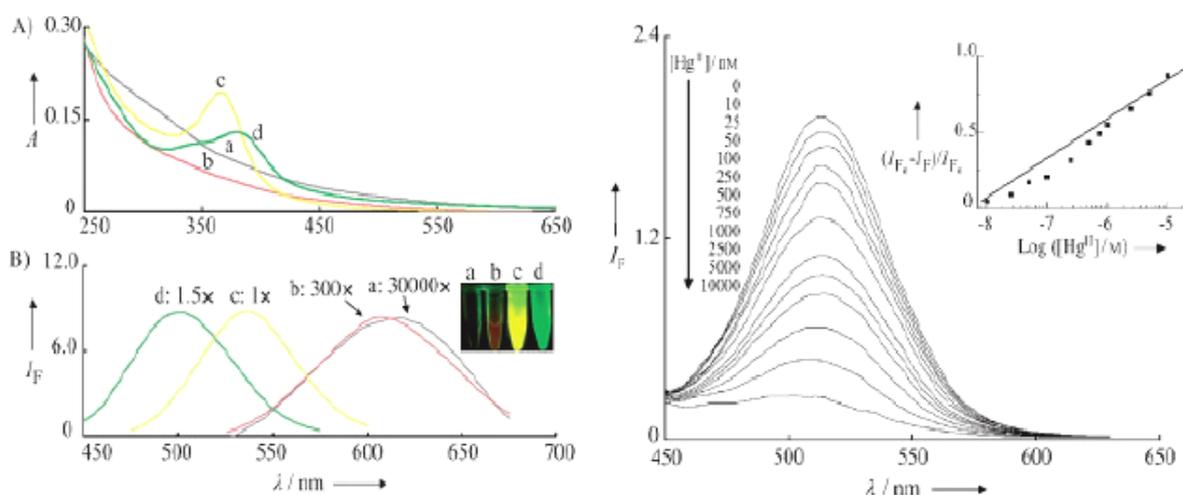


Fig. 2. A) UV/Vis absorbance spectra and B) normalized fluorescence spectra of Au NPs (a), 2-ME-Au NPs (b), 6-MH-Au NPs (c), and 11-MU-Au NPs (d). Inset to (B): photograph of the fluorescence of the various Au NPs upon excitation under a hand-held UV lamp (365 nm). The normalized fluorescence intensities (I_F) are plotted in arbitrary units; excitation wavelength: 365 nm. The concentration ratio of the Au NPs, 2-ME-Au NPs, 6-MH-Au NPs, and 11-MU-Au NPs was 30000:300:1:1.5 in (B).

Hai Chen, Kai Zhou, Guanghua, Zhao (2018) thought that gold nanoparticles exhibit distinguishable optical characteristic in different aggregated states and thus have been developed into simple colorimetric sensors for the

quick detection of chemical contaminants in food samples, and have great potential to be applied as power sensing tools for food safety screening.

2.3 Raman Spectroscopy for Detection of Heavy Metal Ions

Toma et al. used TMT (2, 4, 6-trimercapto-1, 3, 5-triazine) functionalized gold nanoparticles to detect Hg^{2+} and Cd^{2+} . TMT contains three sulfhydryl groups (-SH), in addition to coordination with gold nanoparticles. It can also be used as a detection element to coordinate with Hg^{2+} and Cd^{2+} . Therefore, a more stable structure can be formed, which can be detected by Raman spectroscopy, and can reach 2×10^{-7} - 2×10^{-6} mol L⁻¹ for Hg^{2+} , and can be used for Cd^{2+} for Hg^{2+} . It reaches 2.5×10^{-7} - 3×10^{-6} mol L⁻¹. A new method for detecting heavy metal ions was developed by Raman spectroscopy for the detection of heavy metal ions.

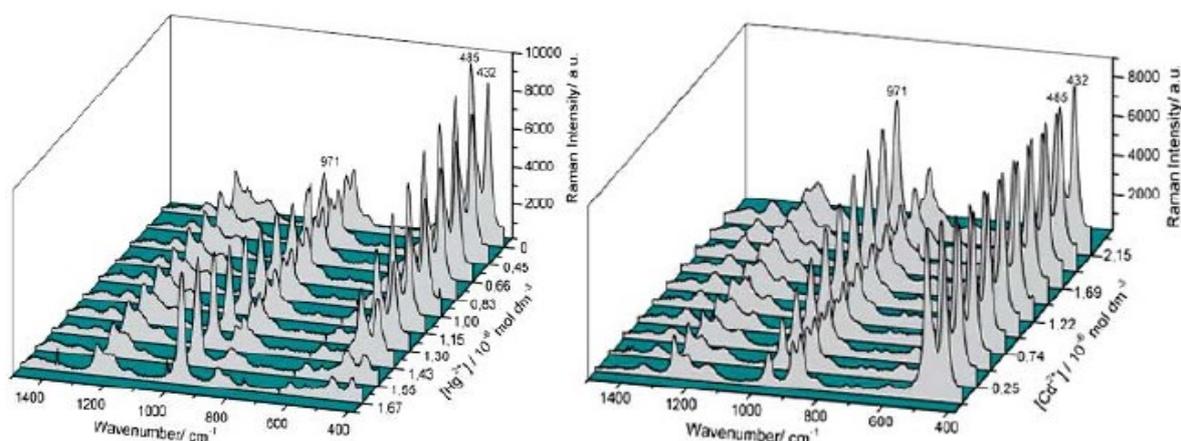


Fig. 3. SERS spectral profiles for a TMT-AuNP aqueous suspension, recorded at several concentrations of Hg^{2+} ions (left). SERS spectral profiles for a TMT-AuNP solution, recorded at several concentrations of Cd^{2+} ions (right).

In 2007, Nie Shuming's research group reported the use of non-toxic, biocompatible polyethylene glycol surface modified nano gold particles for the detection and localization of tumor cells by surface-enhanced Raman scattering SERS. The detection of tumor cells by Raman spectroscopy was carried out in vivo in mice, and large-scale optical enhancement was used to accurately detect tumors in living animals. Tumor cells co-localized with nanoparticles are localized, such as single-stranded variable fragment (antibody) antibodies, and conjugated nanoparticles can be used as tumor markers for epidermal growth factor receptors to achieve human cancer cells and xenograft models.

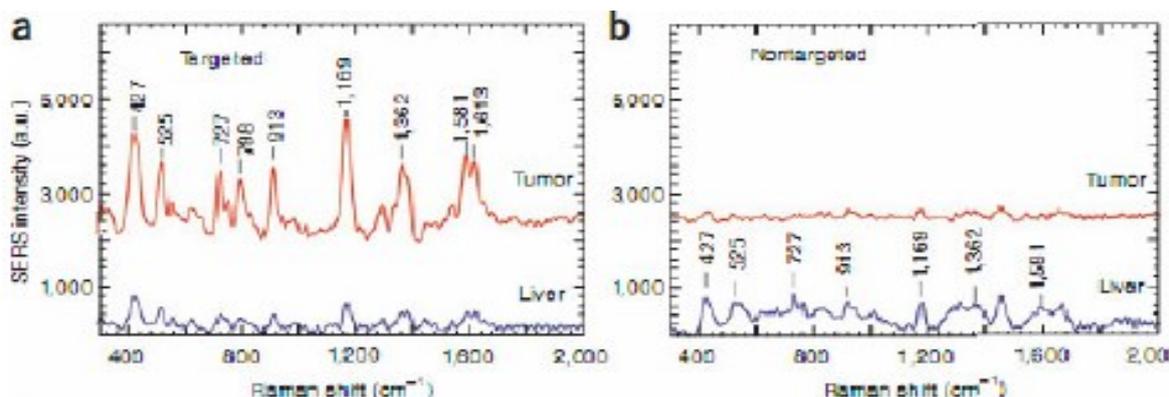


Fig. 4. In vivo cancer targeting and surface enhanced Raman detection by using ScFv antibody conjugated gold nanoparticles that recognize the tumor biomarker EGFR. (a, b) SERS spectra obtained from the tumor and the liver locations by using targeted (a) and nontargeted (b) nanoparticles.

Metallic nanoparticles have been used with good results in separation techniques, electrochemical methods, and optical analytical methods (Berlina et al. 2015); Bittar et al. 2017). Surface plasmon resonance, a characteristic of silver nanoparticles, is a fundamental feature for many analytical applications following a signal change based on ultraviolet visible spectroscopy (Oliveira et al. 2015). Spectral modifications induced by the nanoparticles formed in solution are influenced by their size and shape but also by the dielectric constant of the environment where the particles are generated (Lance et al. 2003). Changes due to nanoparticle shape and size, and to dielectric constant of the environment lead to a large number of peaks, which are, finally, summarized in absorption bands characteristic for plasmonic response of nanoparticles (Oliveira et al. 2015). Functionalized silver nanoparticles may be considered as candidates for developing good sensing response in the ultraviolet-visible range.

3. *Application of Aptamer Functionalized Gold Nanoparticle Colorimetry*

Gold nanoparticles have special optical and physical properties, and can be uniquely functionalized by adsorption and binding with different molecules, or the aggregation state can be changed to change the color and absorption spectrum of the system. The method of optical detection using this effect of gold nanoparticles is called gold nanoparticle colorimetry. As a promising optical detection technology, gold nanoparticle colorimetry has the advantages of simple and easy principle, low experimental cost, easy preparation of raw materials, short experimental period and easy observation of experimental results (Hepel M, Coopersmith K. 2012). The aggregation state of the gold nanoparticles is affected by the intermolecular attraction and repulsive force, thereby exhibiting a state of aggregation or uniform dispersion. Therefore, when the object to be tested is capable of destroying the mutual repulsion or agglomeration between the gold nanoparticles, causing aggregation or dispersion of the gold nanoparticles, resulting in changes in color and spectrum, the target can be compared. Color detection (Hoyos, et al. 2018). When the gold nanoparticle colorimetric method detects the target, it is not only easy to operate, but also the detection result can be determined only by the change of the absorption peak or the change of the color of the system, and is very suitable for the non-professional on-site rapid detection of a specific substance. At present, gold nanoparticles have been widely used as colorimetric probes.

After modification by different reactive groups, gold nanoparticles can be charged with different charges, which are divided into positively charged gold nanoparticles and negatively charged gold nanoparticles. The mercaptoethylamine-modified gold nanoparticles are positively charged and can bind to the negatively charged nucleic acid aptamers due to electrostatic adsorption. The commonly used negatively charged gold nanoparticles are modified by citrate, which is prone to agglomeration in a certain concentration of salt solution, resulting in a change in the color of the system (Ah C S, Kim W J, Wan S Y, et al. 2013). Based on the above principles, common gold nanoparticle nucleic acid aptamer sensors are classified into the following two types:

The first is the application of nucleic acid aptamer colorimetry based on positively charged gold nanoparticles. The mercaptoethylamine-modified gold nanoparticles are positively charged, and the nucleic acid aptamers are electrostatically adsorbed by the negatively charged phosphate groups, causing agglomeration of the gold nanoparticles, and the gold nanoparticles are blue-violet; after adding the target the nucleic acid aptamer specifically binds to the target, releasing gold nanoparticles, and the color of the system will change from blue-violet to burgundy, and the ultraviolet absorption spectrum also changes accordingly. Using this principle, many gold nanoparticle colorimetric methods have been successful in detecting targets.

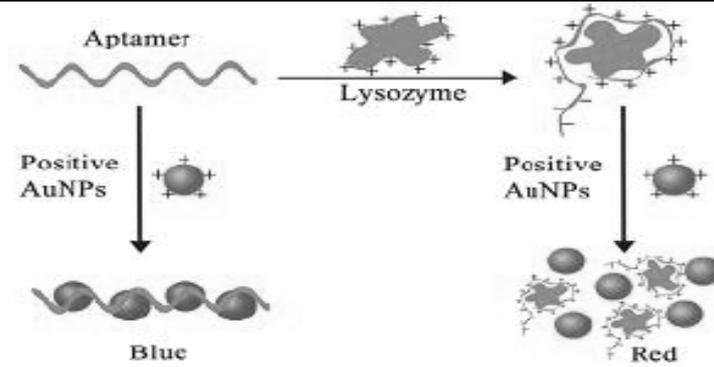


Fig. 5. Scheme of the visual detection of lysozyme based on colorimetric aptasensor.

The second is the application of nucleic acid aptamer colorimetric method based on negative gold nanoparticles. The colorimetric sensor established by negatively charged gold nanoparticles and nucleic acid aptamers is mainly based on the following principle: when the nucleic acid aptamer is adsorbed on the surface of the negatively charged gold nanoparticles, the anti-agglomeration effect of the gold nanoparticles in the salt solution is caused, that is, Adsorption of the nucleic acid aptamer on the surface inhibits the salt effect of the gold nanoparticles. At this time, if the target of the nucleic acid aptamer is added to the system, the configuration of the nucleic acid aptamer in combination with the target changes, and generally changes from a randomly distributed free-stretching structure to a hairpin structure, a neck ring structure, or a G-four. The polymer structure, which has less active groups exposed, so it is difficult to adsorb on the surface of the gold nanoparticles. The gold nanoparticles lose the protection of the surface nucleic acid chain, and agglomeration occurs in the salt solution. The color of the system changes from wine red. In blue and purple. Based on the above principles, many gold nanoparticle nucleic acid aptamer colorimetric methods were established.

Wei et al., based on thrombin, established a nanoparticle colorimetric method based on the above principle to detect proteins. As shown in the schematic diagram of 1.2: When a nucleic acid aptamer of thrombin is added to the gold nanoparticle solution, the nucleic acid aptamer binds to the surface of the gold nanoparticle and inhibits the agglomeration of the nanoparticles caused by the sodium chloride solution, so the gold nanoparticle remains The distribution is evenly distributed, and the system presents wine red. When the target thrombin is present, the nucleic acid aptamer decouples from the surface of the gold nanoparticle and binds to thrombin, and the spatial structure becomes a G-tetramer configuration, which is difficult to adsorb. On the surface of gold nanoparticles, gold nanoparticles lost the protective effect of nucleic acid aptamers, and agglomeration occurred under the action of sodium chloride. The color of the system changed from wine red to blue purple.

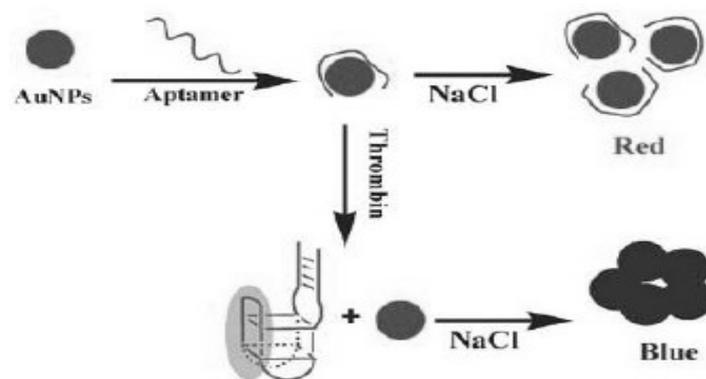


Fig. 6. Scheme of Au NPs colorimetric aptasensor strategy for thrombin detection.

In the research of aptamer functionalized gold nanoparticles for the detection of heavy metal ions, DaidiTan, YueHe et al. (2013) proposed a method for the detection of Hg^{2+} using Hg^{2+} specific DNA (MSD) functionalized gold nanoparticles (AuNPs) based on the formation of T– Hg^{2+} –T complex and the excellent quenching fluorescence property of AuNPs. Hg^{2+} detection can be easily realized by monitoring the change of fluorescence signal of AuNPs–MSD probes. Hg^{2+} can be detected in a range of 0.02–1.0 μM with a detection limit of 16 nM. In terms of sensing events, nano-materials have emerged as one of the most promising candidate to revolutionize conventional analytic methods, resulting in new generation of analytic tools (Behpour, Ghoreishi, Honarmand, & Salavati-Niasari, 2011; Motaghedifard, Ghoreishi, Behpour, Moghadam, & Salavati-Niasari, 2012). These minuscule nano-materials conform to the development tendency of modern analysis as compared to the conventionally approaches by favoring feasible on-site analysis, without the need of any inert gas and high voltage inputs (Priyadarshini & Pradhan, 2017). Elisabete Oliveira, Cristina Nunez et al. (2015) pointed out that as hybrid materials combining large surfaces with important optic and electronic properties demonstrate to be highly sensitive to the presence of metal ions in their surroundings. Gold, silver and alloys nanoparticles as fluorescent and/or colorimetric systems for detection of metals have wide applications in the presence of heavy and toxic metal ions in their review paper.

II. CONCLUSIONS

In summary, gold nanoparticles have strong surface plasmon resonance fluorescence and surface-enhanced Raman properties due to their excellent properties. These properties make gold and silver nanoparticles in biomarkers, molecular recognition, bioassays, and molecular devices, medical diagnosis and treatment, biochip pharmaceutical, drug delivery, infrared hyperthermia and other aspects have a wide range of applications. The preparation of various types of gold nanoparticles, their size, shape and structure control, and the corresponding physical properties have always been at the forefront of materials science and related fields. The surface functionalization of gold nanoparticles and its application in biological detection, recognition and labeling have always been hot topics in analytical science research. It has great application prospects in photoelectron, biomolecule detection, heavy metal ion detection and nano biomedicine.

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