CHEMICAL REVIEWS

Review

pubs.acs.org/CR

Gold Nanoparticles in Chemical and Biological Sensing

Krishnendu Saha, Sarit S. Agasti, Chaekyu Kim, Xiaoning Li, and Vincent M. Rotello*

Department of Chemistry, University of Massachusetts, 710 North Pleasant Street, Amherst, Massachusetts 01003, United States

CONTENTS

1. INTRODUCTION

Detection of chemical and biological agents plays a fundamental role in biomedical, forensic and environmental sciences[1−4] as well as in anti bioterrorism applications.[5−7] The development of highly sensitive, cost-effective, miniature sensors requires advanced technology coupled with fundamental knowledge in chemistry, biology, and material sciences.[8−13] In general, sensors feature two functional components: a recognition element to provide selective/specific binding with the target analytes and a transducer component for signaling the binding event. An efficient sensor relies heavily on these two components for the recognition process in terms of response time, signal-to-noise (S/N) ratio, selectivity, and

Received: April 11, 2011
Published: February 2, 2012

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739–2779

limits of detection (LOD).[14,15] Therefore, designing sensors with higher efficacy depends on the development of novel materials to improve both the recognition and transduction processes. Nanomaterials feature unique physicochemical properties that can be of great utility in creating new recognition and transduction processes for chemical and biological sensors,[15−27] as well as improving the S/N ratio by miniaturization of the sensor elements.[28]

Gold nanoparticles (AuNPs) possess distinct physical and chemical attributes that make them excellent scaffolds for the fabrication of novel chemical and biological sensors (Figure 1).[29−37] First, AuNPs can be synthesized in a straightforward

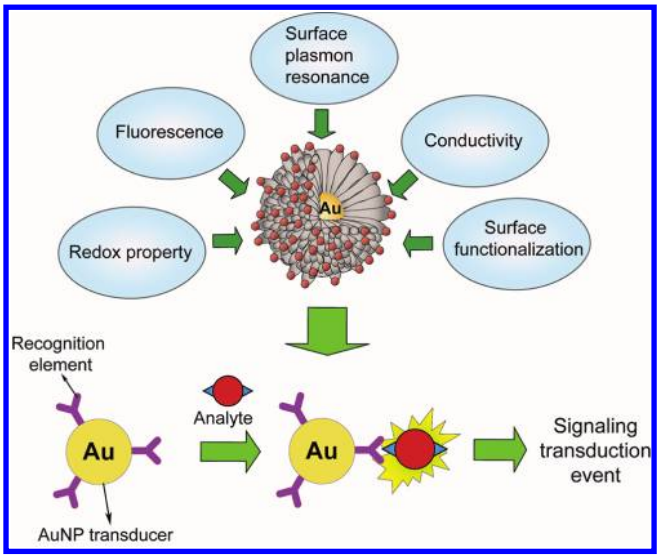

Figure 1. Physical properties of AuNPs and schematic illustration of a AuNP-based detection system.

manner and can be made highly stable. Second, they possess unique optoelectronic properties. Third, they provide high surface-to-volume ratio with excellent biocompatibility using appropriate ligands.[30] Fourth, these properties of AuNPs can be readily tuned by varying their size, shape, and the surrounding chemical environment. For example, the binding event between the recognition element and the analyte can alter physicochemical properties of transducer AuNPs, such as plasmon resonance absorption, conductivity, redox behavior, etc., that in turn can generate a detectable response signal. Finally, AuNPs offer a suitable platform for multifunctionalization with a wide range of organic or biological ligands for the selective binding and detection of small molecules and biological targets.[30−32,36] Each of these attributes of AuNPs has allowed researchers to develop novel sensing strategies with improved sensitivity, stability and selectivity. In the past decade of research, the advent of AuNP as a sensory element provided us a broad spectrum of innovative approaches for the detection of metal ions, small molecules, proteins, nucleic acids, malignant cells, etc., in a rapid and efficient manner.[38]

In this current review, we will highlight the several synthetic routes and properties of AuNPs that make them excellent probes for different sensing strategies. Furthermore, we will discuss various sensing strategies and major advances in the last two decades of research utilizing AuNPs in the detection of variety of target analytes including metal ions, organic molecules, proteins, nucleic acids, and microorganisms.

2. SYNTHESIS AND SURFACE FUNCTIONALIZATION

Numerous preparative methods for AuNPs have been reported, including both "top-down" (physical manipulation) and "bottom-up" (chemical transformation) approaches.[30] During the last two decades, considerable effort has been devoted to synthesis of AuNPs, focusing on control over their size, shape, solubility, stability, and functionality. It is worth noting that the term colloid and cluster are frequently used interchangeably; the former generally refers to particles having diameters more than 10 nm, while the latter commonly refers to smaller particles.

2.1. Citrate and Related Particle Preparation Methods

The scientific synthesis of colloidal gold can be traced back to Michael Faraday's work in 1857, in which the gold hydrosols were prepared by reduction of an aqueous solution of chloroaurate with phosphorus dissolved in carbon disulfide.[39] Later in 1951, Turkevich developed one of the most popular approaches for the synthesis of AuNPs, using citrate reduction of $HAuCl_4$ in water.[40] In this method, citric acid acts as both reducing and stabilizing agent and provides AuNPs with diameters of 20 nm. Further studies by G. Frens enabled control over AuNPs size by varying the feed ratio of gold salt to sodium citrate.[41] The kinetics of the Turkevich process was provided by Chow and Zukoski.[42] Detailed studies and evolution of the Turkevich reaction have been reported and employed in numerous applications.[43−49]

2.2. The Brust−Schiffrin Method for Thiol-protected AuNPs

After Mulvaney's initial attempt of stabilizing AuNPs with alkanethiols,[50] a significant breakthrough in the field of AuNP synthesis was achieved by Brust and Schiffrin in 1994. They reported a two-phase synthetic strategy, (the Brust−Schiffrin method), utilizing strong thiol−gold interactions to protect AuNPs with thiol ligands (Figure 2). In this method, $AuCl_4^-$ is

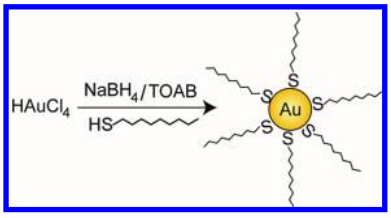

Figure 2. Brust−Schiffrin method for two-phase synthesis of AuNPs by reduction of gold salts in presence of external thiol ligands.

transferred from aqueous phase to toluene using the surfactant tetraoctylammonium bromide (TOAB) and reduced by sodium borohydride ($NaBH_4$) in presence of dodecanethiol.[51] On addition of $NaBH_4$, a quick color change from orange to deep brown takes place in organic phase. The AuNPs are generated in toluene with controlled diameters in the range 1.5−5 nm. These thiol-protected AuNPs feature superior stability because of the strong thiol−gold interaction and they can be easily handled, characterized, and functionalized. The nanoparticles can be thoroughly dried and then redispersed in organic solvents without any aggregation or decomposition. Various reaction conditions, such as gold/thiol ratio, temperature, and reduction rate, can be used to tune the particle size.[52] Immediate quenching after reduction or use of sterically bulky ligands gives a higher portion of small core NPs (≤2 nm).[53−57] With the translation of this synthesis into single-phase system,[58−60] many modifications have been reported to

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

obtain functional thiols-stabilized AuNPs. Isolable, water-soluble gold clusters protected by monolayers of tiopronin have been generated with an average core size of 1.8 nm.[61] Arenethiol ligands generate relatively larger and thermally less stable AuNPs than the alkanethiol protected clusters.[54] All-aromatic monolayer-protected clusters with potential value for enhanced rates of electron transfer can be synthesized by differential extraction of the polyanionic products using benzenethiolates.[62] Alkylthiosulfates (Bunte salts) can be used as ligand precursors to synthesize thiol-stabilized AuNPs[63] and water-soluble AuNPs at a larger size as well.[64,65] AuNPs of mixed monolayer[66,67] and single-component monolayer[68] of thymine moieties have been prepared for assembly studies via molecular recognition. A recent study on the identification and quantification of the precursor species in the Brust-Schiffrin method was also reported.[69] Superhydride,[70] hexadecylaniline (inter alia),[71] organometallic reagents (2-propylmagnesium bromide),[72] 9-borabicyclo[3.3.1]nonane (9-BBN),[73] and glutathione[74] have been used as alternative reagents to $NaBH_4$ for the reduction of Au (III) in synthesis of thiol-protected AuNPs.

2.3. Place Exchange Method to form Mixed Monolayer AuNPs

Place exchange, that is, substitution of thiol ligands by different thiols was reported by Murray et al.[55,75,76] This versatile technique introduces chemical functionality onto the AuNPs monolayer in a divergent fashion. In this method, the initially anchored thiol ligands are exchanged in by free thiol ligands (Figure 3, top). The reaction time and the feed ratio of the

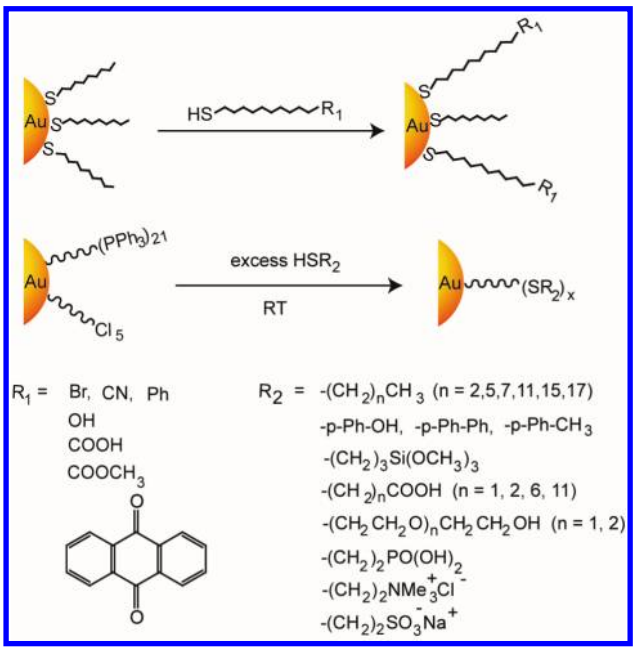

Figure 3. General scheme for place exchange reaction for alkanethiol-protected AuNPs using functionalized thiols, giving examples of particles that can be rapidly generated.

functional ligands control the loading efficiency onto AuNPs surface. Moreover, introducing two or more functional ligands during the place exchange reaction can provide mixed monolayer protected AuNPs for synergistic applications. The ligands on the AuNPs surface also interact with each other (leading to a rigid monolayer)[77] and show a certain level of intramonolayer mobility providing optimization of the interaction with the analytes.[78] Under appropriate conditions, ligands can also slowly hop between NPs.[79] However, recent EPR studies from Chechik group has demonstrated that the mobility of the ligand on AuNP surface is restricted to several factors including organic monolayer packing[80] and temperature.[81] Place exchange is efficient for ultrasmall 1.1 nm diameter phenylethanethiolate-stabilized AuNPs.[82,83] Therefore, a range of functional groups can be employed in the synthesis of AuNPs by the use of functionalized thiols to place exchange with phosphine stabilized nanoparticles (Figure 3, bottom).[84,85]

2.4. Physical Methods for Particle Modification

Physical methods enable further manipulation of the structure and hence properties of AuNPs. Thermolysis,[86,87] digestive ripening,[88,89] and conventional ripening[90,91] have significantly reduced average particle size and polydispersity and triggered formation of superlattices in 2D and 3D. UV and laser irradiation are other parameters that can modify particle structure.[92−97] Ultrasonic fields provide an approach to control the reduction rate of $AuCl_4^-$ in aqueous solutions and therefore affect core sizes with the intensity of the ultrasound and the reactor position.[98−103] Control of the particle size can also be provided by radiolysis.[104−106] Once formed, size-exclusion chromatography can separate suspended AuNPs by shape and size.[107]

2.5. Polymer-Stabilized AuNPs

Polymer-stabilized AuNPs were first reported by Helcher in 1718, though the characterization was rather limited.[108] Polymers commonly used for stabilization include poly(*N*-vinylpyrrolidone) (PVP),[109−111] poly(ethylene glycol) (PEG),[112−115] poly(4-vinylpyridine),[116−118] poly(vinyl alcohol) (PVA),[119] poly(vinyl methyl ether) (PVME),[120] chitosan,[121] polyethyleneimine (PEI),[122] poly(diallyl dimethylammonium chloride) (PDDA),[123] poly(methyl methacrylate) (PMMA),[124,125] polystyrene-block polymers,[126,127] poly(dG)-poly(dC),[128] and poly(*N*-isopropylacrylamide) (PNIPam).[129,130]

There are four strategies widely used for creating polymer-functionalized nanoparticles. (1) The "grafting from" approach consists of polymer chain growth from small initiators attached to AuNPs.[131−134] This technique provides a very dense polymer brush. Frequently used methods include living radical polymerization (LRP)[124] and surface-initiated atom-transfer radical polymerization (SI-ATRP).[116,135] (2) "Grafting to" enables one-pot synthesis of AuNPs stabilized by sulfur-containing polymers,[136−142] and generally produces a sparser coverage.[137] (3) Physisorption using block copolymer micelles (nanoreactors), water-soluble polymers, or star block copolymers.[143−149] (4) "Post-modification of pre-formed AuNPs". In this method, AuNPs are generated in the first stage through conventional methods such as Brust−Schiffrin method, followed by the exchange or modification with polymers.[150,151]

2.6. Other Capping Ligands

While most AuNP functionalization has been done using thiol/thiolated ligands, a variety of other ligands have been used to passivate and functionalize AuNPs. Other sulfur-containing ligands include disulfides,[152−159] multivalent (and hence more stable) di-[160] and trithiols,[161,162] thioethers,[163,164] xanthates,[165] and resorcinarene tetrathiols.[166] Iodine can be used to oxidize and decompose these thiol-stabilized AuNPs.[167] Amine-capped AuNPs were reported using primary amines.[168] Self-assembled

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

gold(I) amine precursors including [AuCl(NH_2R)] (R = C_8H_{17}, $C_{12}H_{25}$, and $C_{16}H_{33}$) yield AuNPs upon decomposition through air exposure or in tetrahydrofuran (THF).[169,170] Laurylamine (LAM) or octadecylamine (ODA) has been used to generate monodispersed particles.[171] Oleyl amine (OLA),[172] aromatic amines,[173] amino acids,[174−178] diamines,[179] tetraoctylammonium,[180] porphyrins,[181] and hyperbranched polyethylenimine[182] have been used as reducing/capping agents in synthesis of AuNPs, while a direct one-pot synthesis of amine-stabilized AuNPs using 3-(trimethoxysilylpropyl)-diethylenetriamine has been reported.[183] The controlled synthesis of AuNPs in quaternary ammonium ionic liquids by simple heating has been developed recently,[184] and piperazine derivatives have been used as reducing/capping agents.[185] Tri-*n*-octylphosphine oxide (TOPO) has been used in the presence of stabilizer octadecylamine.[186,187] Studies using phosphine,[188,189] carboxylate ligands,[190−193] lactic acid,[194] and hydroquinone[195] as stabilizing ligands have also been documented.

3. PHYSICAL PROPERTIES

3.1. Size-Dependent Electronic and Optoelectronic Properties

AuNPs possess quantum size effect that leads to discrete electron transition energy levels. For example, hexanethiol-functionalized AuNPs (Au_{147}, d = 1.62 nm) display 15 redox states at room temperature,[196] demonstrating that AuNPs can possess molecule-like redox properties.[197] Moreover, the quantized capacitance charging behavior of AuNPs can be tuned by external ligands, magnetic fields and electrolyte ions, leading to potential applications in electronic devices and electrochemical labels.[198,199]

In addition to their redox activity, AuNPs feature surface plasmon resonance (SPR).[200] The SPR is the result from the collective oscillation of the conduction electrons across the nanoparticle (diameter $d \ll \lambda$, where λ is the wavelength of the light) because of the resonant excitation by the incoming photons. In 1908, Mie first elucidated the origin of this phenomenon by solving Maxwell's electromagnetic equation for small homogeneous spherical particles interacting with an electromagnetic field.[201] For AuNPs, the resonance condition is satisfied at visible wavelengths, therefore attributing for its intense color.[202−204] The SPR is influenced not only by size but also by solvent, ligand, interparticle distance, and temperature. Murray and co-workers have observed spectral shift induced by solvent refractive index changes that are consistent with Mie theory.[205] The core charge, as mentioned above, is influential in determining surface plasmon band (SPB) energy causing shifts to higher energy with excess electronic charge and to a lower one with electron deficiency.[205−208] SPR is also influenced by electronic dephasing[209,210] and it has been proposed that only electron−electron interactions are involved in this process rather than electron−phonon coupling.[211] However, experimental data from femtosecond light scattering confirmed the occurrence of both processes in the individual AuNPs.[212] Furthermore, the SPR frequency is sensitive to the proximity of other nanoparticles. Therefore, the aggregation of nanoparticles results in significant red-shifting (from ~520 to ~650 nm) and broadening in the SPB, changing the solution color from red to blue due to the interparticle plasmon coupling.[213,214] This phenomenon has made AuNPs an attractive candidate for colorimetric sensors (vide infra).

The size dispersity of AuNPs from batch to batch makes it difficult to obtain an accurate estimation of its concentration. El Sayed et al. have reported a theoretical calculation of the extinction coefficient of AuNPs of different size, shape, and composition.[200] For instance, molar extinction coefficient (ε) of AuNPs with a diameter of 40 nm is 7.66×10^9 M^{-1} cm^{-1} at 528 nm, substantially higher than common organic dyes, such as rhodamine-6G ($\varepsilon = 1.16 \times 10^5$ M^{-1} cm^{-1} at 530 nm) and malachite green ($\varepsilon = 1.49 \times 10^5$ M^{-1} cm^{-1} at 617 nm).[215] Later the size and concentration of AuNPs were also determined from its UV−vis spectra/extinction spectra both theoretically and experimentally.[216,217] Likewise, the extinction coefficients of AuNPs with different stabilizing ligands have also been reported.[218]

3.2. Fluorescence Quenching

Early fluorescence studies on AuNPs focused on fluorescent ligands, such as pyrenyl,[219] polyoctylthiophenyl,[220] fluorenyl,[221] and other probes.[222−225] Photoluminescence was reported later for both dendrimer-encapsulated,[226,227] and polymer stabilized AuNPs.[228] These nanoclusters have shown size-tunable emission maxima, which shifts to higher wavelengths with increasing size. However, Lee et al. later reported strong blue photoluminescence from neutral PAMAM dendrimers in the absence of AuNPs, which made the initial findings controversial.[229] Recently, Orrit group have reported a combined technique using atomic force microscopy, absorption (photothermal), and fluorescence microscopy for the detection of AuNPs of various core sizes, from 5 to 80 nm. By correlating the height of the surface-immobilized AuNPs measured with atomic force microscopy with the absorption and fluorescence signals from the same individual NPs, they were able to compare and measure the fluorescence quantum yield at single particle level.[230] AuNPs also show enhancement in fluorescence at appropriate fluorophore-to-metal distances on solid substrates.[231] It is believed that this phenomenon is due to the reflected far-field radiation from the fluorophore back onto itself.

Fluorescence quenching is a commonly observed consequence when fluorophores are appended onto AuNPs. The resonant energy transfer has led to applications in biophotonics[232] and materials science.[233−235] This quenching occurs when the emission spectrum overlaps with the gold surface plasmon band.[236−238] Both radiative and nonradiative rates are particle dependent, with higher efficiencies of quenching occurring with small nanoparticles.[239−242] A long-range molecular ruler, termed as nanosurface energy transfer (NSET), was demonstrated for breaking the "FRET barrier".[243] NSET is similar to FRET but is capable of measuring nearly 2-fold greater distances, making nanoparticles smaller than 2 nm of particular interest in bionanotechnology.[244,245] Another process that quenches fluorophores is photoinduced electron transfer (PET) to nanoparticles that can be modulated by charging/discharging the gold core.[246,247]

4. COLORIMETRIC SENSING

The aggregation of AuNPs of appropriate sizes (d > 3.5 nm) induces interparticle surface plasmon coupling, resulting in a visible color change from red to blue at nanomolar concentrations.[214] The color change during AuNP aggregation (or redispersion of an aggregate) provides a practical platform for absorption-based colorimetric sensing of any target analyte

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

that directly or indirectly triggers the AuNP aggregation or redispersion.[16,248,249]

4.1. Detection of Metal Ions

4.1.1. Alkali and Alkaline Earth Metal Ions. AuNP-based colorimetric sensing for metal ions generally requires the incorporation of chelating agents onto the nanoparticle surface. The presence of analyte ion induces the nanoparticle aggregation by forming multidentate interparticle complexes with the chelating ligand (Figure 4). For example, AuNPs

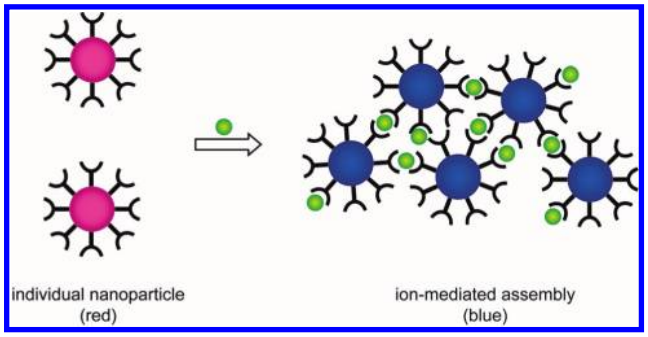

Figure 4. Schematic depiction of red-to-blue color colorimetric sensing of metal ions using AuNPs functionalized with chelating ligands.

carrying 15-crown-5 moieties have been fabricated for the colorimetric detection of potassium ions (K^+) via formation of a 2:1 sandwich complex between 15-crown-5 moiety and K^+.[250] Most attractively, this sensor system showed micromolar recognition and colorimetric response toward K^+ even in the presence of physiologically important cations, such as Li^+, Cs^+, NH_4^+, Mg^{2+}, Ca^{2+}, and excess Na^+. Later the performance of this sensor system was improved by bifunctionalizing the AuNPs with thioctic acid and crown thiols.[251] The increased rate of K^+ recognition from this system has been attributed to a cooperative effect that allows crown moiety to be preorganized by the negatively charged carboxylate moiety of the thioctic acid for K^+ recognition. Utilizing this principle the analogous detection of Na^+ in urine has been achieved by incorporating 12-crown-4 onto the AuNP surface together with the thioctic acid.[251] In a similar fashion Li^+ has been detected by utilizing phenanthroline-functionalized 4 nm AuNPs,[252] and lactose-functionalized 16 nm AuNPs have been used to detect Ca^{2+}[253] through metal ion-mediated carbohydrate−carbohydrate interactions.

4.1.2. Heavy Metal Ions. Heavy metal ions such as Pb^{2+}, Cd^{2+}, and Hg^{2+} pose significant public health hazards. Hupp et al. have reported a simple colorimetric technique for the sensing of aqueous heavy metal ions utilizing 11-mercaptoundecanoic acid (MUA)-functionalized 13 nm AuNPs.[254] The color change (red to blue) is driven by a heavy-metal ion chelation process where the surface carboxylates act as metal ion receptors. Colorimetric response was observed from Pb^{2+}, Cd^{2+}, and Hg^{2+} ($\geq$400 μM), whereas Zn^{2+} displayed no response to this assay process. The ion driven aggregation process was also detected using the enhanced hyper-Rayleigh scattering (HRS) response from the nanoparticle aggregates, leading to a more sensitive (25 μM) detection of Pb^{2+} ion. Chang and co-workers have significantly improved the selectivity and sensitivity of this system by fine-tuning of the buffer composition and monolayer structure,[255] achieving 100 nM sensitivity. A colorimetric sensor for Pb^{2+} was developed by Chen and co-workers that utilized mixed monolayer-protected AuNPs carrying both carboxylate and 15-crown-5 functionalities.[256] In this system, initial aggregates of AuNPs were formed due to hydrogen bonding interactions between carboxylic acid residues in a methanol/water solvent system. Addition of Pb^{2+} disrupts the hydrogen-bonded assembly by associating with crown ether moiety and generating an electrostatic repulsion between the AuNPs, resulting in a blue-to-red color change. This system showed high sensitivity and selectivity over other metal ions including Cd^{2+} and Hg^{2+}. Colorimetric detection of Cu^{2+} and Hg^{2+} has been achieved using AuNPs decorated with cysteine and peptide functionality.[257,258] Quaternary ammonium-functionalized AuNPs have been utilized by Liu et al. to devise a simple colorimetric sensor for Hg^{2+} at room temperature with the abstraction of AuNP stabilizing thiols by Hg^{2+} inducing aggregation.[259] Mirkin and co-workers have employed DNA-functionalized AuNPs for the selective and sensitive detection of Hg^{2+}.[260] This thiolated-DNA based detection system relies on the thymidine-Hg^{2+}-thymidine coordination chemistry and the melting temperature (T_m) of the nanoparticle aggregates. For the assay, AuNPs were functionalized with two different thiolated-DNA sequences (designated as probe **1** and probe **2** in Figure 5). When mixed together, probe **1** and probe **2** formed aggregates with lower T_m because of T−T mismatches in their base sequence. Presence

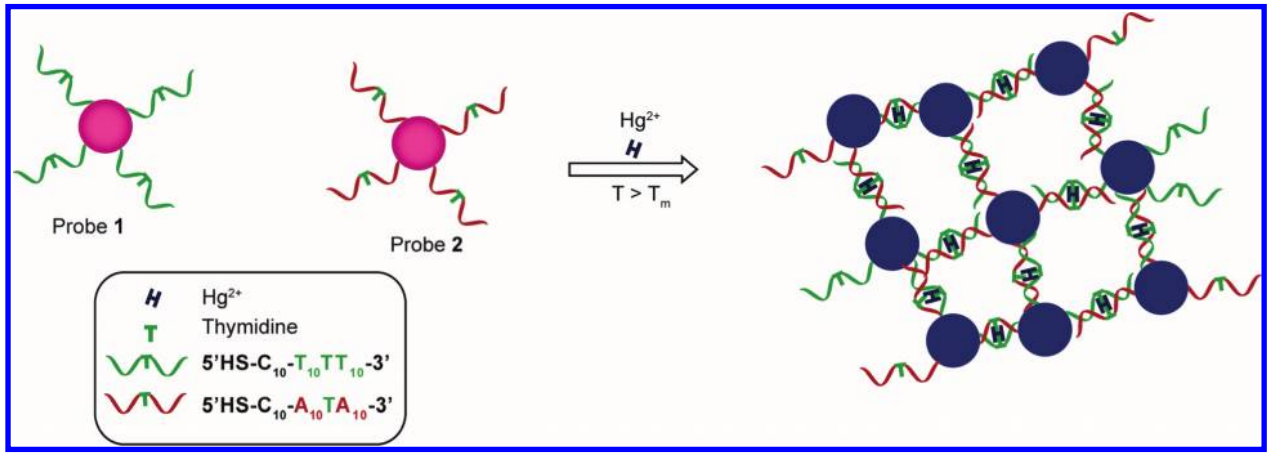

Figure 5. Colorimetric detection of Hg^{2+} using DNA functionalized AuNPs exploiting thymidine−Hg^{2+}−thymidine coordination chemistry.

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739–2779

of Hg^{2+} in the system raised the T_m of the AuNP aggregates through selectively coordinating with the T−T mismatches to form stable T−Hg^{2+}−T base pairs, providing detection down to 100 nM Hg^{2+}.[260] However, this method requires an electronic heating element coupled with the sensor system for careful monitoring of T_m during the detection process. To avoid this need for heating during the read-out process Liu and co-workers have optimized the number of T units in the DNA strands so that the system operates at ambient temperature.[261] Chang and co-workers have reported a visual Hg^{2+} sensing method based on Hg^{2+}-induced conformation change of a T-rich single-stranded DNA (ssDNA).[262] Recently, simple thymine functionalized AuNPs have been employed for the colorimetric detection of Hg^{2+} ion.[263] Specific interaction of Hg^{2+} with thymine residues from two AuNPs induces the aggregation process and corresponding color change. Mirkin and co-workers have reported the discrimination of cysteine from other amino acids utilizing T−Hg^{2+}−T coordination chemistry and employing the DNA-based probes.[264] AuNPs modified with 5,5′-dithiobis (2-nitrobenzoic acid) were also used for the detection of trace levels Cr^{3+} (99.6 ppb) in the presence of 15 other metal ions in aqueous solution.[265]

DNAzymes are DNA-based catalysts.[266−271] Liu and Lu have fabricated highly selective lead biosensors using DNAzyme-directed assembly of AuNPs,[272−275] allowing the tuning of sensitivity over several orders of magnitude. These DNAzymes were obtained through the combinatorial method systematic evolution of ligands by exponential enrichment (SELEX). In their sensor design, a DNAzyme specific to the Pb^{2+} ion was chosen as the target recognition element and DNA-functionalized AuNPs were used as the signal transducer element. The Pb^{2+}-specific DNAzyme is comprised of an enzyme strand and a substrate strand. In the presence of Pb^{2+} ion, the enzyme strand carries out catalytic reactions involving hydrolytic cleavage of the substrate strand. When incubated with DNAzyme, the DNA-functionalized AuNPs form blue-colored assemblies through Watson−Crick base pairing as shown in Figure 6. The DNAzyme is activated in the presence of Pb^{2+} in the solution. Activated DNAzyme cleaves the substrate strand to dissemble the AuNPs, resulting in a blue-to-red color change. The sensor was capable of detecting Pb^{2+} concentration of 100 nM. More importantly, other divalent metal ions such as Ca^{2+}, Co^{2+}, Ni^{2+}, and Cd^{2+} did not induce any color change. Optimization to control the AuNP orientation in the assemblies allowed fast detection of Pb^{2+} (<10 min) at ambient temperature.[275] Later, a highly selective and sensitive colorimetric sensor for uranyl (UO_2^{2+}) based on AuNP and UO_2^{2+} selective DNAzyme has been reported using both labeled and label-free methods.[276]

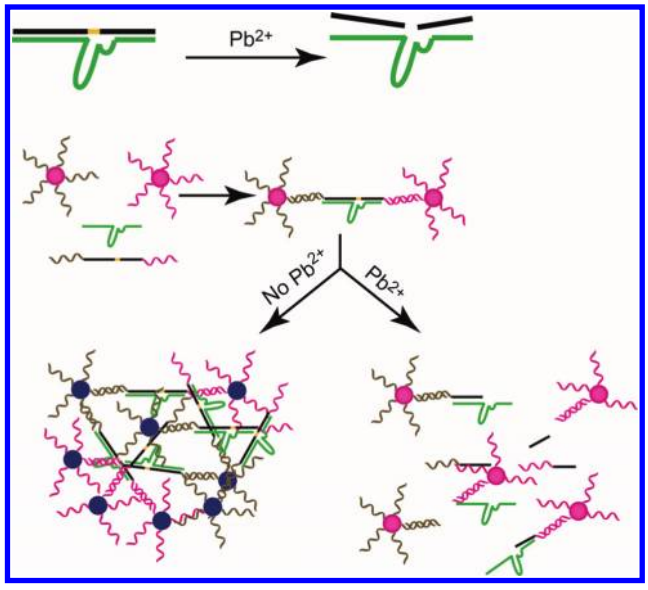

Figure 6. Pb^{2+}-directed assembly of AuNPs by the DNAzymes resulting in detection.

4.1.3. Other Metal Ions. Hutchison and co-workers have developed a sensitive and selective trivalent lanthanide (Ln^{3+}) ions sensor based upon tetramethylmalonamide (TMMA) functionalized AuNPs.[277] The presence of Ln^{3+} ions in the AuNP solution initiates AuNP cross-linking and concomitant red to blue color change through the formation of 2:1 TMMA-Ln^{3+} chelating complex. An immediate colorimetric response to the Ln^{3+} ions was detected, with sensitivity down to ∼50 nM for Eu^{3+} and Sm^{3+}. Recently, Wang and co-workers have devised a colorimetric method for detecting Al^{3+} based on pentapeptide (CALNN) functionalized AuNPs.[278] The affinity of Al^{3+} toward the functional carboxylic group of the pentapeptide induces AuNP aggregation and color change. This assay was successfully applied for sensing of the Al^{3+} on living cellular surfaces under physiological conditions.

4.2. Detection of Anions

Numerous efforts have been devoted to the development of sensor system for anionic species.[279−281] Designing recognition motifs for anions is challenging because of their lower charge to radius ratio, pH sensitivity, wide range of geometries, and solvent dependent binding affinity and selectivity.[281] Kubo et al. have attached isothiouronium groups onto AuNP surface and demonstrated sensing of oxanions, such as AcO^-, HPO_4^{2-}, and malonate in 10% (v/v) H_2O-MeOH solution.[282] Colorimetric sensing of hydrophilic anions (e.g., dihydrogen phosphate) has been achieved in dichloromethane using AuNPs with phenyl urea anion binders.[283] AuNPs coated with ethylene glycol-appended isothiouronium units were used to detect F^- in water using 3-nitrophenylboronic acid as a mediator at pH 5.5.[284] Ionic liquid functionalized AuNPs have been applied for anion sensing.[285,286] For example, Itoh et al. have used ionic liquids based on the imidazolium cation for colorimetric sensing of I^- and PF_6^-.[285] AuNPs coated with thioglucose groups have been used by Watanabe et al. to sense fluoride anions over a relatively narrow concentration range (20−40 mM) in water,[287] with high selectivity against other anions such as Cl^-, Br^-, I^-, AcO^-, and NO_3^-. Ahn et al. have reported selective sensing of trans-dicarboxylates such as fumarate (one of the key components generated in the Krebs cycle) over its cis-isomer, maleate utilizing AuNPs functionalized with an anion-recognition motif.[288,289] Utilizing this system, discrimination of benzene-1,4-dicarboxylate from its isomers benzene-1,2- and benzene-1,3-dicarboxylate in water was also possible.[289]

Fast and sensitive detection of CN^- is important for environmental monitoring and the evaluation of food safety.[290,291] Han et al. reported a colorimetric detection method for cyanide anions in aqueous solution employing adenosine triphosphate-stabilized AuNPs and a Cu^{2+}-phenanthroline complex as the receptor unit.[292] In their sensing ensemble, exposure of CN^- to Cu^{2+}-phenanthroline complex induced a decomplexation process to generate free phenanthroline, which subsequently caused the ATP-stabilized AuNPs to

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

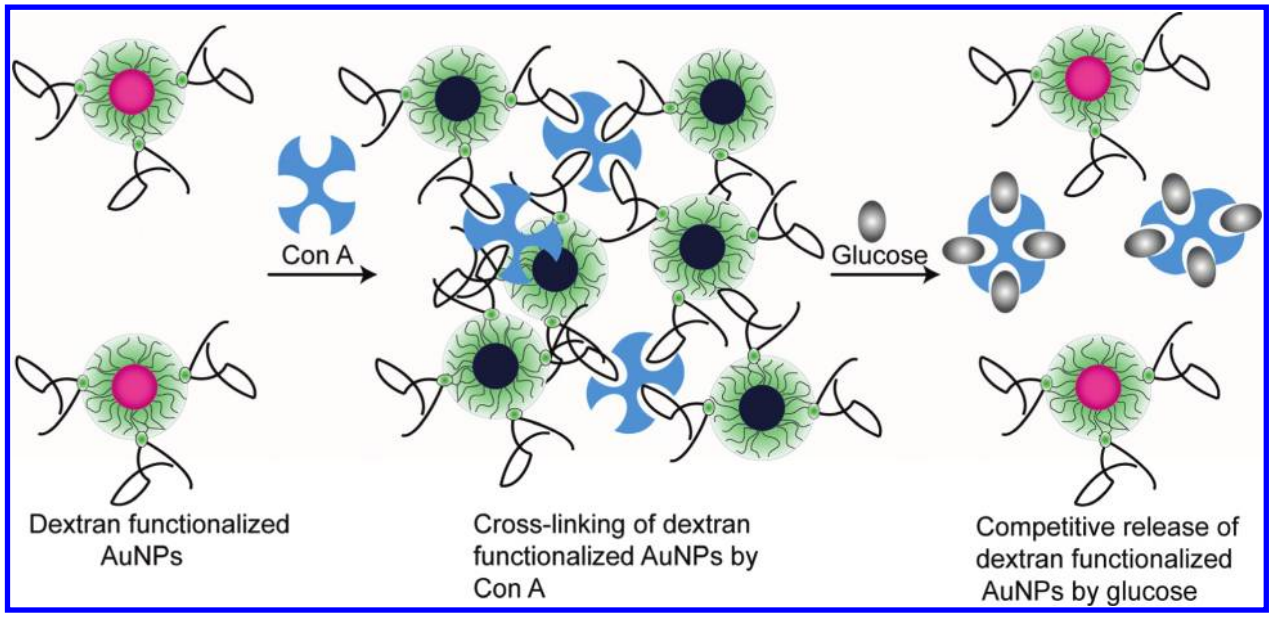

Figure 7. Colorimetric glucose sensing via the dissociation of Con A-aggregated dextran coated AuNPs. The presence of Con A cross-links dextran-coated AuNPs with concomitant blue-shift in SPR. The addition of glucose diminishes the Con A-AuNPs interaction releasing the individual dextran-coated AuNPs.

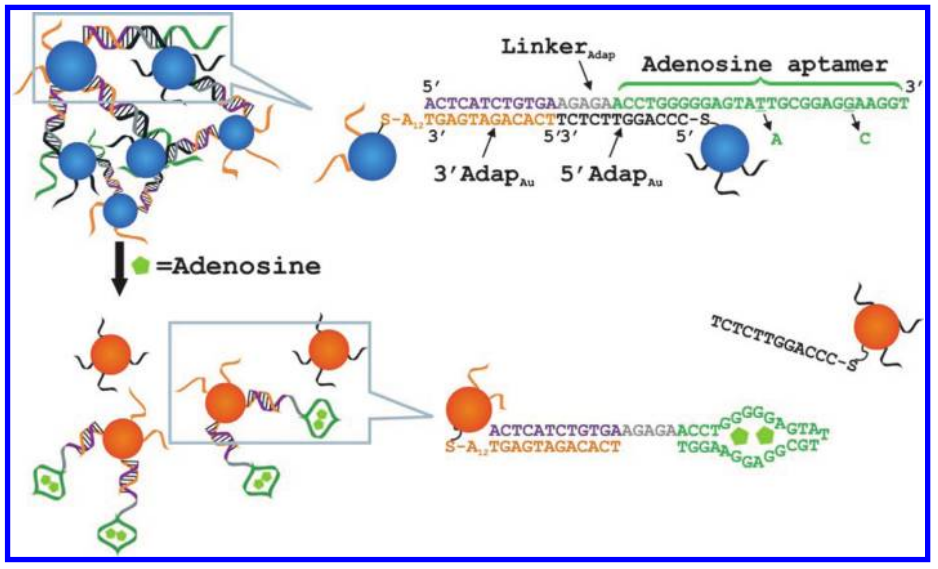

Figure 8. Schematic representation of colorimetric sensing of adenosine using aptamer linked AuNPs (left panel). The mutated linker with two mutations denoted by short black arrows was used as a control. Reprinted with permission from *Angew. Chem., Int. Ed.* (ref 306). Copyright 2006 Wiley-VCH Verlag & Co. KGaA, Weinheim, Germany.

aggregate resulting in color change. Utilizing this system 10^{-5} M CN^- was detected in neutral aqueous solution. Han et al. have reported a AuNP-embedded plasticized poly(vinyl chloride) (PVC) membrane for sensing of iodide anions in the presence of F^-, Cl^-, Br^-, N_3^-, NO_2^-, NO_3^-, and CH_3COO^-.[293] Yuan et al. have employed AuNPs decorated with a zinc(II) dipicolylamine-phosphate binding group for the colorimetric detection of bis-phosphorylated peptides.[294] Li et al. have utilized a "click" reaction coupled with the AuNP probes for the visual detection of ascorbic acid.[295] Mirkin et al. have employed the Griess reaction (coupling of sulfanilamide and naphthylethylenediamine by nitrite) for the AuNP-based colorimetric detection of nitrite.[296]

4.3. Detection of Small Organic Molecules

Geddes et al. have demonstrated a competitive colorimetric glucose assay using assemblies of concanavalin A (Con A) and dextran-functionalized AuNPs.[297,298] As shown in Figure 7, multivalent binding with Con A cross-links dextran-coated nanoparticles. The presence of glucose in the system competitively binds Con A, releasing the dextran-coated AuNPs that can be readily monitored by either conventional UV/vis spectrometry[297] or wavelength-ratiometric resonance light scattering with a glucose dynamic sensing range of 1−40 mM.[298] Because of the wide detection range, this system can potentially be useful to diagnose the blood glucose level in healthy people (3−8 mM) and in diabetics (2−40 mM). Molecularly imprinted polymers (MIP) with embedded AuNPs (Au-MIP) have been used by Sugimoto et al. as a colorimetric

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

sensor for adrenaline.[299] In the absence of adrenaline, the shrunken MIP gel provides close proximity of AuNPs. Adrenaline swells the MIP gel and causes a blue shift in the plasmon absorption band of the immobilized AuNPs, with a dynamic range from 5 μM to 2 mM. AuNPs surface functionalized with water-soluble copolymers [poly(*N*-*n*-isopropylacrylamide-co-acryloyldiethyletriamine)] have been employed by Uehare et al. for the detection of glutathione.[300] In their system, the AuNP aggregates form upon mixing the AuNP solution with the polymer. Addition of glutathione results in spontaneous disassembly of the aggregates with concomitant colorimetric response. AuNPs conjugated with thermoresponsive copolymers have been utilized for the colorimetric sensing of thiol compounds.[301,302] Recently, cysteamine-modified AuNPs have been employed for the colorimetric detection of melamine[303] and 2,4,6-Trinitrotoluene (TNT)[304] in real world matrices.

Aptamers are single-stranded oligonucleic acid-based binding molecules that are generated by SELEX, an in vitro selection process.[305] These functional DNA or RNA structures can bind a wide variety of targets with high affinity and specificity. Aptamer-based analytical methods have been used with the AuNP-based platform for colorimetric detection of small organic molecules.[306−312] For example, Lu and co-workers designed an adenosine sensor system,[306] which is composed of nanoparticle aggregates having three functional components: two kinds of ssDNA-modified AuNPs and a linker DNA molecule that carries adenosine aptamer (Figure 8). Initially, AuNPs and the linker DNA were suspended in solution to generate purple AuNPs. In the AuNP aggregation process, the linker DNA molecule pairs respectively with two ssDNA-functionalized AuNPs where a part of adenosine aptamer also takes part in the DNA hybridization process. When adenosine is present in the system, the aptamer changes its structure to bind with adenosine. This adenosine binding process results in the disassembly of the AuNP aggregates with a concomitant blue-to-red color change. Utilizing this system, adenosine was detected in concentrations from 0.3 to 2 mM. To demonstrate the generality of this system, Lu and co-workers have further constructed a colorimetric sensor for cocaine employing a cocaine aptamer.[306] Interestingly, the use of a mixture of different aptamers provided smart materials with cooperative responses to adenosine and cocaine.[307] The generality of the approach has been further demonstrated by introducing a third aptamer/nanoparticle component (responsive to potassium ions[313]) with this system. Lu and co-workers have also immobilized both adenosine and cocaine aptamer-linked nanoparticle aggregates onto a lateral flow device, resulting in a more sensitive "dipstick" test which can be performed in complex sample matrices such as human blood serum.[312] Stone et al. have reported a AuNP-based colorimetric detection system for theophylline using a theophylline recognizing aptamer.[311] Recently, an aptamer-based colorimetric biosensor for Ochratoxin A (OTA) has been reported by Marty et al.[309] Highly specific target recognition property of aptazymes has been utilized to devise colorimetric sensor for small organic molecules.[314] For example, Lu et al. have devised an adenosine biosensor based on the adenosine recognizing aptazyme-directed assembly of AuNPs.[315] RNA aptazyme-tethered AuNP was employed by Ogawa et al. for developing a sensing system to visually detect ligands of a cleavase-like RNA aptazyme at room temperature.[316] Gu et al. have employed a highly specific oxytetracycline binding ssDNA aptamer to discriminate oxytetracycline from other tetracyclines, such as doxycycline and tetracycline.[317]

4.4. Detection of Oligonucleotides

Detection of genetic mutations provides a crucial target for diagnostics,[318,319] leading to a growing interest in nucleic acid-based detection tests for the early diagnosis of many diseases including cancer. Fluorescent and radioactive detection readout methods (e.g., PCR, RT-PCR, Northern blot, Southern blot, and high density microarrays) are the conventional techniques for the detection of oligonucleotides.[320−323] AuNP-based colorimetric assays have been demonstrated to be a highly competitive technology for oligonucleotide targets.[324,325]

DNA-meditated AuNP assembly was demonstrated by Mirkin in 1996.[326] Fabrication of AuNPs functionalized with thiolated DNA strand allowed researchers to tailor the properties of the nanoparticle probes according to the assay method. This discovery has stimulated extensive use of oligonucleotide-directed AuNP aggregation for colorimetric detection of oligonucleotides[324,327−334] and fabrication of structured assemblies.[335] In this approach, two ssDNA-modified AuNP probes were used for colorimetric detection of target oligonucleotides. The base sequences in the AuNP probes are designed so they are complementary to both ends of the target oligonucleotides (Figure 9). AuNP aggregation with

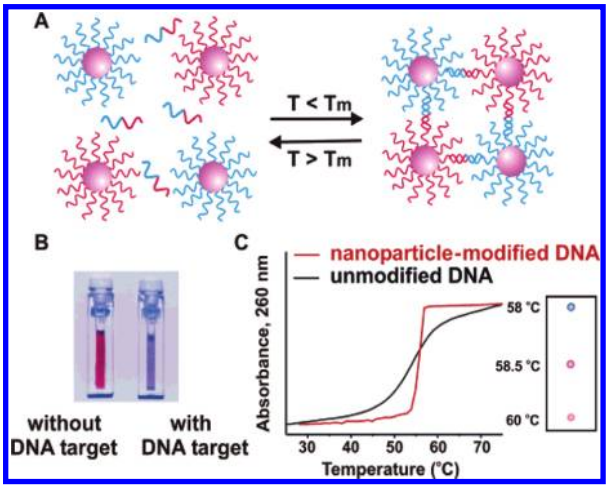

Figure 9. Aggregation of oligonucleotide AuNPs in presence of complementary target DNA (A), leading to change in color of solution from red to blue (B). Reprinted with permission from *Science* and *Chem. Rev.* (refs 327 and 16). Copyrights 1997 American Association for the Advancement of Science and 2005 American Chemical Society.

concomitant color change is triggered by the presence of target oligonucleotides as a result of hybridization of the DNA strand. Highly specific base-pairing of DNA strands coupled with the intense absorptivity of AuNPs enables the subpicomolar quantitative colorimetric detection of oligonucleotides.[330] Maeda et al. have shown that the aggregation of DNA-functionalized AuNPs can also be induced by hybridization of target DNA that does not cross-link the AuNPs,[336] with an unusual sensitivity of this system toward single-base mismatches. Rothberg et al. have shown that citrate-stabilized AuNPs can discern ssDNA and double-stranded DNA (dsDNA) at the level of 100 fmol through simple electrostatic interactions.[337] Mismatches even at the level of single base-pair have been easily detected through this way. A nearly "universal" sensing strategy employing an ssDNA probe, unmodified

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

AuNPs, and a positively charged, water-soluble conjugated polyelectrolyte has been demonstrated by Xia et al. to detect a broad range of targets including DNA, proteins, small molecules, and inorganic ions.[338]

Another important application of oligonucleotide-directed AuNP assembly is for the colorimetric screening and triplex DNA binders.[339,340] Screening of triplex DNA binders uses three components: two sets of AuNPs functionalized with noncomplementary ssDNA strand and a free strand of ssDNA that can form triplex structure with the DNA (Figure 10).[339] At

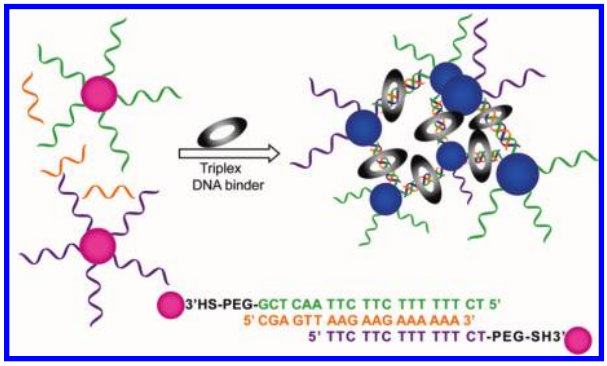

Figure 10. Schematic illustration of structure and color change of DNA functionalized AuNPs in presence of triplex DNA binders.

room temperature, no aggregation of ssDNA functionalized AuNPs takes place because of the low stability of the triplex structure. However, the presence of appropriate triplex DNA binders (e.g., benzo[e]pyridoindole and coralyne (CORA)) stabilizes the triplex structure, inducing the AuNP aggregation and corresponding color change. The simplicity of this approach makes a convenient and high-throughput method for identifying triplex binders from large combinatorial libraries. Oligonucleotide-directed AuNP assembly has also been applied for determining the relative binding strengths of molecules to duplex DNA by colorimetric assay, providing a strategy for identifying DNA binding drugs.[341,342]

4.5. Detection of Proteins

Many disease states (e.g., cancer) are often associated with the presence of certain biomarker proteins or irregular protein concentrations. AuNPs have been successfully applied for colorimetric detection of proteins. A diverse range of carbohydrate functionalized AuNPs have been prepared for the detection of carbohydrate binding proteins.[343−353] For example, the aggregation of β-D-lactopyranoside (Lac)-functionalized AuNPs has been utilized by Kataoka et al. for the detection of Recinus communis agglutinin (RCA_{120}).[351] The degree of colloidal aggregation was proportional to the protein concentration, thus allowing this method to be useful in quantitative detection of lectin. Significantly, a high sensitivity of lectin detection (lectin concentration of 1 ppm), has been achieved with this system.[351] Later, the density of Lac moiety on the particle surface has been modulated for controlling the concentration range of lectin detection.[352] The investigation showed that a critical Lac density (>20%) is required to trigger lectin-induced aggregation. The protein-directed assembly of gold glyconanoparticles has also been developed for facile and sensitive identification of protein−protein interactions. In an interesting study, binding partners of Con A have been identified by utilizing the assemblies of Con A and mannose-modified AuNPs, since the protein−protein interactions disrupt the initial nanoparticle−protein assemblies.[354] Similarly, a series of gluco- and manno-oligosaccharide-functionalized AuNPs have been used to sense carbohydrate−protein using the lectin Con A.[355] Recently, a novel fluorescent based competition binding assay was also reported by Wang et al. to measure the binding affinity of glyconanoparticles (AuNPs conjugated with underivatized mono-, oligo-, and polysaccharides) with model protein (lectin Con A).[356] Lactose-stabilized gold glyconanoparticles have been employed by Russell et al. to measure calcium ion-mediated carbohydrate−carbohydrate interactions.[253] The controlled aggregation of lactose-stabilized ~16 nm AuNPs has been harnessed to obtain colorimetric detection of cholera toxin at nanomolar levels.[357] AuNPs functionalized with a series of synthetic sugar probes have been utilized by Uzawa et al. for discriminating ricin toxin.[358] By utilizing biotin-functionalized AuNPs deposited on glass substrates, label-free optical methods to study biomolecular interactions in real time have been developed by Chilkoti et al.[359,360] Likewise, 15 nm sialic acid functionalized AuNPs have been employed to the optical detection of JC virus VLPs through sialic acid recognition.[361]

In an aptamer-based strategy, AuNP probes carrying platelet-derived growth factors (PDGFs)-specific aptamers have been employed by Chang et al. to detect PDGFs at nanomolar concentrations.[362] Additionally, by conducting a competitive binding assay, this aptamer−AuNP−PDGF assembly has been used to detect PDGF receptors.[362] Dong et al. have reported an even simpler aptamer-based colorimetric protein sensing method using unmodified AuNP probes.[363] In their sensor design, unmodified AuNPs were initially stabilized with thrombin-binding aptamers. In the presence of thrombin, the aptamers fold into a G-quadruplex/duplex structure due to the aptamer-protein recognition. As the apatamers fold, their relatively rigid structure induces AuNP aggregation with a detection limit of 0.83 nM. Likewise, glass surfaces have been modified with thrombin-specific aptamer to achieve thrombin sensing.[364] Since thrombin includes two binding sites for the aptamer, this process leads to a "sandwich" complex. Later, this method was extended by further enlargement of the immobilized AuNPs in a growth solution containing $HAuCl_4$, CTAB, and NADH.[365] This process initiates the SPR coupling interactions between the adjacent AuNPs, and provided sensitivity limit of 2 nM for thrombin. A general antigen−antibody interaction has also been applied for the AuNP aggregation-based immunoassay for proteins.[366] Utilizing this method, Rosenzweig et al. have demonstrated a detection limit of 2 μg/mL of antiprotein in serum samples.[367]

Dithiols can cross-link AuNPs,[368] in particular, dithiol-functionalized peptides have been used to generate AuNP assemblies for the colorimetric detection of proteases.[369] Scrimin et al. have designed two C- and N-terminal cysteinyl derivatives of peptide substrates specific to thrombin and lethal factor.[370] For their assay, the peptides were first treated with the analytes. Subsequently, the solution was incubated with citrate-stabilized 12 nm AuNPs. Nanoparticle aggregation was induced by the intact peptides in the absence of target proteases, whereas the protease-cleaved peptides do not bridge the AuNPs. Later, Stevens et al. further simplified this two-stage approach by employing AuNPs decorated with Fmoc-protected peptides that bear a cysteine anchor.[371] Presence of thermolysin in the system cleaved the peptide ligands, leading to AuNPs dispersion in the solution along with a blue-to-red color change (Figure 11) with enhanced sensitivity. On the basis of the

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

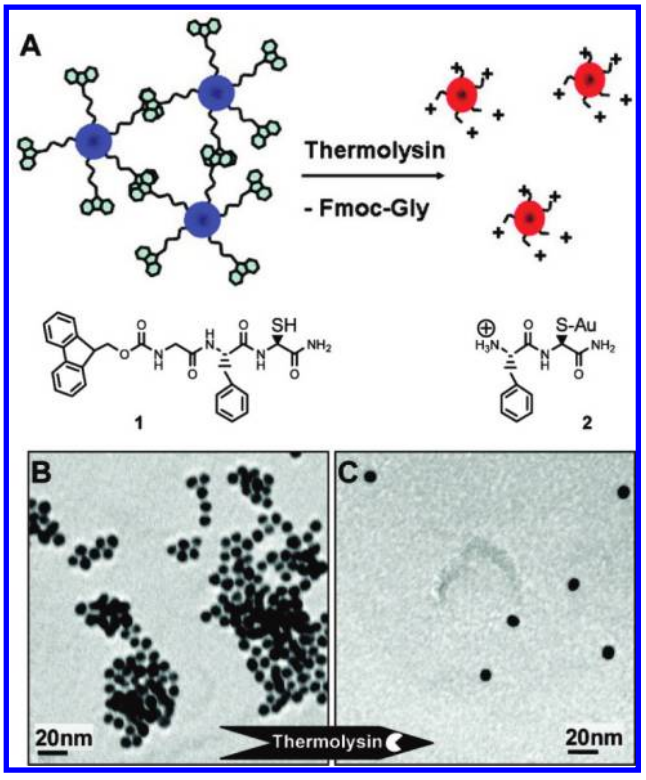

Figure 11. Schematic illustration of thermolysin triggered dispersion of AuNP assemblies (A). TEM images of AuNPs (functionalized with **1**) before (B) and after (C) addition of thermolysin and generation of **2**. Reprinted with permission from *J. Am. Chem. Soc.* (ref 371). Copyright 2007 American Chemical Society.

enzymatic cleavage of DNA molecules, Mirkin et al. have developed a real-time colorimetric screening method for endonuclease activity by using DNA-mediated AuNP assemblies.[372] Simultaneous determination of the efficiencies of endonuclease inhibitors (e.g., molecules with DNA-binding ability) has been achieved utilizing the colorimetric endonuclease-inhibition assay. Similarly, detection of kinase,[373] phosphatases,[374,375] β-lactamase,[376] and aminopeptidase,[377] along with the screening of their activity have been achieved utilizing the enzyme-triggered AuNP assembly/disassembly approach. Zare et al. have demonstrated a colorimetric sensor for protein conformational changes by utilizing AuNP probes.[378]

5. FLUORESCENCE-BASED SENSING

5.1. FRET-Based Detection of Metal Ions and Small Molecules

AuNPs can serve as excellent fluorescence quenchers for FRET-based assays[236] due to their extraordinary high molar extinction coefficients and broad energy bandwidth.[379] Murray and co-workers have reported a FRET based assay for the detection of various metal ions.[380] Electrostatic complexation of anionic tiopronin-coated AuNPs and $[Ru(bpy)_3]^{3+}$, a well-known cationic fluorophore, results in fluorescence quenching of $[Ru(bpy)_3]^{3+}$. The complexes can then be dissociated by addition of electrolytes and the fluorescence of $[Ru(bpy)_3]^{3+}$ restored. AuNP FRET quenching has been utilized in Hg^{2+} sensing.[381] Chang et al. reported that selectivity of the optimized Rhodamine B-absorbed AuNPs system for Hg^{2+} is 50 times higher than that of other metal ions (e.g., Pb^{2+}, Cd^{2+}, Co^{2+}) with a detection limit of 2.0 ppb. A FRET-based Cu^{2+} ion sensor has been developed using bispyridyl perylene bridged AuNPs by Zhu and collaborators.[382] In the absence of the Cu^{2+} ion, the fluorescence of the bispyridyl perylene on AuNPs is quenched. The Cu^{2+} ions then replace the bispyridyl perylene from the AuNPs, restoring fluorescence. Thomas et al. have used lanthanide complexes of bipyridine-functionalized AuNPs as phosphorescent sensors for alkaline earth metal ions and transition metal ions.[383]

Besides detecting metal ions, FRET based AuNP assays have been utilized for sensing small organic molecules. Chang et al. have used AuNPs in which Nile red noncovalently attached to AuNPs for sensing thiols at submicromolar levels.[384] As another example, Tang et al. have designed a FRET based cholesterol sensor by using β-cyclodextrin (β-CD) functionalized AuNPs.[385] Inclusion of fluorescein (FL) into cavity of CD on AuNPs causes complexation of AuNP-CD-FL construct, resulting in fluorescence quenching of FL through FRET. In the presence of cholesterol, FL inside CD is replaced by the cholesterol because of their higher binding affinity to CD, restoring FL fluorescence for detection of cholesterol at nanomolar concentrations. FRET-based AuNP assays have also been reported for detecting homocysteine.[386,387] Because of the strong fluorescent properties of AuNP smaller than 1.2 nm, AuNPs have been used to detect metal ions and proteins, using aggregation induced quenching or enhanced fluorescence of AuNPs.[388−391]

5.2. AuNP-Based Molecular Beacons

Hairpin FRET-based systems for sensing DNA have been created by labeling molecular beacons with AuNPs.[221] As shown in Figure 12, the nucleic acid probe conjugated with the

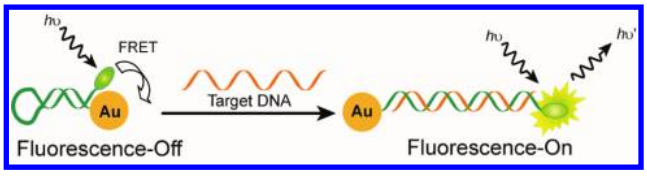

Figure 12. Schematic illustration of DNA detection, showing the conformational changes of dye-oligonucleotide−AuNP conjugates before and after hybridization with the target DNA.

organic dye is self-complementary, forming the hairpin structure on AuNP with effective FRET fluorescence quenching. The hairpin structure changes to rodlike through complementary hybridization with the target DNA, resulting in an increase in fluorescence of the dye. By employing similar principle, Nie et al. have shown that single stranded oligonucleotide-functionalized AuNPs with fluorophore-termini can assemble into a constrained arch like conformation.[392] In this conformation, the fluorophore is efficiently quenched by AuNP due to close donor and acceptor distance. Upon binding with the target DNA, the constrained conformation opens and the fluorophore is separated from the AuNP, affording fluorescence turn-on. AuNP-based FRET assays have also been used to monitor the cleavage of DNA by nucleases.[244]

Mirkin et al. have developed AuNP probes, (nanoflares) that are designed to detect and quantify intracellular analytes, for example, mRNA in cells.[393−395] Hybridization of dye-terminated DNA reporter sequences with oligonucleotide-functionalized AuNPs quenches fluorescence of the reporter. The presence of a target then displaces and releases the

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

reporter from AuNPs by constructing more stable duplex between the target and the oligonucleotide on AuNPs. Bai et al. have fabricated a FRET based AuNP assay to identify organic molecules that stabilize G-quadruplexes.[396] Initially, AuNPs carrying fluorescein-tagged probe DNA quench the fluorescence of the probe. Upon specific binding of a target organic molecule, intramolecular folding of the linear probe DNA into G-quadruplexes formation increases the distance between the AuNP and the probe DNA with concomitant enhancement of fluorescence. Fan et al. have reported multicolor fluorescent AuNP-based molecular beacons to detect target molecular analytes.[397] In their system, the multicolor dye-labeled aptamers are duplexed with DNA probes on AuNPs through complementary hybridization, resulting in fluorescence quenching of the dyes. In the presence of target molecules, the dye-labeled aptamer-target molecule binding separates the duplex, leading to fluorescence recovery of the dyes. FRET-based AuNP assay labeled with fluorescence probes has also been reported to detect Hg^{2+}.[398]

5.3. Sensors Based on FRET between QDs and AuNPs

Semiconductor quantum dots (QDs) have been utilized for FRET-based AuNPs assays for detection of proteins, utilizing the high efficiency and stability of these fluorophores.[399] Malvin et al. have reported a fluorescent competitive assay for DNA identification using QDs and AuNPs, where AuNPs were assembled with CdSe QDs through short cDNA strands, causing fluorescence quenching of the CdSe QDs.[400] Addition of complementary oligonucleotides then displaces the AuNP-DNA from the QD-DNA, resulting in QD fluorescence restoration. Similarly, Kim et al. have fabricated an enzyme inhibition assay using biotinylated AuNPs and streptavidin-coated QDs as a FRET donor–acceptor couple (Figure 13).[401]

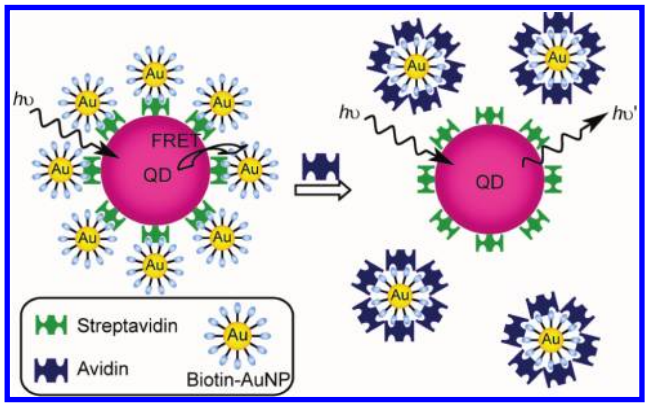

Figure 13. Competitive inhibition assay for the detection of avidin using QD–AuNP conjugates.

The biotinylated AuNPs specifically bind with the streptavidin-functionalized QDs forming quenched assemblies. The presence of avidin then releases the biotinylated AuNPs from QDs through a competitive binding with the biotinylated AuNPs. The authors have also demonstrated an approach for the rapid and simple detection of protein glycosylation by using dextran-functionalized QDs and Con A-coated AuNPs.[402]

Yu et al. have used assembly of Con A conjugated QDs and β-CD-modified AuNPs for determination of glucose in serum.[403] In practice, β-CD-modified AuNP is displaced by glucose due to its higher binding affinity to β-CD than Con A, resulting in release of Con A-conjugated QDs and recovery of QD fluorescence. Guo et al. have designed an inhibition assay for identification of Pb^{2+} based on the modulation in FRET efficiency between QDs and AuNPs.[404] Initially, the positively charged QDs form FRET donor–acceptor assemblies with negatively charged AuNPs by electrostatic interaction. The presence of Pb^{2+} aggregates AuNPs via an ion-templated chelation, inhibiting the FRET process, with a detection limit of 30 ppb of Pb^{2+}. Lu et al. have reported the simultaneous colorimetric and fluorescent detection of adenosine and cocaine in a single solution with QD-encoded aptamer sensors.[405]

5.4. "Chemical Nose" Approach for the Detection of Proteins, Pathogens and Mammalian Cells

The above FRET based assays employ specific interactions. Array-based sensing, that is, "chemical nose/tongue" strategies provides a useful alternative that uses differential selective interactions to generate patterns that can be used to identify analytes or changes in complex mixtures.[8] Recently, Rotello et al. have developed a protein sensor using chemical nose technology.[406] The prototype sensor array was generated using six cationic AuNPs of differing structures and an anionic poly (*p*-phenyleneethynylene) (PPE) polymer. As illustrated in Figure 14a, electrostatic complexation of AuNPs and polymer

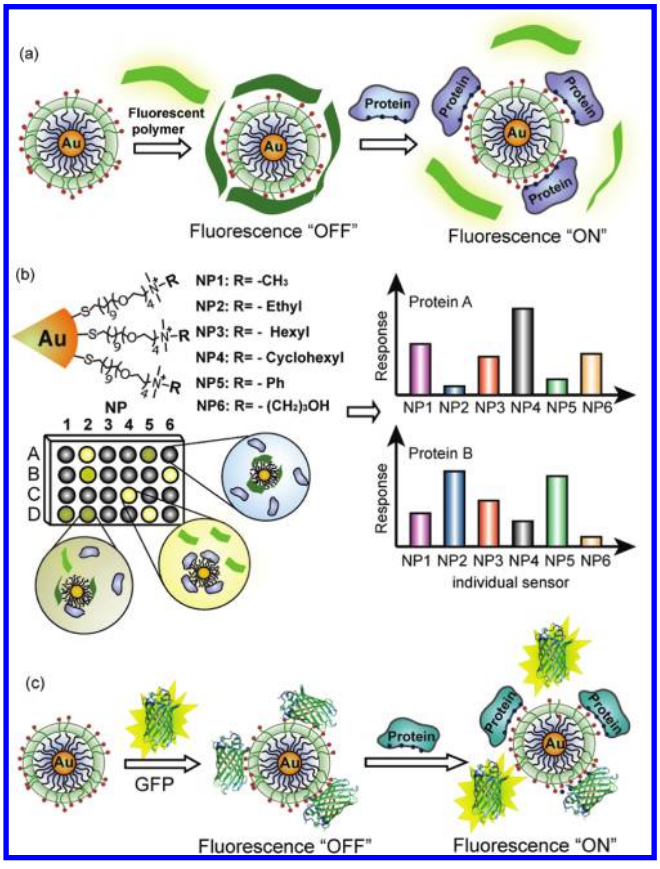

Figure 14. Schematic illustration of "chemical nose" sensor array based on AuNP-fluorescent polymer/GFP conjugates. (a) The competitive binding between protein and quenched polymer-AuNP complexes leads to the restoration of fluorescence (b) The combination of an array of sensors generates fingerprint response patterns for individual proteins. (c) The competitive binding between protein and nanoparticle–GFP complexes leads to fluorescence light-up.

results in fluorescence quenching of the polymer (fluorescence "OFF") through energy transfer. Addition of protein analytes

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739–2779

then disrupts the quenched polymer-AuNPs complexes via competitive binding, causing fluorescence recovery of the polymer (fluorescence "ON"). The protein-nanoparticle interactions are differential,[407,408] leading to a fingerprint fluorescence response pattern for individual proteins (Figure 14b) that was characterized using linear discriminate analysis (LDA). By employing the same principle, a AuNP-green fluorescent protein construct was used to detect and identify proteins at 500 nM in undiluted human serum (~1 mM overall protein concentration) (Figure 14c).[409]

Analogous AuNP-conjugated polymer systems have been used to detect and identify bacteria.[410] Three cationic AuNPs and one anionic PPE polymer were used to generate the sensor. Presence of bacteria disrupts the initially quenched assemblies leading to fluorescence restoration of PPE. From the distinct fluorescence response patterns, the sensor array was capable of identifying 12 bacteria including both Gram-positive (e.g., *A. azurea, B. subtilis*) and Gram-negative (e.g., *E. coli, P. putida*) species, as well as three different strains of *E. coli* (Figure 15).

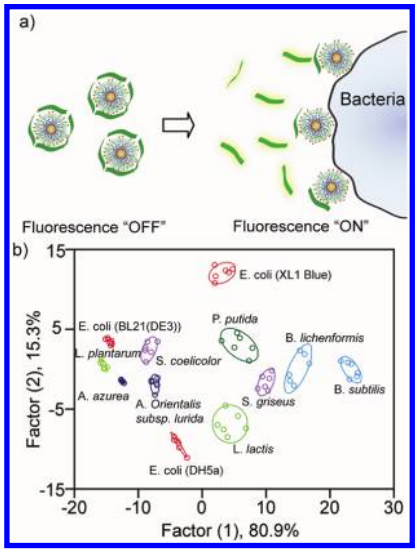

Figure 15. Array-based sensing of bacteria. (a) Displacement assay between bacteria and the AuNP-PPE complex. (b) Canonical score plot for the first two factors of simplified fluorescence response patterns obtained with NP-PPE assembly arrays against bacteria (95% confidence ellipses shown). Reprinted with permission from *Angew. Chem. Int. Ed.* (ref 410). Copyright 2008 Wiley-VCH Verlag & Co. KGaA.

The AuNP-conjugated polymer systems have been used for rapid and effective differentiation between normal, cancerous, and metastatic cells.[411−413] The fluorescence responses analyzed by LDA were capable of distinguishing (1) different cell types; (2) normal, cancerous, and metastatic human breast cells; and (3) isogenic normal, cancerous, and metastatic murine epithelial cell lines (Figure 16).

Rotello et al. have also reported an enzyme−AuNP sensor array for detecting proteins in which the sensitivity is amplified via enzymatic activity.[414] In this system, cationic AuNPs are combined with β-galactosidase (β-Gal) through electrostatic interaction, inhibiting the β-Gal enzymatic activity. Addition of analyte proteins releases the β-Gal from AuNPs and restores the β-Gal activity, providing an amplified readout of the binding event (Figure 17). Using a similar strategy, recently a

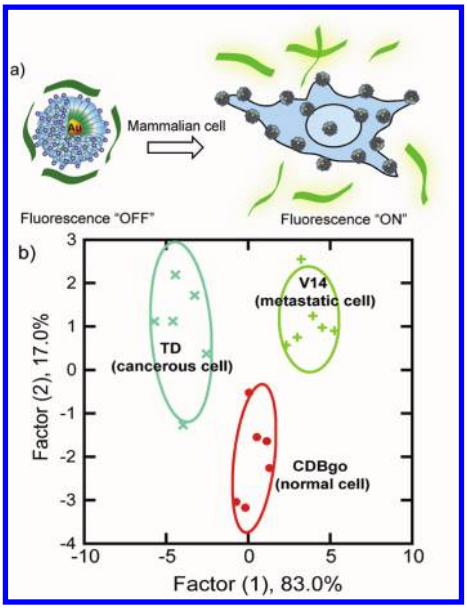

Figure 16. (a) Schematic depiction of the fluorophore-displacement cell detection array. Displacement of quenched fluorescent polymer by a cell with consequent restoration of polymer fluorescence. (b) Canonical score plot for the first two factors of simplified fluorescence response patterns obtained with AuNP-conjugated polymer assembly arrays against different mammalian cell types. Reprinted with permission from *Proc. Natl. Acad. Sci. U.S.A.* (ref 411). Copyright 2009 National Academy of Sciences.

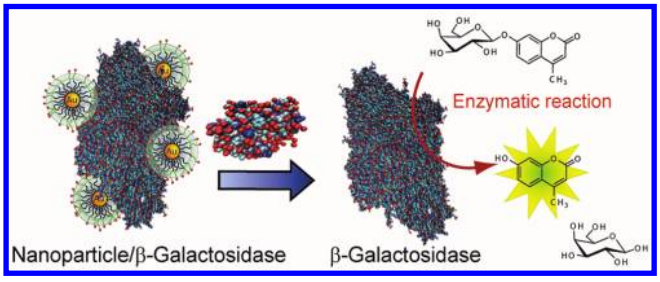

Figure 17. Schematic representation of the sensor system comprised of β-galactosidase (β-Gal) and cationic AuNPs. β-Gal is displaced from the β-Gal/AuNP complex by protein analytes, restoring the catalytic activity of β-Gal toward the fluorogenic substrate 4-methylumbelliferyl-β-D-galactopyranoside, resulting in an amplified signal for detection. Reprinted with permission from *J. Am. Chem. Soc.* (ref 414). Copyright 2010 American Chemical Society.

colorimetric test-strip sensor was developed for the detection of *E. coli.* with high sensitivity (1×10^4 bacteria/mL).[415]

6. ELECTRICAL AND ELECTROCHEMICAL SENSING

AuNPs feature excellent conductivity, high surface area and catalytic properties[416] that make them excellent materials for the electrochemical detection of a wide range of analytes.[15,417−432] In this section, we will summarize the use of AuNPs for electrocatalytic and electrochemical sensing.

6.1. Vapor Sensing

The electronic properties of self-assembled films of monolayer-protected AuNPs can be varied by tuning the particle size, interparticle separation, surface functionality, and chemical environments.[433] Chemiresistors are solid-state devices that rely on this sensitivity through changes in electrical resistance upon interaction with a chemical species. Over the past decade, there

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

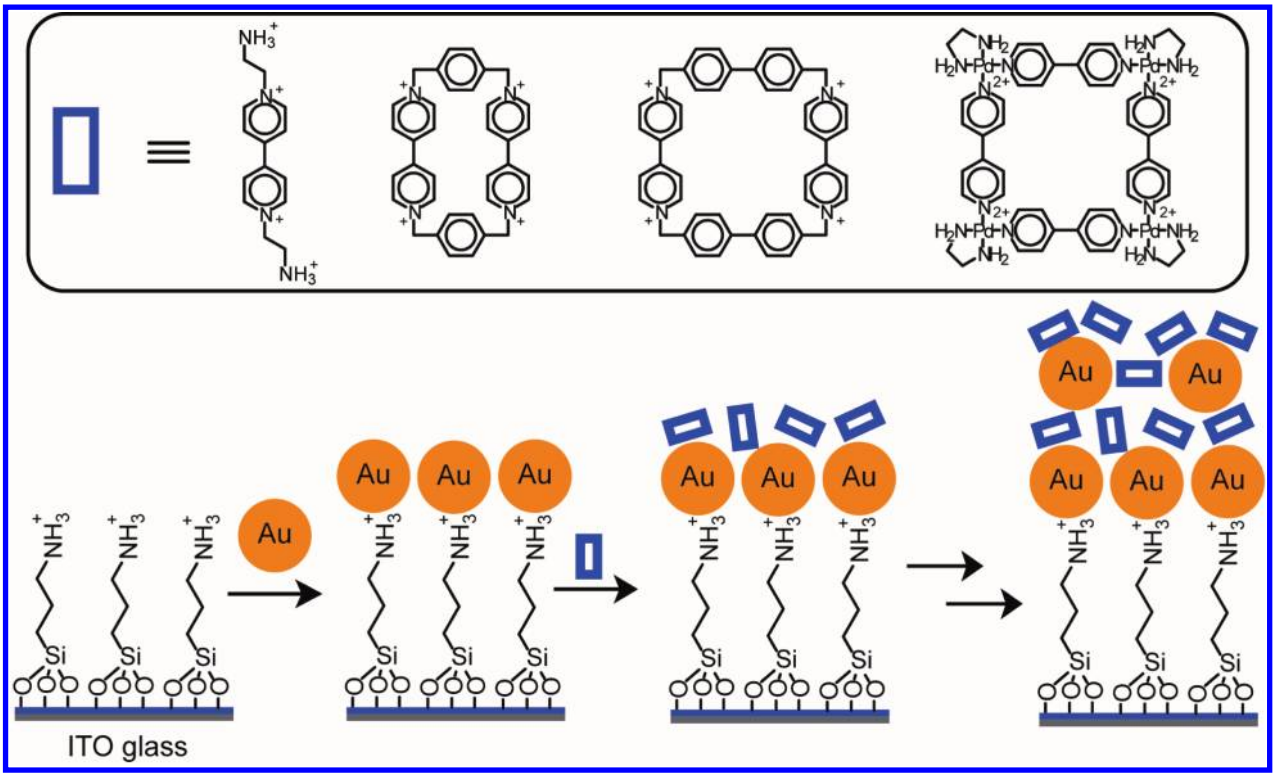

Figure 18. Electroactive multilayers formed by the simultaneous deposition of anionic AuNPs and oligocationic cyclophanes. In these systems, AuNPs provide a rough conductive array while the macrocycles serve as π-acceptors to bind with π-donor analytes (e.g., hydroquinone), generating electrochemical responses.

have been a number of chemiresistor vapor sensors based on thiol functionalized AuNPs.[434−440] For example, Wohltjen and Snow have fabricated a chemiresistor by deposition of a thin film of octanethiol-coated AuNPs ($d \approx 2$ nm) onto an interdigitated microelectrode.[441] A rapid decrease in the conductance due to film swelling was observed in presence of toluene and tetrachloroethylene, with a detection limit of ~1 ppm. Later, Shen and co-workers have shown that aromatic-functionalized AuNPs exhibited different sensory responses depending on the nature of the terminal functionality (OH, CH_3, NH_2, COOH) of aromatic thiols.[442,443]

Vossmeyer et al. have systematically investigated the sensing of toluene and tetrachloroethylene using films consisting of dodecylamine-stabilized AuNPs and dithiols with different chain lengths (C_6, C_9, C_{12}, C_{16}).[444] At a given concentration of toluene, it was observed that the resistance responses increase exponentially with increase of $-CH_2$ units. This effect was attributed to the augmentation of sorption sites with increasing ligand length. Zhong and co-workers have proved the correlation between the vapor-response sensitivity and the interparticle spacing properties.[149,445] Recently, Wieczorek and co-workers successfully detected dissolved organic analytes using a thin film of hexanethiol protected AuNPs inkjet-printed onto microelectrodes.[446] On exposure to toluene, dichloromethane, and ethanol dissolved in 1 M KCl solution, an increase in impedance at 1 Hz was observed with detection limits of 0.1, 10, and 3000 ppm, respectively. Further studies by this group revealed that morphology, ionic strength and hydrophobic−hydrophilic character of nanoparticle film play an essential role in sensing.[447,448]

Mixed monolayer surfaces of AuNPs have been used to develop "electronic-tongue"-type sensor arrays by varying the ratios of the different ligands on the nanoparticle surface.[449,450] For example, AuNPs of two different thiol ligands have been fabricated by Kim et al.[450] that showed different chemical selectivities and produced rapid and reversible responses toward the vapors of 1-propanol, acetone, and cyclohexane. AuNP-dendrimer composites have also been explored in vapor sensing.[451−455] In these layer-by-layer (LBL) self-assemblies, the AuNPs provide the conductive film material while the dendrimers serve to cross-link the nanoparticles and to provide sites for the selective sorption of analyte molecules. An interesting bioconjugate material has been synthesized by simple reaction of the spider silk with aqueous chloroauric acid.[456] The environment-dependent expansion/contraction phenomenon of spider-silk modulates electron transport between nanoparticles, differentiating the polarity of alcohol vapors (from methanol to butanol) by distinct conductivity changes.

6.2. Electronic AuNP Sensors Employing Macrocyclic Complexation

The synergistic combination of electroactive AuNPs and macrocyclic compounds provides useful sensor systems.[457−460] Willner and co-workers have constructed nanostructured assemblies via electrostatic cross-linking of citrate-stabilized AuNPs (12 ± 1 nm) and oligocationic cyclophanes (molecular squares). The assembly process was repeated in a stepwise manner to attain LBL assembly of anionic AuNPs and oligocationic cyclophanes (Figure 18). For sensing, the bipyridinium cyclophanes serve as π-acceptors[461] for the association of π-donor substrates such as hydroquinone in their cavities, generating an electrochemical response.[462] The sensitivity of the resulting sensor can be tuned via the number of assembled layers on the conductive surface.[457] The binding

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

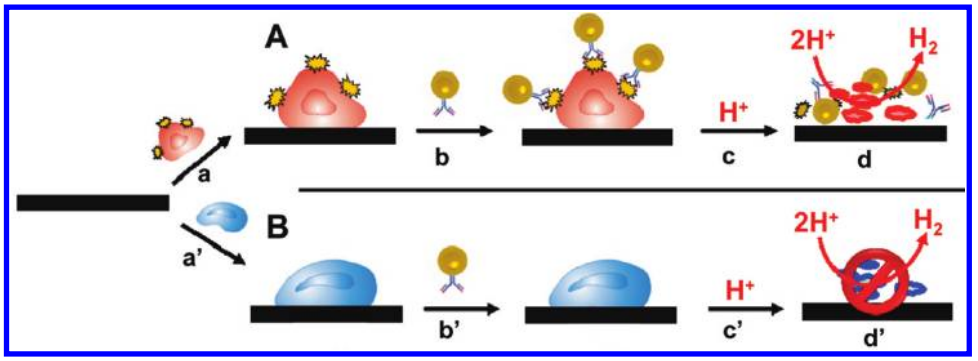

Figure 19. Specific identification of (A) Tumoral Cell Line (HMy2) expressing surface HLA-DR molecules compared to a (B) PC-3 Cell Line that is negative to this marker using AuNP-conjugated antibody coupled with an electrochemical sensor. The specific binding of AuNPs with tumor cells catalyzes hydrogen evolution in the acidic environment, generating electrochemical responses. Reprinted with permission from *Anal. Chem.* (ref 594). Copyright 2009 Americal Chemical Society.

affinity between the macrocycles and the analytes determines the selectivity of the electrodes, with cyclobis(paraquat-*p*-phenylene) cyclophane responding to hydroquinone, while the enlarged cyclophane cyclobis(paraquat-*p*-biphenylene) responds only to dihydroxymethyl ferrocene.[460] Sensing studies with anionic π-donor analytes such as 3,4-dihydroxyphenylacetic acid and an acyclic cross-linker *N*,*N*′-diaminoethyl-4,4′-bipyridinium were also performed.[459] Willner and co-workers have also developed a sensing interface by assembling a film consisting of polyethyleneimine, AuNPs and cyclobis(paraquat-*p*-phenylene) on the Al_2O_3 insulating layer of an ion-sensitive field-effect transistors.[463,464] This device is able to sense charged analytes that are attached to the cyclophane, regardless of their redox activity. Detection of adrenaline was accomplished by measuring either the source-drain current or the gate-source voltage, with a detection limit of 1×10^{-6} M.[464]

6.3. AuNPs as Platforms for Electrocatalyic and Electrochemical Sensors

AuNPs feature catalytic activity that results from their large surface area-to-volume ratio and their interface-dominated properties.[465−468] AuNPs can decrease the overpotentials of many electroanalytical reactions and maintain the reversibility of redox reactions.[469] Numerous approaches such as electrostatic interaction,[457−460] electrochemical deposition,[470−474] and mixing with components in a composite electrode matrix,[475] have been applied to deposit AuNPs on electrode surfaces. For example, AuNPs have been used as electrochemical enhancers for electrogenerated chemiluminescence (ECL) sensors.[476−478]

6.3.1. Detection of Small Molecules. AuNPs have been used for enhanced electrochemical detection of numerous small molecules[479−491] including glucose,[492−501] dopamine,[502−507] uric acid,[508−514] ascorbic acid,[510−512,515−518] epinephrine,[514,519−522] bisphenol A,[523] nitrite,[524−527] etc. Identification of several phenolic compounds;[528] e.g. catechol,[529] and aliphatic dicarboxylic acids; oxalic, succinic, malic, and tartaric[530] were also reported. For example, Wang and co-workers have electrocatalytically detected epinephrine using a self-assembled dithiothreitol(DTT)−dodecanethiol(DDT)−Au colloid modified gold electrode. The electrode reaction of epinephrine is significantly improved at the nano-Au electrode, providing a detection limit of 60 nM.[520] Recently, Luczak reported a voltammetric sensor for detection of norepinephrine using AuNPs, cystamine (CA) and 3, 3′-dithiodipropionic acid (DTDPA) modified gold electrodes. Moreover, the system is able to detect norepinephrine in presence of interferents ascorbic and uric acids.[531] Further, Zhang et al. have reported the superior electrocatalytic acitivity of positively charged AuNPs over negatively charged AuNPs using 4-dimethylaminopyridine (DMAP) coated AuNPs/L-cysteine film on gold electrode. Compared with electrodes modified by negatively charged AuNPs/L-cysteine, or L-cysteine alone, the electrode modified by the positively charged AuNPs/L-cysteine exhibited enhanced electrochemical behavior toward the oxidation of biomolecules such as ascorbic acid, dopamine and hydrogen peroxide.[532] Recently, Willner et al. reported an electrochemical sensor for enhanced detection of TNT using imprinted AuNP composites cross-linked via electropolymerization. The enhanced sensitivities were accomplished using π-donor−acceptor interaction between TNT and π-donor modified electrode or π-donor cross-linked AuNPs conjugated to the electrode. The functionalized AuNP electrodes were constructed by the electropolymerization of thioaniline-capped AuNPs and imprinting substrates on the electrodes. The imprint substrates were then removed by extraction. The electrochemical aggregation of AuNPs bridged by oligoaniline units on the Au electrode detected TNT with a detection limit of 2 nM as a result of the formation of a high content of π-donor sites on the electrode surface as well as the three-dimensional conductivity of the AuNP matrix.[533] Similar strategy was further used by this group using change in surface plasmon resonance reflection of cross-linked AuNP composites to detect explosives, including TNT[534] and RDX,[535] amino acids,[536] antibiotics,[537] and mono/disaccharides.[538]

6.3.2. Detection of Toxic Chemicals and Drugs. AuNP-based electrodes have been used to detect toxic ions, such as arsenic,[539−544] mercury,[539,545−548] antimony,[549] and chromium.[550,551] Several groups also reported high catalytic activity of AuNP-modified electrodes for electrocatalytic oxidation and detection of carbon monoxide,[552,553] nitric oxide,[554−559] and hydrazine.[560−564] Hydrogen peroxide (H_2O_2) was detected using AuNP decorated electrodes through enzymatic,[565−575] nonenzymatic,[576−580] and microfluidic electrochemical[581] approaches. Various pesticides, for example, atrazine,[582] methyl parathion,[583,584] paraoxon ethyl,[585] carbofuran,[584] phoxim,[584] and different drugs, such as paracetamol,[518,586] atenolol,[587] prednisolone,[588] ethamsylate,[589] were also detected using AuNP-modified electrodes. Recently, Raj has detected isoniazid, a popular antituberculosis drug, by chemisorbing 70−100 nm AuNPs on a sol−gel-derived 3D silicate network with a detection sensitivity of 0.1 nM.[590]

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

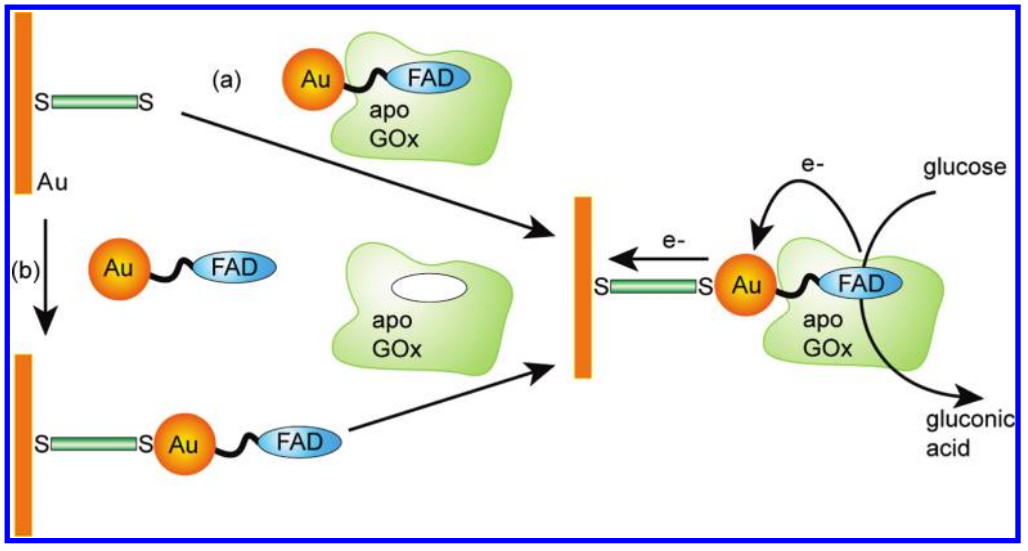

Figure 20. Fabrication of GOx electrode by the reconstitution of GOx on a FAD-functionalized AuNP: (a) The adsorption of AuNP-reconstituted of apo-GOx to a dithiol monolayer assembled on a gold electrode and (b) the adsorption of FAD-AuNPs to a dithiol-modified gold electrode followed by the reconstitution of apo-GOx onto functional AuNPs. Reprinted with permission from *Science* (ref 628). Copyright 2003 American Association for the Advancement of Science.

6.3.3. Detection of Mammalian Cells using AuNP-Modified Electrodes. AuNPs/chitosan nanocomposite gels were used for electrochemical monitoring of adhesion, proliferation, and apoptosis of cells on electrodes. Living cells immobilized on glassy carbon electrode (GCE) demonstrated an irreversible voltammetric response and enhanced the electron-transfer resistance with a limit of detection of 8.71×10^2 cells/mL.[591] Later, K562 leukemia cells were immobilized onto a microporous cellulose membrane modified with AuNPs and the effectiveness of antitumor drug methotrexate effect was monitored through the electrochemical response from cells.[592] Similarly, living pancreatic adenocarcinoma cells were immobilized on a composite electrode using AuNPs and carbon paste and used to determine the cytotoxic effect of antitumor drug adriamycin.[593] Recently, de la Escosura-Muñiz et al. have developed an electrocatalytic platform/sensor for the specific identification of tumor cells. In their system, molecules on cell surfaces are recognized by antibodies conjugated with AuNPs (Figure 19) with catalytic hydrogen reduction used to provide cell detection.[594]

6.4. AuNP-Based Electrochemical Enzymatic Biosensors

6.4.1. AuNPs act as "Electron Wires" Facilitating Direct Electron Transfer. The direct electrical communication of redox enzymes with electrodes is a useful strategy for biochemical sensoring.[595] However, the redox center of most oxidoreductases is electrically insulated by the protein. AuNP-based electrodes acting as "electron wires" can facilitate direct electron transfer between redox proteins and bulk electrode materials, thus allowing electrochemical sensing without redox mediators,[596−605] exploiting the physical properties of AuNPs.[606−609] One practical method to develop AuNP-based enzyme electrodes uses immobilization of the enzyme on AuNPs deposited directly on the surface of the bulk electrode.[610] Different strategies have been applied to immobilize enzymes onto AuNPs, such as direct attachment by the use of cysteine,[611] via thiol linkers,[612] and through covalent bonds.[613] The codeposition of redox enzymes and AuNPs on the electrode surfaces reduces the insulating effect of protein shell providing an excellent biosensor platform[614,615] to detect various biomolecules.[616−622] Moreover, adsorption of biomolecules onto AuNPs surface can preserve their bioactivity using biocompatible AuNPs.[623,624] Again, the immobilization of enzymes onto AuNPs can increase their turnover rates,[625−627] enhancing sensitivity. Willner and co-workers have constructed a AuNP based bioelectrocatalytic system with highly efficient electrical contact of glucose oxidase (GOx) with the electrode support. In their system, electron transfer between the enzyme active sites and the electrode support was facilitated through the reconstitution of apo-glucose oxidase (apo-GOx) on a 1.4 nm AuNP-functionalized with the cofactor flavin adenine dinucleotide (FAD) (Figure 20).[628] The resulting AuNP-reconstituted enzyme electrodes featured high electron-transfer turnover rate of ~5000 s^{-1} (7-fold higher than that of native GOx). This approach was further explored to pyrroloquinoline quinine (PQQ)-dependent enzymes by the reconstitution of apo-glucose dehydrogenase (GDH) on a PQQ-functionalized AuNP-modified gold electrode.[629] Kerman et al. have demonstrated a streptavidin-coated AuNP-based sensing strategy to monitor protein phosphorylation.[630]

Hemoglobin (Hb) has been extensively studied as a redox protein for direct electron transfer to AuNP-modified electrodes. Hb has very slow electron transfer rate to bulk electrodes, however, AuNPs can greatly enhance the electron transfer between Hb and electrodes with[631] or without redox mediator.[632−642] Yuan has used this system for amperometric sensing of H_2O_2 using Hb immobilized on multiwall carbon nanotubes (MWCNT)/AuNPs[643] and onto AuNPs/MWCNT/chitosan composite matrices[644] on GCE surface. Amperometric nitrite sensors have used Hb immobilized on AuNP-modified screen printed electrode[645] and onto one-dimensional AuNP assemblies.[646] Similarly, direct electrochemistry of myoglobin (Mb), an oxygen transporter in muscle tissues, was used to detect H_2O_2 using a variety of AuNP-modified electrodes.[647−651] Also, an electrochemical H_2O_2 biosensor was created by immobilizing Mb and colloidal AuNPs onto Nafion-modified GCE. The immobilized Mb exhibited excellent electrocatalytic response to the reduction of H_2O_2 with a detection limit of 0.5 μM.[652]

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

Direct electron transfer to electrodes of P450 enzymes, CYP2B6[653] and CYP11A1[654] were applied to detect drugs and cholesterol respectively. Similarly, the electrocatalytic activity of cytochrome c immobilized on AuNP-modified electrodes[655−657] was used to sense H_2O_2. LBL assembly methods based on electrostatic interaction have been employed to interface redox proteins by facilitating direct electron transfer.[658,659] For example, multilayer films of GOx/AuNPs on gold electrodes using cysteamine as a covalent cross-linker were prepared by LBL technique. The bioelectrocatalytic response was directly correlated to the number of deposited bilayers.[660] Chen et al. have reported a H_2O_2 biosensor following the similar approach based on horseradish peroxidase (HRP) immobilization on an LBL assembly of films of AuNPs and toluidine blue that responded rapidly to H_2O_2 with a detection limit of 70 nM.[661] Zhu and co-workers have fabricated the composite C@SiO_2 with AuNPs (AuNPs−C@SiO_2) by LBL assembly technique to sense H_2O_2.[662] Cobalt hexacyanoferrate-modified AuNPs were alternated with poly(vinylsulfonic acid) layers on indium tin oxide (ITO) electrodes and used as a platform for immobilization of GOx in the presence of bovine serum albumin (BSA) using glutaraldehyde as a cross-linker. This hybrid electrode successfully measured amperometric response of glucose at 0.0 V vs saturated calomel electrode (SCE).[663]

6.4.2. Enzyme Biosensors using AuNPs Composite Electrode Matrices. The incorporation of nanomaterials into composite electrode matrices presents another approach to enzyme biosensors, providing low background currents, straightforward surface generation, and the ability to incorporate of different substances into the bulk electrode matrix. AuNP-based composite electrode matrices have been used to detect phenol,[475] hypoxanthine,[664] H_2O_2,[665,666] atenolol,[667] glucose,[668] etc. Similarly, tyrosinase biosensors consisting of composite graphite-Teflon electrodes modified with AuNPs have been developed by Pingarrón et al. to detect different alkyl- and chlorophenols. The presence of AuNPs in the composite matrix increased the kinetics of the enzyme reaction and the electrochemical reduction of *o*-quinones at the electrodes, thus allowing nanomolar detection of phenolic compounds.[669]

AuNPs are often conjugated to other nanomaterials to improve their binding efficiency on electrode matrices.[670−673] Electrodes fetauring AuNPs conjugated with carbon nanotubes (CNT) provide excellent electrocatalytic ability[674] enabling electrochemical biosensors for detection of glucose,[675−679] cytochrome c,[680] tryptophan,[681] hydroxylamine,[682] bisphenol A,[683] etc. For example, an electrochemical sensor platform was constructed by covalent integration of AuNPs and CNTs onto a poly(thionine) modified GCE. Using HRP, the synergistic effect of the combined matrix in the presence of redox polymer mediator provided faster electron transfer and higher enzyme immobilization efficiency for detection of H_2O_2.[684]

6.4.3. AuNP/Polymer Matrices for Novel Electrochemical Biosensors. Electropolymerization provides a strategy for biomolecule immobilization on the electrode surfaces in the presence of AuNPs. For example, Au-polypyrrole,[685] Au-polyaniline,[686] and AuNP-(3-mercaptopropyl)-trimethoxysilane (MPS) nanocomposite[687] bioelectrodes have been fabricated to detect glucose as an analyte. AuNPs were assembled onto an AgCl@polyaniline nanocomposite-modified GCE, providing an amperometric glucose biosensor based on GOx. The hybrid electrode system showed superior electrocatalytic activity and reproducibility, detecting glucose at 4 pM.[688] Similarly, a AuNP/polyaniline/AgCl/gelatin matrix has been successfully used for glucose biosensing.[689] A H_2O_2 biosensor has been created by electropolymerization of *p*-aminobenzene sulfonic acid using cyclic voltammetry. In this approach, AuNPs were assembled in an interface containing amine groups of thionine followed by HRP adsorption and the resulting biosensor responded to H_2O_2 with a detection limit of 0.64 μM.[690] Zhu et al. have reported the use of a AuNP/nafion/polythionine/gelatin matrix on Pt disk electrodes to immobilize HRP for H_2O_2 sensing.[691] Recently, a surface molecular self-assembly strategy for molecular imprinting in electropolymerized polyaminothiophenol (PATP) membranes at the surface of AuNP-modified GCE was reported for the electrochemical detection of the pesticide chlorpyrifos (CPF).[692]

Several groups have used the biopolymer chitosan to immobilize enzymes due to its biocompatibility and high mechanical strength. Using this approach, amperometric biosensors have been fabricated including GOx[693−698] to detect glucose, HRP[618,699−705] to detect H_2O_2, tyrosinase[706] to detect phenolic compounds, acetylcholinesterase (AChE) to measure drug sensitivity[707] or malathion activity.[708] A novel in situ interfacing of AuNPs with a chitosan hydrogel was achieved by one-step electrochemical deposition of tetrachloroauric (III) acid and chitosan on gold electrodes (Figure 21).[709] The deposited interface showed excellent biocompatibility and stability. With AChE as a model enzyme, rapid amperometric sensing of the pesticides malathion and monocrotophos was achieved with a detection limit of 1 ng/mL.

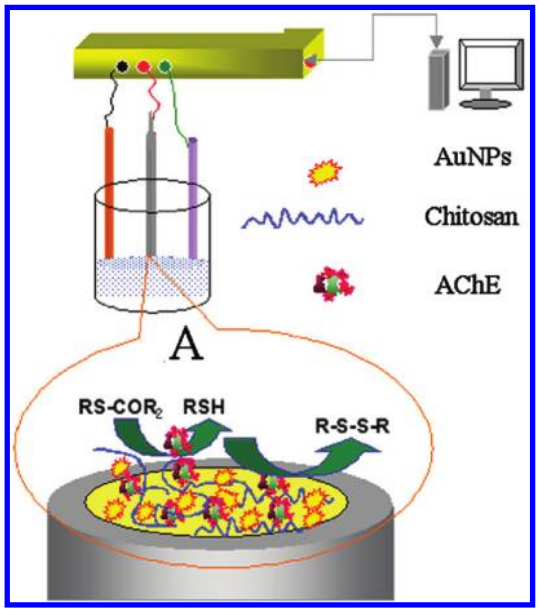

Figure 21. Acetylcholinesterase enzyme biosensor constructs using AuNPs/chitosan hydrogel matrices for the detection of pestisides. (A) Megascopic interface of AChE/Chitosan−AuNP modified gold electrode. Reprinted with permission from *J. Electroanal. Chem.* (ref 709). Copyright 2007 Elsevier B.V.

6.5. AuNP-Based Electrochemical Detection of Oligonucleotides

The unique electronic/electrochemical properties of AuNPs offer an alternative platform for optical sensing of oligonucleo-

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

tides,[710−718] providing an efficient tool for immobilizing DNA on electrodes[719] as well as a label to signal the hybridization event.[720−722] For example, an oligonucleotide with a mercaptohexyl group at the 5′-phosphate end was attached onto a AuNP-modified gold electrode, increasing nucleic acid loading efficiency to 1×10^{14} molecules/cm^2, ∼10 times higher than a bare gold electrode.[723] A variety of AuNP-based DNA sensing strategies (Figure 22) have been developed, including

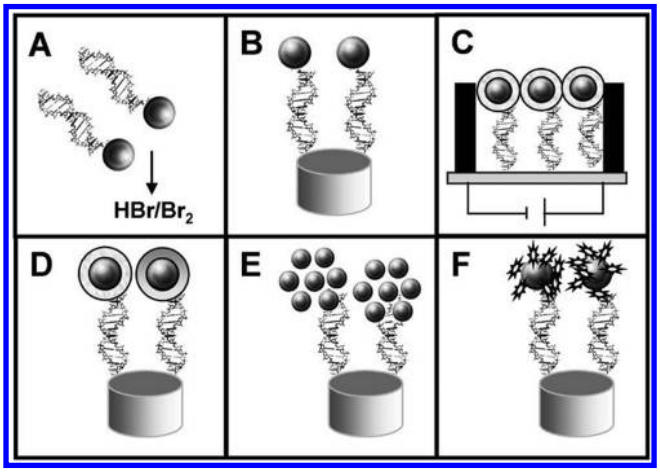

Figure 22. Schematic procedure of the different strategies used for the integration of AuNPs into DNA sensing systems: (A) previous dissolving of AuNPs by using HBr/Br_2 mixture followed by Au(III) ions detection, (B) direct detection of AuNPs anchored onto the surface of the genosensor, (C) conductometric detection, (D) enhancement with silver or gold followed by detection, (E) AuNPs as carriers of other AuNPs, and (F) AuNPs as carriers of other electroactive labels. Reprinted with permission from *Electroanalysis* (ref 711). Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany.

AuNP dissolution by acid,[724−728] direct detection of AuNP/DNA conjugates anchored onto sensor surfaces,[729−731] and AuNPs as carriers for other electroactive labels.[732−737] Sensing enhancement by precipitation of silver[738−746] and gold[747] onto AuNPs labels have been used to achieve amplified signals. Recently, Bonanni et al. have used streptavidin-coated AuNPs to provide impedimetric signal amplification for detecting DNA hybridization events. The probe oligomer was adsorbed on a graphite/epoxy composite electrode and the impedance measurement was performed using a ferrocyanide/ferricyanide redox marker. The coating with streptavidin favored the rapid formation of conjugates with biotinylated target DNA hybrid with a limit of detection 11.8 pM.[748]

DNA sensing has likewise been performed using AuNP-DNA conjugates on GCEs using methylene blue (MB) as an electroactive label and differential pulse voltammetry (DPV). The resulting system enhanced the response signal during immobilization and hybridization by increasing the density of redox active sites.[749] Fang and co-workers have immobilized an oligonucleotide with a mercaptohexyl group at the 5′-phosphate end onto 16 nm AuNPs self-assembled on a cystamine-modified gold electrode. The modified electrode immobilized 10-fold greater quantities of ssDNA than planar gold electrodes.[750]

AuNPs can change the conductivity across a microelectrode gap, providing highly sensitive electronic detection of DNA hybridization.[751,752] Mirkin and co-workers have reported an electronic DNA detection method where a short capture oligonucleotide was immobilized between electrodes in a microelectrode array with 20 μm gaps. Using a three-component sandwich approach, hybridized target DNA and AuNPs functionalized with oligonucleotides were bound between the electrodes leads followed by silver deposition onto AuNPs to enhance conductivity (Figure 23). Using this method, a sensitivity of 500 fM has been achieved with a point mutation selectivity factor of 10^5:1 in target DNA.[752] Following the same principle, Urban et al. have studied the changes of resistance across the microelectrode gap resulting from AuNP-labeled DNA in a parallel array readout system.[753] Additionally Diessel and co-workers have further demonstrated the utility of this strategy for the detection of single-nucleotide polymorphism.[754]

The redox properties of AuNPs have been used as electrochemical labels for DNA detection. For example, Ozsoz et al. have developed a sandwich-type electrochemical genosensor where the labeled target was captured by probe strands immobilized onto a graphite electrode and hybridization detected by electrochemical gold oxidation.[755] The response is enhanced because of the many oxidizable gold atoms in each nanoparticle label, with the detection limit as low as 0.78 fmol DNA for PCR amplicons. Similarly, another design was used to determine a specific binding event between *E. coli* ssDNA binding protein (SSB) and single-stranded oligonucleotides conjugated to AuNPs. SSB was adhered onto a SAM of single-stranded oligonucleotide modified AuNPs, and the resulting Au-tagged SSB was used as the hybridization label. Binding of Au tagged SSB to the probe was monitored through Au oxidation signal change, providing a detection limit of 2.17 pM target DNA.[756] Willner et al. reported an amplified electrochemical DNA detection method using aggregation of AuNPs on electrodes.[757] In their sensor, MB acts as a specific electrochemical indicator for the dsDNA aggregation of the AuNPs, while the AuNP assemblies facilitate the electrical communication of the intercalated MB with the electrodes, achieving a detection limit of 0.1 pM for a 27-mer DNA. More recently, a new strategy for the label-free electrochemical DNA detection has been developed using a AuNP/poly(neutral red) modified electrode that transduces hybridization through current decrease, with a detection limit of 4.2 pM.[758]

In addition to DNA recognition, AuNP-DNA-modified electrodes have been used to study the interaction of DNA with small molecules. For example, a DNA-modified electrode was fabricated by self-assembling (3-aminopropyl) trimethoxysilane and AuNPs and electrochemically immobilizing DNA onto ITO electrode. This DNA-modified electrode was used to detect the synthetic abortifacient, mifepristone with a detection limit of 200 nM.[759] Likewise, interfacial interactions between immobilized DNA probes and DNA binding drugs were investigated using impedance spectroscopy. Use of AuNP functionalized substrates resulted in detection limits of 5 nM for nogalamycin, 10 nM for mythramycin, and 40 nM for netropsin, 15−40-fold lower compared to flat gold substrates.[760] A norepinephrine biosensor was designed using an electrodeposited DNA membrane doped with AuNPs with a detection limit of 5 nM.[761]

6.6. AuNP-Based Electrochemical Immunosensors

Electrochemical immunosensors based on AuNPs enhance the electrochemical signal transduction of the binding event

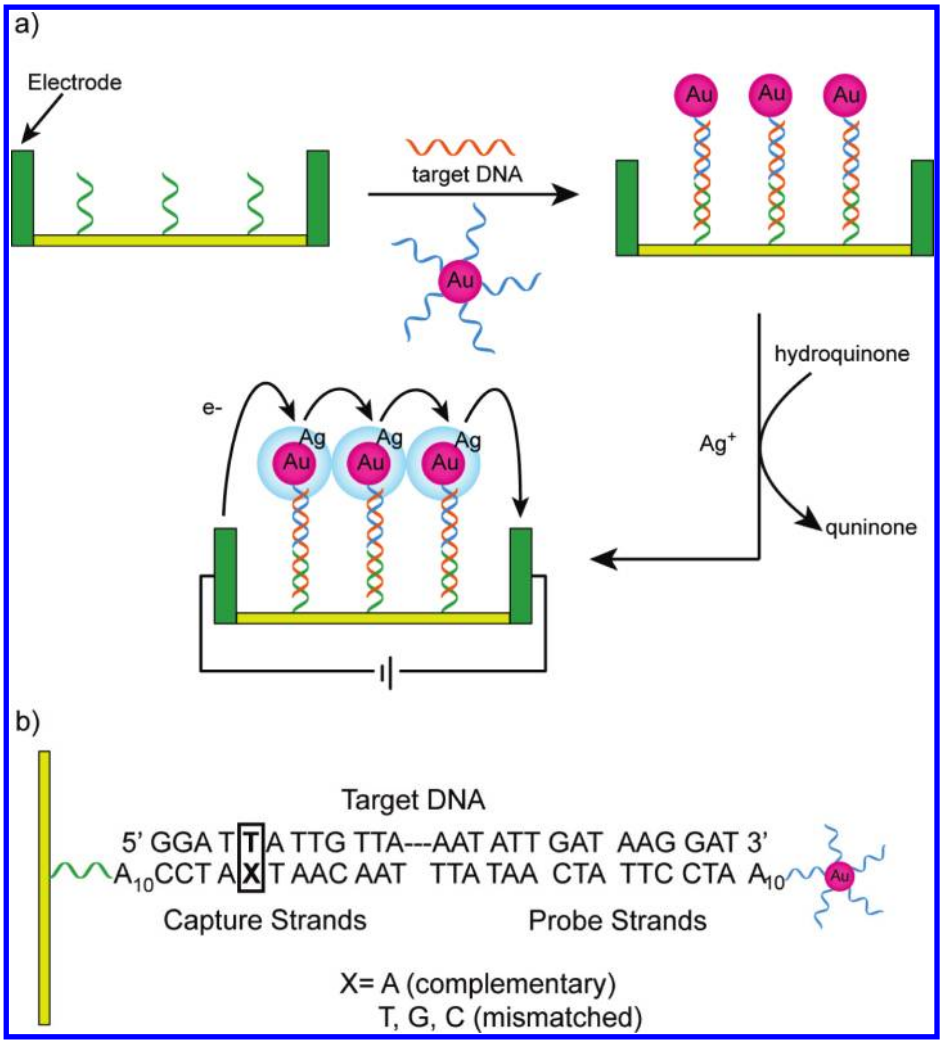

Figure 23. (a) Schematic illustration of electrical detection of DNA based on "sandwich" hybridization with DNA functionalized AuNPs followed by silver enhancement. (b) Sequences of capture, target, and probe DNA strands. Reproduced with permission from *Science* (ref 752). Copyright 2002 American Association for the Advancement of Science.

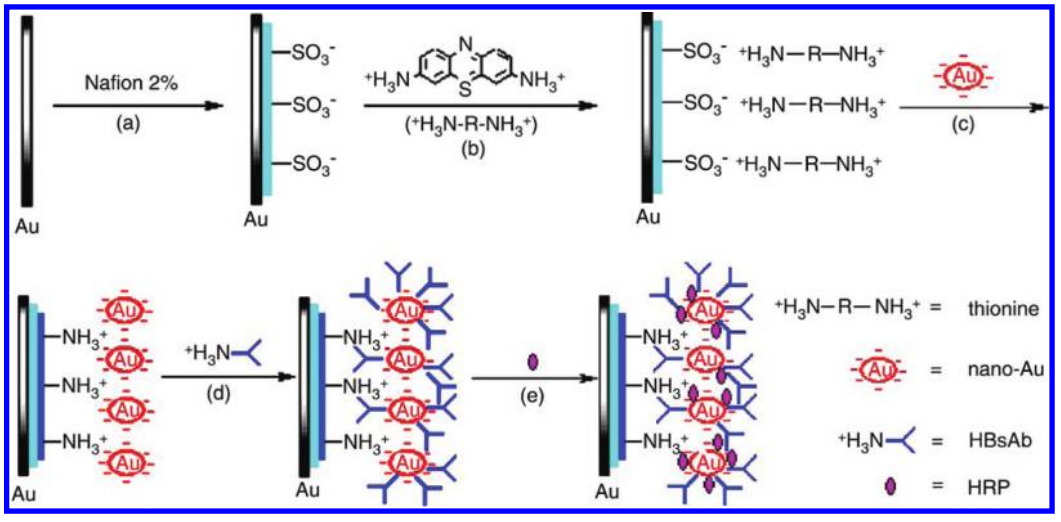

Figure 24. Schematic illustration of the stepwise immunosensor fabrication process to detect HBsAg: (a) formation of nafion monolayer, (b) adsorption of thionine, (c) formation of AuNP-monolayer, (d) HBsAb loading, and (e) blocking with HRP. Reprinted with permission from *Anal. Chim. Acta* (ref 772). Copyright 2005 Elsevier B.V.

between antigen and antibody, providing a better surface for maintaining immunoreagent stability upon immobilization.[762]

6.6.1. Detection of Viral Surface Antigens and Others.

Antibody immobilization onto AuNP-modified electrodes has

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739–2779

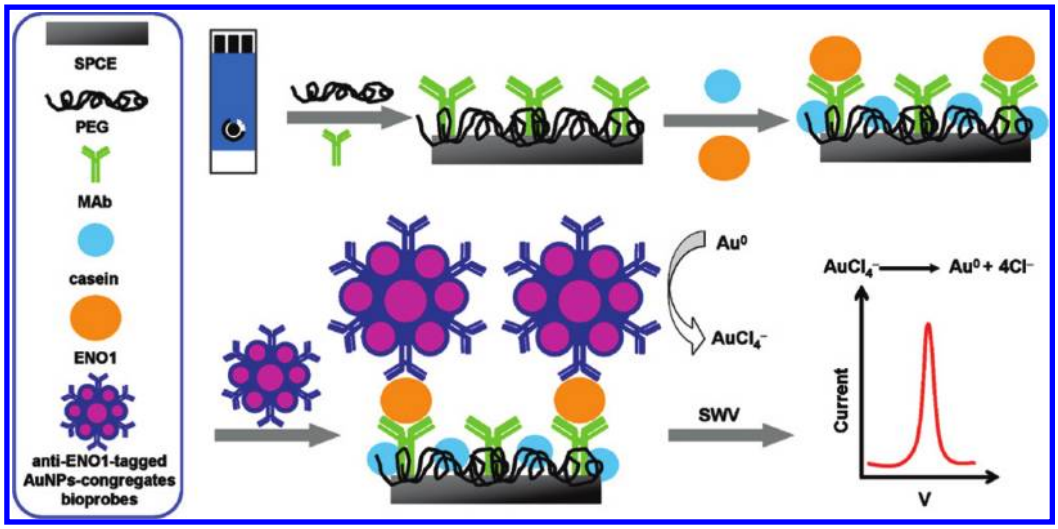

Figure 25. Schematic representation of the operation of the electrochemical immunosensor for the detection of ENO1. Reprinted with permission from *Anal. Chem.* (ref 858). Copyright 2010 American Chemical Society.

been used to detect Hepatitis B virus surface antigen (HBsAg) with detection limits of 50 ng/L[763] and 7.8 ng/mL.[764] Similarly, HBsAg detection was performed by electrostatic adsorption of the corresponding antibody onto AuNP/tris(2,2-bipyridyl)-cobalt(III) multilayer films,[765] AuNPs entrapped on polyvinyl butyral/nafion film coated PtE surface,[766] and cysteamine/AuNP-modified gold electrodes.[767] Other studies have used a nanoporous gold electrode with HRP labeled secondary antibody–AuNPs bioconjugates,[768] self-assembling AuNPs to a thiol-containing sol–gel network and assembling hepatitis B surface antibody on to the surface of AuNPs[769,770] and immobilizing hepatitis B surface antibody on a platinum disk electrode based on a AuNP/nafion/gelatin matrix.[771] An alternate strategy involving AuNPs and HRP modified gold electrode was used to build an amperometric immunosensor for HBsAg (Figure 24). The sensor was comparable to a BSA-blocked immunosensor in terms of linearity and sensitivity and detected HBsAg as low as 0.85 ng/mL.[772] Recently, a label-free amperometric immunosensor based on chitosan-branched ferrocene (CS-Fc) and AuNPs was developed to detect HBsAg. The decrease of amperometric signal corresponding to specific antigen–antibody binding was proportional to HBsAg concentration with a detection limit 0.016 ng/mL.[773] A copper-enhanced AuNP tag provided improved electrochemical performance for detecting HBsAg with a detection limit of 87 pg/mL.[774]

Diphtheria antigen was detected through diphtheria antibody immobilization on PtE modified with AuNPs[775,776] and silica/silver/AuNPs[777] in polyvinyl butyral matrices. A modified approach using a mixture of AuNPs and silica nanoparticles provided higher sensitivity, better reproducibility, and long-term stability of the system.[778] A label-free amperometric immunosensor based on multilayer assembly of polymerized *o*-phenylenediamine and AuNPs was used to detect Japanese B encephalitis vaccine with a detection limit of 6×10^{-9} log pfu/mL (pfu/mL is plaque forming unit).[779]

Electrochemical AuNP-based immunosensors have been used to detect a wide array of small molecule analytes, including carcinogenic substances (Aflatoxin B1,[780,781] Ochratoxin A,[782,783] naphthalene,[784] paraoxon),[785] herbicides (atrazine,[786,787] picloram[788]), and hormones (human chorionic gonadotrophin hormone (pregnancy test marker),[789–794] progesterone,[795,796] phytohormone abscisic acid,[797] 17β-estradiol,[798,799] human growth hormone[800]). Furthermore, detection of different proteins such as transferrin,[801,802] human serum albumin,[803,804] thrombin,[805] hemoglobin,[806] protein A,[807] and apolipoprotein A-I[808] has also been successfully achieved.

6.6.2. Detection of Biomarkers for Cancer and Other Disease States. α-Fetoprotein (AFP) is a tumor-marker for metastatic cancer. Several groups have used AuNP-based immunosensors to detect AFP by immobilizing AFP antibodies onto AuNP-decorated thionine/nafion membranes,[809,810] through electro-deposition of AuNPs and prussian blue on ITO electrode,[811] using carbon paste electrode constructed with an ionic liquid and AuNPs,[812] with AFP-antibody functionalized AuNPs,[813] using chitosan-AuNP composite film on a GCE,[814] using films of MWCNT/DNA/thionine/AuNPs,[815] using 1,1′-bis-(2-mercapto)-4,4′-bipyridinium dibromide functionalized AuNPs onto GCE,[816] and by immobilizing AFP-antigen onto GCE modified with AuNPs and a CNT doped chitosan film.[817] AuNPs and enzyme amplification have been applied to develop an immunosensor to detect AFP based microelectrodes and microwells systems fabricated by SU-8 photoresist on silicon wafer with a detection limit of 5 ng/mL.[818]

Another biomarker, carcinoma antigen 125 (CA125), was electrochemically detected by immobilizing anti-CA125 on a thionine and AuNP-modified carbon paste electrode.[819] Anti-CA125 was later immobilized on AuNPs stabilized with a cellulose acetate membrane on a GCE surface. Using *o*-phenylenediamine and H_2O_2 as enzyme substrates, the sensor provided a competitive immunoassay format to detect CA125, with HRP-labeled CA125 antibody as a tracer.[820] Similarly, various antigens were successfully detected by several groups using AuNP-based immunosensors, for example, carbohydrate antigen 19–9,[821] carbohydrate antigen 125,[822] prostate-specific antigen,[823–827] and mammary cancer 15–3 antigen.[828]

A wide range of additional biomarkers have been detected besides cancer biomarkers, including cholera toxin,[829] interleukin-6,[830–832] vascular endothelial growth factors,[833] Annexin II and MUC5AC antigens,[834] *Schistosoma japonicum* antigen,[835,836] *Salmonella typhi* antigen,[837,838] foodborne pathogen *Escherichia coli* O157:H7,[839] osteoprotegerin,[840] and protein

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739–2779

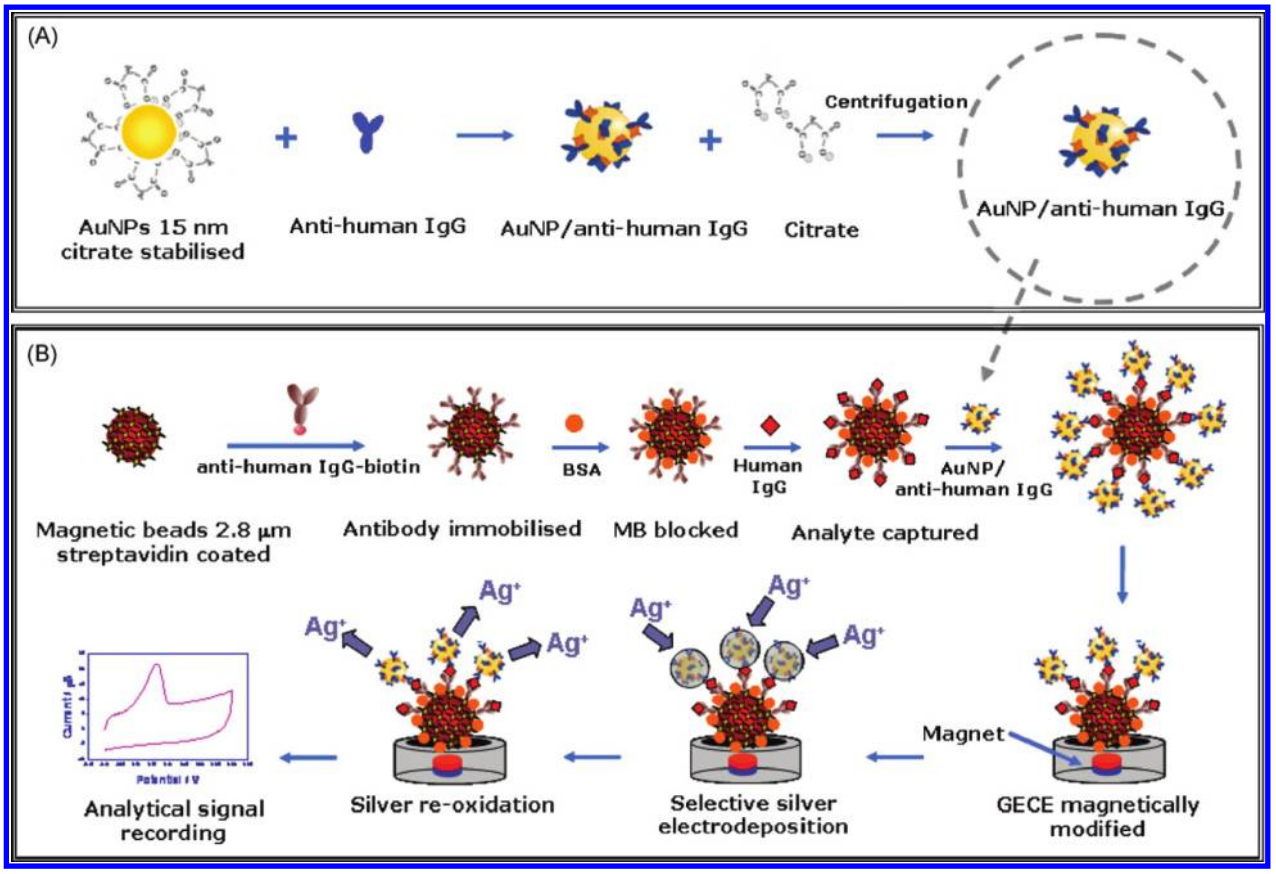

Figure 26. (A) AuNP conjugation with antihuman IgG. (B) Analytical procedure for the sandwich type assay and the obtaining of the analytical signal based on the catalytic effect of AuNPs on the silver electrodeposition. Reprinted with permission from *Biosens. Bioelectron.* (ref 884). Copyright 2009 Elsevier B.V.

markers for acute myocardial infarction (AMI) e.g. myoglobin, cardiac troponin complex and the MB isoform of the enzyme creatine kinase,[841] dust mite allergen Der f2,[842] carcinoembryonic antigen (CEA),[843−857] etc. Recently, Ho et al. have reported a AuNP-based electrochemical sandwich immunosensor for enolase (ENO1) antigen, a potential diagnostic marker for lung cancer. The immunosensor operates through physisorption of anti-ENO1 monoclonal antibody on polyethylene glycol-modified disposable screen-printed electrodes followed by using anti-ENO1-tagged AuNP congregate bioprobes as electrochemical signal probes (Figure 25) with a detection limit as low as 11.9 fg (equivalent to 5 μL of a 2.38 pg/mL solution).[858] Recently, Ju and co-workers have developed a disposable reagentless electrochemical immunoassay array for multianalyte determination by immobilizing AuNPs modified with HRP-labeled antibodies on screen printed electrodes. Chitosan/sol−gel was used to trap the corresponding antigens of the analytes from the sample solutions.[859,860] Upon formation of immunocomplex, the direct electrochemical signal of the HRP decreased because of increasing steric blocking.

6.6.3. Detection of Immunoglobulins. Immunoglobulins are important biomarkers for a wide variety of disease states. Numerous examples of determining human immunoglobulin G (IgG),[861−876] as well as immunoglobulin E (IgE),[877] via AuNP-based electrochemical immunosensors can be found in literature. For example, Velev and Kaler designed a conductivity immunoassay system that used silver metallization to enhance sensitivity.[878] Mao et al. have reported an electrochemical method based on copper precipitation onto AuNP tags to detect human IgG and anodic stripping voltammetry (ASV) reaching a detection limit of 0.5 ng/mL.[879] Pioneering work using AuNPs as electrochemical labels for voltammetric detection of proteins were performed by Costa-García et al.[880,881] and Limoges et al.[882] For example, Limoges and co-workers reported an electrochemical immunoassay for IgG using AuNP-labeled antibodies and ASV. In this approach, the AuNP-labeled antibody forms sandwich complexes with the goat IgG target and the immobilized antibody. After removal of the unbound labeled antibody, AuNPs were dissolved in an acidic bromine-bromide solution to release gold ions that were electrochemically detected, providing an IgG detection limit of 3 pM,[882] competitive with ELISA. Likewise, human IgG has been detected by ASV using cyclic accumulation of AuNPs. In this sensor, the probe antibody in the sandwich complexes is labeled with dethiobiotin and avidin-AuNPs. The alternating treatment of the system with biotin solution and avidin-AuNPs resulted in cyclic accumulation of AuNPs. The detection limit of this method was 0.1 ng/mL of human IgG.[883] Recently, Merkoçi and co-workers reported an electrocatalytic silver-enhanced metalloimmunoassay using AuNPs as labels and microparamagnetic beads (MBs) as platforms for primary antibody immobilization to detect human IgG with a very low detection limit of 23 fg/mL (Figure 26).[884] Finally, on the basis of the catalytic effect of AuNPs on the electroreduction of silver ions, Huang and co-workers have reported the sensitivity enhancement for an electrochemical immunoassay by the autocatalytic deposition of Au^{3+} onto AuNPs. By coupling the

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

autocatalytic deposition with square-wave stripping voltammetry, the model analyte rabbit IgG could be determined quantitatively with a detection limit 1.6 fM.[885]

The rather analogous mouse IgG was identified with a detection limit of 1 ng/mL using a reagentless amperometric immunosensor based on AuNPs on a nafion modified GCE with 3,3′,5,5′-tetramethylbenzidine (TMB) as redox mediator.[886] A polymer-membrane based potentiometric IgG sensing method using silver enlargement of AuNPs tracers was reported by Chumbimuni-Torres et al. to detect mouse IgG with a detection limit of ~12.5 pmol in the 50 μL sample.[887] A novel DNA-free ultrasensitive sandwich-type heterogeneous electrochemical immunosensor using AuNP nanocatalyst labels was reported by Das et al.[888] As illustrated in Figure 27**a** partially

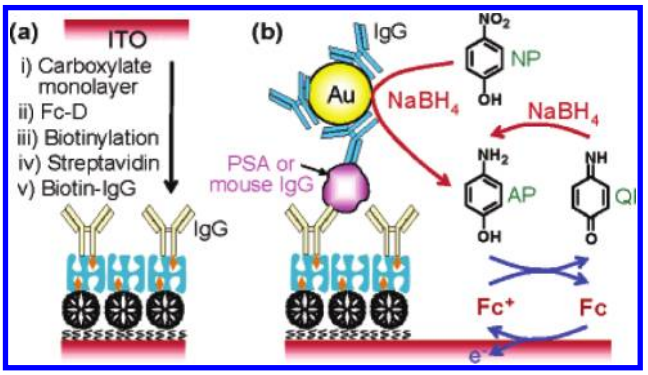

Figure 27. (a) Schematic representation of the preparation of an immunosensing layer. (b) Schematic view of electrochemical detection of mouse IgG or PSA. Reprinted with permission from *J. Am. Chem. Soc.* (ref 888). Copyright 2006 American Chemical Society.

ferrocenyltethered dendrimer (Fc-D) was immobilized to the ITO electrode by covalent bonding between dendrimer amines and carboxylic acids of a phosphonate self-assembled monolayer. Unreacted amines of Fc-D were modified with biotin groups to allow the specific binding of streptavidin. Then, biotinylated antibodies were immobilized to the streptavidin-modified ITO electrode. An IgG-nanocatalyst conjugate was also prepared via direct adsorption of IgG on 10 nm AuNPs. Mouse IgG and prostate specific antigen (PSA) were chosen as target analytes (Figure 27**b**).[888] The signal amplification was achieved by the catalytic reduction of *p*-nitrophenol (NP) to *p*-aminophenol (AP) using gold AuNP catalyst labels as well as through the $NaBH_4$ mediated chemical reduction of *p*-quinone imine (QI). This DNA-free method can detect 1 fg/mL of PSA, comparable to that of the biobarcode assay.[889] An extension of this model using magnetic beads for easy magnetic separation and immunoreactions leads to greater signal amplification by AuNPs, detecting mouse IgG as low as 7 aM using CV and 0.7 aM using DPV measurements.[890]

7. AUNP-BASED SURFACE PLASMON RESONANCE SENSORS

The interaction of light at the surface of the noble metal film excites surface electromagnetic waves and sets them to resonate with incident light wave, resulting in the absorption of the light. This phenomenon is known as surface plasmon resonance (SPR)[891,892] and depends on the refractive index of the interfacial region. Metal nanoparticles, such as gold[240,893−895] and silver,[896,897] exhibit localized surface plasmon resonance (LSPR) at specific incident wavelengths, generating strong light scattering and the appearance of intense surface plasmon absorption bands. The intensity and the frequency of the absorption band is a characteristic of the particular metal nanoparticles and highly dependent on their size and shape, as well as the surrounding environment.[898−902] Using this phenomenon many LSPR-based chemical and biological sensors have been developed.[14,322,903−915] Although numerous biosensors have been developed using silver nanoparticles,[916−923] we will focus on AuNP based sensors.[914,924−935]

7.1. Sensors Based on Change in LSPR Absorption of AuNPs

The general principle behind LSPR-based sensors is the wavelength shift in the LSPR spectrum arising from local dielectric changes caused by analyte adsorption. LSPR assays have been conducted both in solution phase[936−938] and on surfaces coated with nanoparticle monolayers.[939−942] In examples of the former, absorption maxima of LSPR was red-shifted when AuNPs functionalized with monoclonal antibodies interacted with analytes.[943,944] Moreover, the wavelength shift was found to be proportional to the amount of ligands.[944]

Most AuNP-based SPR sensors, however, have been fabricated by immobilizing nanoparticles onto surface.[945,946] The introduction of AuNPs onto the sensing surface provides an effective way to increase the sensitivity of SPR sensors owing to the high dielectric constants of AuNPs and the electromagnetic coupling between AuNPs and the metal film on the surface.[947] For example, a gold film-coated chip was used to detect dopamine in nanomolar concentration by immobilizing an MIP gel with embedded AuNPs.[948] Various substrates, such as quartz, optical fibers, ITO glass, sol−gel matrix, etc., have been used for supports for AuNPs, allowing the detection of numerous analytes such as human serum albumin,[949] BSA,[950,951] human IgG,[952] streptavidin,[953] interleukin-1β,[954] propanethiol,[955] etc. Recently, AuNPs encapsulated by hydroxyl/thiol-functionalized fourth generation PAMAM dendrimer were immobilized onto maleimide terminated SAMs to detect insulin.[956] The resulting AuNP-modified dendrimer surface provided high stability and enhanced sensitivity with a detection limit of 0.5 pM. The sensor was further testified by analyzing human serum samples from normal and diabetic patients with good correlation to standard methods.[956]

The aggregation of AuNPs leads to an alteration in surface absorption band that gives rise to a visible color change. Exploting this principle, Mirkin et al. have developed a colorimetric sensor for DNA hybridization assay using oligonucletide functionalized AuNPs both in dispersions as well as on surface (see section 4.4). Other SPR based sensors using aggregation of AuNPs have been reported to detect proteins (via antigen−antibody or biotin-streptavidin interaction),[367,957,958] and lectin.[344,351]

7.2. AuNP-Mediated SPR Signal Amplification

AuNPs have been used to enhance the signals of the propagating SPR spectroscopic signals to increase sensor sensitivity.[959−963] The signal amplification was explained by the electronic coupling interaction of the propagating surface plasmons with localized surface plasmons of AuNPs[964,965] and depends on various factors such as size, shape, and the distance from the metal generating SPR.[966,967]

7.2.1. Sensing of Proteins. Protein sensing through antigen−antibody interaction can be detected exploiting AuNP-amplified SPR phenomena. For example, Natan et al. have reported a AuNP-enhanced SPR immunosensing system

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

using either antigen or secondary antibody functionalized AuNPs as signal enhancers.[924] In an example of this sandwich strategy, a gold film coated with F_c specific monoclonal goat antihuman IgG (α-h-IgG(F_c)) generates a small plasmon shift upon addition of human IgG and the second free antibody. The plasmon shift, however, increases 28-fold times compared to an unamplified assay when the secondary free antibody is replaced by an electrostatic conjugate between AuNPs and α-h-IgG(F_c). Using this method picomolar detection of human IgG has been achieved. Similarly, several competitive and sandwich immunoassays have been developed using AuNP-enhanced SPR signals to detect human tissue inhibitor of metalloproteinases-2,[968] antiglutamic acid decarboxylase antibody,[969] allergen,[970] TNT,[971] human IgE,[972] and testosterone.[973] The sensitivity of these assays can be enhanced using fluorescence-labeled antibodies decorated with AuNPs, leading to the technique called localized surface plasmon resonance coupled fluorescence fiber optic sensor.[974−977]

7.2.2. Sensing of Oligonucleotides. The sensitivity of oligonucleotide detection can be improved by using AuNP-amplified SPR.[978,979] Keating et al. developed a sandwich approach where 12-mer oligonucleotides were first linked covalently onto a gold substrate followed by hybridization of one-half of the target DNA molecules. Then, a sequence complementary to the other half of the target was added with or without tagging of AuNPs. The AuNP-tagged surface demonstrated a 10-fold increase in angle shift concomitant with a 1000-fold improvement in sensitivity and a ~10 pM detection limit for the target 24-mer oligonucleotide.[980] For example, Zhou et al. have shown that an intermediate carboxylated dextran layer between gold film and the immobilized DNA molecules effectively eliminates the nonspecific adsorption of oligonucleotide functionalized AuNPs, resulting femtomolar level of detection for 39-mer DNA (Figure 28).[981] In a representative study, real time multicolor DNA detection has been achieved exploiting AuNP-amplified diffraction, where ssDNA-modified AuNPs and micropatterned chemoresponsive diffraction gratings were used to interrogate simultaneously at multiple laser wavelengths.[982]

7.3. Sensors Based on AuNP Plasmon Resonance Scattering

In addition to changes in LSPR absorption, the plasmon resonance scattering phenomenon of AuNPs provides a useful tool for sensor design.[200,983] The plasmon scattering of 36 nm diameter AuNPs is 10−100 times stronger than dyes or quantum dots. Exploiting this nanoscale phenomena, several groups have developed immunoassays to detect human IgG,[984] kanamycin,[985] and lysozyme in human urine.[986] For example, Ren and co-workers have developed a highly selective and sensitive homogeneous immunoassay and DNA hybridization assay using plasmon scattering of single AuNP probe. The sandwich immunoassay was used to detect cancer biomarkers such as CEA, AFP in femtomolar range, and aptamer recognition for thrombin as low as 2.72 pM.[987] Recently, Ling et al. have reported an LSPR light scattering sensor for Ag^+ with unmodified AuNPs exploiting the specific recognition property of Ag^+ with a cytosine-cytosine mismatch base pair. The addition of Ag^+ removes the oligonucleotide from the AuNP surface causing aggregation concomitant with dramatic increment of LSPR scattering intensity. The LSPR light scattering intensity was proportional to concentration of Ag^+, with a limit of detection of 62 nM.[988] El Sayed et al. have

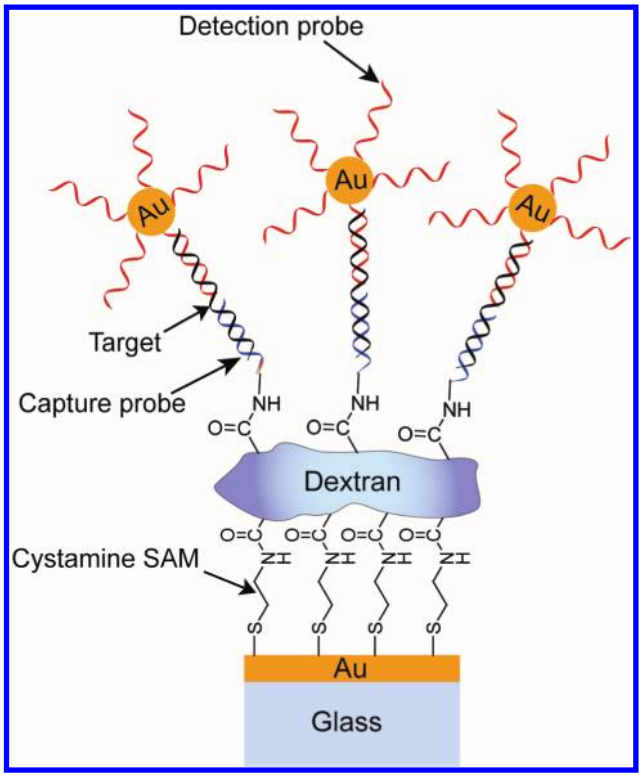

Figure 28. Schematic representation of sandwich DNA detection assay via AuNP-mediated SPR signal amplification. The SPR measurements were carried out by injecting the oligonucleotide functionalized AuNPs into the flow cell housing sensors covered with various duplexes or capture probes. The intermediate dextran layer reduces the nonspecific adsorption of AuNPs, improving detection sensitivity. Reproduced with permission from *Anal. Biochem.* (ref 981). Copyright 2006 Elevier B.V.

demonstrated a biosensor technique using SPR scattering images and SPR absorption spectra from anti-EGFR functionalized AuNPs for the diagnosis of oral epithelial cancer cells in vitro.[989] The anti-EGFR functionalized AuNPs bind 600% stronger to oral malignant cells HOC 313 clone 8 and HSC 3 than normal cell HaCaT, resulting in a sharper SPR absorption band with a red shift (Figure 29).

8. SURFACE ENHANCED RAMAN SCATTERING (SERS)-BASED SENSING

The physical phenomenon behind the Raman spectroscopy is the inelastic scattering of photons by a molecule having quantized vibrational level/signature.[990] Raman scattering is sensitive to different vibrational modes and consequently can provide a "fingerprint" of the target molecules.[991] However, the direct application of this technique in sensitive detection and identification of analyte molecules is severely restricted owing to the low efficiency of inelastic photon scattering by molecules leading to a weak signal.[992] The inherent limitation of low scattering intensity arises from the fact that the Raman scattering cross sections for molecules are usually small, typically 10^{-30}−10^{-25} cm^2/molecule, 10−15 orders of magnitude smaller than that of fluorescence cross section. In the presence of plasmonic nanoparticles or rough metal surfaces, however, the Raman scattering intensity from a molecule can be enhanced by up to 10^{14} order of magnitudes.[993−997] This phenomenon has been attributed to a local electromagnetic field enhancement induced by the

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

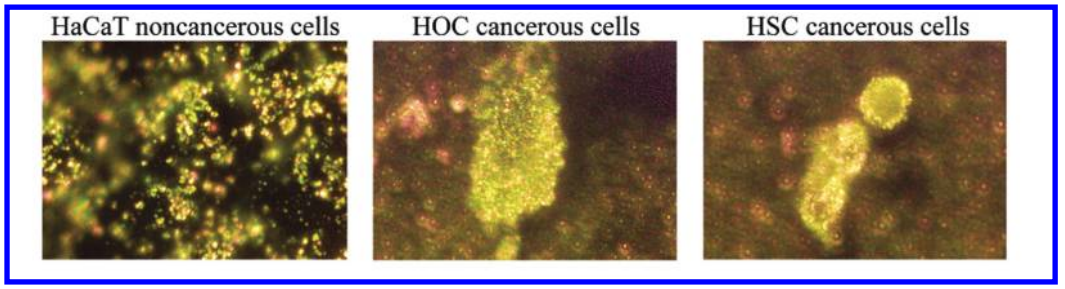

Figure 29. SPR light scattering images to distinguish between normal cells (left panel, HaCaT) and cancerous cells (middle and right panel, HOC and HSC) after incubation with anti-EGFR conjugated AuNPs. The anti-EGFR conjugated AuNPs bind specifically to the surface of cancer cells resulting in a sharper SPR band with a red-shifted maxima. Reproduced with permission from *Nano Lett.* (ref 989). Copyright 2005 American Chemical Society.

plasmon resonance of surfaces and is called surface enhanced Raman scattering (SERS).[998−1001] The field enhancement is dependent on the size, shape, orientation, and aggregation of the nanoparticle. The large enhancement in detectable signal coupled with the unique molecular fingerprints generated has made SERS a powerful tool for the multiplex detection of analytes, with the ability to achieve a detection of single molecule level.[996,997]

8.1. Detection of Small Organic Molecules

AuNPs have been utilized for the SERS-based detection of small organic molecules including explosives.[1002−1005] For example, Ray et al. have used AuNPs modified with cysteine as label-free SERS probe for highly selective and sensitive recognition of TNT.[1002] Cysteine modified AuNPs undergo aggregation in the presence of TNT because of the formation of donor−acceptor Meisenheimer complex between TNT and cysteine. The resulting "hot spots" for enhancement of the Raman signal provided a sensitivity of 2 pM level. Kneipp et al. have shown that SERS nanosensor made from AuNP nanoaggregates and 4-mercaptobenzoic acid attached as a reporter can be used for monitoring changes in local pH of the cellular compartments of living cells.[1006]

8.2. Detection of Oligonucleotides

Mirkin et al. have utilized AuNP probes labeled with oligonucleotides and Raman-active dyes for the SERS-based multiplexed detection of DNA and RNA targets (Figure 30).[1007] To detect the presence of specific target DNA strands, a three-component sandwich assay in a microarray format was used. For the assay, dye-labeled AuNP probes were captured by the target oligonucleotide strands, followed by silver enhancement, generating detectable SERS signals exclusively from the Raman dyes immobilized on the particles, with a limit of detection of 20 fM. More importantly, this method was able to discriminate single nucleotide polymorphisms relating to six different viruses. Irudayaraj et al. have incorporated non-fluorescent Raman tags onto DNA-conjugated AuNP (∼30 nm) probes for the SERS detection of DNA.[1008] In their system, the surface coverage of the Raman tags on the AuNP surface has been modulated to control the intensity of Raman signal from the probes. Simultaneous identification of up to eight probes with a detection limit of ∼100 nM without further metal enhancement was achieved. A DNA sensor using SERS from AuNP aggregates formed via DNA photoligation has been described by Maenosono et al.[1009] In their system, SERS signals arise after hybridization from the Raman-active molecules present in the NP aggregates. Liu et al. have reported a sequence-specific DNA detection using SERS spectroscopic

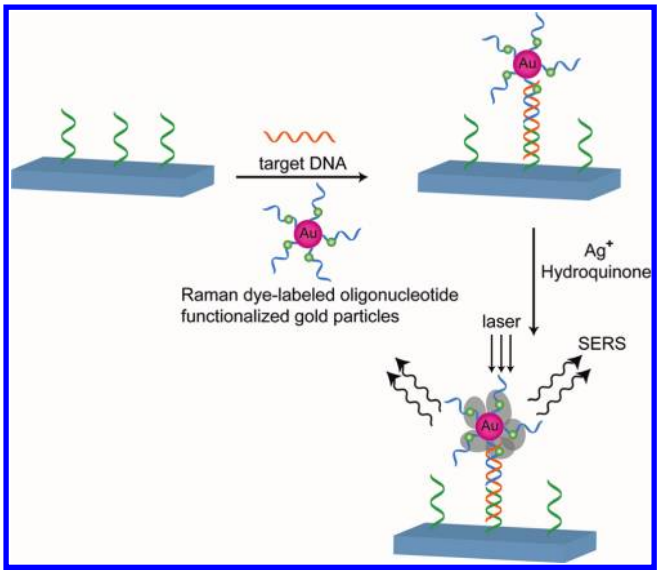

Figure 30. Schematic representation of three-component sandwich assay for SERS-based oligonucleotide detection. Reproduced with permission from *Science* (ref 1007). Copyright 2002 American Association for the Advancement of Science.

fingerprint from thiol-oligonucleotide-modified ZnO/Au nanocomposite probes.[1010] Nie et al. have developed a SERS beacons using DNA conjugated AuNP probe.[1011] Signals from this AuNP-based SERS beacons can be turned on and off by biomolecular binding and dissociation events. Using both distance dependent SERS enhancement of the isolated AuNPs and the "hot spots" created by two conjugated AuNPs, Hu et al. have developed a novel nanojunction based biosensor for the detection of subattomolar HIV-1 DNA.[1012] Johnson et al. have demonstrated an indirect capture model assay for SERS-based detection of DNA using AuNPs.[1013] SERS based approach utilizing AuNP probes for identifying and quantifying multiple gene segments extracted from cells has been described by Irudayaraj et al.[1014] Multiple AuNP-on-wire systems as a SERS sensing platform for viral DNA have been developed by Kang and co-workers.[1015] Their particle-on-wire sensor provided SERS signals only in the presence of target DNA, leading to the detection of DNA concentration ranging from 10 pM to 10 nM. Raman dye labeled AuNP probes have also been applied for SERS based in vivo and in vitro imaging.[1016−1021]

8.3. Detection of Proteins

AuNPs have been widely used in SERS based immunoassays of proteins.[1022−1029] For example, Grubisha et al. reported an

dx.doi.org/10.1021/cr2001178 | *Chem. Rev.* 2012, 112, 2739−2779

immunoassay using 30 nm AuNPs functionalized with a monolayer of an intrinsically strong Raman scatterer (5-thiol-2-nitrobenzoate) followed by a layer of covalently linked antibodies.[1024] In this system, a sandwich assay format based on monoclonal antibodies has been used for the detection of free PSA. The sensitivity from this system has been drastically enhanced because of their unique senor design, which not only minimizes the separation between label and particle surface but also maximizes the number of labels on each particle. The detection limit of this immunoassay was ~1 pg mL^{-1} in human serum. Kim et al. have demonstrated a label-free detection system for avidin via avidin-mediated self-assembly between biotinylated Au nanowires and biotinylated AuNPs. The avidin induced self-assembly process created 'hot spots' between the nanowire and AuNPs that strongly enhanced the Raman signal.[1030] An aptasensor based on the formation of SERS "hot spots" between nanowires and AuNPs has also been used to detect human α-thrombin in serum.[1031] Hu et al. have used AuNPs functionalized with thrombin specific aptamer for the detection of thrombin.[1032] Their electrostatic interaction based assay approach provided a detection limit of 20 pM. Mirkin et al. have used AuNPs functionalized with either protein ligands or antibodies and Raman dyes to perform multiplexed screening of protein-small molecule interactions and protein−protein interactions in a microarray format.[1033] Reich et al. have employed DNA-bridged AuNP assemblies for the detection of protein−DNA interactions via SERS.[1034] Self-assembly of peptide functionalized AuNPs has been used for the SERS based detection of proteases.[1035] Wang et al. demonstrated a microarray approach based on SERS for the detection of peptide−protein or protein−antibody interactions.[1036] A SERS-based assay technique was developed by Gu et al. to detect the activity of alkaline phosphatase enzyme at ultralow concentrations.[1037] SERS based rapid screening of pathogenic bacteria has also been achieved utilizing AuNPs.[1038,1039]

9. AUNPS IN QUARTZ CRYSTAL MICROBALANCE-BASED SENSING

Quartz crystal microbalances (QCM) are ultrasensitive piezoelectric devices that use frequency changes on a quartz crystal resonator to monitor changes in mass arising from analyte binding. This technique has been widely used to sense chemical vapors, microorganisms, and DNA probes because of its high sensitivity and label-free detection.[1040−1046] The incorporation of AuNPs into QCM-based sensing systems[1047] can enhance detection sensitivity by their high surface area and by serving as a "mass enhancer" by amplifying the frequency changes.[1048] On the small molecule front, AuNPs and AuNP-dendrimer composite behaving as sorptive materials have been utilized to detect chemical vapors.[1049−1052]

9.1. Detection of Oligonucleotides

Several groups have reported QCM-based oligonucleotide sensors incorporating AuNPs.[1053] For example, Duan and co-workers have shown the introduction of AuNPs greatly enhances the immobilization capacity and the detection limit for oligonucleotide sensing using QCM.[1054] In their findings, the immobilization of ~12 nm diameter AuNPs onto a gold coated QCM resulted in easier attachment of thiol containing ssDNA, resulting in higher sensitivity upon addition of target oligonucleotides. Sandwich-based approaches using ssDNA-modified AuNPs, can significantly improve the detection limit, where one end of the target oligonucleotide hybridizes with the immobilized ssDNA (recognition element) while the other end hybridizes with AuNPs (mass enhancer).[1055−1063] It should be noted, however, the nonspecific adsorption of AuNPs to the gold film of QCM should be avoided to prevent the overestimation of signal amplification.[1064] On the other hand, catalytic deposition of gold films onto amplifier AuNPs has been proved to enhance the sensitivity of the QCM approach for DNA detection with a detection limit of 1 fM.[1065] Microcantilever-based DNA sensors are a parallel method that monitors mass changes on much smaller platforms. The sensor element, however, in comparison to QCM, is at least 100 times smaller, providing a high density sensor array for multiplexed detection. Using the sandwich approach together with AuNP-mediated amplification on a microcantilever, Dravid et al. obtained a detection limit of 23 pM for a 30-mer DNA.[1066]

9.2. Detection of Proteins

Several sandwich type assays on QCM using AuNPs have been reported for immunosensing of proteins.[1067−1072] For example, detection of streptavidin on a QCM has been achieved using AuNPs as signal amplifiers.[1073] The experimental set up involves the immobilization of biotinylated BSA on the gold surface of the QCM electrode. Addition of streptavidin generates a small frequency change that is amplified by incubation with biotin functionalized AuNP providing a detection limit of 1 ng/mL. A similar approach has been described by Kim et al. to detect C-reactive protein.[1074] To attain further sensitivity Su et al. developed a QCM biosensor using primary AuNP-amplified sandwich immunoassay with the silver enhancement technique. The AuNP-promoted silver reduction and the deposition of silver improved the detection of human IgG with 2-fold of magnitudes.[1075] Other QCM-based biosensors have also been reported for the detection of pathogens,[1076−1078] antisperm antibody,[1079] human carcinoma cells,[1080] lectin,[1081] and dengue virus[1082] exploiting analogous AuNP-enhanced signal amplification.

10. AUNP-BASED BIO-BARCODE ASSAYS

A multiplexed and ultrasensitive detection for proteins and nucleic acids has been developed by Mirkin et al. using a AuNP-based biobarcode assay to amplify the target molecules.[16,1083,1084] The biobarcode assay was first utilized for identifying PSA.[889] As illustrated in Figure 31a, the target of interest PSA was captured by targeting antibodies immobilized on magnetic microparticles. A AuNP encoding double-stranded barcode DNAs and PSA targeting antibodies then bound with the magnetic microparticle. After magnetic separation of the complexes, thermal dehybridization of the barcode DNAs on AuNPs was carried out to afford the single-stranded free barcode DNA and the ssDNA encoded AuNPs. The free barcode ssDNAs were analyzed by using the PCR amplification to determine the presence of PSA, providing a limit of detection of 3 aM. When the ssDNA-encoded AuNP probes were analyzed by using chip-based hybridization followed by silver amplification, PSA was detected at 30 aM.[889]

Exploiting the same principle, a AuNP-based biobarcode assay to detect DNA has also been reported.[1085−1087] As shown in Figure 31b, specific ssDNA replaced the antibodies on magnetic microparticle in the protein detection system. Upon complementary binding with the target DNA, both magnetic microparticle and biobarcoded AuNPs form sandwich assemblies. The magnetic separation of the sandwich assemblies

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739−2779

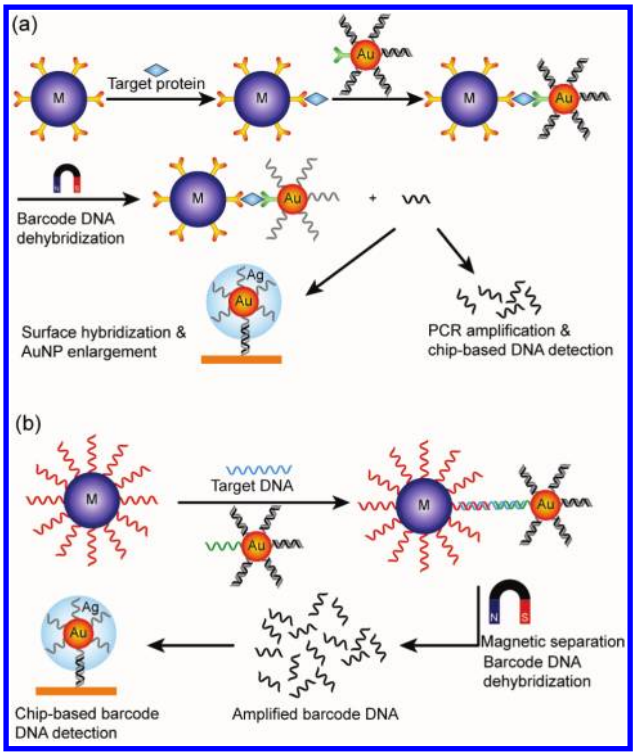

Figure 31. AuNP-based biobarcode assay of (a) proteins and (b) DNA.

followed by thermal dehybridization released the free bar-code DNA for analysis. Scanometric detection of this method provides 500 zeptomolar sensitivity, comparable to many PCR-based approaches.[1086] The authors also demonstrated that the biobarcoded amplification method can be used for identifying multiple DNA targets and bacterial genomic DNA.[1088]

The biobarcode assay has been applied to detect specific targets for many diseases.[1089,1090] This approach has also been used to measure the concentration of amyloid-β-derived diffusible ligand (ADDL), a soluble pathogenic Alzheimer's disease marker in the cerebrospinal fluid (CSF).[1091] In this work, the biobarcode assay was used to detect ADDL in CSF at clinically relevant concentrations (<1 pM) that were not detectable by conventional ELISA or blotting assay. Mirkin et al. also reported a biobarcode assay for detecting human telomerase, a biomarker for cancer diagnosis.[1092,1093] Recently, AuNP-based biobarcode assay has been conducted to detect PSA in the serum of patients who have experienced radical prostatectomy for prostate cancer.[1094] The assay is ~300 times more sensitive than commercial immunoassays.

The AuNP-based biobarcode assay has been employed for multiplexed detection of protein cancer markers by using a mixture of different biobarcoded AuNP probes.[1095,1096] During the detection process, the released barcode DNA molecules can be specifically immobilized onto DNA functionalized surfaces followed by hybridization with ssDNA–AuNP and silver amplification. The multiplexed barcode assay can detect the target markers at low-femtomolar concentrations in serum.

An analogous fluorophore labeled biobarcode amplification method simplifies the detection process of the previously reported biobarcode AuNPs assay by eliminating the requirement for barcode sorting.[1097] Quantification of the assay is analyzed by measuring the fluorescence intensity of the released fluorophore-labeled barcode DNA. When the assay was tested with PSA, a detection limit of 300 aM was obtained without enzymatic amplification or microarray analysis. Wolff et al. have reported fluorescent DNA barcode-based assay for detecting avian influenza virus with PCR-like sensitivity.[1098]

A colorimetric biobarcode amplification assay has been developed by Groves et al. for the protein detection.[1099,1100] In this system, the released barcode DNAs serve as a bridging agent for two ssDNA-functionalized AuNPs, inducing aggregation of the AuNPs and consequent red-to-blue color change to detect target molecules. The authors showed that cytokine, a biomarker for immunodeficiency-related diseases, was detected up to 30 aM concentration, 3 orders of magnitude more sensitive than conventional cytokine detection assays.

11. CONCLUDING REMARKS

The physical properties, ease of synthesis, and functionalization make AuNPs a versatile platform for chemical and biological sensors. The adaptable functionalization of both selective and specific recognition elements and environmentally responsive optoelectronic properties of AuNPs can be utilized to accomplish the transduction of the binding event with appropriate affinity and selectivity toward target analytes. Functionalized AuNPs may act as both molecular receptor and signal transducer in a single sensing motif, thereby simplifying the sensor design as improving the sensitivity. In addition, taking advantage of the particular chemistry at the surface of AuNPs, the sensing accuracy can be improved and the sensor system can be expanded over a broad range of biological condition.

A variety of factors including the analyte, the recognition partner, and the transduction process can influence the sensitivity of AuNP-based sensors. As we have summarized throughout the review, the detection limit of the AuNP-based sensors spans from micromolar to zeptomolar depending on the target species as well as the sensor design. In general the subpico-/femtomolar detection limit can be achieved with proteins and DNA as target analytes, which meets their theoretical detection limit using microfluidic nanoscale sensors.[28] However, this detection limit is predominantly due to the analyte transport limitation, demonstrating the importance of directed transport of biomolecules for further improvements in sensitivity.

Advanced nanodiagnostic techniques have paved the way for affording easy, rapid, low-cost, and multiplexed identification of biomarkers. However, optimization of parameters for the sensing systems is still required to meet the demands of clinical diagnostics for the future development of personalized medicine. In particular, the development of efficient sensors to detect analytes in complex biological fluids such as urine, serum, and blood remains a challenge. Additionally, efficient detection of disease markers often requires multiplex analysis which demands fabrication of high amount of pertinent specific recognition elements. These issues can be addressed in two parallel manners: (1) further miniaturization that increases the number of recognition elements or (2) use of a differential sensor array approach which relies on the selective rather than specific capture of analyte.[10] For the second strategy, the ease of surface functionalization of AuNPs can generate an efficient sensor array with limited number of elements that can perform a high-throughput screening of different target analytes. Taken together, both optoelectronic properties of the core of AuNPs and its tunable surface properties hold great promises for the development of chemical and biological sensors of high

dx.doi.org/10.1021/cr2001178 | Chem. Rev. 2012, 112, 2739–2779

performance. As described in this review, there have been numerous AuNP-based sensor systems fashioned to date of both fundamental and clinical importance. The fundamental advantages of AuNPs have generated an exponential increase in their use in sensing that will continue to revolutionize the field of diagnostics for years to come.

AUTHOR INFORMATION

Corresponding Author

*E-mail: rotello@chem.umass.edu.

Biographies

Krishnendu Saha received his B.Sc. in Chemistry from Jadavpur University, India in 2006 and M.Sc. in Chemistry from Indian Institute of Technology-Madras, India in 2008. He is currently pursuing his Ph.D. at the Department of Chemistry, University of Massachusetts at Amherst, U.S.A. under the supervision of Professor Vincent M. Rotello. His current research interest involves the use of gold nanoparticles for cell-surface recognition, cancer diagnosis, and delivery applications.

Sarit S. Agasti received his B.Sc. in Chemistry from the Calcutta University, India in 2003 and M.Sc. from the Indian Institute of Technology-Kanpur, India in 2005. He then joined the Department of Chemistry at University of Massachusetts-Amherst to pursue doctoral studies. There he worked under the tutelage of Dr. Vincent M. Rotello. He received his PhD in 2011. His doctoral research was oriented toward developing surface functionalized gold nanoparticles with tailored monolayers for biological applications, including protein surface recognition and creating delivery systems for therapeutic applications. Currently, he is working as a postdoctoral fellow in the Dr. Ralph Weissleder group at Massachusetts General Hospital and Harvard Medical School.

Chaekyu Kim obtained B.E. in Chemical engineering in 2002 and M.E. in Polymer science and engineering in 2005 from Inha University in South Korea. He is currently pursuing his PhD in Chemistry in Umass-Amherst with Professor Vincent Rotello since 2006. His research interests focus on bionanotechnological applications via engineering the interface between biomacromolecules and nanomaterials. He is working on synthesis and characterization of gold nanoparticles for cancer therapeutic strategies.

Xiaoning Li received her B.Sc. in Chemistry from University of Science and Technology of China, China in 2008. She is currently pursuing her Ph.D. at the Department of Chemistry, University of Massachusetts at Amherst, U.S.A. under the guidance of Professor Vincent M. Rotello. Her current research interest focuses on gold nanoparticle-fabricated biosensors.

Vincent Rotello is the Charles A. Goessmann Professor of Chemistry at the University of Massachusetts at Amherst, He has been the recipient of the NSF CAREER and Cottrell Scholar awards, as well as the Camille Dreyfus Teacher-Scholar, the Sloan Fellowships, and the Langmuir Lectureship, and is a Fellow of the American Association for

the Advancement of Science (AAAS) and of the Royal Society of Chemistry (U.K.). His research program focuses on using synthetic organic chemistry to engineer the interface between hard and soft materials, and spans the areas of devices, polymers, and nanotechnology/bionanotechnology, with over 340 papers published to date.

ACKNOWLEDGMENTS

We acknowledge the support of the NIH (EB012246, GM077173) and the NSF (CHE-0808945, VR), MRSEC facilities, and the Center for Hierarchical Manufacturing (DMI-0531171).

REFERENCES

(1) Diamond, D. *Principles of Chemical and Biological Sensors*; John Wiley & Sons, Inc.: New York, NY, 1998.
(2) Sadik, O. A.; Land, W. H.; Wang, J. *Electroanalysis* **2003**, *15*, 1149.
(3) El-Sherif, M.; Bansal, L.; Yuan, J. M. *Sensors* **2007**, *7*, 3100.
(4) Sapsford, K. E.; Bradburne, C.; Detehanty, J. B.; Medintz, I. L. *Mater. Today* **2008**, *11*, 38.
(5) Burnworth, M.; Rowan, S. J.; Weder, C. *Chem.—Eur. J.* **2007**, *13*, 7828.
(6) Paddle, B. M. *Biosens. Bioelectron.* **1996**, *11*, 1079.
(7) Russell, A. J.; Berberich, J. A.; Drevon, G. E.; Koepsel, R. R. *Annu. Rev. Biomed. Eng.* **2003**, *5*, 1.
(8) Miranda, O. R.; Creran, B.; Rotello, V. M. *Curr. Opin. Chem. Biol.* **2010**, *14*, 728.
(9) De, M.; Ghosh, P. S.; Rotello, V. M. *Adv. Mater.* **2008**, *20*, 4225.
(10) Anslyn, E. V.; Rotello, V. M. *Curr. Opin. Chem. Biol.* **2010**, *14*, 683.
(11) Cote, G. L.; Lec, R. M.; Pishko, M. V. *IEEE Sens. J.* **2003**, *3*, 251.
(12) Sanchez, C.; Julian, B.; Belleville, P.; Popall, M. *J. Mater. Chem.* **2005**, *15*, 3559.
(13) Thomas, S. W.; Joly, G. D.; Swager, T. M. *Chem. Rev.* **2007**, *107*, 1339.
(14) Anker, J. N.; Hall, W. P.; Lyandres, O.; Shah, N. C.; Zhao, J.; Van Duyne, R. P. *Nat. Mater.* **2008**, *7*, 442.
(15) Shipway, A. N.; Katz, E.; Willner, I. *ChemPhysChem* **2000**, *1*, 18.
(16) Rosi, N. L.; Mirkin, C. A. *Chem. Rev.* **2005**, *105*, 1547.
(17) Agasti, S. S.; Rana, S.; Park, M. H.; Kim, C. K.; You, C. C.; Rotello, V. M. *Adv. Drug Delivery Rev.* **2010**, *62*, 316.
(18) Alivisatos, P. *Nat. Biotechnol.* **2004**, *22*, 47.
(19) Asefa, T.; Duncan, C. T.; Sharma, K. K. *Analyst* **2009**, *134*, 1980.
(20) Cheng, M. M. C.; Cuda, G.; Bunimovich, Y. L.; Gaspari, M.; Heath, J. R.; Hill, H. D.; Mirkin, C. A.; Nijdam, A. J.; Terracciano, R.; Thundat, T.; Ferrari, M. *Curr. Opin. Chem. Biol.* **2006**, *10*, 11.
(21) Pandey, P.; Datta, M.; Malhotra, B. D. *Anal. Lett.* **2008**, *41*, 159.
(22) Parak, W. J.; Gerion, D.; Pellegrino, T.; Zanchet, D.; Micheel, C.; Williams, S. C.; Boudreau, R.; Le Gros, M. A.; Larabell, C. A.; Alivisatos, A. P. *Nanotechnology* **2003**, *14*, R15.
(23) Niemeyer, C. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 4128.
(24) Tansil, N. C.; Gao, Z. Q. *Nano Today* **2006**, *1*, 28.
(25) Welser, K.; Adsley, R.; Moore, B. M.; Chan, W. C.; Aylott, J. W. *Analyst* **2011**, *136*, 29.
(26) West, J. L.; Halas, N. J. *Curr. Opin. Biotechnol.* **2000**, *11*, 215.
(27) Khanna, V. K. *Def. Sci. J.* **2008**, *58*, 608.
(28) Sheehan, P. E.; Whitman, L. J. *Nano Lett.* **2005**, *5*, 803.
(29) Boisselier, E.; Astruc, D. *Chem. Soc. Rev.* **2009**, *38*, 1759.
(30) Daniel, M. C.; Astruc, D. *Chem. Rev.* **2004**, *104*, 293.
(31) Haick, H. *J. Phys. D: Appl. Phys* **2007**, *40*, 7173.
(32) Zayats, M.; Baron, R.; Popov, I.; Willner, I. *Nano Lett.* **2005**, *5*, 21.
(33) Zhao, W.; Brook, M. A.; Li, Y. F. *ChemBioChem* **2008**, *9*, 2363.
(34) Bunz, U. H. F.; Rotello, V. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 3268.
(35) Sperling, R. A.; Rivera Gil, P.; Zhang, F.; Zanella, M.; Parak, W. J. *Chem. Soc. Rev.* **2008**, *37*, 1896.
(36) Radwan, S. H.; Azzazy, H. M. E. *Expert Rev. Mol. Diagn.* **2009**, *9*, 511.
(37) Zeng, S. W.; Yong, K. T.; Roy, I.; Dinh, X. Q.; Yu, X.; Luan, F. *Plasmonics* **2011**, *6*, 491.
(38) Wilson, R. *Chem. Soc. Rev.* **2008**, *37*, 2028.
(39) Faraday, M. *Philos. Trans. R. Soc. London* **1857**, *147*, 145.
(40) Turkevich, J.; Stevenson, P. C.; Hillier, J. *Discuss. Faraday Soc* **1951**, 55.
(41) Frens, G. *Nature: Phys. Sci* **1973**, *241*, 20.
(42) Chow, M. K.; Zukoski, C. F. *J. Colloid Interface Sci.* **1994**, *165*, 97.
(43) Ji, X. H.; Song, X. N.; Li, J.; Bai, Y. B.; Yang, W. S.; Peng, X. G. *J. Am. Chem. Soc.* **2007**, *129*, 13939.
(44) Kimling, J.; Maier, M.; Okenve, B.; Kotaidis, V.; Ballot, H.; Plech, A. *J. Phys. Chem. B* **2006**, *110*, 15700.
(45) Nguyen, D. T.; Kim, D. J.; So, M. G.; Kim, K. S. *Adv. Powder Technol.* **2010**, *21*, 111.
(46) Polte, J.; Ahner, T. T.; Delissen, F.; Sokolov, S.; Emmerling, F.; Thunemann, A. F.; Kraehnert, R. *J. Am. Chem. Soc.* **2010**, *132*, 1296.
(47) Pong, B. K.; Elim, H. I.; Chong, J. X.; Ji, W.; Trout, B. L.; Lee, J. Y. *J. Phys. Chem. C* **2007**, *111*, 6281.
(48) Uppal, M. A.; Kafizas, A.; Ewing, M. B.; Parkin, I. P. *New J. Chem.* **2010**, *34*, 2906.
(49) Uppal, M. A.; Kafizas, A.; Lim, T. H.; Parkin, I. P. *New J. Chem.* **2010**, *34*, 1401.
(50) Giersig, M.; Mulvaney, P. *Langmuir* **1993**, *9*, 3408.
(51) Brust, M.; Walker, M.; Bethell, D.; Schiffrin, D. J.; Whyman, R. *J. Chem. Soc., Chem. Commun.* **1994**, 801.
(52) Hostetler, M. J.; Wingate, J. E.; Zhong, C. J.; Harris, J. E.; Vachet, R. W.; Clark, M. R.; Londono, J. D.; Green, S. J.; Stokes, J. J.; Wignall, G. D.; Glish, G. L.; Porter, M. D.; Evans, N. D.; Murray, R. W. *Langmuir* **1998**, *14*, 17.
(53) Chen, S. W. *Langmuir* **1999**, *15*, 7551.
(54) Chen, S. W.; Murray, R. W. *Langmuir* **1999**, *15*, 682.
(55) Hostetler, M. J.; Green, S. J.; Stokes, J. J.; Murray, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 4212.
(56) Ingram, R. S.; Hostetler, M. J.; Murray, R. W. *J. Am. Chem. Soc.* **1997**, *119*, 9175.
(57) Templeton, A. C.; Wuelfing, M. P.; Murray, R. W. *Acc. Chem. Res.* **2000**, *33*, 27.
(58) Brust, M.; Fink, J.; Bethell, D.; Schiffrin, D. J.; Kiely, C. *J. Chem. Soc., Chem. Commun.* **1995**, 1655.
(59) Kanaras, A. G.; Kamounah, F. S.; Schaumburg, K.; Kiely, C. J.; Brust, M. *Chem. Commun.* **2002**, 2294.
(60) Zheng, M.; Li, Z. G.; Huang, X. Y. *Langmuir* **2004**, *20*, 4226.
(61) Templeton, A. C.; Chen, S. W.; Gross, S. M.; Murray, R. W. *Langmuir* **1999**, *15*, 66.
(62) Price, R. C.; Whetten, R. L. *J. Am. Chem. Soc.* **2005**, *127*, 13750.
(63) Shon, Y. S.; Gross, S. M.; Dawson, B.; Porter, M.; Murray, R. W. *Langmuir* **2000**, *16*, 6555.
(64) Shon, Y. S.; Wuelfing, W. P.; Murray, R. W. *Langmuir* **2001**, *17*, 1255.
(65) Lohse, S. E.; Dahl, J. A.; Hutchison, J. E. *Langmuir* **2010**, *26*, 7504.
(66) Boal, A. K.; Ilhan, F.; DeRouchey, J. E.; Thurn-Albrecht, T.; Russell, T. P.; Rotello, V. M. *Nature* **2000**, *404*, 746.
(67) Itoh, H.; Tahara, A.; Naka, K.; Chujo, Y. *Langmuir* **2004**, *20*, 1972.
(68) Zhou, J. F.; Beattie, D. A.; Sedev, R.; Ralston, J. *Langmuir* **2007**, *23*, 9170.
(69) Goulet, P. J. G.; Lennox, R. B. *J. Am. Chem. Soc.* **2010**, *132*, 9582.
(70) Yee, C. K.; Jordan, R.; Ulman, A.; White, H.; King, A.; Rafailovich, M.; Sokolov, J. *Langmuir* **1999**, *15*, 3486.
(71) Ascencio, J. A.; Perez, M.; Jose-Yacaman, M. *Surf. Sci.* **2000**, *447*, 73.
(72) Sugie, A.; Hatta, T.; Kanie, K.; Muramatsu, A.; Mori, A. *Chem. Lett.* **2009**, *38*, 562.
(73) Sardar, R.; Shumaker-Parry, J. S. *Chem. Mater.* **2009**, *21*, 1167.

(74) Negishi, Y.; Takasugi, Y.; Sato, S.; Yao, H.; Kimura, K.; Tsukuda, T. *J. Am. Chem. Soc.* **2004**, *126*, 6518.
(75) Templeton, A. C.; Hostetler, M. J.; Kraft, C. T.; Murray, R. W. *J. Am. Chem. Soc.* **1998**, *120*, 1906.
(76) Hostetler, M. J.; Templeton, A. C.; Murray, R. W. *Langmuir* **1999**, *15*, 3782.
(77) Jadzinsky, P. D.; Calero, G.; Ackerson, C. J.; Bushnell, D. A.; Kornberg, R. D. *Science* **2007**, *318*, 430.
(78) Boal, A. K.; Rotello, V. M. *J. Am. Chem. Soc.* **2000**, *122*, 734.
(79) Zachary, M.; Chechik, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 3304.
(80) Ionita, P.; Wolowska, J.; Chechik, V.; Caragheorgheopol, A. *J. Phys. Chem. C* **2007**, *111*, 16717.
(81) Ionita, P.; Volkov, A.; Jeschke, G.; Chechik, V. *Anal. Chem.* **2008**, *80*, 95.
(82) Donkers, R. L.; Lee, D.; Murray, R. W. *Langmuir* **2004**, *20*, 1945.
(83) Wang, W.; Murray, R. W. *Langmuir* **2005**, *21*, 7015.
(84) Woehrle, G. H.; Warner, M. G.; Hutchison, J. E. *J. Phys. Chem. B* **2002**, *106*, 9979.
(85) Woehrle, G. H.; Brown, L. O.; Hutchison, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 2172.
(86) Leff, D. V.; Ohara, P. C.; Heath, J. R.; Gelbart, W. M. *J. Phys. Chem.* **1995**, *99*, 7036.
(87) Tao, A. R.; Habas, S.; Yang, P. D. *Small* **2008**, *4*, 310.
(88) Prasad, B. L. V.; Stoeva, S. I.; Sorensen, C. M.; Klabunde, K. J. *Langmuir* **2002**, *18*, 7515.
(89) Prasad, B. L. V.; Stoeva, S. I.; Sorensen, C. M.; Klabunde, K. J. *Chem. Mater.* **2003**, *15*, 935.
(90) Zhong, C. J.; Zhang, W. X.; Leibowitz, F. L.; Eichelberger, H. H. *Chem. Commun.* **1999**, 1211.
(91) Maye, M. M.; Zheng, W. X.; Leibowitz, F. L.; Ly, N. K.; Zhong, C. J. *Langmuir* **2000**, *16*, 490.
(92) Kurita, H.; Takami, A.; Koda, S. *Appl. Phys. Lett.* **1998**, *72*, 789.
(93) Sau, T. K.; Pal, A.; Jana, N. R.; Wang, Z. L.; Pal, T. *J. Nanopart. Res.* **2001**, *3*, 257.
(94) Mossmer, S.; Spatz, J. P.; Moller, M.; Aberle, T.; Schmidt, J.; Burchard, W. *Macromolecules* **2000**, *33*, 4791.
(95) Meltzer, S.; Resch, R.; Koel, B. E.; Thompson, M. E.; Madhukar, A.; Requicha, A. A. G.; Will, P. *Langmuir* **2001**, *17*, 1713.
(96) Mallick, K.; Wang, Z. L.; Pal, T. *J. Photochem. Photobiol., A* **2001**, *140*, 75.
(97) Sobhan, M. A.; Withford, M. J.; Goldys, E. M. *Langmuir* **2010**, *26*, 3156.
(98) Chen, W.; Cai, W. P.; Liang, C. H.; Zhang, L. D. *Mater. Res. Bull.* **2001**, *36*, 335.
(99) Chen, W.; Cai, W. P.; Zhang, L.; Wang, G. Z.; Zhang, L. D. *J. Colloid Interface Sci.* **2001**, *238*, 291.
(100) Niidome, Y.; Hori, A.; Sato, T.; Yamada, S. *Chem. Lett.* **2000**, 310.
(101) Pol, V. G.; Gedanken, A.; Calderon-Moreno, J. *Chem. Mater.* **2003**, *15*, 1111.
(102) Reed, J. A.; Cook, A.; Halaas, D. J.; Parazzoli, P.; Robinson, A.; Matula, T. J.; Grieser, F. *Ultrason. Sonochem* **2003**, *10*, 285.
(103) Zhou, Y.; Wang, C. Y.; Zhu, Y. R.; Chen, Z. Y. *Chem. Mater.* **1999**, *11*, 2310.
(104) Dawson, A.; Kamat, P. V. *J. Phys. Chem. B* **2000**, *104*, 11842.
(105) Gachard, E.; Remita, H.; Khatouri, J.; Keita, B.; Nadjo, L.; Belloni, J. *New J. Chem.* **1998**, *22*, 1257.
(106) Henglein, A.; Meisel, D. *Langmuir* **1998**, *14*, 7392.
(107) Wei, G. T.; Liu, F. K.; Wang, C. R. C. *Anal. Chem.* **1999**, *71*, 2085.
(108) Helcher, H. H. *Aurum Potabile oder Gold Tinstur*; J. Herbord Klossen: Breslau and Leipzig, 1718.
(109) Meguro, K.; Nakamura, Y.; Hayashi, Y.; Torizuka, M.; Esumi, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 347.
(110) Carotenuto, G. *Appl. Organomet. Chem.* **2001**, *15*, 344.
(111) Seoudi, R.; Fouda, A. A.; Elmenshawy, D. A. *Phys. B* **2010**, *405*, 906.
(112) Hayat, M. A. *Colloidal Gold, Principles, Methods, and Applications.*; Academic Press: New York, 1989.
(113) Oh, E.; Susumu, K.; Goswami, R.; Mattoussi, H. *Langmuir* **2010**, *26*, 7604.
(114) Susumu, K.; Mei, B. C.; Mattoussi, H. *Nat. Protoc.* **2009**, *4*, 424.
(115) Tracy, J. B.; Kalyuzhny, G.; Crowe, M. C.; Balasubramanian, R.; Choi, J. P.; Murray, R. W. *J. Am. Chem. Soc.* **2007**, *129*, 6706.
(116) Li, D. X.; He, Q.; Cui, Y.; Li, J. B. *Chem. Mater.* **2007**, *19*, 412.
(117) Bohrisch, J.; Wendler, U.; Jaeger, W. *Macromol. Rapid Commun.* **1997**, *18*, 975.
(118) Harnish, B.; Robinson, J. T.; Pei, Z. C.; Ramstrom, O.; Yan, M. D. *Chem. Mater.* **2005**, *17*, 4092.
(119) Pucci, A.; Bernabo, M.; Elvati, P.; Meza, L. I.; Galembeck, F.; Leite, C. A. D.; Tirelli, N.; Ruggeri, G. *J. Mater. Chem.* **2006**, *16*, 1058.
(120) Bhattacharjee, R. R.; Chakraborty, M.; Mandal, T. K. *J. Phys. Chem. B* **2006**, *110*, 6768.
(121) Huang, H. Z.; Yang, X. R. *Biomacromolecules* **2004**, *5*, 2340.
(122) Sun, X. P.; Dong, S. J.; Wang, E. K. *Polymer* **2004**, *45*, 2181.
(123) Gole, A.; Murphy, C. J. *Chem. Mater.* **2005**, *17*, 1325.
(124) Mandal, T. K.; Fleming, M. S.; Walt, D. R. *Nano Lett.* **2002**, *2*, 3.
(125) Yilmaz, E.; Suzer, S. *Appl. Surf. Sci.* **2010**, *256*, 6630.
(126) Spatz, J. P.; Mossmer, S.; Moller, M. *Angew. Chem., Int. Ed.* **1996**, *35*, 1510.
(127) Spatz, J. P.; Roescher, A.; Moller, M. *Adv. Mater.* **1996**, *8*, 337.
(128) Zikich, D.; Borovok, N.; Molotsky, T.; Kotlyar, A. *Bioconjugate Chem* **2010**, *21*, 544.
(129) Zhu, M. Q.; Wang, L. Q.; Exarhos, G. J.; Li, A. D. Q. *J. Am. Chem. Soc.* **2004**, *126*, 2656.
(130) Morones, J. R.; Frey, W. *J. Nanopart. Res.* **2010**, *12*, 1401.
(131) Ohno, K.; Koh, K.; Tsujii, Y.; Fukuda, T. *Macromolecules* **2002**, *35*, 8989.
(132) Raula, J.; Shan, J.; Nuopponen, M.; Niskanen, A.; Jiang, H.; Kauppinen, E. I.; Tenhu, H. *Langmuir* **2003**, *19*, 3499.
(133) Kim, D. J.; Kang, S. M.; Kong, B.; Kim, W. J.; Paik, H. J.; Choi, H.; Choi, I. S. *Macromol. Chem. Phys.* **2005**, *206*, 1941.
(134) Nuss, S.; Bottcher, H.; Wurm, H.; Hallensleben, M. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 4016.
(135) Yoon, K. R.; Ramaraj, B.; Lee, S. M.; Kim, D. P. *Surf. Interface Anal.* **2008**, *40*, 1139.
(136) Wuelfing, W. P.; Gross, S. M.; Miles, D. T.; Murray, R. W. *J. Am. Chem. Soc.* **1998**, *120*, 12696.
(137) Corbierre, M. K.; Cameron, N. S.; Lennox, R. B. *Langmuir* **2004**, *20*, 2867.
(138) Shan, J.; Nuopponen, M.; Jiang, H.; Kauppinen, E.; Tenhu, H. *Macromolecules* **2003**, *36*, 4526.
(139) Kim, B. J.; Bang, J.; Hawker, C. J.; Kramer, E. J. *Macromolecules* **2006**, *39*, 4108.
(140) Suzuki, D.; Kawaguchi, H. *Langmuir* **2005**, *21*, 8175.
(141) Hussain, I.; Graham, S.; Wang, Z. X.; Tan, B.; Sherrington, D. C.; Rannard, S. P.; Cooper, A. I.; Brust, M. *J. Am. Chem. Soc.* **2005**, *127*, 16398.
(142) Huang, H. M.; Chang, C. Y.; Liu, I. C.; Tsai, H. C.; Lai, M. K.; Tsiang, R. C. C. *J. Polym. Sci., Part A: Polym. Chem* **2005**, *43*, 4710.
(143) Shan, J.; Tenhu, H. *Chem. Commun.* **2007**, 4580.
(144) Kim, F.; Connor, S.; Song, H.; Kuykendall, T.; Yang, P. D. *Angew. Chem., Int. Ed.* **2004**, *43*, 3673.
(145) Salvati, R.; Longo, A.; Carotenuto, G.; De Nicola, S.; Pepe, G. P.; Nicolais, L.; Barone, A. *Appl. Surf. Sci.* **2005**, *248*, 28.
(146) Ah, C. S.; Yun, Y. J.; Park, H. J.; Kim, W. J.; Ha, D. H.; Yun, W. S. *Chem. Mater.* **2005**, *17*, 5558.
(147) Chen, Y.; Gu, X.; Nie, C. G.; Jiang, Z. Y.; Xie, Z. X.; Lin, C. J. *Chem. Commun.* **2005**, 4181.
(148) Hoppe, C. E.; Lazzari, M.; Pardinas-Blanco, I.; Lopez-Quintela, M. A. *Langmuir* **2006**, *22*, 7027.
(149) Wang, L. Y.; Kariuki, N. N.; Schadt, M.; Mott, D.; Luo, J.; Zhong, C. J.; Shi, X. J.; Zhang, C.; Hao, W. B.; Lu, S.; Kim, N.; Wang, J. Q. *Sensors* **2006**, *6*, 667.

(150) Corbierre, M. K.; Cameron, N. S.; Sutton, M.; Mochrie, S. G. J.; Lurio, L. B.; Ruhm, A.; Lennox, R. B. *J. Am. Chem. Soc.* **2001**, *123*, 10411.
(151) Kang, Y. J.; Taton, T. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 409.
(152) Shelley, E. J.; Ryan, D.; Johnson, S. R.; Couillard, M.; Fitzmaurice, D.; Nellist, P. D.; Chen, Y.; Palmer, R. E.; Preece, J. A. *Langmuir* **2002**, *18*, 1791.
(153) Hasan, M.; Bethell, D.; Brust, M. *J. Am. Chem. Soc.* **2002**, *124*, 1132.
(154) Porter, L. A.; Ji, D.; Westcott, S. L.; Graupe, M.; Czernuszewicz, R. S.; Halas, N. J.; Lee, T. R. *Langmuir* **1998**, *14*, 7378.
(155) Yonezawa, T.; Yasui, K.; Kimizuka, N. *Langmuir* **2001**, *17*, 271.
(156) Manna, A.; Chen, P. L.; Akiyama, H.; Wei, T. X.; Tamada, K.; Knoll, W. *Chem. Mater.* **2003**, *15*, 20.
(157) Torigoe, K.; Esumi, K. *J. Phys. Chem. B* **1999**, *103*, 2862.
(158) Letsinger, R. L.; Elghanian, R.; Viswanadham, G.; Mirkin, C. A. *Bioconjugate Chem* **2000**, *11*, 289.
(159) Rouhana, L. L.; Jaber, J. A.; Schlenoff, J. B. *Langmuir* **2007**, *23*, 12799.
(160) Resch, R.; Baur, C.; Bugacov, A.; Koel, B. E.; Echternach, P. M.; Madhukar, A.; Montoya, N.; Requicha, A. A. G.; Will, P. *J. Phys. Chem. B* **1999**, *103*, 3647.
(161) Li, Z.; Jin, R. C.; Mirkin, C. A.; Letsinger, R. L. *Nucleic Acids Res.* **2002**, *30*, 1558.
(162) Tan, Y. W.; Li, Y. F.; Zhu, D. B. *Langmuir* **2002**, *18*, 3392.
(163) Maye, M. M.; Chun, S. C.; Han, L.; Rabinovich, D.; Zhong, C. J. *J. Am. Chem. Soc.* **2002**, *124*, 4958.
(164) Li, X. M.; de Jong, M. R.; Inoue, K.; Shinkai, S.; Huskens, J.; Reinhoudt, D. N. *J. Mater. Chem.* **2001**, *11*, 1919.
(165) Tzhayik, O.; Sawant, P.; Efrima, S.; Kovalev, E.; Klug, J. T. *Langmuir* **2002**, *18*, 3364.
(166) Balasubramanian, R.; Kim, B.; Tripp, S. L.; Wang, X. J.; Lieberman, M.; Wei, A. *Langmuir* **2002**, *18*, 3676.
(167) Sun, L.; Crooks, R. M.; Chechik, V. *Chem. Commun.* **2001**, 359.
(168) Leff, D. V.; Brandt, L.; Heath, J. R. *Langmuir* **1996**, *12*, 4723.
(169) Gomez, S.; Philippot, K.; Colliere, V.; Chaudret, B.; Senocq, F.; Lecante, P. *Chem. Commun.* **2000**, 1945.
(170) Heath, J. R.; Knobler, C. M.; Leff, D. V. *J. Phys. Chem. B* **1997**, *101*, 189.
(171) Kumar, A.; Mandal, S.; Selvakannan, P. R.; Pasricha, R.; Mandale, A. B.; Sastry, M. *Langmuir* **2003**, *19*, 6277.
(172) Aslam, M.; Fu, L.; Su, M.; Vijayamohanan, K.; Dravid, V. P. *J. Mater. Chem.* **2004**, *14*, 1795.
(173) Newman, J. D. S.; Blanchard, G. J. *Langmuir* **2006**, *22*, 5882.
(174) Bhargava, S. K.; Booth, J. M.; Agrawal, S.; Coloe, P.; Kar, G. *Langmuir* **2005**, *21*, 5949.
(175) Selvakannan, P. R.; Mandal, S.; Phadtare, S.; Pasricha, R.; Sastry, M. *Langmuir* **2003**, *19*, 3545.
(176) Selvakannan, P.; Mandal, S.; Phadtare, S.; Gole, A.; Pasricha, R.; Adyanthaya, S. D.; Sastry, M. *J. Colloid Interface Sci.* **2004**, *269*, 97.
(177) Leontowich, A. F. G.; Calver, C. F.; Dasog, M.; Scott, R. W. J. *Langmuir* **2010**, *26*, 1285.
(178) Mandal, S.; Selvakannan, P.; Phadtare, S.; Pasricha, R.; Sastry, M. *Proc. Indian Acad. Sci. Chem. Sci* **2002**, *114*, 513.
(179) Selvakannan, P. R.; Kumar, P. S.; More, A. S.; Shingte, R. D.; Wadgaonkar, P. P.; Sastry, M. *Langmuir* **2004**, *20*, 295.
(180) Isaacs, S. R.; Cutler, E. C.; Park, J. S.; Lee, T. R.; Shon, Y. S. *Langmuir* **2005**, *21*, 5689.
(181) Kotiaho, A.; Lahtinen, R.; Efimov, A.; Lehtivuori, H.; Tkachenko, N. V.; Kanerva, T.; Lemmetyinen, H. *J. Photochem. Photobiol., A* **2010**, *212*, 129.
(182) Duan, H. W.; Nie, S. M. *J. Am. Chem. Soc.* **2007**, *129*, 2412.
(183) Zhu, H. G.; Pan, Z. W.; Hagaman, E. W.; Liang, C. D.; Overbury, S. H.; Dai, S. *J. Colloid Interface Sci.* **2005**, *287*, 360.
(184) Huang, W.; Chen, S. M.; Liu, Y. S.; Fu, H. Y.; Wu, G. Z. *Nanotechnology* **2011**, *22*, 025602.
(185) Das, A. K.; Raj, C. R. *J. Colloid Interface Sci.* **2011**, *353*, 506.
(186) Green, M.; O'Brien, P. *Chem. Commun.* **2000**, 183.
(187) Fleming, D. A.; Williams, M. E. *Langmuir* **2004**, *20*, 3021.
(188) Weare, W. W.; Reed, S. M.; Warner, M. G.; Hutchison, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 12890.
(189) Moores, A.; Goettmann, F.; Sanchez, C.; Le Floch, P. *Chem. Commun.* **2004**, 2842.
(190) Yamamoto, M.; Nakamoto, M. *Chem. Lett.* **2003**, *32*, 452.
(191) Shakeri-Zadeh, A.; Ghasemifard, M.; Mansoor, G. A. *Phys. E* **2010**, *42*, 1272.
(192) Sarkar, A.; Shukla, S. P.; Adhikari, S.; Mukherjee, T. *Int. J. Nano. Technol* **2010**, *7*, 1027.
(193) Wang, W. X.; Chen, Q. F.; Jiang, C.; Yang, D. Z.; Liu, X. M.; Xu, S. K. *Colloid. Surface. A* **2007**, *301*, 73.
(194) Yin, X. J.; Chen, S. G.; Wu, A. G. *Micro Nano Lett.* **2010**, *5*, 270.
(195) Sirajuddin; Mechler, A.; Torriero, A. A. J.; Nafady, A.; Lee, C. Y.; Bond, A. M.; O'Mullane, A. P.; Bhargava, S. K. *Colloids Surf., A* **2010**, *370*, 35.
(196) Quinn, B. M.; Liljeroth, P.; Ruiz, V.; Laaksonen, T.; Kontturi, K. *J. Am. Chem. Soc.* **2003**, *125*, 6644.
(197) Antonello, S.; Holm, A. H.; Instuli, E.; Maran, F. *J. Am. Chem. Soc.* **2007**, *129*, 9836.
(198) Schmid, G.; Simon, U. *Chem. Commun.* **2005**, 697.
(199) Subramaniam, C.; Pradeep, T.; Chakrabarti, J. *Phys. Rev. Lett.* **2005**, *95*, 164501.
(200) Jain, P. K.; Lee, K. S.; El-Sayed, I. H.; El-Sayed, M. A. *J. Phys. Chem. B* **2006**, *110*, 7238.
(201) Mie, G. *Ann. Phys* **1908**, *25*, 377.
(202) Halas, N. J.; Lal, S.; Chang, W. S.; Link, S.; Nordlander, P. *Chem. Rev.* **2011**, *111*, 3913.
(203) Jain, P. K.; Huang, X.; El-Sayed, I. H.; El-Sayed, M. A. *Acc. Chem. Res.* **2008**, *41*, 1578.
(204) Link, S.; El-Sayed, M. A. *Annu. Rev. Phys. Chem.* **2003**, *54*, 331.
(205) Templeton, A. C.; Pietron, J. J.; Murray, R. W.; Mulvaney, P. *J. Phys. Chem. B* **2000**, *104*, 564.
(206) Link, S.; Mohamed, M. B.; El-Sayed, M. A. *J. Phys. Chem. B* **1999**, *103*, 3073.
(207) Yan, B. H.; Yang, Y.; Wang, Y. C. *J. Phys. Chem. B* **2003**, *107*, 9159.
(208) Rechberger, W.; Hohenau, A.; Leitner, A.; Krenn, J. R.; Lamprecht, B.; Aussenegg, F. R. *Opt. Commun.* **2003**, *220*, 137.
(209) Heilweil, E. J.; Hochstrasser, R. M. *J. Chem. Phys.* **1985**, *82*, 4762.
(210) Klar, T.; Perner, M.; Grosse, S.; von Plessen, G.; Spirkl, W.; Feldmann, J. *Phys. Rev. Lett.* **1998**, *80*, 4249.
(211) Link, S.; El-Sayed, M. A. *J. Phys. Chem. B* **1999**, *103*, 4212.
(212) Itoh, T.; Asahi, T.; Masuhara, H. *Appl. Phys. Lett.* **2001**, *79*, 1667.
(213) Su, K. H.; Wei, Q. H.; Zhang, X.; Mock, J. J.; Smith, D. R.; Schultz, S. *Nano Lett.* **2003**, *3*, 1087.
(214) Srivastava, S.; Frankamp, B. L.; Rotello, V. M. *Chem. Mater.* **2005**, *17*, 487.
(215) Du, H.; Fuh, R. C. A.; Li, J. Z.; Corkan, L. A.; Lindsey, J. S. *Photochem. Photobiol.* **1998**, *68*, 141.
(216) Haiss, W.; Thanh, N. T. K.; Aveyard, J.; Fernig, D. G. *Anal. Chem.* **2007**, *79*, 4215.
(217) Khlebtsov, N. G. *Anal. Chem.* **2008**, *80*, 6620.
(218) Liu, X. O.; Atwater, M.; Wang, J. H.; Huo, Q. *Colloids Surf., B* **2007**, *58*, 3.
(219) Thomas, K. G.; Kamat, P. V. *J. Am. Chem. Soc.* **2000**, *122*, 2655.
(220) Xu, P.; Yanagi, H. *Chem. Mater.* **1999**, *11*, 2626.
(221) Dubertret, B.; Calame, M.; Libchaber, A. J. *Nat. Biotechnol.* **2001**, *19*, 365.
(222) Sarathy, K. V.; Narayan, K. S.; Kim, J.; White, J. O. *Chem. Phys. Lett.* **2000**, *318*, 543.
(223) Makarova, O. V.; Ostafin, A. E.; Miyoshi, H.; Norris, J. R.; Meisel, D. *J. Phys. Chem. B* **1999**, *103*, 9080.
(224) Gu, T.; Whitesell, J. K.; Fox, M. A. *Chem. Mater.* **2003**, *15*, 1358.

(225) Dulkeith, E.; Morteani, A. C.; Niedereichholz, T.; Klar, T. A.; Feldmann, J.; Levi, S. A.; van Veggel, F.; Reinhoudt, D. N.; Moller, M.; Gittins, D. I. *Phys. Rev. Lett.* **2002**, *89*, 203002.
(226) Zheng, J.; Petty, J. T.; Dickson, R. M. *J. Am. Chem. Soc.* **2003**, *125*, 7780.
(227) Zheng, J.; Zhang, C. W.; Dickson, R. M. *Phys. Rev. Lett.* **2004**, *93*, 077402.
(228) Schaeffer, N.; Tan, B.; Dickinson, C.; Rosseinsky, M. J.; Laromaine, A.; McComb, D. W.; Stevens, M. M.; Wang, Y.; Petit, L.; Barentin, C.; Spiller, D. G.; Cooper, A. I.; Levy, R. *Chem. Commun.* **2008**, 3986.
(229) Lee, W. I.; Bae, Y. J.; Bard, A. J. *J. Am. Chem. Soc.* **2004**, *126*, 8358.
(230) Gaiduk, A.; Yorulmaz, M.; Orrit, M. *ChemPhysChem*, **2011**, *12*, 1536.
(231) Lakowicz, J. R. *Anal. Biochem.* **2005**, *337*, 171.
(232) Imahori, H.; Fukuzumi, S. *Adv. Mater.* **2001**, *13*, 1197.
(233) Imahori, H.; Arimura, M.; Hanada, T.; Nishimura, Y.; Yamazaki, I.; Sakata, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **2001**, *123*, 335.
(234) Lakowitca, J. R. *Principles of Fluorescence Spectroscopy*; Klumer: New York, 1999.
(235) Wilcoxon, J. P.; Martin, J. E.; Parsapour, F.; Wiedenman, B.; Kelley, D. F. *J. Chem. Phys.* **1998**, *108*, 9137.
(236) Sapsford, K. E.; Berti, L.; Medintz, I. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 4562.
(237) Gersten, J.; Nitzan, A. *J. Chem. Phys.* **1981**, *75*, 1139.
(238) Oh, E.; Hong, M. Y.; Lee, D.; Nam, S. H.; Yoon, H. C.; Kim, H. S. *J. Am. Chem. Soc.* **2005**, *127*, 3270.
(239) Bigioni, T. P.; Whetten, R. L.; Dag, O. *J. Phys. Chem. B* **2000**, *104*, 6983.
(240) Link, S.; El-Sayed, M. A. *Int. Rev. Phys. Chem.* **2000**, *19*, 409.
(241) Mohamed, M. B.; Volkov, V.; Link, S.; El-Sayed, M. A. *Chem. Phys. Lett.* **2000**, *317*, 517.
(242) Dulkeith, E.; Ringler, M.; Klar, T. A.; Feldmann, J.; Javier, A. M.; Parak, W. J. *Nano Lett.* **2005**, *5*, 585.
(243) Yun, C. S.; Javier, A.; Jennings, T.; Fisher, M.; Hira, S.; Peterson, S.; Hopkins, B.; Reich, N. O.; Strouse, G. F. *J. Am. Chem. Soc.* **2005**, *127*, 3115.
(244) Ray, P. C.; Fortner, A.; Darbha, G. K. *J. Phys. Chem. B* **2006**, *110*, 20745.
(245) Jennings, T. L.; Singh, M. P.; Strouse, G. F. *J. Am. Chem. Soc.* **2006**, *128*, 5462.
(246) Kamat, P. V.; Barazzouk, S.; Hotchandani, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2764.
(247) Thomas, K. G.; Kamat, P. V. *Acc. Chem. Res.* **2003**, *36*, 888.
(248) Liu, R. R.; Liew, R. S.; Zhou, H.; Xing, B. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 8799.
(249) Jiang, Y.; Zhao, H.; Lin, Y. Q.; Zhu, N. N.; Ma, Y. R.; Mao, L. Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 4800.
(250) Lin, S. Y.; Liu, S. W.; Lin, C. M.; Chen, C. H. *Anal. Chem.* **2002**, *74*, 330.
(251) Lin, S. Y.; Chen, C. H.; Lin, M. C.; Hsu, H. F. *Anal. Chem.* **2005**, *77*, 4821.
(252) Obare, S. O.; Hollowell, R. E.; Murphy, C. J. *Langmuir* **2002**, *18*, 10407.
(253) Reynolds, A. J.; Haines, A. H.; Russell, D. A. *Langmuir* **2006**, *22*, 1156.
(254) Kim, Y. J.; Johnson, R. C.; Hupp, J. T. *Nano Lett.* **2001**, *1*, 165.
(255) Huang, C. C.; Chang, H. T. *Chem. Commun.* **2007**, 1215.
(256) Lin, S. Y.; Wu, S. H.; Chen, C. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 4948.
(257) Yang, W. R.; Gooding, J. J.; He, Z. C.; Li, Q.; Chen, G. N. *J. Nanosci. Nanotechnol.* **2007**, *7*, 712.
(258) Si, S.; Kotal, A.; Mandal, T. K. *J. Phys. Chem. C* **2007**, *111*, 1248.
(259) Liu, D. B.; Qu, W. S.; Chen, W. W.; Zhang, W.; Wang, Z.; Jiang, X. Y. *Anal. Chem.* **2010**, *82*, 9606.
(260) Lee, J. S.; Han, M. S.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4093.
(261) Xue, X. J.; Wang, F.; Liu, X. G. *J. Am. Chem. Soc.* **2008**, *130*, 3244.
(262) Liu, C. W.; Hsieh, Y. T.; Huang, C. C.; Lin, Z. H.; Chang, H. T. *Chem. Commun.* **2008**, 2242.
(263) Liu, X. J.; Cheng, X. H.; Bing, T.; Fang, C. L.; Shangguan, D. H. *Anal. Sci.* **2010**, *26*, 1169.
(264) Lee, J. S.; Ulmann, P. A.; Han, M. S.; Mirkin, C. A. *Nano Lett.* **2008**, *8*, 529.
(265) Dang, Y. Q.; Li, H. W.; Wang, B.; Li, L.; Wu, Y. Q. *ACS Appl. Mater. Interfaces* **2009**, *1*, 1533.
(266) Joyce, G. F. *Annu. Rev. Biochem.* **2004**, *73*, 791.
(267) Achenbach, J. C.; Chiuman, W.; Cruz, R. P. G; Li, Y. *Curr. Pharm. Biotechnol.* **2004**, *5*, 321.
(268) Breaker, R. R. *Nat. Biotechnol.* **1997**, *15*, 427.
(269) Breaker, R. R. *Science* **2000**, *290*, 2095.
(270) Lu, Y. *Chem.—Eur. J.* **2002**, *8*, 4589.
(271) Sen, D.; Geyer, C. R. *Curr. Opin. Chem. Biol.* **1998**, *2*, 680.
(272) Liu, J. W.; Lu, Y. *J. Am. Chem. Soc.* **2003**, *125*, 6642.
(273) Liu, J. W.; Lu, Y. *J. Am. Chem. Soc.* **2004**, *126*, 12298.
(274) Liu, J. W.; Lu, Y. *Chem. Mater.* **2004**, *16*, 3231.
(275) Liu, J.; Lu, Y. *J. Am. Chem. Soc.* **2005**, *127*, 12677.
(276) Lee, J. H.; Wang, Z. D.; Liu, J. W.; Lu, Y. *J. Am. Chem. Soc.* **2008**, *130*, 14217.
(277) Lisowski, C. E.; Hutchison, J. E. *Anal. Chem.* **2009**, *81*, 10246.
(278) Li, X. K.; Wang, J. N.; Sun, L. L.; Wang, Z. X. *Chem. Commun.* **2010**, *46*, 988.
(279) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609.
(280) Martinez-Manez, R.; Sancenon, F. *Chem. Rev.* **2003**, *103*, 4419.
(281) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486.
(282) Kubo, Y. *Tetrahedron Lett.* **2005**, *46*, 4369.
(283) Kado, S.; Furui, A.; Akiyama, Y.; Nakahara, Y.; Kimura, K. *Anal. Sci.* **2009**, *25*, 261.
(284) Minami, T.; Kaneko, K.; Nagasaki, T.; Kubo, Y. *Tetrahedron Lett.* **2008**, *49*, 432.
(285) Itoh, H.; Naka, K.; Chujo, Y. *J. Am. Chem. Soc.* **2004**, *126*, 3026.
(286) Garcia-Etxarri, A.; Aizpurua, J.; Molina-Aldareguia, J.; Marcilla, R.; Pomposo, J. A.; Mecerreyes, D. *Front. Phys. China* **2010**, *5*, 330.
(287) Watanabe, S.; Seguchi, H.; Yoshida, K.; Kifune, K.; Tadaki, T.; Shiozaki, H. *Tetrahedron Lett.* **2005**, *46*, 8827.
(288) Youk, K. S.; Kim, K. M.; Chatterjee, A.; Ahn, K. H. *Tetrahedron Lett.* **2008**, *49*, 3652.
(289) Chatterjee, A.; Oh, D. J.; Kim, K. M.; Youk, K. S.; Ahn, K. H. *Chem. Asian. J.* **2008**, *3*, 1962.
(290) Muir, G. D. *Hazards in the Chemical Laboratory*, 2nd ed.; The Chemical Society: London, 1977.
(291) Baskin, S. I. B., T., G. *Medical Aspects of Chemical and Biological Warfare*; TMM Publications: Washington, DC, 1997.
(292) Kim, M. H.; Kim, S.; Jang, H. H.; Yi, S.; Seo, S. H.; Han, M. S. *Tetrahedron Lett.* **2010**, *51*, 4712.
(293) Lee, K. Y.; Kim, D. W.; Heo, J.; Kim, J. S.; Yang, J. K.; Cheong, G. W.; Han, S. W. *Bull. Korean Chem. Soc.* **2006**, *27*, 2081.
(294) Zhang, S. H.; Wang, J.; Han, L. A.; Li, C. G.; Wang, W.; Yuan, Z. *Sens. Actuat. B Chem.* **2010**, *147*, 687.
(295) Zhang, Y. F.; Li, B. X.; Xu, C. L. *Analyst* **2010**, *135*, 1579.
(296) Daniel, W. L.; Han, M. S.; Lee, J. S.; Mirkin, C. A. *J. Am. Chem. Soc.* **2009**, *131*, 6362.
(297) Aslan, K.; Lakowicz, J. R.; Geddes, C. D. *Anal. Biochem.* **2004**, *330*, 145.
(298) Aslan, K.; Lakowicz, J. R.; Geddes, C. D. *Anal. Chem.* **2005**, *77*, 2007.
(299) Matsui, J.; Akamatsu, K.; Nishiguchi, S.; Miyoshi, D.; Nawafune, H.; Tamaki, K.; Sugimoto, N. *Anal. Chem.* **2004**, *76*, 1310.
(300) Uehara, N.; Ookubo, K.; Shimizu, T. *Langmuir* **2010**, *26*, 6818.
(301) Shimada, T.; Ookubo, K.; Komuro, N.; Shimizu, T.; Uehara, N. *Langmuir* **2007**, *23*, 11225.
(302) Okubo, K.; Shimada, T.; Shimizu, T.; Uehara, N. *Anal. Sci.* **2007**, *23*, 85.

(303) Liang, X. S.; Wei, H. P.; Cui, Z. Q.; Deng, J. Y.; Zhang, Z. P.; You, X. Y.; Zhang, X. E. *Analyst* **2011**, *136*, 179.
(304) Jiang, Y.; Zhao, H.; Zhu, N. N.; Lin, Y. Q.; Yu, P.; Mao, L. Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 8601.
(305) Bunka, D. H. J.; Stockley, P. G. *Nat. Rev. Microbiol.* **2006**, *4*, 588.
(306) Liu, J. W.; Lu, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 90.
(307) Liu, J. W.; Lu, Y. *Adv. Mater.* **2006**, *18*, 1667.
(308) Liu, J.; Lu, Y. *Nat. Protoc.* **2006**, *1*, 246.
(309) Cheng, Y.; Yong, W.; Marty, J. L.; Xiurong, Y. *Biosens. Bioelectron.* **2010**, *26*, 2724.
(310) Liu, X. P.; Zhou, Z. H.; Zhang, L. L.; Tan, Z. Y.; Shen, G. L.; Yu, R. Q. *Chin. J. Chem.* **2009**, *27*, 1855.
(311) Chavez, J. L.; Lyon, W.; Kelley-Loughnane, N.; Stone, M. O. *Biosens. Bioelectron.* **2010**, *26*, 23.
(312) Liu, J. W.; Mazumdar, D.; Lu, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 7955.
(313) Wang, L. H.; Liu, X. F.; Hu, X. F.; Song, S. P.; Fan, C. H. *Chem. Commun.* **2006**, 3780.
(314) Zhao, W. A.; Chiuman, W.; Brook, M. A.; Li, Y. F. *ChemBioChem* **2007**, *8*, 727.
(315) Liu, J. W.; Lu, Y. *Anal. Chem.* **2004**, *76*, 1627.
(316) Ogawa, A. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 155.
(317) Kim, Y. S.; Kim, J. H.; Kim, I. A.; Lee, S. J.; Jurng, J.; Gu, M. B. *Biosens. Bioelectron.* **2010**, *26*, 1644.
(318) Ludwig, J. A.; Weinstein, J. N. *Nat. Rev. Cancer* **2005**, *5*, 845.
(319) Cairns, P. *Nat. Rev. Cancer* **2007**, *7*, 531.
(320) Lien, K.-Y.; Lee, G.-B. *Analyst* **2010**, *135*, 1499.
(321) Marti, A. A.; Jockusch, S.; Stevens, N.; Ju, J. Y.; Turro, N. J. *Acc. Chem. Res.* **2007**, *40*, 402.
(322) Sassolas, A.; Leca-Bouvier, B. D.; Blum, L. J. *Chem. Rev.* **2008**, *108*, 109.
(323) Kolpashchikov, D. M. *Chem. Rev.* **2010**, *110*, 4709.
(324) Thaxton, C. S.; Georganopoulou, D. G.; Mirkin, C. A. *Clin. Chim. Acta* **2006**, *363*, 120.
(325) Sato, K.; Hosokawa, K.; Maeda, M. *Anal. Sci.* **2007**, *23*, 17.
(326) Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature* **1996**, *382*, 607.
(327) Elghanian, R.; Storhoff, J. J.; Mucic, R. C.; Letsinger, R. L.; Mirkin, C. A. *Science* **1997**, *277*, 1078.
(328) Storhoff, J. J.; Elghanian, R.; Mucic, R. C.; Mirkin, C. A.; Letsinger, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 1959.
(329) Storhoff, J. J.; Lucas, A. D.; Garimella, V.; Bao, Y. P.; Muller, U. R. *Nat. Biotechnol.* **2004**, *22*, 883.
(330) Reynolds, R. A.; Mirkin, C. A.; Letsinger, R. L. *J. Am. Chem. Soc.* **2000**, *122*, 3795.
(331) Cao, Y. C.; Jin, R. C.; Thaxton, S.; Mirkin, C. A. *Talanta* **2005**, *67*, 449.
(332) Li, H. X.; Rothberg, L. J. *J. Am. Chem. Soc.* **2004**, *126*, 10958.
(333) Chakrabarti, R.; Klibanov, A. M. *J. Am. Chem. Soc.* **2003**, *125*, 12531.
(334) Li, J. H.; Chu, X.; Liu, Y. L.; Jiang, J. H.; He, Z. M.; Zhang, Z. W.; Shen, G. L.; Yu, R. Q. *Nucleic Acids Res.* **2005**, *33*, 9.
(335) Feldkamp, U.; Niemeyer, C. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 1856.
(336) Sato, K.; Hosokawa, K.; Maeda, M. *J. Am. Chem. Soc.* **2003**, *125*, 8102.
(337) Li, H. X.; Rothberg, L. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 14036.
(338) Xia, F.; Zuo, X. L.; Yang, R. Q.; Xiao, Y.; Kang, D.; Vallee-Belisle, A.; Gong, X.; Yuen, J. D.; Hsu, B. B. Y.; Heeger, A. J.; Plaxco, K. W. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 10837.
(339) Han, M. S.; Lytton-Jean, A. K. R.; Mirkin, C. A. *J. Am. Chem. Soc.* **2006**, *128*, 4954.
(340) Chen, C. E.; Song, G. T.; Yang, X. J.; Ren, J. S.; Qu, X. G. *Biochimie* **2010**, *92*, 1416.
(341) Han, M. S.; Lytton-Jean, A. K. R.; Oh, B. K.; Heo, J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1807.
(342) Hurst, S. J.; Han, M. S.; Lytton-Jean, A. K. R.; Mirkin, C. A. *Anal. Chem.* **2007**, *79*, 7201.
(343) Schofield, C. L.; Haines, A. H.; Field, R. A.; Russell, D. A. *Langmuir* **2006**, *22*, 6707.
(344) Watanabe, S.; Yoshida, K.; Shinkawa, K.; Kumagawa, D.; Seguchi, H. *Colloids Surf., B* **2010**, *81*, 570.
(345) Narain, R.; Housni, A.; Gody, G.; Boullanger, P.; Charreyre, M. T.; Delair, T. *Langmuir* **2007**, *23*, 12835.
(346) Nakamura-Tsuruta, S.; Kishimoto, Y.; Nishimura, T.; Suda, Y. *J. Biochem.* **2008**, *143*, 833.
(347) Schofield, C. L.; Mukhopadhyay, B.; Hardy, S. M.; McDonnell, M. B.; Field, R. A.; Russell, D. A. *Analyst* **2008**, *133*, 626.
(348) Barrientos, A. G.; de la Fuente, J. M.; Jimenez, M.; Solis, D.; Canada, F. J.; Martin-Lomas, M.; Penades, S. *Carbohydr. Res.* **2009**, *344*, 1474.
(349) Thygesen, M. B.; Sorensen, K. K.; Clo, E.; Jensen, K. J. *Chem. Commun.* **2009**, 6367.
(350) Chuang, Y. J.; Zhou, X. C.; Pan, Z. W.; Turchi, C. *Biochem. Biophys. Res. Commun.* **2009**, *389*, 22.
(351) Otsuka, H.; Akiyama, Y.; Nagasaki, Y.; Kataoka, K. *J. Am. Chem. Soc.* **2001**, *123*, 8226.
(352) Takae, S.; Akiyama, Y.; Otsuka, H.; Nakamura, T.; Nagasaki, Y.; Kataoka, K. *Biomacromolecules* **2005**, *6*, 818.
(353) Toyoshima, M.; Miura, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 1412.
(354) Tsai, C. S.; Yu, T. B.; Chen, C. T. *Chem. Commun.* **2005**, 4273.
(355) Halkes, K. M.; de Souza, A. C.; Maljaars, C. E. P.; Gerwig, G. J.; Kamerling, J. P. *Eur. J. Org. Chem.* **2005**, 3650.
(356) Wang, X.; Ramstrom, O.; Yan, M. D. *Anal. Chem.* **2010**, *82*, 9082.
(357) Schofield, C. L.; Field, R. A.; Russell, D. A. *Anal. Chem.* **2007**, *79*, 1356.
(358) Uzawa, H.; Ohga, K.; Shinozaki, Y.; Ohsawa, I.; Nagatsuka, T.; Seto, Y.; Nishida, Y. *Biosens. Bioelectron.* **2008**, *24*, 923.
(359) Nath, N.; Chilkoti, A. *Anal. Chem.* **2002**, *74*, 504.
(360) Nath, N.; Chilkoti, A. *Anal. Chem.* **2004**, *76*, 5370.
(361) Niikura, K.; Nagakawa, K.; Ohtake, N.; Suzuki, T.; Matsuo, Y.; Sawa, H.; Ijiro, K. *Bioconjugate Chem.* **2009**, *20*, 1848.
(362) Huang, C. C.; Huang, Y. F.; Cao, Z. H.; Tan, W. H.; Chang, H. T. *Anal. Chem.* **2005**, *77*, 5735.
(363) Wei, H.; Li, B. L.; Li, J.; Wang, E. K.; Dong, S. J. *Chem. Commun.* **2007**, 3735.
(364) Pavlov, V.; Xiao, Y.; Shlyahovsky, B.; Willner, I. *J. Am. Chem. Soc.* **2004**, *126*, 11768.
(365) Xiao, Y.; Pavlov, V.; Levine, S.; Niazov, T.; Markovitch, G.; Willner, I. *Angew. Chem., Int. Ed.* **2004**, *43*, 4519.
(366) Dykman, L. A.; Bogatyrev, V. A.; Khlebtsov, B. N.; Khlebtsov, N. G. *Anal. Biochem.* **2005**, *341*, 16.
(367) Thanh, N. T. K.; Rosenzweig, Z. *Anal. Chem.* **2002**, *74*, 1624.
(368) Brust, M.; Bethell, D.; Schiffrin, D. J.; Kiely, C. J. *Adv. Mater.* **1995**, *7*, 795.
(369) You, C. C.; Arvizo, R. R.; Rotello, V. M. *Chem. Commun.* **2006**, 2905.
(370) Guarise, C.; Pasquato, L.; De Filippis, V.; Scrimin, P. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 3978.
(371) Laromaine, A.; Koh, L. L.; Murugesan, M.; Ulijn, R. V.; Stevens, M. M. *J. Am. Chem. Soc.* **2007**, *129*, 4156.
(372) Xu, X. Y.; Han, M. S.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3468.
(373) Wang, Z. X.; Levy, R.; Fernig, D. G.; Brust, M. *J. Am. Chem. Soc.* **2006**, *128*, 2214.
(374) Choi, Y.; Ho, N. H.; Tung, C. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 707.
(375) Zhao, W. A.; Chiuman, W.; Lam, J. C. F.; Brook, M. A.; Li, Y. F. *Chem. Commun.* **2007**, 3729.
(376) Jiang, T. T.; Liu, R. R.; Huang, X. F.; Feng, H. J.; Teo, W. L.; Xing, B. G. *Chem. Commun.* **2009**, 1972.
(377) Uehara, N.; Fujita, M.; Shimizu, T. *Anal. Sci.* **2009**, *25*, 267.

(378) Chah, S.; Hammond, M. R.; Zare, R. N. *Chem. Biol.* **2005**, *12*, 323.
(379) Jain, P. K.; El-Sayed, I. H.; El-Sayed, M. A. *Nano Today* **2007**, *2*, 18.
(380) Huang, T.; Murray, R. W. *Langmuir* **2002**, *18*, 7077.
(381) Huang, C.-C.; Chang, H.-T. *Anal. Chem.* **2006**, *78*, 8332.
(382) He, X. R.; Liu, H. B.; Li, Y. L.; Wang, S.; Li, Y. J.; Wang, N.; Xiao, J. C.; Xu, X. H.; Zhu, D. B. *Adv. Mater.* **2005**, *17*, 2811.
(383) Ipe, B. I.; Yoosaf, K.; Thomas, K. G. *J. Am. Chem. Soc.* **2006**, *128*, 1907.
(384) Chen, S.-J.; Chang, H.-T. *Anal. Chem.* **2004**, *76*, 3727.
(385) Zhang, N.; Liu, Y. Y.; Tong, L. L.; Xu, K. H.; Zhuo, L. H.; Tang, B. *Analyst* **2008**, *133*, 1176.
(386) Lin, J. H.; Chang, C. W.; Tseng, W. L. *Analyst* **2010**, *135*, 104.
(387) Huang, C. C.; Tseng, W. L. *Anal. Chem.* **2008**, *80*, 6345.
(388) Huang, C. C.; Yang, Z.; Lee, K. H.; Chang, H. T. *Angew. Chem., Int. Ed.* **2007**, *46*, 6824.
(389) Huang, C. C.; Chen, C. T.; Shiang, Y. C.; Lin, Z. H.; Chang, H. T. *Anal. Chem.* **2009**, *81*, 875.
(390) Chen, C. T.; Chen, W. J.; Liu, C. Z.; Chang, L. Y.; Chen, Y. C. *Chem. Commun.* **2009**, 7515.
(391) Chen, W. B.; Tu, X. J.; Guo, X. Q. *Chem. Commun.* **2009**, 1736.
(392) Maxwell, D. J.; Taylor, J. R.; Nie, S. M. *J. Am. Chem. Soc.* **2002**, *124*, 9606.
(393) Seferos, D. S.; Giljohann, D. A.; Hill, H. D.; Prigodich, A. E.; Mirkin, C. A. *J. Am. Chem. Soc.* **2007**, *129*, 15477.
(394) Zheng, D.; Seferos, D. S.; Giljohann, D. A.; Patel, P. C.; Mirkin, C. A. *Nano Lett.* **2009**, *9*, 3258.
(395) Prigodich, A. E.; Seferos, D. S.; Massich, M. D.; Giljohann, D. A.; Lane, B. C.; Mirkin, C. A. *ACS Nano* **2009**, *3*, 2147.
(396) Jin, Y.; Li, H. Y.; Bai, J. Y. *Anal. Chem.* **2009**, *81*, 5709.
(397) Zhang, J.; Wang, L. H.; Zhang, H.; Boey, F.; Song, S. P.; Fan, C. H. *Small* **2010**, *6*, 201.
(398) Wang, H.; Wang, Y. X.; Jin, J. Y.; Yang, R. H. *Anal. Chem.* **2008**, *80*, 9021.
(399) Medintz, I. L.; Clapp, A. R.; Mattoussi, H.; Goldman, E. R.; Fisher, B.; Mauro, J. M. *Nat. Mater.* **2003**, *2*, 630.
(400) Dyadyusha, L.; Yin, H.; Jaiswal, S.; Brown, T.; Baumberg, J. J.; Booy, F. P.; Melvin, T. *Chem. Commun.* **2005**, 3201.
(401) Oh, E.; Hong, M.-Y.; Lee, D.; Nam, S.-H.; Yoon, H. C.; Kim, H.-S. *J. Am. Chem. Soc.* **2005**, *127*, 3270.
(402) Oh, E.; Lee, D.; Kim, Y. P.; Cha, S. Y.; Oh, D. B.; Kang, H. A.; Kim, J.; Kim, H. S. *Angew. Chem., Int. Ed.* **2006**, *45*, 7959.
(403) Tang, B.; Cao, L. H.; Xu, K. H.; Zhuo, L. H.; Ge, J. H.; Li, Q. F.; Yu, L. J. *Chem.—Eur. J.* **2008**, *14*, 3637.
(404) Wang, X.; Guo, X. Q. *Analyst* **2009**, *134*, 1348.
(405) Liu, J. W.; Lee, J. H.; Lu, Y. *Anal. Chem.* **2007**, *79*, 4120.
(406) You, C. C.; Miranda, O. R.; Gider, B.; Ghosh, P. S.; Kim, I. B.; Erdogan, B.; Krovi, S. A.; Bunz, U. H. F.; Rotello, V. M. *Nat. Nanotechnol.* **2007**, *2*, 318.
(407) You, C. C.; De, M.; Han, G.; Rotello, V. M. *J. Am. Chem. Soc.* **2005**, *127*, 12873.
(408) De, M.; You, C. C.; Srivastava, S.; Rotello, V. M. *J. Am. Chem. Soc.* **2007**, *129*, 10747.
(409) De, M.; Rana, S.; Akpinar, H.; Miranda, O. R.; Arvizo, R. R.; Bunz, U. H. F.; Rotello, V. M. *Nat. Chem* **2009**, *1*, 461.
(410) Phillips, R. L.; Miranda, O. R.; You, C. C.; Rotello, V. M.; Bunz, U. H. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2590.
(411) Bajaj, A.; Miranda, O. R.; Kim, I. B.; Phillips, R. L.; Jerry, D. J.; Bunz, U. H. F.; Rotello, V. M. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 10912.
(412) Bajaj, A.; Miranda, O. R.; Phillips, R.; Kim, I. B.; Jerry, D. J.; Bunz, U. H. F.; Rotello, V. M. *J. Am. Chem. Soc.* **2010**, *132*, 1018.
(413) Bajaj, A.; Rana, S.; Miranda, O. R.; Yawe, J. C.; Jerry, D. J.; Bunz, U. H. F.; Rotello, V. M. *Chem. Sci* **2010**, *1*, 134.
(414) Miranda, O. R.; Chen, H. T.; You, C. C.; Mortenson, D. E.; Yang, X. C.; Bunz, U. H. F.; Rotello, V. M. *J. Am. Chem. Soc.* **2010**, *132*, 5285.
(415) Miranda, O. R.; Li, X.; Garcia-Gonzalez, L.; Zhu, Z.-J.; Yan, B.; Bunz, U. H. F.; Rotello, V. M. *J. Am. Chem. Soc.* **2011**, *133*, 9650.
(416) Katz, E.; Willner, I.; Wang, J. *Electroanalysis* **2004**, *16*, 19.
(417) Guo, S. J.; Wang, E. K. *Anal. Chim. Acta* **2007**, *598*, 181.
(418) Pumera, M.; Sanchez, S.; Ichinose, I.; Tang, J. *Sens. Actuat. B Chem* **2007**, *123*, 1195.
(419) Willner, I.; Willner, B. *Pure Appl. Chem.* **2002**, *74*, 1773.
(420) Lucarelli, F.; Tombelli, S.; Minunni, M.; Marrazza, G.; Mascini, M. *Anal. Chim. Acta* **2008**, *609*, 139.
(421) Shipway, A. N.; Lahav, M.; Willner, I. *Adv. Mater.* **2000**, *12*, 993.
(422) Pingarron, J. M.; Yanez-Sedeno, P.; Gonzalez-Cortes, A. *Electrochim. Acta* **2008**, *53*, 5848.
(423) Wang, J. *Analyst* **2005**, *130*, 421.
(424) Hernandez-Santos, D.; Gonzalez-Garcia, M. B.; Garcia, A. C. *Electroanalysis* **2002**, *14*, 1225.
(425) Wang, J. *Anal. Chim. Acta* **2003**, *500*, 247.
(426) Erdem, A. *Talanta* **2007**, *74*, 318.
(427) Fritzsche, W.; Taton, T. A. *Nanotechnology* **2003**, *14*, R63.
(428) Kerman, K.; Saito, M.; Yamamura, S.; Takamura, Y.; Tamiya, E. *TrAC, Trends Anal. Chem* **2008**, *27*, 585.
(429) Yanez-Sedeno, P.; Pingarron, J. M. *Anal. Bioanal. Chem.* **2005**, *382*, 884.
(430) Merkoci, A. *FEBS J.* **2007**, *274*, 310.
(431) Kerman, K.; Kobayashi, M.; Tamiya, E. *Meas. Sci. Technol.* **2004**, *15*, R1.
(432) Mao, X.; Liu, G. D. *J. Biomed. Nanotechnol.* **2008**, *4*, 419.
(433) Zamborini, F. P.; Leopold, M. C.; Hicks, J. F.; Kulesza, P. J.; Malik, M. A.; Murray, R. W. *J. Am. Chem. Soc.* **2002**, *124*, 8958.
(434) Ahn, H.; Chandekar, A.; Kang, B.; Sung, C.; Whitten, J. E. *Chem. Mater.* **2004**, *16*, 3274.
(435) Im, J.; Chandekar, A.; Whitten, J. E. *Langmuir* **2009**, *25*, 4288.
(436) Joseph, Y.; Peic, A.; Chen, X. D.; Michl, J.; Vossmeyer, T.; Yasuda, A. *J. Phys. Chem. C* **2007**, *111*, 12855.
(437) Ibanez, F. J.; Zamborini, F. P. *ACS Nano* **2008**, *2*, 1543.
(438) Joseph, Y.; Guse, B.; Vossmeyer, T.; Yasuda, A. *J. Phys. Chem. C* **2008**, *112*, 12507.
(439) Guo, J. L.; Pang, P. F.; Cai, Q. Y. *Sens. Actuat. B Chem.* **2007**, *120*, 521.
(440) Ibanez, F. J.; Gowrishetty, U.; Crain, M. M.; Walsh, K. M.; Zamborini, F. P. *Anal. Chem.* **2006**, *78*, 753.
(441) Wohltjen, H.; Snow, A. W. *Anal. Chem.* **1998**, *70*, 2856.
(442) Evans, S. D.; Johnson, S. R.; Cheng, Y. L.; Shen, T. *J. Mater. Chem.* **2000**, *10*, 183.
(443) Zhang, H. L.; Evans, S. D.; Henderson, J. R.; Miles, R. E.; Shen, T. H. *Nanotechnology* **2002**, *13*, 439.
(444) Joseph, Y.; Besnard, I.; Rosenberger, M.; Guse, B.; Nothofer, H.-G.; Wessels, J. M.; Wild, U.; Knop-Gericke, A.; Su, D.-S.; Schlögl, R.; Yasuda, A.; Vossmeyer, T. *J. Phys. Chem. B* **2003**, *107*, 7406.
(445) Wang, L. Y.; Shi, X. J.; Kariuki, N. N.; Schadt, M.; Wang, G. R.; Rendeng, Q.; Choi, J.; Luo, J.; Lu, S.; Zhong, C. J. *J. Am. Chem. Soc.* **2007**, *129*, 2161.
(446) Raguse, B.; Chow, E.; Barton, C. S.; Wieczorek, L. *Anal. Chem.* **2007**, *79*, 7333.
(447) Chow, E.; Herrmann, J.; Barton, C. S.; Raguse, B.; Wieczorek, L. *Anal. Chim. Acta* **2009**, *632*, 135.
(448) Raguse, B.; Barton, C. S.; Muller, K. H.; Chow, E.; Wieczorek, L. *J. Phys. Chem. C* **2009**, *113*, 15390.
(449) Chow, E.; Gengenbach, T. R.; Wieczorek, L.; Raguse, B. *Sens. Actuat. B Chem* **2010**, *143*, 704.
(450) Kim, Y. J.; Yang, Y. S.; Ha, S. C.; Cho, S. M.; Kim, Y. S.; Kim, H. Y.; Yang, H.; Kim, Y. T. *Sens. Actuat. B Chem* **2005**, *106*, 189.
(451) Krasteva, N.; Besnard, I.; Guse, B.; Bauer, R. E.; Müllen, K.; Yasuda, A.; Vossmeyer, T. *Nano Lett.* **2002**, *2*, 551.
(452) Krasteva, N.; Fogel, Y.; Bauer, R. E.; Mullen, K.; Matsuzawa, N.; Yasuda, A.; Vossmeyer, T. *Adv. Funct. Mater.* **2007**, *17*, 881.
(453) Krasteva, N.; Guse, B.; Besnard, I.; Yasuda, A.; Vossmeyer, T. *Sens. Actuat. B Chem.* **2003**, *92*, 137.

(454) Vossmeyer, T.; Guse, B.; Besnard, I.; Bauer, R. E.; Mullen, K.; Yasuda, A. *Adv. Mater.* **2002**, *14*, 238.
(455) Park, M. H.; Ofir, Y.; Samanta, B.; Rotello, V. M. *Adv. Mater.* **2009**, *21*, 2323.
(456) Singh, A.; Hede, S.; Sastry, M. *Small* **2007**, *3*, 466.
(457) Shipway, A. N.; Lahav, M.; Blonder, R.; Willner, I. *Chem. Mater.* **1999**, *11*, 13.
(458) Lahav, M.; Gabai, R.; Shipway, A. N.; Willner, I. *Chem. Commun.* **1999**, 1937.
(459) Lahav, M.; Shipway, A. N.; Willner, I. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1925.
(460) Lahav, M.; Shipway, A. N.; Willner, I.; Nielsen, M. B.; Stoddart, J. F. *J. Electroanal. Chem.* **2000**, *482*, 217.
(461) Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed.* **1988**, *27*, 1547.
(462) Blonder, R.; Sheeney, L.; Willner, I. *Chem. Commun.* **1998**, 1393.
(463) Kharitonov, A. B.; Shipway, A. N.; Katz, E.; Willner, I. *Rev. Anal. Chem.* **1999**, *18*, 255.
(464) Kharitonov, A. B.; Shipway, A. N.; Willner, I. *Anal. Chem.* **1999**, *71*, 5441.
(465) Thompson, D. T. *Nano Today* **2007**, *2*, 40.
(466) Valden, M.; Lai, X.; Goodman, D. W. *Science* **1998**, *281*, 1647.
(467) Haruta, M.; Date, M. *Appl. Catal., A* **2001**, *222*, 427.
(468) Turner, M.; Golovko, V. B.; Vaughan, O. P. H; Abdulkin, P.; Berenguer-Murcia, A.; Tikhov, M. S.; Johnson, B. F. G.; Lambert, R. M. *Nature* **2008**, *454*, 981.
(469) Li, Y. Y.; Schluesener, H. J.; Xu, S. Q. *Gold Bull.* **2010**, *43*, 29.
(470) Li, Y.; Shi, G. Q. *J. Phys. Chem. B* **2005**, *109*, 23787.
(471) Guerin, S.; Attard, G. S. *Electrochem. Commun.* **2001**, *3*, 544.
(472) Ueda, M.; Dietz, H.; Anders, A.; Kneppe, H.; Meixner, A.; Plieth, W. *Electrochim. Acta* **2002**, *48*, 377.
(473) Plieth, W.; Dietz, H.; Anders, A.; Sandmann, G.; Meixner, A.; Weber, M.; Kneppe, H. *Surf. Sci.* **2005**, *597*, 119.
(474) Lin, T. H.; Hung, W. H. *J. Electrochem. Soc.* **2009**, *156*, D45.
(475) Liu, S. Q.; Yu, J. H.; Ju, H. X. *J. Electroanal. Chem.* **2003**, *540*, 61.
(476) Cui, H.; Dong, Y. P. *J. Electroanal. Chem.* **2006**, *595*, 37.
(477) Sun, X. P.; Du, Y.; Dong, S. J.; Wang, E. K. *Anal. Chem.* **2005**, *77*, 8166.
(478) Zhang, L. H.; Xu, Z. A.; Sun, X. P.; Dong, S. J. *Biosens. Bioelectron.* **2007**, *22*, 1097.
(479) Jena, B. K.; Raj, C. R. *Electroanalysis* **2007**, *19*, 816.
(480) Feng, K. J.; Sun, C. H.; Kang, Y.; Chen, J. W.; Jiang, J. H.; Shen, G. L.; Yu, R. Q. *Electrochem. Commun.* **2008**, *10*, 531.
(481) Goyal, R. N.; Oyama, M.; Singh, S. P. *Electroanalysis* **2007**, *19*, 575.
(482) Mora, L.; Hernandez, P.; Vicente, J.; Galan, F.; Hernandez, L. *Electroanalysis* **2008**, *20*, 2084.
(483) Liu, Y. J.; Nie, L. H.; Tao, W. Y.; Yao, S. Z. *Electroanalysis* **2004**, *16*, 1271.
(484) Cubukcu, M.; Timur, S.; Anik, U. *Talanta* **2007**, *74*, 434.
(485) Yang, S. L.; Qu, L. B.; Li, G.; Yang, R.; Liu, C. C. *J. Electroanal. Chem.* **2010**, *645*, 115.
(486) Zhang, J.; Wang, Y. Q.; Lv, R. H.; Xu, L. *Electrochim. Acta* **2010**, *55*, 4039.
(487) Cheng, H.; Chen, C. D.; Zhang, S. A. *Anal. Sci.* **2009**, *25*, 1221.
(488) Kannan, P.; John, S. A. *Anal. Chim. Acta* **2010**, *663*, 158.
(489) Wei, X. H.; Wang, F.; Yin, Y. M.; Liu, Q. Y.; Zou, L. N.; Ye, B. X. *Analyst* **2010**, *135*, 2286.
(490) Liu, D.; Luo, P.; Sun, W. W.; Zhang, L. P.; Wang, Z. *Anal. Biochem.* **2010**, *404*, 14.
(491) Han, L.; Hang, X. L. *Electroanalysis* **2009**, *21*, 124.
(492) Kurniawan, F.; Tsakova, V.; Mirsky, V. M. *Electroanalysis* **2006**, *18*, 1937.
(493) Li, Y.; Song, Y. Y.; Yang, C.; Xia, X. H. *Electrochem. Commun.* **2007**, *9*, 981.
(494) Jena, B. K.; Raj, C. R. *Chem.—Eur. J.* **2006**, *12*, 2702.
(495) Sun, Y. Y.; Bai, Y.; Yang, W. W.; Sun, C. Q. *Electrochim. Acta* **2007**, *52*, 7352.
(496) Chen, M.; Diao, G. W. *Talanta* **2009**, *80*, 815.
(497) Liu, X. Y.; Zeng, X. D.; Mai, N. N.; Liu, Y.; Kong, B.; Li, Y. H.; Wei, W. Z.; Luo, S. L. *Biosens. Bioelectron.* **2010**, *25*, 2675.
(498) Jia, F.; Shan, C. S.; Li, F. H.; Niu, L. *Biosens. Bioelectron.* **2008**, *24*, 945.
(499) Wang, J. W.; Wang, L. P.; Di, J. W.; Tu, Y. F. *Sens. Actuat. B Chem.* **2008**, *135*, 283.
(500) Zheng, B. Z.; Qian, L.; Yuan, H. Y.; Xiao, D.; Yang, X. P.; Paau, M. C.; Choi, M. M. F. *Talanta* **2010**, *82*, 177.
(501) Labib, M.; Hedstrom, M.; Amin, M.; Mattiasson, B. *Anal. Chim. Acta* **2010**, *659*, 194.
(502) Raj, C. R.; Okajima, T.; Ohsaka, T. *J. Electroanal. Chem.* **2003**, *543*, 127.
(503) Li, M. G.; Gao, F.; Yang, P.; Wang, L.; Fang, B. *Surf. Sci.* **2008**, *602*, 151.
(504) Zhang, L.; Jiang, X. *J. Electroanal. Chem.* **2005**, *583*, 292.
(505) Hu, G. Z.; Zhang, D. P.; Wu, W. L.; Yang, Z. S. *Colloids Surf. B* **2008**, *62*, 199.
(506) Huang, X.; Li, Y. X.; Wang, P.; Wang, L. *Anal. Sci.* **2008**, *24*, 1563.
(507) Li, J.; Lin, X. Q. *Sens. Actuat. B Chem.* **2007**, *124*, 486.
(508) Zhang, S. J.; Xu, M. L.; Zhang, Y. Z. *Electroanalysis* **2009**, *21*, 2607.
(509) Raj, C. R.; Ohsaka, T. *J. Electroanal. Chem.* **2003**, *540*, 69.
(510) Hu, G. Z.; Ma, Y. G.; Guo, Y.; Shao, S. J. *Electrochim. Acta* **2008**, *53*, 6610.
(511) Kannan, P.; John, S. A. *Anal. Biochem.* **2009**, *386*, 65.
(512) Kalimuthu, P.; John, S. A. *J. Electroanal. Chem.* **2008**, *617*, 164.
(513) Lu, L. P.; Lin, X. Q. *Anal. Sci.* **2004**, *20*, 527.
(514) Li, J.; Lin, X. Q. *Anal. Chim. Acta* **2007**, *596*, 222.
(515) Wang, J. L.; Wang, F.; Zou, X. Q.; Xu, Z. A.; Dong, S. J. *Electrochem. Commun.* **2007**, *9*, 343.
(516) Sivanesan, A.; Kannan, P.; John, S. A. *Electrochim. Acta* **2007**, *52*, 8118.
(517) Ragupathy, D.; Gopalan, A. I.; Lee, K. P. *Sens. Actuat. B Chem.* **2010**, *143*, 696.
(518) Nair, S. S.; John, S. A.; Sagara, T. *Electrochim. Acta* **2009**, *54*, 6837.
(519) Jin, B. K.; Zhang, H. *Anal. Lett.* **2002**, *35*, 1907.
(520) Wang, L.; Bai, J. Y.; Huang, P. F.; Wang, H. J.; Zhang, L. Y.; Zhao, Y. Q. *Electrochem. Commun.* **2006**, *8*, 1035.
(521) Luczak, T. *Electrochim. Acta* **2009**, *54*, 5863.
(522) Zhang, H.; Gui, X. Q.; Xu, Y.; Jin, B. K. *Chin. Chem. Lett.* **2002**, *13*, 153.
(523) Yin, H. S.; Zhou, Y. L.; Ai, S. Y.; Han, R. X.; Tang, T. T.; Zhu, L. S. *Microchim. Acta* **2010**, *170*, 99.
(524) Zhao, M. L.; Ni, D. D.; Wang, J. W.; Di, J. W.; Tu, Y. F. *Chin. J. Anal. Chem.* **2008**, *36*, 1729.
(525) Li, J. *Chin. J. Chem.* **2009**, *27*, 2373.
(526) Liu, Y.; Gu, H. Y. *Microchim. Acta* **2008**, *162*, 101.
(527) Jiang, Y. N.; Luo, H. Q.; Li, N. B. *Int. J. Environ. Anal. Chem.* **2007**, *87*, 295.
(528) Sanz, V. C.; Mena, M. L.; Gonzalez-Cortes, A.; Yanez-Sedeno, P.; Pingarron, J. M. *Anal. Chim. Acta* **2005**, *528*, 1.
(529) Su, L.; Mao, L. Q. *Talanta* **2006**, *70*, 68.
(530) El-Cheick, F. M.; Rashwan, F. A.; Mahmoud, H. A.; El-Rouby, M. *J. Solid State Electrochem.* **2010**, *14*, 1425.
(531) Luczak, T. *Electroanalysis* **2009**, *12*, 1539.
(532) Zhang, L. Y.; Yuan, R.; Chai, Y. Q.; Li, X. L. *Anal. Chim. Acta* **2007**, *596*, 99.
(533) Riskin, M.; Tel-Vered, R.; Bourenko, T.; Granot, E.; Willner, I. *J. Am. Chem. Soc.* **2008**, *130*, 9726.
(534) Riskin, M.; Tel-Vered, R.; Lioubashevski, O.; Willner, I. *J. Am. Chem. Soc.* **2009**, *131*, 7368.
(535) Riskin, M.; Tel-Vered, R.; Willner, I. *Adv. Mater.* **2010**, *22*, 1387.

(536) Riskin, M.; Tel-Vered, R.; Frasconi, M.; Yavo, N.; Willner, I. *Chem.—Eur. J.* **2010**, *16*, 7114.
(537) Frasconi, M.; Tel-Vered, R.; Riskin, M.; Willner, I. *Anal. Chem.* **2010**, *82*, 2512.
(538) Ben-Amram, Y.; Riskin, M.; Willner, I. *Analyst* **2010**, *135*, 2952.
(539) Jena, B. K.; Raj, C. R. *Anal. Chem.* **2008**, *80*, 4836.
(540) Song, Y. S.; Muthuraman, G.; Chen, Y. Z.; Lin, C. C.; Zen, J. M. *Electroanalysis* **2006**, *18*, 1763.
(541) Dai, X.; Compton, R. G. *Electroanalysis* **2005**, *17*, 1325.
(542) Baron, R.; Sljukic, B.; Salter, C.; Crossley, A.; Compton, R. G. *Russ. J. Phys. Chem. A* **2007**, *81*, 1443.
(543) Xiao, L.; Wildgoose, G. G.; Compton, R. G. *Anal. Chim. Acta* **2008**, *620*, 44.
(544) Majid, E.; Hrapovic, S.; Liu, Y. L.; Male, K. B.; Luong, J. H. T. *Anal. Chem.* **2006**, *78*, 762.
(545) Zhu, Z. Q.; Su, Y. Y.; Li, J.; Li, D.; Zhang, J.; Song, S. P.; Zhao, Y.; Li, G. X.; Fan, C. H. *Anal. Chem.* **2009**, *81*, 7660.
(546) Dominguez-Renedo, O.; Alonso-Lomillo, M. A.; Ferreira-Goncalves, L.; Arcos-Martinez, M. J. *Talanta* **2009**, *79*, 1306.
(547) Xu, H.; Zeng, L. P.; Xing, S. J.; Shi, G. Y.; Xian, Y. Z.; Lin, L. T. *Electrochem. Commun.* **2008**, *10*, 1839.
(548) Abollino, O.; Giacomino, A.; Malandrino, M.; Piscionieri, G.; Mentasti, E. *Electroanalysis* **2008**, *20*, 75.
(549) Renedo, O. D.; Martinez, M. J. A. *Anal. Chim. Acta* **2007**, *589*, 255.
(550) Liu, B. Z.; Lu, L. Y.; Wang, M.; Zi, Y. Q. *J. Chem. Sci.* **2008**, *120*, 493.
(551) Liu, G. D.; Lin, Y. Y.; Wu, H.; Lin, Y. *Environ. Sci. Technol.* **2007**, *41*, 8129.
(552) Maye, M. M.; Lou, Y. B.; Zhong, C. J. *Langmuir* **2000**, *16*, 7520.
(553) Diao, P.; Zhang, D. F.; Guo, M.; Zhang, Q. *J. Catal.* **2007**, *250*, 247.
(554) Milsom, E. V.; Novak, J.; Oyama, M.; Marken, F. *Electrochem. Commun.* **2007**, *9*, 436.
(555) Gu, H. Y.; Yu, A. M.; Yuan, S. S.; Chen, H. Y. *Anal. Lett.* **2002**, *35*, 647.
(556) Kannan, P.; John, S. A. *Electrochim. Acta* **2010**, *55*, 3497.
(557) Varatharajan, S.; Kumar, K. S.; Berchmans, S.; Amutha, R.; Kiruthiga, P. V.; Devi, K. P. *Analyst* **2010**, *135*, 2348.
(558) Zhu, M.; Liu, M.; Shi, G. Y.; Xu, F.; Ye, X. Y.; Chen, J. S.; Jin, L. T.; Jin, J. Y. *Anal. Chim. Acta* **2002**, *455*, 199.
(559) Yu, A. M.; Liang, Z. J.; Cho, J. H.; Caruso, F. *Nano Lett.* **2003**, *3*, 1203.
(560) Jena, B. K.; Raj, C. R. *J. Phys. Chem. C* **2007**, *111*, 6228.
(561) Maduraiveeran, G.; Ramaraj, R. *Electrochem. Commun.* **2007**, *9*, 2051.
(562) Baron, R.; Sljukic, B.; Salter, C.; Crossley, A.; Compton, R. G. *Electroanalysis* **2007**, *19*, 1062.
(563) Li, J.; Lin, X. Q. *Sens. Actuat. B Chem.* **2007**, *126*, 527.
(564) Yi, Q. F.; Yu, W. Q. *J. Electroanal. Chem.* **2009**, *633*, 159.
(565) Yin, H. S.; Ai, S. Y.; Shi, W. J.; Zhu, L. S. *Sens. Actuat. B Chem.* **2009**, *137*, 747.
(566) Xu, X. X.; Liu, S. Q.; Ju, H. X. *Sensors* **2003**, *3*, 350.
(567) Xiao, Y.; Ju, H. X.; Chen, H. Y. *Anal. Chim. Acta* **1999**, *391*, 73.
(568) Xu, S. Y.; Peng, B.; Han, X. Z. *Biosens. Bioelectron.* **2007**, *22*, 1807.
(569) Wang, L.; Wang, E. K. *Electrochem. Commun.* **2004**, *6*, 225.
(570) Li, X. L.; Wu, J.; Gao, N.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2006**, *117*, 35.
(571) Xu, S. Y.; Han, X. Z. *Biosens. Bioelectron.* **2004**, *19*, 1117.
(572) Wang, J. W.; Wang, L. P.; Di, J. W.; Tu, Y. F. *Talanta* **2009**, *77*, 1454.
(573) Zheng, Y.; Lin, X. Q. *Chin. J. Anal. Chem.* **2008**, *36*, 604.
(574) Patolsky, F.; Gabriel, T.; Willner, I. *J. Electroanal. Chem.* **1999**, *479*, 69.
(575) Xu, S. Y.; Tu, G. L.; Peng, B.; Han, X. Z. *Anal. Chim. Acta* **2006**, *570*, 151.
(576) Liu, A. P.; Dong, W. J.; Liu, E. J.; Tang, W. H.; Zhu, J. Q.; Han, J. C. *Electrochim. Acta* **2010**, *55*, 1971.
(577) Qiu, J. D.; Peng, H. Z.; Liang, R. P.; Li, J.; Xia, X. H. *Langmuir* **2007**, *23*, 2133.
(578) Pandey, P. C.; Singh, B. *Biosens. Bioelectron.* **2008**, *24*, 842.
(579) Li, Y. L.; Zhang, J.; Zhu, H.; Yang, F.; Yang, X. R. *Electrochim. Acta* **2010**, *55*, 5123.
(580) Hung, C. C.; Wen, T. C.; Wei, Y. *Mater. Chem. Phys.* **2010**, *122*, 392.
(581) Chikkaveeraiah, B. V.; Liu, H. Y.; Mani, V.; Papadimitrakopoulos, F.; Rusling, J. F. *Electrochem. Commun.* **2009**, *11*, 819.
(582) Kim, G. Y.; Shim, J.; Kang, M. S.; Moon, S. H. *J. Hazard. Mater.* **2008**, *156*, 141.
(583) Kang, T. F.; Wang, F.; Lu, L. P.; Zhang, Y.; Liu, T. S. *Sens. Actuat. B Chem.* **2010**, *145*, 104.
(584) Yin, H. S.; Ai, S. Y.; Xu, J.; Shi, W. J.; Zhu, L. S. *J. Electroanal. Chem.* **2009**, *637*, 21.
(585) Upadhyay, S.; Rao, G. R.; Sharma, M. K.; Bhattacharya, B. K.; Rao, V. K.; Vijayaraghavan, R. *Biosens. Bioelectron.* **2009**, *25*, 832.
(586) Goyal, R. N.; Gupta, V. K.; Oyama, M.; Bachheti, N. *Electrochem. Commun.* **2005**, *7*, 803.
(587) Goyal, R. N.; Gupta, V. K.; Oyama, M.; Bachheti, N. *Electrochem. Commun.* **2006**, *8*, 65.
(588) Goyal, R. N.; Oyama, M.; Bachheti, N.; Singh, S. P. *Bioelectrochemistry* **2009**, *74*, 272.
(589) Yang, G. J.; Qu, X. L.; Shen, M.; Wang, C. Y.; Qu, Q. S.; Hu, X. Y. *Sens. Actuat. B Chem* **2007**, *128*, 258.
(590) Jena, B. K.; Raj, C. R. *Talanta* **2010**, *80*, 1653.
(591) Ding, L.; Hao, C.; Xue, Y. D.; Ju, H. X. *Biomacromolecules* **2007**, *8*, 1341.
(592) Yan, F.; Chen, J.; Ju, H. X. *Electrochem. Commun.* **2007**, *9*, 293.
(593) Du, D.; Liu, S. L.; Chen, J.; Ju, H. X.; Lian, H. Z.; Li, J. X. *Biomaterials* **2005**, *26*, 6487.
(594) de la Escosura-Muniz, A.; Sanchez-Espinel, C.; Diaz-Freitas, B.; Gonzalez-Fernandez, A.; Maltez-da Costa, M.; Merkoci, A. *Anal. Chem.* **2009**, *81*, 10268.
(595) Ghindilis, A. L.; Atanasov, P.; Wilkins, E. *Electroanalysis* **1997**, *9*, 661.
(596) Brown, K. R.; Fox, A. P.; Natan, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 1154.
(597) Wang, L.; Wang, E. K. *Electrochem. Commun.* **2004**, *6*, 49.
(598) Murata, K.; Suzuki, M.; Kajiya, K.; Nakamura, N.; Ohno, H. *Electrochem. Commun.* **2009**, *11*, 668.
(599) Xiao, Y.; Ju, H. X.; Chen, H. Y. *Anal. Biochem.* **2000**, *278*, 22.
(600) Zhao, J. G.; Henkens, R. W.; Stonehuerner, J.; Odaly, J. P.; Crumbliss, A. L. *J. Electroanal. Chem.* **1992**, *327*, 109.
(601) Li, F.; Feng, Y.; Wang, Z.; Yang, L. M.; Zhuo, L. H.; Tang, B. *Biosens. Bioelectron.* **2010**, *25*, 2244.
(602) Xiang, C.; Zou, Y.; Sun, L. X.; Xu, F. *Sens. Actuat. B Chem* **2009**, *136*, 158.
(603) Liu, Y.; Yuan, R.; Chai, Y. Q.; Tang, D. P.; Dai, J. Y.; Zhong, X. *Sens. Actuat. B Chem* **2006**, *115*, 109.
(604) Xu, Q.; Cai, W. Y.; Zhu, J. J. *Chem. Lett.* **2005**, *34*, 832.
(605) Guo, S. F.; Wang, L. H.; Lu, T. H.; Ding, X. L.; Huang, X. H. *J. Electroanal. Chem.* **2010**, *644*, 80.
(606) Liu, S. Q.; Leech, D.; Ju, H. X. *Anal. Lett.* **2003**, *36*, 1.
(607) Zhao, S.; Zhang, K.; Bai, Y.; Yang, W. W.; Sun, C. Q. *Bioelectrochemistry* **2006**, *69*, 158.
(608) Du, D.; Ding, J. W.; Cai, J.; Zhang, J. M.; Liu, L. *Talanta* **2008**, *74*, 1337.
(609) Zhang, H.; Hu, N. *Biosens. Bioelectron.* **2007**, *23*, 393.
(610) Zhao, J. G.; ODaly, J. P.; Henkens, R. W.; Stonehuerner, J.; Crumbliss, A. L. *Biosens. Bioelectron.* **1996**, *11*, 493.
(611) Andreescu, S.; Luck, L. A. *Anal. Biochem.* **2008**, *375*, 282.
(612) Lei, C. X.; Hu, S. Q.; Gao, N.; Shen, G. L.; Yu, R. Q. *Bioelectrochemistry* **2004**, *65*, 33.
(613) Zhang, S. X.; Wang, N.; Yu, H. J.; Niu, Y. M.; Sun, C. Q. *Bioelectrochemistry* **2005**, *67*, 15.

(614) Crumbliss, A. L.; Perine, S. C.; Stonehürner, J.; Tubergen, K. R.; Zhao, J. G.; Henkens, R. W. *Biotechnol. Bioeng.* **1992**, *40*, 483.
(615) Shulga, O.; Kirchhoff, J. R. *Electrochem. Commun.* **2007**, *9*, 935.
(616) Bharathi, S.; Nogami, M. *Analyst* **2001**, *126*, 1919.
(617) Zhou, N.; Wang, J.; Chen, T.; Yu, Z. G.; Li, G. X. *Anal. Chem.* **2006**, *78*, 5227.
(618) Lin, J. H.; Zhang, L. J.; Zhang, S. S. *Anal. Biochem.* **2007**, *370*, 180.
(619) Cai, W. Y.; Xu, Q.; Zhao, X. N.; Zhu, J. H.; Chen, H. Y. *Chem. Mater.* **2006**, *18*, 279.
(620) Wang, X. Y.; Zhong, H.; Lv, Y.; Chen, H. Y. *Chem. Lett.* **2003**, *32*, 1054.
(621) Zhang, J. J.; Zhu, J. J. *Sci. China, Ser. B* **2009**, *52*, 815.
(622) Mena, M. L.; Yanez-Sedeno, P.; Pingarron, J. M. *Anal. Biochem.* **2005**, *336*, 20.
(623) Gole, A.; Dash, C.; Ramakrishnan, V.; Sainkar, S. R.; Mandale, A. B.; Rao, M.; Sastry, M. *Langmuir* **2001**, *17*, 1674.
(624) Gole, A.; Vyas, S.; Phadtare, S.; Lachke, A.; Sastry, M. *Colloids Surf. B* **2002**, *25*, 129.
(625) You, C. C.; Agasti, S. S.; De, M.; Knapp, M. J.; Rotello, V. M. *J. Am. Chem. Soc.* **2006**, *128*, 14612.
(626) Pandey, P.; Singh, S. P.; Arya, S. K.; Gupta, V.; Datta, M.; Singh, S.; Malhotra, B. D. *Langmuir* **2007**, *23*, 3333.
(627) Ahirwal, G. K.; Mitra, C. K. *Sensors* **2009**, *9*, 881.
(628) Xiao, Y.; Patolsky, F.; Katz, E.; Hainfeld, J. F.; Willner, I. *Science* **2003**, *299*, 1877.
(629) Zayats, M.; Katz, E.; Baron, R.; Willner, I. *J. Am. Chem. Soc.* **2005**, *127*, 12400.
(630) Kerman, K.; Chikae, M.; Yamamura, S.; Tamiya, E. *Anal. Chim. Acta* **2007**, *588*, 26.
(631) Ma, L. P.; Yuan, R.; Chai, Y. Q.; Chen, S. H.; Ling, S. J. *Bioprocess Biosyst. Eng.* **2009**, *32*, 537.
(632) Zhang, L.; Jiang, X. U.; Wang, E. K.; Dong, S. J. *Biosens. Bioelectron.* **2005**, *21*, 337.
(633) Fang, B.; Wang, G. F.; Yang, X. H.; Zha, Q. Q.; Zhang, W. Z.; Kan, X. W. *Anal. Lett.* **2004**, *37*, 2911.
(634) Ruo, Y.; ShuRui, C.; Yaqin, C.; FengXian, G.; Oing, Z.; MingYu, T.; ZhongQiang, T.; Yi, X. *Sci. China, Ser. B* **2007**, *50*, 620.
(635) Yang, G.; Yuan, R.; Chai, Y. Q. *Colloids Surf. B* **2008**, *61*, 93.
(636) Liu, Y.; Jiang, Q. Y.; Lu, S. Y.; Zhang, Y.; Gu, H. Y. *Appl. Biochem. Biotechnol.* **2009**, *152*, 418.
(637) Guo, H. L.; Liu, D. Y.; Yu, X. D.; Xia, X. H. *Sens. Actuat. B Chem* **2009**, *139*, 598.
(638) Tang, M. Y.; Chen, S. H.; Yuan, R.; Chai, Y. Q.; Gao, F. X.; Xie, Y. *Anal. Sci.* **2008**, *24*, 487.
(639) Li, J. X.; Zhou, L. H.; Han, X.; Liu, H. L. *Sens. Actuat. B Chem* **2008**, *135*, 322.
(640) Gu, H. Y.; Yu, A. M.; Chen, H. Y. *J. Electroanal. Chem.* **2001**, *516*, 119.
(641) Han, X. J.; Cheng, W. L.; Zhang, Z. L.; Dong, S. J.; Wang, E. K. *Biochim. Biophys. Acta* **2002**, *1556*, 273.
(642) Feng, J. J.; Xu, J. J.; Chen, H. Y. *J. Electroanal. Chem.* **2005**, *585*, 44.
(643) Chen, S. H.; Yuan, R.; Chai, Y. Q.; Zhang, L. Y.; Wang, N.; Li, X. L. *Biosens. Bioelectron.* **2007**, *22*, 1268.
(644) Chen, S. H.; Ynan, R.; Chai, Y. Q.; Yin, B.; Xu, Y. *Electroanalysis* **2008**, *20*, 2141.
(645) Xu, X. X.; Liu, S. Q.; Li, B.; Ju, H. X. *Anal. Lett.* **2003**, *36*, 2427.
(646) Hong, J. M.; Dai, Z. H. *Sens. Actuat. B Chem* **2009**, *140*, 222.
(647) Zhang, J. D.; Oyama, M. *J. Electroanal. Chem.* **2005**, *577*, 273.
(648) Liu, S. Q.; Ju, H. X. *Electroanalysis* **2003**, *15*, 1488.
(649) Cao, W.; Wei, C. M.; Hu, J. B.; Li, Q. L. *Electroanalysis* **2008**, *20*, 1925.
(650) Zhang, H.; Hu, N. F. *J. Phys. Chem. B* **2007**, *111*, 10583.
(651) Zhang, H.; Lu, H. Y.; Hu, N. F. *J. Phys. Chem. B* **2006**, *110*, 2171.
(652) Yang, W. W.; Li, Y. C.; Bai, Y.; Sun, C. Q. *Sens. Actuat. B Chem.* **2006**, *115*, 42.
(653) Liu, S. Q.; Peng, L.; Yang, X. D.; Wu, Y. F.; He, L. *Anal. Biochem.* **2008**, *375*, 209.
(654) Shumyantseva, V. V.; Carrara, S.; Bavastrello, V.; Riley, D. J.; Bulko, T. V.; Skryabin, K. G.; Archakov, A. I.; Nicolini, C. *Biosens. Bioelectron.* **2005**, *21*, 217.
(655) Ju, H. X.; Liu, S. Q.; Ge, B. X.; Lisdat, F.; Scheller, F. W. *Electroanalysis* **2002**, *14*, 141.
(656) Li, S. Q.; Xia, J.; Liu, C. Y.; Cao, W.; Hu, J. B.; Li, Q. L. *J. Electroanal. Chem.* **2009**, *633*, 273.
(657) Xiang, C. L.; Zou, Y. J.; Sun, L. X.; Xu, F. *Electrochem. Commun.* **2008**, *10*, 38.
(658) Hoshi, T.; Sagae, N.; Daikuhara, K.; Anzai, J. *Talanta* **2007**, *71*, 644.
(659) Hoshi, T.; Sagae, N.; Daikuhara, K.; Takahara, K.; Anzai, J. I. *Mater. Sci. Eng., C* **2007**, *27*, 890.
(660) Yang, W. W.; Wang, J. X.; Zhao, S.; Sun, Y. Y.; Sun, C. Q. *Electrochem. Commun.* **2006**, *8*, 665.
(661) Chen, S. H.; Yuan, R.; Chai, Y. Q.; Xu, L.; Wang, N.; Li, X. N.; Zhang, L. Y. *Electroanalysis* **2006**, *18*, 471.
(662) Wang, Y. Y.; Chen, X. J.; Zhu, J. J. *Electrochem. Commun.* **2009**, *11*, 323.
(663) Crespilho, F. N.; Ghica, M. E.; Florescu, M.; Nart, F. C.; Oliveira, O. N.; Brett, C. M. A. *Electrochem. Commun.* **2006**, *8*, 1665.
(664) Agui, L.; Manso, J.; Yanez-Sedeno, P.; Pingarron, J. M. *Sens. Actuat. B Chem* **2006**, *113*, 272.
(665) Lei, C. X.; Hu, S. Q.; Shen, G. L.; Yu, R. Q. *Talanta* **2003**, *59*, 981.
(666) Liu, S. Q.; Ju, H. X. *Anal. Biochem.* **2002**, *307*, 110.
(667) Behpour, M.; Honarmand, E.; Ghoreishi, S. M. *Bull. Korean Chem. Soc.* **2010**, *31*, 845.
(668) Liu, S. Q.; Ju, H. X. *Biosens. Bioelectron.* **2003**, *19*, 177.
(669) Carralero, V.; Mena, M. L.; Gonzalez-Cortes, A.; Yanez-Sedeno, P.; Pingarron, J. M. *Biosens. Bioelectron.* **2006**, *22*, 730.
(670) Li, J. L.; Han, T.; Wei, N. N.; Du, J. Y.; Zhao, X. W. *Biosens. Bioelectron.* **2009**, *25*, 773.
(671) Wei, Y. Y.; Li, Y.; Zhang, N. D.; Shi, G. Y.; Jin, L. T. *Ultrason. Sonochem* **2010**, *17*, 17.
(672) Wang, H. C.; Wang, X. S.; Zhang, X. Q.; Qin, X.; Zhao, Z. X.; Miao, Z. Y.; Huang, N.; Chen, Q. *Biosens. Bioelectron.* **2009**, *25*, 142.
(673) Kang, Q.; Yang, L. X.; Cai, Q. Y. *Bioelectrochemistry* **2008**, *74*, 62.
(674) Liu, Y.; Wang, M. K.; Zhao, F.; Guo, Z. H.; Chen, H. J.; Dong, S. J. *J. Electroanal. Chem.* **2005**, *581*, 1.
(675) Manso, J.; Mena, M. L.; Yanez-Sedeno, P.; Pingarron, J. *J. Electroanal. Chem.* **2007**, *603*, 1.
(676) Liu, Y.; Wu, S.; Ju, H. X.; Xu, L. *Electroanalysis* **2007**, *19*, 986.
(677) Wang, Y.; Wei, W. Z.; Liu, X. Y.; Zeng, X. D. *Mater. Sci. Eng., C* **2009**, *29*, 50.
(678) Wu, B. Y.; Hou, S. H.; Yin, F.; Zhao, Z. X.; Wang, Y. Y.; Wang, X. S.; Chen, Q. *Biosens. Bioelectron.* **2007**, *22*, 2854.
(679) Manesh, K. M.; Kim, J. H.; Santhosh, P.; Gopalan, A. Y.; Lee, K. P.; Kang, H. D. *J. Nanosci. Nanotechnol.* **2007**, *7*, 3365.
(680) Wu, Y. H.; Hu, S. S. *Colloids Surf. B* **2005**, *41*, 299.
(681) Guo, Y. J.; Guo, S. J.; Fang, Y. X.; Dong, S. J. *Electrochim. Acta* **2010**, *55*, 3927.
(682) Bui, M. P. N; Pham, X. H.; Han, K. N.; Li, C. A.; Lee, E. K.; Chang, H. J.; Seong, G. H. *Electrochem. Commun.* **2010**, *12*, 250.
(683) Tu, X. M.; Yan, L. S.; Luo, X. B.; Luo, S. L.; Xie, Q. J. *Electroanalysis* **2009**, *21*, 2491.
(684) Feng, H.; Wang, H.; Zhang, Y.; Yan, B.; Shen, G.; Yu, R. Q. *Anal. Sci.* **2007**, *23*, 235.
(685) Njagi, J.; Andreescu, S. *Biosens. Bioelectron.* **2007**, *23*, 168.
(686) Xian, Y. Z.; Hu, Y.; Liu, F.; Xian, Y.; Wang, H. T.; Jin, L. T. *Biosens. Bioelectron.* **2006**, *21*, 1996.
(687) Zhong, X.; Yuan, R.; Chai, Y. Q.; Liu, Y.; Dai, J. Y.; Tang, D. P. *Sens. Actuat. B Chem* **2005**, *104*, 191.
(688) Yan, W.; Feng, X. M.; Chen, X. J.; Hou, W. H.; Zhu, J. J. *Biosens. Bioelectron.* **2008**, *23*, 925.

(689) Ozdemir, C.; Yeni, F.; Odaci, D.; Timur, S. *Food Chem.* **2010**, *119*, 380.
(690) Gao, F. X.; Yuan, R.; Chai, Y. Q.; Chen, S. H.; Cao, S. R.; Tang, M. Y. *J. Biochem. Biophys. Methods* **2007**, *70*, 407.
(691) Zhu, Q.; Yuan, R.; Chai, Y. Q.; Zhuo, Y.; Zhang, Y.; Li, X. L.; Wang, N. *Anal. Lett.* **2006**, *39*, 483.
(692) Xie, C. G.; Li, H. F.; Li, S. Q.; Wu, J.; Zhang, Z. P. *Anal. Chem.* **2010**, *82*, 241.
(693) Luo, X. L.; Xu, J. J.; Du, Y.; Chen, H. Y. *Anal. Biochem.* **2004**, *334*, 284.
(694) Wu, B. Y.; Hou, S. H.; Yin, F.; Li, J.; Zhao, Z. X.; Huang, J. D.; Chen, Q. *Biosens. Bioelectron.* **2007**, *22*, 838.
(695) Xue, M. H.; Xu, Q.; Zhou, M.; Zhu, J. J. *Electrochem. Commun.* **2006**, *8*, 1468.
(696) Du, Y.; Luo, X. L.; Xu, J. J.; Chen, H. Y. *Bioelectrochemistry* **2007**, *70*, 342.
(697) Shan, C. S.; Yang, H. F.; Han, D. X.; Zhang, Q. X.; Ivaska, A.; Niu, L. *Biosens. Bioelectron.* **2010**, *25*, 1070.
(698) Zeng, X. D.; Li, X. F.; Xing, L.; Liu, X. Y.; Luo, S. L.; Wei, W. Z.; Kong, B.; Li, Y. H. *Biosens. Bioelectron.* **2009**, *24*, 2898.
(699) Luo, X. L.; Xu, J. J.; Zhang, Q.; Yang, G. J.; Chen, H. Y. *Biosens. Bioelectron.* **2005**, *21*, 190.
(700) Tangkuaram, T.; Ponchio, C.; Kangkasomboon, T.; Katikawong, P.; Veerasai, W. *Biosens. Bioelectron.* **2007**, *22*, 2071.
(701) Zhao, X. J.; Mai, Z. B.; Kang, X. H.; Zou, X. Y. *Biosens. Bioelectron.* **2008**, *23*, 1032.
(702) Xu, Q.; Mao, C.; Liu, N. N.; Zhu, J. J.; Sheng, J. *Biosens. Bioelectron.* **2006**, *22*, 768.
(703) Wang, J. F.; Yuan, R.; Chai, Y. Q.; Li, W. J.; Fu, P.; Min, L. G. *Colloids Surf. B* **2010**, *75*, 425.
(704) Li, W. J.; Yuan, R.; Chai, Y. Q.; Zhou, L.; Chen, S. H.; Li, N. *J. Biochem. Biophys. Methods* **2008**, *70*, 830.
(705) Lin, J. H.; Qu, W.; Zhang, S. S. *Anal. Biochem.* **2007**, *360*, 288.
(706) Liu, Z. M.; Wang, H.; Yang, Y.; Yang, H. F.; Hu, S. Q.; Shen, G. L.; Yu, R. Q. *Anal. Lett.* **2004**, *37*, 1079.
(707) Du, D.; Chen, S. Z.; Cai, J.; Song, D. D. *J. Electroanal. Chem.* **2007**, *611*, 60.
(708) Du, D.; Ding, J. W.; Cai, J.; Zhang, A. D. *Sens. Actuat. B Chem.* **2007**, *127*, 317.
(709) Du, D.; Ding, J. W.; Cai, J.; Zhang, A. D. *J. Electroanal. Chem.* **2007**, *605*, 53.
(710) Drummond, T. G.; Hill, M. G.; Barton, J. K. *Nat. Biotechnol.* **2003**, *21*, 1192.
(711) Castaneda, M. T.; Alegret, S.; Merkoci, A. *Electroanalysis* **2007**, *19*, 743.
(712) Moller, R.; Fritzsche, W. *Curr. Pharm. Biotechnol.* **2007**, *8*, 274.
(713) Fang, Y. Z.; Xu, Y.; He, P. G. *J. Biomed. Nanotechnol.* **2005**, *1*, 276.
(714) Selvaraju, T.; Das, J.; Jo, K.; Kwon, K.; Huh, C. H.; Kim, T. K.; Yang, H. *Langmuir* **2008**, *24*, 9883.
(715) Ma, H. Y.; Zhang, L. P.; Pan, Y.; Zhang, K. Y.; Zhang, Y. Z. *Electroanalysis* **2008**, *20*, 1220.
(716) Zhang, Z. L.; Pang, D. W.; Yuan, H.; Cai, R. X.; Abruna, H. *Anal. Bioanal. Chem.* **2005**, *381*, 833.
(717) Zhang, K. I.; Ma, H. Y.; Zhang, L. P.; Zhang, Y. Z. *Electroanalysis* **2008**, *20*, 2127.
(718) Fu, Y. Z.; Yuan, R.; Xu, L.; Chai, Y. Q.; Zhong, X.; Tang, D. P. *Biochem. Eng. J.* **2005**, *23*, 37.
(719) Lin, X. Q.; Miao, Q.; Jin, B. K. *Chin. Chem. Lett.* **1999**, *10*, 157.
(720) Yang, J.; Yang, T.; Feng, Y. Y.; Jiao, K. *Anal. Biochem.* **2007**, *365*, 24.
(721) Liu, S. F.; Li, Y. F.; Li, J. R.; Jiang, L. *Biosens. Bioelectron.* **2005**, *21*, 789.
(722) Lin, X. Q.; Zheng, S. J.; Miao, Q.; Jin, B. K. *Anal. Lett.* **2002**, *35*, 1373.
(723) Wu, Z. S.; Jiang, J. H.; Shen, G. L.; Yu, R. Q. *Hum. Mutat.* **2007**, *28*, 630.
(724) Authier, L.; Grossiord, C.; Brossier, P.; Limoges, B. *Anal. Chem.* **2001**, *73*, 4450.
(725) Wang, J.; Xu, D. K.; Kawde, A. N.; Polsky, R. *Anal. Chem.* **2001**, *73*, 5576.
(726) Wang, J.; Polsky, R.; Xu, D. K. *Langmuir* **2001**, *17*, 5739.
(727) Wang, J.; Xu, D. K.; Polsky, R. *J. Am. Chem. Soc.* **2002**, *124*, 4208.
(728) Kawde, A. N.; Wang, J. *Electroanalysis* **2004**, *16*, 101.
(729) Pumera, M.; Castaneda, M. T.; Pividori, M. I.; Eritja, R.; Merkoci, A.; Alegret, S. *Langmuir* **2005**, *21*, 9625.
(730) Castaneda, M. T.; Merkoci, A.; Pumera, M.; Alegret, S. *Biosens. Bioelectron.* **2007**, *22*, 1961.
(731) Kerman, K.; Saito, M.; Morita, Y.; Takamura, Y.; Ozsoz, M.; Tamiya, E. *Anal. Chem.* **2004**, *76*, 1877.
(732) Wang, J.; Li, J. H.; Baca, A. J.; Hu, J. B.; Zhou, F. M.; Yan, W.; Pang, D. W. *Anal. Chem.* **2003**, *75*, 3941.
(733) Baca, A. J.; Zhou, F. M.; Wang, J.; Hu, J. B.; Li, J. H.; Wang, J. X.; Chikneyan, Z. S. *Electroanalysis* **2004**, *16*, 73.
(734) Jin, Y.; Lu, W.; Hu, J. Q.; Yao, X.; Li, J. H. *Electrochem. Commun.* **2007**, *9*, 1086.
(735) Wang, J. X.; Zhu, X.; Tu, Q. Y.; Guo, Q.; Zarui, C. S.; Momand, J.; Sun, X. Z.; Zhou, F. M. *Anal. Chem.* **2008**, *80*, 769.
(736) Zhang, J.; Song, S. P.; Zhang, L. Y.; Wang, L. H.; Wu, H. P.; Pan, D.; Fan, C. H. *J. Am. Chem. Soc.* **2006**, *128*, 8575.
(737) Wang, J.; Zhang, S. J.; Zhang, Y. Z. *Anal. Biochem.* **2010**, *396*, 304.
(738) Li, L. L.; Cai, H.; Lee, T. M. H.; Barford, J.; Hsing, I. M. *Electroanalysis* **2004**, *16*, 81.
(739) Wang, M. J.; Sun, C. Y.; Wang, L. Y.; Ji, X. H.; Bai, Y. B.; Li, T. J.; Li, J. H. *J. Pharm. Biomed. Anal.* **2003**, *33*, 1117.
(740) Cai, H.; Wang, Y. Q.; He, P. G.; Fang, Y. H. *Anal. Chim. Acta* **2002**, *469*, 165.
(741) Lee, T. M. H.; Li, L. L.; Hsing, I. M. *Langmuir* **2003**, *19*, 4338.
(742) Cai, H.; Shang, C.; Hsing, I. M. *Anal. Chim. Acta* **2004**, *523*, 61.
(743) Lee, T. M. H.; Cai, H.; Hsing, I. M. *Electroanalysis* **2004**, *16*, 1628.
(744) Cai, H.; Wang, Y. Q.; He, P. G.; Fang, Y. Z. *Chem. J. Chinese Univ.* **2003**, *24*, 1390.
(745) Lee, T. M. H.; Cai, H.; Hsing, I. M. *Analyst* **2005**, *130*, 364.
(746) Hanaee, H.; Ghourchian, H.; Ziaee, A. A. *Anal. Biochem.* **2007**, *370*, 195.
(747) Rochelet-Dequaire, M.; Limoges, B.; Brossier, P. *Analyst* **2006**, *131*, 923.
(748) Bonanni, A.; Esplandiu, M. J.; del Valle, M. *Electrochim. Acta* **2008**, *53*, 4022.
(749) Kang, J. W.; Li, X. N.; Wu, G. F.; Wang, Z. H.; Lu, X. Q. *Anal. Biochem.* **2007**, *364*, 165.
(750) Cai, H.; Xu, C.; He, P. G.; Fang, Y. Z. *J. Electroanal. Chem.* **2001**, *510*, 78.
(751) Moller, R.; Csaki, A.; Kohler, J. M.; Fritzsche, W. *Langmuir* **2001**, *17*, 5426.
(752) Park, S. J.; Taton, T. A.; Mirkin, C. A. *Science* **2002**, *295*, 1503.
(753) Urban, M.; Moller, R.; Fritzsche, W. *Rev. Sci. Instrum.* **2003**, *74*, 1077.
(754) Diessel, E.; Grothe, K.; Siebert, H. M.; Warner, B. D.; Burmeister, J. *Biosens. Bioelectron.* **2004**, *19*, 1229.
(755) Ozsoz, M.; Erdem, A.; Kerman, K.; Ozkan, D.; Tugrul, B.; Topcuoglu, N.; Ekren, H.; Taylan, M. *Anal. Chem.* **2003**, *75*, 2181.
(756) Kerman, K.; Morita, Y.; Takamura, Y.; Ozsoz, M.; Tamiya, E. *Anal. Chim. Acta* **2004**, *510*, 169.
(757) Li, D.; Yan, Y.; Wieckowska, A.; Willner, I. *Chem. Commun.* **2007**, 3544.
(758) Zhang, K. Y.; Zhang, Y. Z. *Electroanalysis* **2010**, *22*, 673.
(759) Xu, J. H.; Zhu, J. J.; Zhu, Y. L.; Gu, K.; Chen, H. Y. *Anal. Lett.* **2001**, *34*, 503.
(760) Li, C. Z.; Liu, Y. L.; Luong, J. H. T. *Anal. Chem.* **2005**, *77*, 478.
(761) Lu, L. P.; Wang, S. Q.; Lin, X. Q. *Anal. Chim. Acta* **2004**, *519*, 161.
(762) de la Escosura-Muniz, A.; Parolo, C.; Merkoci, A. *Mater. Today* **2010**, *13*, 17.

(763) Wang, M. J.; Wang, L. Y.; Wang, G.; Ji, X. H.; Bai, Y. B.; Li, T. J.; Gong, S. Y.; Li, J. H. *Biosens. Bioelectron.* **2004**, *19*, 575.
(764) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Dai, J. Y.; Zhong, X.; Liu, Y. *Bioelectrochemistry* **2004**, *65*, 15.
(765) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Fu, Y. Z.; Dai, J. Y.; Liu, Y.; Zhong, X. *Biosens. Bioelectron.* **2005**, *21*, 539.
(766) Ruo, Y.; Tang, D. P.; Chai, Y. Q.; Zhang, L. Y.; Liu, Y.; Zhong, X.; Dai, J. Y. *Sci. China, Ser. B* **2005**, *48*, 49.
(767) Bin He, Y.; Luo, H. Q.; Li, N. B. *Biosens. Bioelectron.* **2007**, *22*, 2952.
(768) Ding, C. F.; Li, H.; Hu, K. C.; Lin, J. M. *Talanta* **2010**, *80*, 1385.
(769) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Zhong, X.; Liu, Y.; Dai, J. Y. *Clin. Biochem.* **2006**, *39*, 309.
(770) Liang, R. P.; Qiu, H. D.; Cai, P. X. *Anal. Chim. Acta* **2005**, *534*, 223.
(771) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Zhong, X.; Liu, Y.; Dai, J. Y.; Zhang, L. Y. *Anal. Biochem.* **2004**, *333*, 345.
(772) Zhuo, Y.; Yuan, R.; Chai, Y. Q.; Zhang, Y.; Li, X. L.; Zhu, Q.; Wang, N. *Anal. Chim. Acta* **2005**, *548*, 205.
(773) Qiu, J. D.; Liang, R. P.; Wang, R.; Fan, L. X.; Chen, Y. W.; Xia, X. H. *Biosens. Bioelectron.* **2009**, *25*, 852.
(774) Shen, G. Y.; Zhang, Y. *Anal. Chim. Acta* **2010**, *674*, 27.
(775) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Zhang, L. Y.; Zhong, X.; Liu, Y.; Dai, J. Y. *Sens. Actuat. B Chem.* **2005**, *104*, 199.
(776) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Zhong, X.; Liu, Y.; Dai, J. Y. *Biochem. Eng. J.* **2004**, *22*, 43.
(777) Tang, D. P.; Yuan, R.; Chai, Y. Q.; Fu, Y. Z. *Electrochem. Commun.* **2005**, *7*, 177.
(778) Tang, D. P.; Ren, J. J. *Electroanalysis* **2005**, *17*, 2208.
(779) Yuan, R.; Zhang, L. Y.; Li, Q. F.; Chai, Y. Q.; Cao, S. R. *Anal. Chim. Acta* **2005**, *531*, 1.
(780) Liu, Y.; Qin, Z. H.; Wu, X. F.; Jiang, H. *Biochem. Eng. J.* **2006**, *32*, 211.
(781) Sharma, A.; Matharu, Z.; Sumana, G.; Solanki, P. R.; Kim, C. G.; Malhotra, B. D. *Thin Solid Films* **2010**, *519*, 1213.
(782) Bone, L.; Vidal, J. C.; Duato, P.; Castillo, J. R. *Anal. Methods* **2010**, *2*, 335.
(783) Liu, X. P.; Deng, Y. J.; Jin, X. Y.; Chen, L. G.; Jiang, J. H.; Shen, G. L.; Yu, R. Q. *Anal. Biochem.* **2009**, *389*, 63.
(784) Zhang, Y.; Zhuang, H. S. *Chin. J. Anal. Chem.* **2010**, *38*, 153.
(785) Hu, S. Q.; Xie, J. W.; Xu, Q. H.; Rong, K. T.; Shen, G. L.; Yu, R. Q. *Talanta* **2003**, *61*, 769.
(786) Valera, E.; Ramon-Azcon, J.; Sanchez, F. J.; Marco, M. P.; Rodriguez, A. *Sens. Actuat. B Chem.* **2008**, *134*, 95.
(787) Valera, E.; Muniz, D.; Rodriguez, A. *Microelectron. Eng.* **2010**, *87*, 167.
(788) Tang, L.; Zeng, G. M.; Shen, G. L.; Li, Y. P.; Zhang, Y.; Huang, D. L. *Environ. Sci. Technol.* **2008**, *42*, 1207.
(789) Chen, J.; Tang, J. H.; Yan, F.; Ju, H. X. *Biomaterials* **2006**, *27*, 2313.
(790) Idegami, K.; Chikae, M.; Kerman, K.; Nagatani, N.; Yuhi, T.; Endo, T.; Tamiya, D. *Electroanalysis* **2008**, *20*, 14.
(791) Chen, J.; Yan, F.; Tan, F.; Ju, H. X. *Electroanalysis* **2006**, *18*, 1696.
(792) Chai, R.; Yuan, R.; Chai, Y. Q.; Ou, C. F.; Cao, S. R.; Li, X. L. *Talanta* **2008**, *74*, 1330.
(793) Yang, G. M.; Chang, Y. B.; Yang, H.; Tan, L.; Wu, Z. S.; Lu, X. X.; Yang, Y. H. *Anal. Chim. Acta* **2009**, *644*, 72.
(794) Chen, J.; Yan, F.; Du, D.; Wu, J.; Ju, H. X. *Electroanalysis* **2006**, *18*, 670.
(795) Carralero, V.; Gonzalez-Cortes, A.; Yanez-Sedeno, P.; Pingarron, J. M. *Anal. Chim. Acta* **2007**, *596*, 86.
(796) Carralero, V.; Gonzalez-Cortes, A.; Yanez-Sedeno, P.; Pingarron, J. M. *Electroanalysis* **2007**, *19*, 853.
(797) Wang, R. Z.; Li, Y. W.; Li, Q.; Shen, G. L.; Xiao, L. T. *Anal. Lett.* **2009**, *42*, 2893.
(798) Liu, X. Q.; Wong, D. K. Y. *Talanta* **2009**, *77*, 1437.
(799) Liu, X. Q.; Duckworth, P. A.; Wong, D. K. Y. *Biosens. Bioelectron.* **2010**, *25*, 1467.
(800) Rezaei, B.; Khayamian, T.; Majidi, N.; Rahmani, H. *Biosens. Bioelectron.* **2009**, *25*, 395.
(801) Yin, T. J.; Wei, W. Z.; Yang, L.; Gao, X. H.; Gao, Y. P. *Sens. Actuat. B Chem.* **2006**, *117*, 286.
(802) Hu, S. Q.; Xie, Z. M.; Lei, C. X.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2005**, *106*, 641.
(803) Ahirwal, G. K.; Mitra, C. K. *Biosens. Bioelectron.* **2010**, *25*, 2016.
(804) Kim, J. H.; Cho, J. H.; Cha, G. S.; Lee, C. W.; Kim, H. B.; Paek, S. H. *Biosens. Bioelectron.* **2000**, *14*, 907.
(805) Rahman, M. A.; Son, J. I.; Won, M. S.; Shim, Y. B. *Anal. Chem.* **2009**, *81*, 6604.
(806) Qu, L.; Xia, S. H.; Bian, C.; Sun, J. Z.; Han, J. H. *Biosens. Bioelectron.* **2009**, *24*, 3419.
(807) Lin, C. C.; Chen, L. C.; Huang, C. H.; Ding, S. J.; Chang, C. C.; Chang, H. C. *J. Electroanal. Chem.* **2008**, *619*, 39.
(808) Zhang, S.; Huang, F.; Liu, B. H.; Ding, J. J.; Xu, X.; Kong, J. L. *Talanta* **2007**, *71*, 874.
(809) Zhuo, Y.; Yuan, R.; Chai, Y. Q.; Tang, D. P.; Zhang, Y.; Wang, N.; Li, X. L.; Zhu, Q. *Electrochem. Commun.* **2005**, *7*, 355.
(810) Zhuo, Y.; Yuan, R.; Chai, Y. Q.; Zhang, Y.; Li, X. L.; Wang, N.; Zhu, Q. A. *Sens. Actuat. B Chem.* **2006**, *114*, 631.
(811) Li, Y.; Liang, W. B.; Fang, L. C.; Huang, H.; Deng, J.; Zheng, J. S. *J. Chem. Sci.* **2009**, *121*, 1069.
(812) Ding, C. F.; Zhao, F.; Ren, R.; Lin, J. M. *Talanta* **2009**, *78*, 1148.
(813) Tan, L.; Chen, Y. Q.; Yang, H.; Shi, Y.; Si, J. F.; Yang, G. M.; Wu, Z. S.; Wang, P.; Lu, X. X.; Bai, H. P.; Yang, Y. H. *Sens. Actuat. B Chem.* **2009**, *142*, 316.
(814) Liu, Y. X.; Yuan, R.; Chai, Y. Q.; Hong, C. L.; Guan, S. *Bioprocess Biosyst. Eng.* **2010**, *33*, 613.
(815) Ran, X. Q.; Yuan, R.; Chai, Y. Q.; Hong, C. L.; Qian, X. Q. *Colloids Surf. B* **2010**, *79*, 421.
(816) Liang, W. B.; Yi, W. J.; Li, S. H.; Yuan, R.; Chen, A.; Chen, S.; Xiang, G. M.; Hu, C. M. *Clin. Biochem.* **2009**, *42*, 1524.
(817) Lin, J. H.; He, C. Y.; Zhang, L. J.; Zhang, S. S. *Anal. Biochem.* **2009**, *384*, 130.
(818) Xu, Y. Y.; Chao, B. A.; Chen, S. F.; Xia, S. H. *Anal. Chim. Acta* **2006**, *561*, 48.
(819) Tang, D. P.; Yuan, R.; Chai, Y. Q. *Anal. Chim. Acta* **2006**, *564*, 158.
(820) Wu, L. N.; Chen, J.; Du, D.; Ju, H. X. *Electrochim. Acta* **2006**, *51*, 1208.
(821) Du, D.; Xu, X. X.; Wang, S. F.; Zhang, A. D. *Talanta* **2007**, *71*, 1257.
(822) Fu, X. H. *Electroanalysis* **2007**, *19*, 1831.
(823) Kim, D. J.; Lee, N. E.; Park, J. S.; Park, I. J.; Kim, J. G.; Cho, H. J. *Biosens. Bioelectron.* **2010**, *25*, 2477.
(824) Liu, Y. *Thin Solid Films* **2008**, *516*, 1803.
(825) Liu, Z. Y.; Yuan, R.; Chai, Y. Q.; Zhuo, Y.; Hong, C. L. *Acta Chim. Sin.* **2009**, *67*, 637.
(826) Rusling, J. F.; Sotzing, G.; Papadimitrakopoulosa, F. *Bioelectrochemistry* **2009**, *76*, 189.
(827) Mani, V.; Chikkaveeraiah, B. V.; Patel, V.; Gutkind, J. S.; Rusling, J. F. *ACS Nano* **2009**, *3*, 585.
(828) Tang, D. P.; Yuan, R.; Chai, Y. Q. *Biosens. Bioelectron.* **2007**, *22*, 1116.
(829) Loyprasert, S.; Hedstrom, M.; Thavarungkul, P.; Kanatharana, P.; Mattiasson, B. *Biosens. Bioelectron.* **2010**, *25*, 1977.
(830) Liang, K. Z.; Mu, W. J. *Anal. Chim. Acta* **2006**, *580*, 128.
(831) Liang, K. Z.; Mu, W. J.; Huang, M. Y.; Yu, Z. X.; Lai, Q. K. *Electroanalysis* **2006**, *18*, 1505.
(832) Munge, B. S.; Krause, C. E.; Malhotra, R.; Patel, V.; Gutkind, J. S.; Rusling, J. F. *Electrochem. Commun.* **2009**, *11*, 1009.
(833) Kim, G. I.; Kim, K. W.; Oh, M. K.; Sung, Y. M. *Biosens. Bioelectron.* **2010**, *25*, 1717.
(834) Kim, D. M.; Noh, H. B.; Park, D. S.; Ryu, S. H.; Koo, J. S.; Shim, Y. B. *Biosens. Bioelectron.* **2009**, *25*, 456.

(835) Lei, C. X.; Gong, F. C.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2003**, *96*, 582.
(836) Chu, X.; Xiang, Z. F.; Fu, X.; Wang, S. P.; Shen, G. L.; Yu, R. Q. *J. Immunol. Methods* **2005**, *301*, 77.
(837) Dungchai, W.; Siangproh, W.; Chaicumpa, W.; Tongtawe, P.; Chailapakul, O. *Talanta* **2008**, *77*, 727.
(838) Yang, G. J.; Huang, J. L.; Meng, W. J.; Shen, M.; Jiao, X. A. *Anal. Chim. Acta* **2009**, *647*, 159.
(839) Lin, Y. H.; Chen, S. H.; Chuang, Y. C.; Lu, Y. C.; Shen, T. Y.; Chang, C. A.; Lin, C. S. *Biosens. Bioelectron.* **2008**, *23*, 1832.
(840) Singh, K.; Rahman, M. A.; Son, J. I.; Kim, K. C.; Shim, Y. B. *Biosens. Bioelectron.* **2008**, *23*, 1595.
(841) Piras, L.; Reho, S. *Sens. Actuat. B Chem.* **2005**, *111*, 450.
(842) Huang, H. Z.; Ran, P. X.; Liu, Z. G. *Bioelectrochemistry* **2007**, *70*, 257.
(843) Li, X. L.; Yuan, R.; Chai, Y. Q.; Zhang, L. Y.; Zhuo, Y.; Zhang, Y. *J. Biotechnol.* **2006**, *123*, 356.
(844) An, H. Z.; Yuan, R. T.; Tang, D. P.; Chai, Y. Q.; Li, N. *Electroanalysis* **2007**, *19*, 479.
(845) Huang, K. J.; Niu, D. J.; Xie, W. Z.; Wang, W. *Anal. Chim. Acta* **2010**, *659*, 102.
(846) Ou, C. F.; Yuan, R.; Chai, Y. Q.; Tang, M. Y.; Chai, R.; He, X. L. *Anal. Chim. Acta* **2007**, *603*, 205.
(847) Zhong, Z. Y.; Wu, W.; Wang, D.; Wang, D.; Shan, J. L.; Qing, Y.; Zhang, Z. M. *Biosens. Bioelectron.* **2010**, *25*, 2379.
(848) Liu, Z. Y.; Yuan, R.; Chai, Y. Q.; Zhuo, Y.; Hong, C. L.; Yang, X. *Sens. Actuat. B Chem.* **2008**, *134*, 625.
(849) Li, N.; Zhao, H. W.; Yuan, R.; Peng, K. F.; Chai, Y. Q. *Electrochim. Acta* **2008**, *54*, 235.
(850) Shi, Y. T.; Yuan, R.; Chai, Y. Q.; He, X. L. *Electrochim. Acta* **2007**, *52*, 3518.
(851) Shi, Y. T.; Yuan, R.; Chai, Y. Q.; Tang, M. Y.; He, X. L. *J. Electroanal. Chem.* **2007**, *604*, 9.
(852) Zhuo, Y.; Yu, R. J.; Yuan, R.; Chai, Y. Q.; Hong, C. L. *J. Electroanal. Chem.* **2009**, *628*, 90.
(853) He, X. L.; Yuan, R.; Chai, Y. Q.; Shi, Y. T. *J. Biochem. Biophys. Methods* **2008**, *70*, 823.
(854) Song, Z. J.; Yuan, R.; Chai, Y. Q.; Yin, B.; Fu, P.; Wang, J. F. *Electrochim. Acta* **2010**, *55*, 1778.
(855) Yuan, Y. R.; Yuan, R.; Chai, Y. Q.; Zhuo, Y.; Miao, X. M. *J. Electroanal. Chem.* **2009**, *626*, 6.
(856) Tang, H.; Chen, J. H.; Nie, L. H.; Kuang, Y. F.; Yao, S. Z. *Biosens. Bioelectron.* **2007**, *22*, 1061.
(857) Zhang, T. T.; Yuan, R.; Chai, Y. Q.; Liu, K. G.; Ling, S. J. *Microchim. Acta* **2009**, *165*, 53.
(858) Ho, J. A. A.; Chang, H. C.; Shih, N. Y.; Wu, L. C.; Chang, Y. F.; Chen, C. C.; Chou, C. *Anal. Chem.* **2010**, *82*, 5944.
(859) Wu, J.; Yan, F.; Zhang, X. Q.; Yan, Y. T.; Tang, J. H.; Ju, H. X. *Clin. Chem.* **2008**, *54*, 1481.
(860) Wu, J.; Yan, Y. T.; Yan, F.; Ju, H. X. *Anal. Chem.* **2008**, *80*, 6072.
(861) Wu, Z. S.; Li, J. S.; Luo, M. H.; Shen, G. L.; Yu, R. Q. *Anal. Chim. Acta* **2005**, *528*, 235.
(862) Mao, X.; Jiang, J. H.; Huang, Y.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2007**, *123*, 198.
(863) Chen, Z. P.; Peng, Z. F.; Zhang, P.; Jin, X. F.; Jiang, J. H.; Zhang, X. B.; Shen, G. L.; Yu, R. Q. *Talanta* **2007**, *72*, 1800.
(864) Chen, H.; Jiang, J. H.; Huang, Y.; Deng, T.; Li, J. S.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2006**, *117*, 211.
(865) Chu, X.; Fu, X.; Chen, K.; Shen, G. L.; Yu, R. Q. *Biosens. Bioelectron.* **2005**, *20*, 1805.
(866) Fu, Y. Z.; Yuan, R.; Tang, D. P.; Chai, Y. Q.; Xu, L. *Colloids Surf. B* **2005**, *40*, 61.
(867) Carralero, V.; Gonzalez-Cortes, A.; Yanez-Sedeno, P.; Pingarron, J. M. *Anal. Lett.* **2008**, *41*, 244.
(868) Leng, C. A.; Lai, G. S.; Yan, F.; Ju, H. X. *Anal. Chim. Acta* **2010**, *666*, 97.
(869) Cui, R. J.; Huang, H. P.; Yin, Z. Z.; Gao, D.; Zhu, J. J. *Biosens. Bioelectron.* **2008**, *23*, 1666.
(870) Liu, M. Q.; Jiang, J. H.; Feng, Y. L.; Huang, Y.; Shen, G. L.; Yu, R. Q. *Chin. J. Anal. Chem.* **2010**, *38*, 258.
(871) Huang, K. J.; Niu, D. J.; Sun, J. Y.; Zhu, X. L.; Zhu, J. J. *Anal. Bioanal. Chem.* **2010**, *397*, 3553.
(872) Tian, D.; Duan, C.; Wang, W.; Li, N.; Zhang, H.; Cui, H.; Lu, Y. *Talanta* **2009**, *78*, 399.
(873) Tian, D. Y.; Duan, C. F.; Wang, W.; Cui, H. *Biosens. Bioelectron.* **2010**, *25*, 2290.
(874) Marcon, L.; Melnyk, O.; Stievenard, D. *Biosens. Bioelectron.* **2008**, *23*, 1185.
(875) Liu, G. D.; Lin, Y. H. *J. Nanosci. Nanotechnol.* **2005**, *5*, 1060.
(876) Ambrosi, A.; Castaneda, M. T.; Killard, A. J.; Smyth, M. R.; Alegret, S.; Merkoci, A. *Anal. Chem.* **2007**, *79*, 5232.
(877) Chen, C. R.; Liu, D. Y.; Wu, Z. S.; Luo, Q. M.; Shen, G. L.; Yu, R. Q. *Electrochem. Commun.* **2009**, *11*, 1869.
(878) Velev, O. D.; Kaler, E. W. *Langmuir* **1999**, *15*, 3693.
(879) Mao, X.; Jiang, J. H.; Luo, Y.; Shen, G. L.; Yu, R. Q. *Talanta* **2007**, *73*, 420.
(880) Garcia, M. B. G.; Garcia, A. C. *Bioelectrochem. Bioenerg.* **1995**, *38*, 389.
(881) Gonzalez-Garcia, M. B.; Fernandez-Sanchez, C.; Costa-Garcia, A. *Biosens. Bioelectron.* **2000**, *15*, 315.
(882) Dequaire, M.; Degrand, C.; Limoges, B. *Anal. Chem.* **2000**, *72*, 5521.
(883) Mao, X.; Jiang, J.; Chen, J.; Huang, Y.; Shen, G.; Yu, R. *Anal. Chim. Acta* **2006**, *557*, 159.
(884) de la Escosura-Muniz, A.; Costa, M. M. D.; Merkoci, A. *Biosens. Bioelectron.* **2009**, *24*, 2475.
(885) Liao, K. T.; Huang, H. J. *Anal. Chim. Acta* **2005**, *538*, 159.
(886) Wu, Y.; Zheng, J. W.; Li, Z.; Zhao, Y. R.; Zhang, Y. *Biosens. Bioelectron.* **2009**, *24*, 1389.
(887) Chumbimuni-Torres, K. Y.; Dai, Z.; Rubinova, N.; Xiang, Y.; Pretsch, E.; Wang, J.; Bakker, E. *J. Am. Chem. Soc.* **2006**, *128*, 13676.
(888) Das, J.; Aziz, M. A.; Yang, H. *J. Am. Chem. Soc.* **2006**, *128*, 16022.
(889) Nam, J. M.; Thaxton, C. S.; Mirkin, C. A. *Science* **2003**, *301*, 1884.
(890) Selvaraju, T.; Das, J.; Han, S. W.; Yang, H. *Biosens. Bioelectron.* **2008**, *23*, 932.
(891) Tudos, A. J., Schasfoort, R. B. M. *Handbook of Surface Plasmon Resonance*; RSC Publishing: Cambridge, U.K., 2008.
(892) Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. *Chem. Rev.* **2005**, *105*, 1103.
(893) Eustis, S.; El-Sayed, M. A. *Chem. Soc. Rev.* **2006**, *35*, 209.
(894) Mustafa, D. E.; Yang, T. M.; Xuan, Z.; Chen, S. Z.; Tu, H. Y.; Zhang, A. D. *Plasmonics* **2010**, *5*, 221.
(895) Guerrero, E.; Munoz-Marquez, M. A.; Garcia, M. A.; Crespo, P.; Fernandez-Pinel, E.; Hernando, A.; Fernandez, A. *Nanotechnology* **2008**, *19*, 175701.
(896) Haes, A. J.; Zou, S. L.; Schatz, G. C.; Van Duyne, R. P. *J. Phys. Chem. B* **2004**, *108*, 109.
(897) Haes, A. J.; Van Duyne, R. P. *J. Am. Chem. Soc.* **2002**, *124*, 10596.
(898) Underwood, S.; Mulvaney, P. *Langmuir* **1994**, *10*, 3427.
(899) Mulvaney, P. *Langmuir* **1996**, *12*, 788.
(900) Burda, C.; Chen, X. B.; Narayanan, R.; El-Sayed, M. A. *Chem. Rev.* **2005**, *105*, 1025.
(901) Lee, K. S.; El-Sayed, M. A. *J. Phys. Chem. B* **2006**, *110*, 19220.
(902) Zhang, X. M.; Zhang, J. H.; Wang, H. A.; Hao, Y. D.; Zhang, X.; Wang, T. Q.; Wang, Y. N.; Zhao, R.; Zhang, H.; Yang, B. *Nanotechnology* **2010**, *21*, 465702.
(903) Homola, J.; Yee, S. S.; Gauglitz, G. *Sens. Actuat. B Chem.* **1999**, *54*, 3.
(904) Aslan, K.; Lakowicz, J. R.; Geddes, C. D. *Curr. Opin. Chem. Biol.* **2005**, *9*, 538.
(905) Hutter, E.; Fendler, J. H. *Adv. Mater.* **2004**, *16*, 1685.
(906) Haes, A. J.; Van Duyne, R. P. *Anal. Bioanal. Chem.* **2004**, *379*, 920.
(907) Ray, P. C. *Chem. Rev.* **2010**, *110*, 5332.

(908) Homola, J. *Chem. Rev.* **2008**, *108*, 462.
(909) Stewart, M. E.; Anderton, C. R.; Thompson, L. B.; Maria, J.; Gray, S. K.; Rogers, J. A.; Nuzzo, R. G. *Chem. Rev.* **2008**, *108*, 494.
(910) Willets, K. A.; Van Duyne, R. P. *Annu. Rev. Phys. Chem.* **2007**, *58*, 267.
(911) Yonzon, C. R.; Stuart, D. A.; Zhang, X. Y.; McFarland, A. D.; Haynes, C. L.; Van Duyne, R. P. *Talanta* **2005**, *67*, 438.
(912) Yguerabide, J.; Yguerabide, E. E. *Anal. Biochem.* **1998**, *262*, 137.
(913) Jin, R. C.; Cao, Y. C.; Hao, E. C.; Metraux, G. S.; Schatz, G. C.; Mirkin, C. A. *Nature* **2003**, *425*, 487.
(914) Kealley, C. S.; Arnold, M. D.; Porkovich, A.; Cortie, M. B. *Sens. Actuat. B Chem.* **2010**, *148*, 34.
(915) Jain, P. K.; Huang, X.; El-Sayed, I. H.; El-Sayad, M. A. *Plasmonics* **2007**, *2*, 107.
(916) Fan, M. K.; Thompson, M.; Andrade, M. L.; Brolo, A. G. *Anal. Chem.* **2010**, *82*, 6350.
(917) McFarland, A. D.; Van Duyne, R. P. *Nano Lett.* **2003**, *3*, 1057.
(918) Haes, A. J.; Van Duyne, R. P. *Expert Rev. Mol. Diagn.* **2004**, *4*, 527.
(919) Yonzon, C. R.; Jeoungf, E.; Zou, S. L.; Schatz, G. C.; Mrksich, M.; Van Duyne, R. P. *J. Am. Chem. Soc.* **2004**, *126*, 12669.
(920) Lai, T.; Hou, Q. N.; Yang, H. A.; Luo, X. G.; Xi, M. R. *Acta Biochim. Biophys. Sin.* **2010**, *42*, 787.
(921) Endo, T.; Shibata, A.; Yanagida, Y.; Higo, Y.; Hatsuzawa, T. *Mater. Lett.* **2010**, *64*, 2105.
(922) Filippo, E.; Serra, A.; Manno, D. *Sens. Actuat. B Chem.* **2009**, *138*, 625.
(923) Serra, A.; Filippo, E.; Re, M.; Palmisano, M.; Vittori-Antisari, M.; Buccolieri, A.; Manno, D. *Nanotechnology* **2009**, *20*, 165501.
(924) Lyon, L. A.; Musick, M. D.; Natan, M. J. *Anal. Chem.* **1998**, *70*, 5177.
(925) Cheng, S. F.; Chau, L. K. *Anal. Chem.* **2003**, *75*, 16.
(926) Raschke, G.; Kowarik, S.; Franzl, T.; Sonnichsen, C.; Klar, T. A.; Feldmann, J.; Nichtl, A.; Kurzinger, K. *Nano Lett.* **2003**, *3*, 935.
(927) Chen, C. H.; Tsao, T. C.; Li, W. Y.; Shen, W. C.; Cheng, C. W.; Tang, J. L.; Jen, C. P.; Chau, L. K.; Wu, W. T. *Microsyst. Technol.* **2010**, *16*, 1207.
(928) Chau, L. K.; Lin, Y. F.; Cheng, S. F.; Lin, T. J. *Sens. Actuat. B Chem.* **2006**, *113*, 100.
(929) Ye, J.; Bonroy, K.; Nelis, D.; Frederix, F.; D'Haen, J.; Maes, G.; Borghs, G. *Colloids Surf., A* **2008**, *321*, 313.
(930) Uechi, I.; Yamada, S. *Anal. Bioanal. Chem.* **2008**, *391*, 2411.
(931) Park, K. H.; Kim, S.; Yang, S. M.; Park, H. G. *J. Nanosci. Nanotechnol.* **2009**, *9*, 1374.
(932) Kajiura, M.; Nakanishi, T.; Iida, H.; Takada, H.; Osaka, T. *J. Colloid Interface Sci.* **2009**, *335*, 140.
(933) Gao, S. Y.; Koshizaki, N.; Tokuhisa, H.; Koyama, E.; Sasaki, T.; Kim, J. K.; Ryu, J.; Kim, D. S.; Shimizu, Y. *Adv. Funct. Mater.* **2010**, *20*, 78.
(934) Wang, L.; Li, T.; Du, Y.; Chen, C. G.; Li, L.; Zhou, M.; Dong, S. J. *Biosens. Bioelectron.* **2010**, *25*, 2622.
(935) Wang, T. J.; Lin, W. S. *Appl. Phys. Lett.* **2006**, *89*, 173903.
(936) Watanabe, S.; Sonobe, M.; Arai, M.; Tazume, Y.; Matsuo, T.; Nakamura, T.; Yoshida, K. *Chem. Commun.* **2002**, 2866.
(937) Hone, D. C.; Haines, A. H.; Russell, D. A. *Langmuir* **2003**, *19*, 7141.
(938) Fahnestock, K. J.; Manesse, M.; McIlwee, H. A.; Schauer, C. L.; Boukherroub, R.; Szunerits, S. *Analyst* **2009**, *134*, 881.
(939) Kalyuzhny, G.; Vaskevich, A.; Schneeweiss, M. A.; Rubinstein, I. *Chem.—Eur. J.* **2002**, *8*, 3850.
(940) Kalyuzhny, G.; Schneeweiss, M. A.; Shanzer, A.; Vaskevich, A.; Rubinstein, I. *J. Am. Chem. Soc.* **2001**, *123*, 3177.
(941) Deng, J. J.; Song, Y.; Wang, Y. A.; Di, J. W. *Biosens. Bioelectron.* **2010**, *26*, 615.
(942) Tokareva, I.; Minko, S.; Fendler, J. H.; Hutter, E. *J. Am. Chem. Soc.* **2004**, *126*, 15950.
(943) Englebienne, P. *Analyst* **1998**, *123*, 1599.
(944) Englebienne, P.; Van Hoonacker, A.; Verhas, M. *Analyst* **2001**, *126*, 1645.
(945) Prabhakar, A.; Mukherji, S. *Lab Chip* **2010**, *10*, 3422.
(946) Zhu, S. L.; Zhang, J. B.; Yue, L. Y. L.; Hartono, D.; Liu, A. Q. *Adv. Mater. Res.* **2009**, *74*, 95.
(947) Wang, J. *Small* **2005**, *1*, 1036.
(948) Matsui, J.; Akamatsu, K.; Hara, N.; Miyoshi, D.; Nawafune, H.; Tamaki, K.; Sugimoto, N. *Anal. Chem.* **2005**, *77*, 4282.
(949) Frederix, F.; Friedt, J. M.; Choi, K. H.; Laureyn, W.; Campitelli, A.; Mondelaers, D.; Maes, G.; Borghs, G. *Anal. Chem.* **2003**, *75*, 6894.
(950) Azzam, E. M. S.; Bashir, A.; Shekhah, O.; Alawady, A. R. E.; Birkner, A.; Grunwald, C.; Woll, C. *Thin Solid Films* **2009**, *518*, 387.
(951) Kim, H. M.; Jin, S. M.; Lee, S. K.; Kim, M. G.; Shin, Y. B. *Sensors* **2009**, *9*, 2334.
(952) Wang, J.; Wang, L. Y.; Sun, Y.; Zhu, X. N.; Cao, Y. B.; Wang, X. H.; Zhang, H. Q.; Song, D. Q. *Colloids Surf., B* **2010**, *75*, 520.
(953) Lin, Y. B.; Zou, Y.; Mo, Y. Y.; Guo, J. P.; Lindquist, R. G. *Sensors* **2010**, *10*, 9397.
(954) Chiang, C. Y.; Hsieh, M. L.; Huang, K. W.; Chau, L. K.; Chang, C. M.; Lyu, S. R. *Biosens. Bioelectron.* **2010**, *26*, 1036.
(955) Briglin, S. M.; Gao, T.; Lewis, N. S. *Langmuir* **2004**, *20*, 299.
(956) Frasconi, M.; Tortolini, C.; Botre, F.; Mazzei, F. *Anal. Chem.* **2010**, *82*, 7335.
(957) Connolly, S.; Fitzmaurice, D. *Adv. Mater.* **1999**, *11*, 1202.
(958) Shenton, W.; Davis, S. A.; Mann, S. *Adv. Mater.* **1999**, *11*, 449.
(959) Fu, E.; Ramsey, S. A.; Yager, P. *Anal. Chim. Acta* **2007**, *599*, 118.
(960) Ko, S.; Park, T. J.; Kim, H. S.; Kim, J. H.; Cho, Y. J. *Biosens. Bioelectron.* **2009**, *24*, 2592.
(961) Siiman, O.; Burshteyn, A. *J. Phys. Chem. B* **2000**, *104*, 9795.
(962) Manera, M. G.; Spadavecchia, J.; Taurino, A.; Rella, R. *J. Opt.* **2010**, *12*, 035003.
(963) Hutter, E.; Pileni, M. P. *J. Phys. Chem. B* **2003**, *107*, 6497.
(964) Roy, D.; Fendler, J. *Adv. Mater.* **2004**, *16*, 479.
(965) Hutter, E.; Cha, S.; Liu, J. F.; Park, J.; Yi, J.; Fendler, J. H.; Roy, D. *J. Phys. Chem. B* **2001**, *105*, 8.
(966) Hutter, E.; Fendler, J. H.; Roy, D. *J. Phys. Chem. B* **2001**, *105*, 11159.
(967) Chah, S.; Hutter, E.; Roy, D.; Fendler, J. H.; Yi, J. *Chem. Phys.* **2001**, *272*, 127.
(968) Pieper-Furst, U.; Stocklein, W. F. M.; Warsinke, A. *Anal. Chim. Acta* **2005**, *550*, 69.
(969) Cao, C.; Sim, S. J. *Biosens. Bioelectron.* **2007**, *22*, 1874.
(970) Huang, H. Z.; Ran, P. X.; Liu, Z. G. *Sens. Actuat. B Chem.* **2008**, *131*, 417.
(971) Kawaguchi, T.; Shankaran, D. R.; Kim, S. J.; Matsumoto, K.; Toko, K.; Miura, N. *Sens. Actuat. B Chem.* **2008**, *133*, 467.
(972) Wang, J. L.; Munir, A.; Li, Z. H.; Zhou, H. S. *Biosens. Bioelectron.* **2009**, *25*, 124.
(973) Mitchell, J. S.; Lowe, T. E. *Biosens. Bioelectron.* **2009**, *24*, 2177.
(974) Chang, Y. F.; Chen, R. C.; Lee, Y. J.; Chao, S. C.; Su, L. C.; Li, Y. C.; Chou, C. *Biosens. Bioelectron.* **2009**, *24*, 1610.
(975) Hsieh, B. Y.; Chang, Y. F.; Ng, M. Y.; Liu, W. C.; Lin, C. H.; Wu, H. T.; Chou, C. *Anal. Chem.* **2007**, *79*, 3487.
(976) Huang, J. C.; Chang, Y. F.; Chen, K. H.; Su, L. C.; Lee, C. W.; Chen, C. C.; Chen, Y. M. A.; Chou, C. *Biosens. Bioelectron.* **2009**, *25*, 320.
(977) Chang, Y. F.; Wang, S. F.; Huang, J. C.; Su, L. C.; Yao, L.; Li, Y. C.; Wu, S. C.; Chen, Y. M. A.; Hsieh, J. P.; Chou, C. *Biosens. Bioelectron.* **2010**, *26*, 1068.
(978) Yamaguchi, A.; Juodkazis, S.; Matsuo, S.; Misawa, H. *Chem. Lett.* **2002**, 190.
(979) Fang, S. P.; Lee, H. J.; Wark, A. W.; Corn, R. M. *J. Am. Chem. Soc.* **2006**, *128*, 14044.
(980) He, L.; Musick, M. D.; Nicewarner, S. R.; Salinas, F. G.; Benkovic, S. J.; Natan, M. J.; Keating, C. D. *J. Am. Chem. Soc.* **2000**, *122*, 9071.
(981) Yao, X.; Li, X.; Toledo, F.; Zurita-Lopez, C.; Gutova, M.; Momand, J.; Zhou, F. M. *Anal. Biochem.* **2006**, *354*, 220.
(982) Bailey, R. C.; Nam, J. M.; Mirkin, C. A.; Hupp, J. T. *J. Am. Chem. Soc.* **2003**, *125*, 13541.

(983) Du, B. A.; Li, Z. P.; Liu, C. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 8022.
(984) Jans, H.; Liu, X.; Austin, L.; Maes, G.; Huo, Q. *Anal. Chem.* **2009**, *81*, 9425.
(985) Wang, X. Y.; Zou, M. J.; Xu, X.; Lei, R.; Li, K. A.; Li, N. *Anal. Bioanal. Chem.* **2009**, *395*, 2397.
(986) Wang, X. Y.; Xu, Y.; Xu, X. A.; Hu, K.; Xiang, M. H.; Li, L. M.; Liu, F.; Li, N. *Talanta* **2010**, *82*, 693.
(987) Xie, C.; Xu, F. G.; Huang, X. Y.; Dong, C. Q.; Ren, J. C. *J. Am. Chem. Soc.* **2009**, *131*, 12763.
(988) Wu, C. K.; Xiong, C.; Wang, L. J.; Lan, C. C.; Ling, L. S. *Analyst* **2010**, *135*, 2682.
(989) El-Sayed, I. H.; Huang, X. H.; El-Sayed, M. A. *Nano Lett.* **2005**, *5*, 829.
(990) Smith, E., Dent, G. *Modern Raman Spectroscopy—A Practical Approach*; Wiley: Chichester, U.K., 2005.
(991) Kneipp, K.; Kneipp, H.; Itzkan, I.; Dasari, R. R.; Feld, M. S. *Chem. Rev.* **1999**, *99*, 2957.
(992) Banholzer, M. J.; Millstone, J. E.; Qin, L. D.; Mirkin, C. A. *Chem. Soc. Rev.* **2008**, *37*, 885.
(993) Fleischm., M; Hendra, P. J.; McQuilla., Aj *Chem. Phys. Lett.* **1974**, *26*, 163.
(994) Jeanmaire, D. L.; Vanduyne, R. P. *J. Electroanal. Chem.* **1977**, *84*, 1.
(995) Albrecht, M. G.; Creighton, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 5215.
(996) Nie, S. M.; Emory, S. R. *Science* **1997**, *275*, 1102.
(997) Kneipp, K.; Wang, Y.; Kneipp, H.; Perelman, L. T.; Itzkan, I.; Dasari, R.; Feld, M. S. *Phys. Rev. Lett.* **1997**, *78*, 1667.
(998) Stockman, M. I. In *Surface-Enhanced Raman Scattering: Physics and Applications*; Springer: New York, 2006; Vol. *103*.
(999) Schatz, G. C.; Young, M. A.; Van Duyne, R. P. In *Surface-Enhanced Raman Scattering: Physics and Applications*; Springer: New York, 2006; Vol. *103*.
(1000) Moskovits, M. In *Surface-Enhanced Raman Scattering: Physics and Applications*; Springer: Berlin, Heidelberg, New York, 2006; Vol. *103*.
(1001) Otto, A. *J. Raman Spectrosc.* **2006**, *37*, 937.
(1002) Dasary, S. S. R.; Singh, A. K.; Senapati, D.; Yu, H. T.; Ray, P. C. *J. Am. Chem. Soc.* **2009**, *131*, 13806.
(1003) Gupta, S.; Agrawal, M.; Uhlmann, P.; Simon, F.; Oertel, U.; Stamm, M. *Macromolecules* **2008**, *41*, 8152.
(1004) Chang, S. H.; Ko, H. H.; Singamaneni, S.; Gunawidjaja, R.; Tsukruk, V. V. *Anal. Chem.* **2009**, *81*, 5740.
(1005) Ko, H.; Chang, S.; Tsukruk, V. V. *ACS Nano* **2009**, *3*, 181.
(1006) Kneipp, J.; Kneipp, H.; Wittig, B.; Kneipp, K. *J. Phys. Chem. C* **2010**, *114*, 7421.
(1007) Cao, Y. C.; Jin, R.; Mirkin, C. A. *Science* **2002**, *297*, 1536.
(1008) Sun, L.; Yu, C. X.; Irudayaraj, J. *Anal. Chem.* **2007**, *79*, 3981.
(1009) Thuy, N. T. B.; Yokogawa, R.; Yoshimura, Y.; Fujimoto, K.; Koyano, M.; Maenosono, S. *Analyst* **2010**, *135*, 595.
(1010) Liu, Y. C.; Zhong, M. Y.; Shan, G. Y.; Li, Y. J.; Huang, B. Q.; Yang, G. L. *J. Phys. Chem. B* **2008**, *112*, 6484.
(1011) Qian, X. M.; Zhou, X.; Nie, S. M. *J. Am. Chem. Soc.* **2008**, *130*, 14934.
(1012) Hu, J.; Zheng, P. C.; Jiang, J. H.; Shen, G. L.; Yu, R. Q.; Liu, G. K. *Analyst* **2010**, *135*, 1084.
(1013) Harpster, M. H.; Zhang, H.; Sankara-Warrier, A. K.; Ray, B. H.; Ward, T. R.; Kollmar, J. P.; Carron, K. T.; Mecham, J. O.; Corcoran, R. C.; Wilson, W. C.; Johnson, P. A. *Biosens. Bioelectron.* **2009**, *25*, 674.
(1014) Sun, L.; Irudayaraj, J. *J. Phys. Chem. B* **2009**, *113*, 14021.
(1015) Kang, T.; Yoo, S. M.; Yoon, I.; Lee, S. Y.; Kim, B. *Nano Lett.* **2010**, *10*, 1189.
(1016) Maiti, K. K.; Dinish, U. S.; Fu, C. Y.; Lee, J. J.; Soh, K. S.; Yun, S. W.; Bhuvaneswari, R.; Olivo, M.; Chang, Y. T. *Biosens. Bioelectron.* **2010**, *26*, 398.
(1017) Willets, K. A. *Anal. Bioanal. Chem.* **2009**, *394*, 85.
(1018) Qian, X. M.; Peng, X. H.; Ansari, D. O.; Yin-Goen, Q.; Chen, G. Z.; Shin, D. M.; Yang, L.; Young, A. N.; Wang, M. D.; Nie, S. M. *Nat. Biotechnol.* **2008**, *26*, 83.
(1019) Kneipp, J.; Kneipp, H.; Rice, W. L.; Kneipp, K. *Anal. Chem.* **2005**, *77*, 2381.
(1020) Kneipp, K.; Haka, A. S.; Kneipp, H.; Badizadegan, K.; Yoshizawa, N.; Boone, C.; Shafer-Peltier, K. E.; Motz, J. T.; Dasari, R. R.; Feld, M. S. *Appl. Spectrosc.* **2002**, *56*, 150.
(1021) Tang, H. W.; Yang, X. B.; Kirkham, J.; Smith, D. A. *Anal. Chem.* **2007**, *79*, 3646.
(1022) Ni, J.; Lipert, R. J.; Dawson, G. B.; Porter, M. D. *Anal. Chem.* **1999**, *71*, 4903.
(1023) Driskell, J. D.; Uhlenkamp, J. M.; Lipert, R. J.; Porter, M. D. *Anal. Chem.* **2007**, *79*, 4141.
(1024) Grubisha, D. S.; Lipert, R. J.; Park, H. Y.; Driskell, J.; Porter, M. D. *Anal. Chem.* **2003**, *75*, 5936.
(1025) Han, X. X.; Kitahama, Y.; Itoh, T.; Wang, C. X.; Zhao, B.; Ozaki, Y. *Anal. Chem.* **2009**, *81*, 3350.
(1026) Wang, G. F.; Park, H. Y.; Lipert, R. J. *Anal. Chem.* **2009**, *81*, 9643.
(1027) Manimaran, M.; Jana, N. R. *J. Raman Spectrosc.* **2007**, *38*, 1326.
(1028) Lin, C. C.; Yang, Y. M.; Chen, Y. F.; Yang, T. S.; Chang, H. C. *Biosens. Bioelectron.* **2008**, *24*, 178.
(1029) Stevenson, R.; Ingram, A.; Leung, H.; McMillan, D. C.; Graham, D. *Analyst* **2009**, *134*, 842.
(1030) Kang, T.; Yoon, I.; Kim, J.; Hee, H.; Kim, B. *Chem.—Eur. J.* **2010**, *16*, 1351.
(1031) Wang, Y. L.; Lee, K.; Irudayaraj, J. *Chem. Commun.* **2010**, *46*, 613.
(1032) Hu, J.; Zheng, P. C.; Jiang, J. H.; Shen, G. L.; Yu, R. Q.; Liu, G. K. *Anal. Chem.* **2009**, *81*, 87.
(1033) Cao, Y. C.; Jin, R. C.; Nam, J. M.; Thaxton, C. S.; Mirkin, C. A. *J. Am. Chem. Soc.* **2003**, *125*, 14676.
(1034) Bonham, A. J.; Braun, G.; Pavel, I.; Moskovits, M.; Reich, N. O. *J. Am. Chem. Soc.* **2007**, *129*, 14572.
(1035) Maher, R. C.; Maier, S. A.; Cohen, L. F.; Koh, L.; Laromaine, A.; Dick, J. A. G.; Stevens, M. M. *J. Phys. Chem. C* **2010**, *114*, 7231.
(1036) Li, T.; Liu, D. J.; Wang, Z. X. *Biosens. Bioelectron.* **2009**, *24*, 3335.
(1037) Ruan, C. M.; Wang, W.; Gu, B. H. *Anal. Chem.* **2006**, *78*, 3379.
(1038) Huang, P. J.; Tay, L. L.; Tanha, J.; Ryan, S.; Chau, L. K. *Chem.—Eur. J.* **2009**, *15*, 9330.
(1039) Rule, K. L.; Vikesland, P. J. *Environ. Sci. Technol.* **2009**, *43*, 1147.
(1040) Marx, K. A. *Biomacromolecules* **2003**, *4*, 1099.
(1041) Fritz, J. *Analyst* **2008**, *133*, 855.
(1042) Milburn, C.; Zhou, J.; Bravo, O.; Kumar, C.; Soboyejo, W. O. *J. Biomed. Nanotechnol.* **2005**, *1*, 30.
(1043) Wu, G. H.; Datar, R. H.; Hansen, K. M.; Thundat, T.; Cote, R. J.; Majumdar, A. *Nat. Biotechnol.* **2001**, *19*, 856.
(1044) Zhou, X. C.; Huang, L. Q.; Li, S. F. Y. *Biosens. Bioelectron.* **2001**, *16*, 85.
(1045) Oshima, K.; Nakajima, H.; Takahashi, S.; Kera, Y.; Shimomura, M.; Miyauchi, S. *Sens. Actuat. B Chem.* **2005**, *105*, 473.
(1046) Hwang, K. S.; Lee, S. M.; Kim, S. K.; Lee, J. H.; Kim, T. S. *Annu. Rev. Anal. Chem.* **2009**, *2*, 77.
(1047) Saya, D.; Nicu, L.; Guirardel, M.; Tauran, Y.; Bergaud, C. *Rev. Sci. Instrum.* **2004**, *75*, 3010.
(1048) Mao, X. L.; Yang, L. J.; Su, X. L.; Li, Y. B. *Biosens. Bioelectron.* **2006**, *21*, 1178.
(1049) Grate, J. W.; Nelson, D. A.; Skaggs, R. *Anal. Chem.* **2003**, *75*, 1868.
(1050) Grate, J. W. *Anal. Chem.* **2003**, *75*, 6759.
(1051) Han, L.; Daniel, D. R.; Maye, M. M.; Zhong, C. J. *Anal. Chem.* **2001**, *73*, 4441.

(1052) Krasteva, N.; Fogel, Y.; Bauer, R. E.; Mullen, K.; Joseph, Y.; Matsuzawa, N.; Yasuda, A.; Vossmeyer, T. *Adv. Funct. Mater.* **2007**, *17*, 881.
(1053) Han, S. B.; Lin, J. Q.; Satjapipat, M.; Baca, A. J.; Zhou, F. M. *Chem. Commun.* **2001**, 609.
(1054) Lin, L.; Zhao, H. Q.; Li, J. R.; Tang, J. A.; Duan, M. X.; Jiang, L. *Biochem. Biophys. Res. Commun.* **2000**, *274*, 817.
(1055) Zhou, X. C.; O'Shea, S. J.; Li, S. F. Y. *Chem. Commun.* **2000**, 953.
(1056) Patolsky, F.; Ranjit, K. T.; Lichtenstein, A.; Willner, I. *Chem. Commun.* **2000**, 1025.
(1057) Willner, I.; Patolsky, F.; Weizmann, Y.; Willner, B. *Talanta* **2002**, *56*, 847.
(1058) Nie, L. B.; Yang, Y.; Li, S.; He, N. Y. *Nanotechnology* **2007**, *18*, 305501.
(1059) Liu, T.; Tang, J.; Han, M. M.; Jiang, L. *Biochem. Biophys. Res. Commun.* **2003**, *304*, 98.
(1060) Liu, T.; Tang, J.; Jiang, L. *Biochem. Biophys. Res. Commun.* **2004**, *313*, 3.
(1061) Tao, L.; Ji'an, T.; Han, M. M.; Jiang, L. *Chin. Sci. Bull.* **2003**, *48*, 873.
(1062) Liu, S. F.; Li, J. R.; Jiang, L. *Colloids Surf., A* **2005**, *257–58*, 57.
(1063) Li, S. H.; Li, X. C.; Zhang, J. P.; Zhang, Y. K.; Han, J. H.; Jiang, L. *Colloids Surf., A* **2010**, *364*, 158.
(1064) Liu, T.; Tang, J.; Jiang, L. *Biochem. Biophys. Res. Commun.* **2002**, *295*, 14.
(1065) Weizmann, Y.; Patolsky, F.; Willner, I. *Analyst* **2001**, *126*, 1502.
(1066) Su, M.; Li, S. U.; Dravid, V. P. *Appl. Phys. Lett.* **2003**, *82*, 3562.
(1067) Tang, D. Q.; Zhang, D. J.; Tang, D. Y.; Ai, H. *J. Immunol. Methods* **2006**, *316*, 144.
(1068) Jla, X. E.; Xie, Q. J.; Zhang, Y. Y.; Yao, S. Z. *Anal. Sci.* **2007**, *23*, 689.
(1069) Jin, X. Y.; Jin, X. F.; Chen, L. G.; Jiang, J. H.; Shen, G. L.; Yu, R. Q. *Biosens. Bioelectron.* **2009**, *24*, 2580.
(1070) Fu, Y. C.; Xie, Q. J.; Jia, X. E.; Xu, X. H.; Meng, W. H.; Yao, S. Z. *J. Electroanal. Chem.* **2007**, *603*, 96.
(1071) Ding, Y. J.; Wang, H.; Li, J. S.; Shen, G. L.; Yu, R. Q. *Chem. J. Chinese Univ.* **2005**, *26*, 222.
(1072) Chu, X.; Zhao, Z. L.; Shen, G. L.; Yu, R. Q. *Sens. Actuat. B Chem.* **2006**, *114*, 696.
(1073) Kim, N. H.; Baek, T. J.; Park, H. G.; Seong, G. H. *Anal. Sci.* **2007**, *23*, 177.
(1074) Kim, N.; Kim, D. K.; Cho, Y. J. *Curr. Appl. Phys.* **2010**, *10*, 1227.
(1075) Su, X. D.; Li, S. F. Y.; O'Shea, S. J. *Chem. Commun.* **2001**, 755.
(1076) Xia, H.; Wang, F.; Huang, Q.; Huang, J. F.; Chen, M.; Wang, J.; Yao, C. Y.; Chen, Q. H.; Cai, G. R.; Fu, W. L. *Sensors* **2008**, *8*, 6453.
(1077) Wang, L. J.; Wei, Q. S.; Wu, C. S.; Hu, Z. Y.; Ji, J.; Wang, P. *Chin. Sci. Bull.* **2008**, *53*, 1175.
(1078) Chen, S. H.; Wu, V. C. H.; Chuang, Y. C.; Lin, C. S. *J. Microbiol. Methods* **2008**, *73*, 7.
(1079) Shen, G. Y.; Tan, S. Z.; Nie, H. G.; Shen, G. L.; Yu, R. Q. *J. Immunol. Methods* **2006**, *313*, 11.
(1080) Ma, Z. F.; Wu, J. L.; Zhou, T. H.; Chen, Z. H.; Dong, Y. G.; Tang, J. T.; Sui, S. F. *New J. Chem.* **2002**, *26*, 1795.
(1081) Lyu, Y. K.; Lim, K. R.; Lee, B. Y.; Kim, K. S.; Lee, W. Y. *Chem. Commun.* **2008**, 4771.
(1082) Chen, S. H.; Chuang, Y. C.; Lu, Y. C.; Lin, H. C.; Yang, Y. L.; Lin, C. S. *Nanotechnology* **2009**, *20*, 215501.
(1083) Nam, J. M.; Park, S. J.; Mirkin, C. A. *J. Am. Chem. Soc.* **2002**, *124*, 3820.
(1084) Hill, H. D.; Mirkin, C. A. *Nat. Protoc.* **2006**, *1*, 324.
(1085) Stoeva, S. I.; Lee, J. S.; Thaxton, C. S.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 3303.
(1086) Nam, J. M.; Stoeva, S. I.; Mirkin, C. A. *J. Am. Chem. Soc.* **2004**, *126*, 5932.
(1087) Li, J.; Song, S. P.; Liu, X. F.; Wang, L. H.; Pan, D.; Huang, Q.; Zhao, Y.; Fan, C. H. *Adv. Mater.* **2008**, *20*, 497.
(1088) Hill, H. D.; Vega, R. A.; Mirkin, C. A. *Anal. Chem.* **2007**, *79*, 9218.
(1089) Goluch, E. D.; Nam, J. M.; Georganopoulou, D. G.; Chiesl, T. N.; Shaikh, K. A.; Ryu, K. S.; Barron, A. E.; Mirkin, C. A.; Liu, C. *Lab Chip* **2006**, *6*, 1293.
(1090) Liu, M. Y.; Jia, C. P.; Huang, Y. Y.; Lou, X. H.; Yao, S. H.; Jin, Q. H.; Zhao, J. L.; Xiang, J. Q. *Analyst* **2010**, *135*, 327.
(1091) Georganopoulou, D. G.; Chang, L.; Nam, J. M.; Thaxton, C. S.; Mufson, E. J.; Klein, W. L.; Mirkin, C. A. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 2273.
(1092) Zheng, G. F.; Daniel, W. L.; Mirkin, C. A. *J. Am. Chem. Soc.* **2008**, *130*, 9644.
(1093) Kim, N. W.; Piatyszek, M. A.; Prowse, K. R.; Harley, C. B.; West, M. D.; Ho, P. L. C.; Coviello, G. M.; Wright, W. E.; Weinrich, S. L.; Shay, J. W. *Science* **1994**, *266*, 2011.
(1094) Thaxton, C. S.; Elghanian, R.; Thomas, A. D.; Stoeva, S. I.; Lee, J. S.; Smith, N. D.; Schaeffer, A. J.; Klocker, H.; Horninger, W.; Bartsch, G.; Mirkin, C. A. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 18437.
(1095) Stoeva, S. I.; Lee, J. S.; Smith, J. E.; Rosen, S. T.; Mirkin, C. A. *J. Am. Chem. Soc.* **2006**, *128*, 8378.
(1096) Kim, D.; Daniel, W. L.; Mirkin, C. A. *Anal. Chem.* **2009**, *81*, 9183.
(1097) Oh, B. K.; Nam, J. M.; Lee, S. W.; Mirkin, C. A. *Small* **2006**, *2*, 103.
(1098) Cao, C.; Dhumpa, R.; Bang, D. D.; Ghavifekr, Z.; Hogberg, J.; Wolff, A. *Analyst* **2010**, *135*, 337.
(1099) Nam, J. M.; Wise, A. R.; Groves, J. T. *Anal. Chem.* **2005**, *77*, 6985.
(1100) Nam, J. M.; Jang, K.-J.; Groves, J. T. *Nat. Protoc.* **2007**, *2*, 1438.