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CRITICAL REVIEW

# Recent advances in electrochemical sensing for hydrogen peroxide: a review†

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Due to the significance of hydrogen peroxide ($H_2O_2$) in biological systems and its practical applications, the development of efficient electrochemical $H_2O_2$ sensors holds a special attraction for researchers. Various materials such as Prussian blue (PB), heme proteins, carbon nanotubes (CNTs) and transition metals have been applied to the construction of $H_2O_2$ sensors. In this article, the electrocatalytic $H_2O_2$ determinations are mainly focused on because they can provide a superior sensing performance over non-electrocatalytic ones. The synergetic effect between nanotechnology and electrochemical $H_2O_2$ determination is also highlighted in various aspects. In addition, some recent progress for *in vivo* $H_2O_2$ measurements is also presented. Finally, the future prospects for more efficient $H_2O_2$ sensing are discussed.

## 1. Introduction

Hydrogen peroxide ($H_2O_2$) is a very simple compound in nature but with great importance in pharmaceutical, clinical, environmental, mining, textile and food manufacturing applications.[1] In living organisms, besides its well-known cytotoxic effects, $H_2O_2$ also plays an essential role as a signalling molecule in regulating diverse biological processes such as immune cell activation, vascular remodelling, apoptosis, stomatal closure and root growth.[2–4] $H_2O_2$ is also a side product generated from some classic biochemical reactions catalyzed by enzymes such as glucose oxidase (GOx), alcohol oxidase (AlOx), lactate oxidase (LOx), urate oxidase (UOx), cholesterol oxidase (ChoOx), D-amino acid oxidase (DAAO), glutamate oxidase (GlOx), lysine oxidase (LyOx), oxalate oxidase (OxaOx), *etc.* Therefore, the study on $H_2O_2$ detection is of practical significance for both academic and industrial purposes. Conventional techniques for hydrogen peroxide determination such as fluorimetry,[5] chemiluminescence,[6] fluorescence[7] and spectrophotometry[8] are complex, costly and time consuming. In comparison, electrochemistry can offer simple, rapid, sensitive, and cost effective means since $H_2O_2$ is an electroactive molecule.[9]

In electrochemistry, $H_2O_2$ can be either oxidized or reduced directly at ordinary solid electrodes. However, these processes in analytical applications are limited by slow electrode kinetics and high overpotential which will downgrade the sensing performance and may incur large interferences from other existing electroactive species in real samples such as ascorbate, urate, bilirubin, *etc.* Thus, the current research on $H_2O_2$ detection is mainly focused on electrode modifications in order to decrease the overpotential and increase the electron transfer kinetics. For these considerations, a large range of materials such as redox proteins, dyes, transition metals, metal oxides, metal phthalocyanines, metal porphyrins, redox polymers, and carbon nanotubes have been employed to conduct electrocatalytic $H_2O_2$ detection. On the other hand, in recent years, nanomaterials have attracted tremendous research interest because of their desirable chemical, physical and electronic properties that are different from those of bulk materials. Furthermore, the size and structure of nanomaterials can be tailored for designing a novel sensing platform and enhancing sensing performance.[10] Herein, some of the above-mentioned materials tailored into or combined with nanomaterials have shown distinct advantages over conventional materials for $H_2O_2$ sensing.[11–13] The aim of this review is to summarize the recent advances since 2000 and gain an insight into the materials used in the electrocatalytic sensing of $H_2O_2$.

## 2. Materials used for electrocatalytic hydrogen peroxide sensing

### 2.1. Metal hexacyanoferrates

**2.1.1. Ferric hexacyanoferrate.** Ferric hexacyanoferrate or Prussian blue (PB) has been denoted as an "artificial peroxidase" because the reduced form of PB—Prussian white—is capable of catalyzing the reduction of $H_2O_2$ at low potentials (−50 mV (*vs.* Ag/AgCl)) like peroxidases.[14,15] PB also owns good catalytic specificity to $H_2O_2$ due to the polycrystal structure of PB which may allow penetration of only small molecules into its lattice while larger molecules such as ascorbic acid (AA), uric acid

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(UA), and *para*-acetylaminophenol (APAP) are excluded.[16] Therefore, PB or PB-based composites have been intensively studied and widely used in biosensor constructions.[14,17,18] The most straightforward use of PB in $H_2O_2$ sensing is to electrochemically coat the working electrode surface with a PB layer followed by overlaying additional layers which may be used for loading enzyme, stabilizing PB, improving selectivity, *etc.* Various oxidases including GOx,[19–21] choline oxidase (ChOx),[22,23] ChoOx,[24] AlOx,[25] galactose oxidase (GaOx),[26] GlOx,[27] LOx,[28] LyOx,[29,30] OxaOx[31] and xanthine oxidase (XOx)[32] have been combined with PB for biosensor construction. Screen printing technology was also employed to fabricate PB based sensors. O'Halloran *et al.*[33] made the bulk modification of the carbon ink by PB microparticles (<38 μm) and Mattos *et al.*[34] modified Au and Pt screen-printed electrodes with electrochemically deposited PB. Ricci *et al.*[23] modified the graphite ink based screen printed electrode surfaces with *in situ* chemically synthesized PB and found the enhanced life-time and pH stability of resulted sensors.

With the attractive advantages from nanotechnologies, PB based $H_2O_2$ sensing has been developed with nanomaterials. Li *et al.*[35] constructed an amperometric biosensor *via* grafting PB nanoparticles on the polymeric matrix of multiwalled carbon nanotubes (MWCNTs) and poly(4-vinylpyridine) (PVP). The MWCNT/PVP/PB composite films were fabricated by casting films of MWCNTs wrapped with PVP on gold electrodes followed by electrochemical deposition of PB on the MWCNT/PVP matrix. This modified electrode shows largely enhanced sensitivity of 1.3 $\mu A\ \mu M^{-1}\ cm^{-2}$ and a detection limit of 25 nM due to the remarkable synergistic effect of MWCNTs and PB. Li *et al.*[36] deposited PB on the MWCNT modified pyrolytic graphite electrode and found improved electrochemical stability over a wide pH range and larger response to the reduction of hydrogen peroxide compared to a PB modified pyrolytic graphite electrode. One-step electroless depositions of PB nanoparticles on CNTs were carried out by dispersing CNTs in a mixture of $Fe^{3+}$, $[Fe(CN)_6]^{3-}$ and KCl.[37,38] The driving forces for CNT assisted PB nanoparticle synthesis are due to the difference in the redox potentials between CNTs and $Fe^{3+}/Fe^{2+}$ and between CNTs and $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$. Later, Du *et al.*[39] fabricated a porous PB–MWCNT film by the electrochemical co-deposition method. The characterization showed that this PB–MWCNT composite film gave a larger response current to the reduction of $H_2O_2$ with a sensitivity of 856 $\mu A\ mM^{-1}\ cm^{-2}$ and a detection limit of 23 nM. PB has also been electrodeposited on a graphene oxide modified glassy carbon electrode for fabricating a glucose sensor and this graphene oxide/PB hybrid based sensor showed a largely enhanced response to $H_2O_2$.[40,41] PB itself can also be tailored into different nanostructures for sensor constructions. Liu *et al.*[42] synthesized PB nanoparticles (*ca.* 50 nm) self-assembled onto a gold electrode using cysteine as a bridge between the gold surface and the nanoparticles. Zhang *et al.*[43] constructed multi-PB nanocluster/enzyme-immobilized poly (toluidine blue) layers by depositing PB and polymerizing toluidine blue alternately from an acidic solution of ferricyanide. Later, Zhao *et al.*[44] used a layer by layer assembly method to construct multi-PB nanoparticle/enzyme-immobilized polymer layers. A bilayer of poly(diallydimethylammonium chloride) (PDDA) and poly(sodium 4-styrenesulfonate) (PSS) is consecutively adsorbed on 3-mercapto-1-propanesulfonic acid modified Au electrode surfaces, forming stable, ultrathin multilayer films. Subsequently, PDDA protected PB nanoparticles and negatively charged glucose oxidase are consecutively adsorbed onto the PSS-terminated bilayer. This process allows the fabrication of sensing membranes with controlled thickness, structural morphology and biocatalyst loading. The template synthesized PB nanostructures were also achieved by depositing PB in lyotropic liquid crystalline templates[45] and highly ordered porous anodic alumina (PAA) membrane,[46] respectively. Both results demonstrated enhanced sensing performances in comparison with conventional PB based electrodes.

The major drawback of PB in sensing applications is the lack of operational stability in neutral and alkaline solutions because the reduced form of PB, Prussian white, can be dissolved by hydroxide ions.[16,47] Therefore, it is necessary to improve the stability of PB at relatively high pH. Fortunately, some studies demonstrated that surfactants including cetyltrimethylammonium bromide (CTAB), polyvinyl alcohol, polyvinyl pyrrolidone, polyallylamine hydrochloride, polydiallyldimethyldiammonium chloride, tetrabutylammonium toluene-4-sulfonate and polystyrene sulfonate can effectively enhance the electrochemical stability of metal hexacyanoferrate.[27,48–56]

**2.1.2. Other metal hexacyanoferrates.** After the discovery of the electroactivity of PB, other metal hexacyanoferrates including copper,[57–61] nickel,[58,62–65] cobalt,[58,66–69] chromium,[70,71] vanadium,[1] ruthenium[72,73] and manganese[74] hexacyanoferrates have been also investigated for hydrogen peroxide sensing. In comparison with PB based electrodes, these metal hexacyanoferrate based sensors have a similar or lower capability of electrocatalytic reduction for $H_2O_2$, but with more electrochemical stabilities over a wide range of pH.[18,57,74] This advantage is taken into account because it permits the better sensing operation at physiological pHs which are favoured by enzymes. Another advantage is that metal hexacyanoferrates can perform well in solution containing not only potassium but also other alkali metal cations such as lithium, sodium, rubidium or caesium, contrary to PB that only shows good electroactivity in $K^+$ containing electrolytes.[75–78]

## 2.2. Heme proteins

Heme proteins such as horseradish peroxidase (HRP), catalase (CAT), cytochrome c (Cyt c), hemoglobin (Hb), microperoxidase (MP) and myoglobin (Mb) are a category of metalloproteins containing iron centered porphyrin as their prosthetic groups. This iron in the heme can easily undergo oxidation and reduction over a wide range of potentials which are varied by the protein environment around heme groups.[79,80] Due to the redox capability of heme proteins, they have the great potential to be used in bioelectrochemical applications, especially biosensors. The most efficient practice for fabricating redox protein based electrochemical biosensors is to establish direct electron transfer between the protein and electrode (the third generation biosensor). The biosensors based on this configuration can offer better selectivity since they are able to operate in a potential range closer to the redox potential of the protein itself, thus

 

giving less exposure to interfering reactions, unlike the redox mediator based ones (the second generation biosensor) that facilitate not only the electron transfer between the electrode and enzyme but also various interfering reactions.[81,82] The main challenge to construct the third generation biosensor is to optimize the electron transfer between the heme protein and electrode, because the prosthetic group of heme protein is shielded by the polypeptides, which make the electron transfer distance so long that the tunnelling mechanism rarely happens.[82] Thus, a careful design of the biosensor architectures is essential for facilitating direct electron transfer in predefined pathways interconnecting the active centre and the electrode surface.[83] Various strategies such as silica sol–gel,[84] conducting polymer,[85,86] ionic liquid,[87–89] self-assembly monolayer[90] and layer-by-layer assembly[91,92] have been successfully proved effective in building the third generation hydrogen peroxide sensor. Furthermore, with the attractive advantages, more and more nanomaterials have been integrated with heme proteins to construct direct electron transfer based hydrogen peroxide sensors. Table 1 shows the part of recently published heme proteins and nanomaterials based third generation biosensors and their performances.

Though HRP, Hb, CAT, Mb and Cyt c have been used to successfully construct the third generation biosensors, respectively, their differences in direct electrochemistry still remain. Lotzbeyer *et al.*[120] made early investigations on the direct electron transfer capability of HRP, Cyt c, Mb, microperoxidase MP-11 and haemin all of which can catalyze the reduction of hydrogen peroxide. These heme proteins were covalently tethered to self-assembled monolayers on the gold surface. As direct electron transfer processes are predominantly limited by the distance between the active site of the protein and the electrode surface, the highest electrocatalytic efficiency was observed for the smallest heme proteins (*e.g.* microperoxidase MP-11, haemin). Although haemin exhibits a 3300 fold lower catalytic activity for hydrogen peroxide reduction in solution in comparison with HRP, it showed a more than 10 fold higher electrocatalytic activity when immobilized at the monolayer. This tremendous difference could be attributed to a higher surface concentration for the smaller proteins, the improved access for the substrate to their active sites and the increased electron-transfer rate due to the decrease of the distance between the redox site and electrode surface. Wu *et al.*[121] studied the catalysis of Mb, Hb, HRP and CAT in the silk fibroin film on graphite electrodes with direct electrochemistry. At a potential of −0.2 V (*vs.* SCE), at which the reduction of heme Fe(III) does not interfere, the current was monitored with consecutive $H_2O_2$ injection. The result showed that the HRP based electrode possesses the highest sensitivity followed by the CAT modified electrode. Li *et al.*[122] investigated the direct electron transfer reaction of HRP and CAT immobilized by methyl cellulose and found that the HRP based electrode showed about 5 fold higher sensitivity to $H_2O_2$ than the CAT based electrode. Peng *et al.*[123] fabricated a magnetic core–shell $Fe_3O_4$@$Al_2O_3$ nanoparticle attached magnetic glassy carbon electrode for the immobilization of heme proteins including Hb, Mb and HRP. The direct electrochemistry of Hb, Mb and HRP was observed and their apparent Michaelis–Menten constants ($K_M^{app}$) for hydrogen

**Table 1** Examples of heme proteins and nanomaterials based third generation biosensors for $H_2O_2$

| Heme proteins | Nanomaterials | Linear range/μM | Detection limit/μM | References |
|---|---|---|---|---|
| HRP | Au nanoparticles | 41–6.3 × $10^2$ | 5.9 | 93 |
| | | 0.5–5.2 × $10^3$ | 0.1 | 94 |
| | | 15–1.1 × $10^3$ | 9.0 | 95 |
| | Au nanowire array | 0.74–1.5 × $10^4$ | 0.42 | 96 |
| | $TiO_2$ nanotube | 0.5–10 and 50–1.0 × $10^3$ | 0.1 | 97 |
| | Graphene | 3.5–3.29 × $10^2$ | 1.17 | 98 |
| | | 0.33–14.0 | 0.11 | 99 |
| | CNTs | 0.6–1.8 × $10^3$ | 0.3 | 100 |
| | | 1.07–48.4 | 0.357 | 101 |
| | | 5.0–1.05 × $10^3$ | 0.5 | 102 |
| | | 86–1.0 × $10^4$ | 86 | 103 |
| CAT | CNTs | Up to 0.1 | 10 | 104 |
| | | 10–1 × $10^2$ | 1 | 105 |
| | Au nanoparticles | 0.3–6 × $10^2$ | 0.05 | 106 |
| | | 1 × $10^3$–5 × $10^3$ | — | 107 |
| | NiO nanoparticles | 1–1 × $10^3$ | — | 108 |
| Cyt c | Au nanoparticles | 8.5 × $10^2$–1.3 × $10^4$ | 9.8 | 109 |
| | | 50–1.15 × $10^3$ | 3 | 110 |
| | | 10–1.2 × $10^4$ | 6.3 | 111 |
| | | 2–3.0 × $10^2$ | 0.5 | 112 |
| | ZnO nanosheets | 1–1 × $10^3$ | 0.8 | 113 |
| Hb | CNTs | 23.6–1.34 × $10^2$ | 7.87 | 101 |
| | Au nanoparticles | 7.4 × $10^2$–1.3 × $10^4$ | 6.4 | 109 |
| | | 6 × $10^2$–1.7 × $10^3$ and 2 × $10^3$–2.2 × $10^4$ | — | 114 |
| | Pt nanoparticles | 0.44–44 | 2.8 × $10^{-2}$ | 115 |
| | CdTe nanoparticles | 7.44–6.95 × $10^2$ | 2.23 | 116 |
| | $TiO_2$ nanorods | 0–1.02 × $10^2$ | 0.72 | 117 |
| Mb | CNTs | 24.2–1.67 × $10^2$ | 8.07 | 101 |
| | Au nanoparticles | 1.3 × $10^3$–1.3 × $10^4$ | 1.8 | 109 |
| | | 0.1–2.35 × $10^2$ | — | 118 |
| | Nanoporous ZnO | 4.8–2.0 × $10^2$ | 2.0 | 119 |

peroxide reduction were calculated as 0.12 mM, 0.105 mM and 0.083 mM, respectively. This result suggested that the HRP based electrode has the highest affinity to $H_2O_2$ among the three heme protein based electrodes. Wang *et al.*[124] investigated the effects of 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][$BF_4$]) on direct electrochemistry and bioelectrocatalysis of Hb, Mb and CAT entrapped in agarose hydrogel films. The $K_M^{app}$ of CAT, Hb, and Mb based electrodes for $H_2O_2$ reduction was 0.317 mM, 0.755 mM and 0.593 mM, respectively, and the slope of the calibration curves of CAT, Hb, and Mb based electrodes for $H_2O_2$ detection was 2.17 mA $M^{-1}$, 0.24 mA $M^{-1}$ and 0.996 mA $M^{-1}$. All the constants and the slopes indicated that the CAT based electrode has the highest affinity and best sensitivity over Hb and Mb based electrodes for $H_2O_2$ determination. Later, Wang *et al.*[101] studied direct electrochemistry and electrocatalysis of heme proteins including Hb, Mb and HRP immobilized in SWCNT–CTAB nanocomposite film modified electrodes. The electrocatalytic reduction of $H_2O_2$ on these heme protein based electrodes was investigated by amperometry with an applied potential of −0.4 V. The result showed the slope of the calibration curve of HRP, Hb and Mb was 0.133 μA $\mu M^{-1}$, 0.112 μA $\mu M^{-1}$ and 0.094 μA $\mu M^{-1}$, respectively, which suggested that the HRP modified electrode gave the best performance over Hb and Mb based electrodes on $H_2O_2$ determination. The same results were also achieved on HRP, Hb and Mb immobilized Au nanoparticle-bacteria cellulose nanofiber modified electrodes by Wang *et al.*[125]

### 2.3. CNTs and graphene

**2.3.1. CNTs.** CNTs have been widely used for chemical and biological sensing applications due to their high surface area, high electric conductivity, ability to accumulate analyte, alleviation of surface fouling, capability to make surface functionalization and electrocatalytic activity.[126,127] Studies have shown that CNTs can electrocatalyze both the oxidation and reduction of $H_2O_2$. Wang's group fabricated CNT/Nafion modified electrodes[128] and CNT/Teflon modified electrodes[129] based on the dispersion of MWCNTs within Nafion and Teflon as binders, respectively. Significant oxidation and reduction currents around +0.20 V (*vs.* Ag/AgCl) for $H_2O_2$ were observed on both sensor constructions. The performance of the MWCNT/Teflon/GOx electrodes operated at the potentials of +0.6 V and +0.1 V (*vs.* Ag/AgCl) was studied. It was found that low-potential operation results in a highly linear response (over 2–20 mM range), high selectivity and a slower response time (~1 min *vs.* 25 s at +0.6 V) (*vs.* Ag/AgCl). Despite the absence of permselective coating, the sensor response operated at +0.1 V (*vs.* Ag/AgCl) was not affected by the addition of APAP and UA.[129] Manesh *et al.*[130] reported a nanofibrous glucose electrode fabricated by the immobilization of GOx into an electrospun composite membrane consisting of polymethylmethacrylate (PMMA) dispersed with multiwall carbon nanotubes wrapped by a cationic polymer PDDA. This modified electrode recorded significant electrocatalysis for the oxidation and reduction of $H_2O_2$ around 0 mV. The operation potential of this electrode was also at +0.1 V (*vs.* Ag/AgCl) for $H_2O_2$ oxidation. Nafion was necessary to eliminate the interferences from UA and AA in this study. Kachoosangi *et al.*[131] fabricated CNT/ionic liquid *n*-octylpyridinum hexafluorophosphate (OPFP) composite based sensors and found that this configuration showed overwhelming performance over the CNT/mineral oil composite based electrode due to the excellent charge transfer properties and extremely low capacitance of this ion liquid. CNTs dispersed in mineral oil,[132] polyaniline (PANI),[133,134] polypyrrole (PPy),[135] poly(vinyl alcohol) (PVA),[136] poly(pyrocatechol violet) (poly-PCV),[137] poly(3,4-ethylenedioxythiophene) (PEDOT),[138] chitosan[139–142] and nano-$Fe_3O_4$[143] (for magnetic loading) have also shown good electrocatalysis to $H_2O_2$. Interestingly, Gomathi *et al.*[144] reported that MWCNT/chitosan nanocomposite modified electrodes were operated based on the oxidation of $H_2O_2$ at 0.34 V (*vs.* Ag/AgCl). Without a permselective membrane at such a potential, the sensor exhibited no interferences from AA, UA and APAP. Rivas' group studied the electrochemical behaviour of MWCNTs dispersed in polyethylenimine (PEI).[145] This PEI/CNT modified electrode showed an excellent electrocatalytic activity toward $H_2O_2$ because it was found that the overpotentials for the oxidation and reduction of hydrogen peroxide were decreased by 350 mV and 450 mV, respectively, and the currents were also higher than those obtained with other dispersant agents like Nafion, concentrated acids or chitosan. Besides the traditional dispersion, Lin *et al.*[146] developed glucose biosensors based on a CNT nanoelectrode array grown from Ni nanoparticles on a Cr-coated Si substrate. This sensor array was operated at −0.2 V (*vs.* Ag/AgCl) with good selectivity against the interferences from AA, UA, and AC.

To get further insight into the electrocatalysis of CNT to $H_2O_2$, Xu *et al.*[147] compared the nitrogen-doped carbon nanotubes (NCNTs) with MWCNTs. CNTs doped with N can yield a large number of defective sites on nanotube surfaces and have been proved to have largely improved electrocatalysis.[148] In this study, the NCNTs exhibited greatly enhanced electrocatalytic activity toward the oxidation and reduction of $H_2O_2$ at +0.25 V and −0.1 V (*vs.* Ag/AgCl), respectively. Compton's group reported a very interesting finding on the electrocatalytic activity of MWCNTs.[149] By comparing the electrochemical behaviour of Fe(III) oxide modified basal plane pyrolytic graphite (BPPG) electrode and CNT modified BPPG electrode in $H_2O_2$ solution, they found that the electrocatalysis was due to iron oxide particles arising from the chemical vapor deposition nanotube fabrication process rather than due to intrinsic catalysis attributable to the carbon nanotubes arising, for example, from edge plane-like sites/defects.

**2.3.2. Graphene.** Graphene has attracted considerable attention from both scientific and technological communities due to its unique physicochemical properties and various potential applications in recent years.[150] In comparison with CNTs, graphene shows competitive advantages of low cost, ease of processing and safety.[151] Graphene is also an ideal platform for electrochemical research since it is free from the contamination of transition metals which are apt to exist in CNTs. Zhou *et al.*[152] characterized a chemically reduced graphene oxide (CR-GO) modified electrode which shows the much lower onset potential of $H_2O_2$ oxidation/reduction started at 0.2/0.1 V (*vs.* Ag/AgCl) than those of the graphite electrode and bare electrode. The superior electrocatalytic activity of CR-GO is most likely attributed to the high density of edge-plane-like defective sites on

 

CR-GO.[153–155] Niu's group characterized a PVP-protected graphene/polyethylenimine functionalized ionic liquid (PFIL) electrode for $H_2O_2$ electrocatalysis.[156] The more positive reduction potential (onset potential at ~0 V) and more obvious reduction current indicated that the graphene-based modified electrode had much better electrocatalysis toward $H_2O_2$ than the PFIL modified electrode. Later, the same group combined both graphene and gold nanoparticles (AuNPs) dispersed in chitosan to make a glucose biosensor.[157] This modified electrode exhibited the highest electrocatalytic activity toward $H_2O_2$ than the graphene/chitosan, AuNPs/chitosan, and chitosan modified electrodes. This electrocatalysis enhancement might be attributed to the synergistic effect of graphene and AuNPs.[158]

### 2.4. Metals and metal oxides

**2.4.1. Metals.** Transition metals and their compounds are known as good catalysts either because of their ability to adopt multiple oxidation states or, in the case of the metals, to adsorb other substances onto their surface and activate them in the process. On the other hand, nano-sized metals can display unique advantages of enhanced mass transport, high effective surface area, size controlled electrical, chemical and optical properties and effective utilization of expensive materials.[13] Thus, transition metal nanoparticles can be made excellent catalysts due to their high ratio of surface atoms with free valences to the cluster of total atoms.[159] A wide range of transition metals including platinum (Pt),[160] palladium (Pd),[160] copper (Cu),[161–163] rhodium (Rh),[79,80] iridium (Ir)[79,163–165] and ferrum (Fe)[166] have been successfully used for electrocatalyzed $H_2O_2$ determination. As one of the most intensively studied transition metals, various Au nanomaterials with different shapes and structures such as Au nanowire assembling architecture,[167] nanoporous Au,[168] Au nanocages[11] and Au nanoparticles[169] have been investigated for electrocatalytic $H_2O_2$ reduction. It seems that Au nanocage[11] and nanoporous Au[168] slightly outperformed others.

To achieve high loading and reserving high catalytic activities for transition metal nanoparticles, carbon based nanomaterials especially CNTs were extensively utilized as supporting substrates due to their high surface area, high conductivity and high electrocatalytic activity. After the first report of Pt nanoparticle/CNT as a sensing platform,[159] numerous studies have been conducted based on this strategy for $H_2O_2$ sensing though the approaches may slightly vary.[170–175] Other transition metal nanoparticles such as Pd nanoparticles[176] and Ag nanoparticles[177,178] also have been utilized with CNTs for electrocatalytic $H_2O_2$ sensing. Furthermore, besides the most used CNTs, graphene,[103,179,180] graphite nanoplatelet,[13] carbon nanofiber,[181,182] silicon nanowire,[183] and Au nanowire array[184] were also proved to be suitable nanostructural substrates for various transition metal nanoparticles.

In recent years, bimetallic alloy nanoparticles have attracted considerable attention because they have both the favourable catalytic properties over monometallic counterparts and unique advantages from nanomaterials. Xiao *et al.*[185] fabricated AuPt nanoparticles on chitosan–ionic liquid (trihexyltetradecylphosphonium bis(trifluoromethylsulfonyl)imide ([P$(C_6)_3C_{14}$][$Tf_2N$])) film by using an ultrasonic electrodeposition method. Chitosan acted as an adsorbent for the metal ions, and [P$(C_6)_3C_{14}$][$Tf_2N$] played a dual role of matrix and stabilizer in the formation of the nanoparticles. By comparing the electrochemical response of different modified electrodes toward $H_2O_2$ reduction, the AuPt-chitosan-[P$(C_6)_3C_{14}$][$Tf_2N$] modified electrode exhibits the lowest overpotential. This synergistic effect can be attributed to the presence of Au that can reduce the strength of Pt–OH formation.[186,187] Furthermore, this sensor was operated at a low working potential (−0.05 V *vs.* Ag/AgCl) with a sensitivity of 3.98 mA $mM^{-1}$ $cm^{-2}$, a detection limit of 0.3 nM in a linear range of 5–355 nM and a very high selectivity of less than 5% decrease of the 20 nM $H_2O_2$ signal with the existence of a bunch of foreign species. Later, Safavi and Farjami[188] used the same strategy to construct a cholesterol biosensor based on a AuPt-Ch-IL modified electrode and also achieved good performance for $H_2O_2$ determination. Li *et al.*[189] utilized AuPt alloy nanoparticles deposited on MWCNTs to fabricate an $H_2O_2$ based amperometric immunosensor in which AuPt alloy nanoparticles not only could be used to assemble biomolecules with well maintained bioactivity, but also could facilitate the shuttle of electrons. Liu *et al.*[190] reported an amorphous ternary FeNiPt nanomaterial with tunable length to construct an electrochemical sensing platform. The FeNiPt nanorods with large axial ratio exhibit enhanced electrocatalytic activity towards both the oxidation and reduction of $H_2O_2$. $H_2O_2$ is cathodically determined on FeNiPt-nanorod modified glassy carbon electrodes with relatively high selectivity at the appropriate potential of 0 V (*vs.* Ag/AgCl). The anodic $H_2O_2$ detection based on the same electrode showed a sensitivity of 2.45 mA $mM^{-1}$ $cm^{-2}$, which is 4-fold higher than that of the cathodic detection and those Pt nanoparticle-based $H_2O_2$ determination, and the detection limit of 40 nM with a dynamic linear range from 100 nM to 30 mM, which is wider than Pt nanoparticles and binary Pt alloys based detection.

**2.4.2. Metal oxides.** Some transition metal oxides such as manganese oxide,[163,191–198] cobalt oxide,[199] titanium dioxide,[200] copper oxide[201,202] and iridium oxide[203] have been reported to show electrocatalytic activity to $H_2O_2$. However, many of them were based on the electrocatalytic oxidation of $H_2O_2$ in which high potentials were applied on the working electrode. For example, $MnO_2$ nanoparticle and dihexadecyl hydrogen phosphate composite film modified electrode was used for $H_2O_2$ determination at an applied potential of +0.65 V (*vs.* saturated calomel electrode (SCE))[192] and a $TiO_2$/MWCNT modified electrode was employed to detect $H_2O_2$ at an applied potential of +0.4 V (*vs.* Ag/AgCl).[200] From the application point of view, the operation potentials of these sensors are too high to be applied to real biological samples. Xu *et al.*[198] reported the $MnO_2$/MWCNT modified electrode for $H_2O_2$ determination which showed high anti-interference property without any permselective membranes against AA, citric acid and UA in spite of the high operation potential of 0.45 V (*vs.* Ag/AgCl). Bai *et al.*[204] found that $MnO_2$ nanoparticle modified electrodes show bi-direction electrocatalytic ability toward the reduction/oxidation of $H_2O_2$. When this modified electrode was operated at 0 V (*vs.* Ag/AgCl) in the $H_2O_2$ reduction pathway, the interference from AA was greatly depressed. Copper oxide seems a more suitable material for $H_2O_2$ sensing. Luque *et al.*[202] reported that the CuO/carbon paste electrode showed an excellent electrocatalytic activity towards the

oxidation and reduction of $H_2O_2$. This modified electrode was operated at a potential of −0.1 V (*vs.* Ag/AgCl) for glucose detection. Miao *et al.*[201] constructed a CuO nanoparticle/Nafion modified electrode for $H_2O_2$ detection. In 0.1 M NaOH, this sensor exhibited a detection limit of 0.06 μM in the range of 0.15 μM–9.00 mM at an applied potential of −0.3 V (*vs.* SCE). Magnetite has also been reported to own good catalytic activity towards the reduction of $H_2O_2$. Lin and Len[205] constructed a $Fe_3O_4$/chitosan modified glassy carbon rotating disk electrode for a $H_2O_2$ sensor with unique features of electrocatalytic reduction and interference elimination. This magnetite based $H_2O_2$ sensor exhibited the advantages of low applied potential (−0.2 V *vs.* Ag/AgCl), low background current, rapid response and long half-life (9 months at room temperature). Comba *et al.*[206] utilized electrosynthesized $Fe_3O_4$ nanoparticles within a carbon paste electrode to fabricate a glucose sensor. Due to the low operation potential at −0.1 V (*vs.* Ag/AgCl), this sensor showed no response to 0.1 μM AA and 0.4 μM UA with the average sensitivity of 32 ± 4 μA $M^{-1}$ and detection limit of $3.0 \times 10^{-4}$ M.

### 2.5. Other electrocatalytic compounds for hydrogen peroxide sensing

Besides above-mentioned materials, some compounds with reversible redox capabilities have been reported in electrocatalytic $H_2O_2$ sensing. Metallophthalocyanines and metalloporphyrins such as cobalt phthalocyanine,[207,208] cobalt tetraruthenated porphyrin,[209] ether-linked cobalt phthalocyanine–cobalt tetraphenylporphyrin,[210] and iron phthalocyanine[211] are frequently used due to their excellent catalytic properties and high chemical stabilities. Perovskite-type oxides containing transition metals,[212,213] redox polymers,[162,214] redox dyes[215] and iron–sulfur protein[216] have also been proved effective in electrocatalytic $H_2O_2$ sensing.

## 3. *In vivo* applications

When the $H_2O_2$ sensor is applied to *in vivo* measurements, more challenges will arise. The sensor should be able to provide appropriate spatial and temporal resolution within acceptable sensitivity and limits of detection. Due to the complex environment of *in vivo* measurements, sensing selectivity becomes more critical. Sometimes, a trade-off between selectivity and other parameters such as response time is needed. Furthermore, the sensor should be stable enough to conduct the whole experiment. All of these considerations may be balanced to achieve optimum performance according to the specific requirements and conditions of *in vivo* measurements.

Salazar *et al.*[217] constructed PB modified carbon fiber microelectrodes for $H_2O_2$ detection in brain extracellular fluid. To improve stability and selectivity, several polymeric films including Nafion, poly(*o*-phenylenediamine) (PPD), and a hybrid configuration of these two polymers were investigated. The PPD coating was selected due to its excellent anti-interference properties and stabilization capability for PB against solubilisation at high pH though the sensitivity was about 50% loss due to diffusion phenomena across the polymeric film. The result showed that the PPD film significantly enhanced the selectivity against the main endogenous brain interference species, expressed as the ratio of the sensitivity slopes, which was close to 600 for all interference molecules studied. Later, Salazar *et al.*[218] adopted the same sensor configuration based on PB for *in vivo* glucose detection in extracellular fluid of the prefrontal cortex. Due to the addition of GOx, Nafion, PEI and PPD were employed to attenuate oxygen dependence, to stabilize the enzyme and to shield the sensor surface from interferences, respectively. The sensor showed the sufficient sensitivity and stability to monitor multi-phasic and reversible changes in brain extracellular fluid.

Kulagina and Michael[219] reported a cross-linked redox polymer containing a HRP modified carbon fibre electrode which was used for $H_2O_2$ measurements in the brain of anesthetized rats. When implanted in the striatal region of the rat brain, a biphasic response was observed upon electrical stimulation of the dopaminergic pathway that innervates the striatal tissue, while no response was observed at sensors containing no HRP. This study confirmed that amperometric sensors based on carbon fibre microelectrodes can be used for monitoring the kinetic neurochemical activity in the brain. Rui *et al.*[113] constructed Cyt c adsorbed hexagonal ZnO nanosheets based sensors for the extracellular released $H_2O_2$ from living cancer cells. The direct electron transfer of Cyt c was realized on the nanostructured ZnO. The result showed that under the optimized potential of 0 V (*vs.* Ag/AgCl) the electrochemical determination of $H_2O_2$ is free from both anodic interferences and cathodic interference of $O_2$.

A strategy to realize *in vivo* selective detection without sacrifice of response time was reported by Sanford *et al.*[220] The electrochemical technique, background-substrated, fast-scan cyclic voltammetry (FSCV), provides chemical selectivity in addition to high temporal resolution and sensitivity.[221] With this approach, a cyclic voltammogram is generated to serve as a chemical signature for the analyte of interest, allowing discrimination from other electroactive species in the brain.[161] In this study, the first voltammetric characterization of rapid $H_2O_2$ fluctuations at an uncoated carbon fibre microelectrode was demonstrated with unprecedented chemical and spatial resolution. The carbon fibre was electrochemically conditioned on the anodic scan and the irreversible oxidation of peroxide was detected on the cathodic scan. The oxidation potential was dependent on the scan rate which occurred at +1.2 V (*vs.* Ag/AgCl) at a scan rate of 400 V $s^{-1}$. The sensor exhibited a detection limit of 2 μM in a linear range up to 2 mM and was successfully tested in brain slices.

However, *in vivo* biosensors for $H_2O_2$ were mostly developed for animal tissues. The *in vivo* measurements of $H_2O_2$ from oxidative bursts in plant (oilseed rape (*Brassica napus* L.)) which were induced by either biotic or abiotic stresses were successfully achieved by our group.[222–224] The response of the oilseed rape to three different stresses including ultraviolet A and C, *Sclerotinia sclerotiorum* and $Cd^{2+}$ were investigated, respectively. In our studies, a Pt microparticle modified Pt wire electrode with PPD coating as a selectively permeable layer was polarized at −0.1 V (*vs.* Ag/AgCl) which showed good sensitivity and selectivity in living plant tissues.

## 4. Conclusions and future prospects

This review has mainly concentrated on the recent advances of electrocatalytic $H_2O_2$ determination. The utilization of electrocatalytic activity of various materials is for effectively

 

reducing the overpotentials for $H_2O_2$ reduction or oxidation, thus decreasing the possible interferences from other electroactive species. Though the earlier studies based on the conventional materials have shown considerable achievements for efficient $H_2O_2$ determination, the emergence of nanotechnology over the last decade still promoted tremendous progress in this area. Due to their unique physical and chemical properties, nanomaterials not only largely improve the sensitivity and selectivity, but also provide more strategies for $H_2O_2$ sensing. For example, CNTs and graphene can be used either as substrates with high specific area for catalytic materials or as electrocatalysts by themselves. In addition, nanomaterials facilitate the development of the third generation biosensor in which electrons can be more easily transferred from a protein prosthetic group to an electrode surface. For *in vivo* measurements, besides the above-mentioned merits, nanotechnology is expected to provide very high spatial and temporal resolutions for the analyte of interest with less injury to living organisms since the dimension of the probe can be made small enough in comparison with the size of cell.

On the other hand, research on artificial enzymes that mimic natural enzymes such as CAT is very meaningful. Natural enzymes are difficult to be manipulated for biosensor constructions because they are very sensitive to the environment and prone to denature by relatively harsh conditions such as high temperature or organic solvent. The poor stability of natural enzymes quite limits the fabrication process of biosensors and long-time usage in real applications. Furthermore, the cost of enzymes is still high even in mass manufacturing. In comparison, artificial enzymes can be more robust and more easily tailored to the desired properties for biosensor construction and application. For example, some progress has been made in CAT mimics.[225–227]

A wide range of newly introduced nanomaterials and electrocatalytic compounds is expected to continuously advance $H_2O_2$ sensing development. And these sensors will facilitate the understanding of the physiological process participated by $H_2O_2$ in living organisms. Furthermore, tremendous influence of $H_2O_2$ sensing on clinical diagnostic, pharmaceutical development, food safety and environmental monitoring will gradually appear in the near future.

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## Notes and references

1 C. G. Tsiafoulis, P. N. Trikalitis and M. I. Prodromidis, *Electrochem. Commun.*, 2005, **7**, 1398–1404.
2 M. Geiszt and T. L. Leto, *J. Biol. Chem.*, 2004, **279**, 51715–51718.
3 M. Giorgio, M. Trinei, E. Migliaccio and P. G. Pelicci, *Nat. Rev. Mol. Cell Biol.*, 2007, **8**, 722–728.
4 C. Laloi, K. Apel and A. Danon, *Curr. Opin. Plant Biol.*, 2004, **7**, 323–328.
5 J. H. Lee, I. N. Tang and J. B. Weinstein-Lloyd, *Anal. Chem.*, 1990, **62**, 2381–2384.
6 S. Hanaoka, *Anal. Chim. Acta*, 2001, **426**, 57–64.
7 E. Fernandes, A. Gomes and J. L. F. C. Lima, *J. Biochem. Biophys. Methods*, 2005, **65**, 45–80.
8 M. C. O. R. F. P. Nogueira and W. C. Paterlini, *Talanta*, 2005, **66**, 86–91.
9 J. Wang, *Biosens. Bioelectron.*, 2006, **21**, 1887–1892.
10 J. Wang, *Analyst*, 2005, **130**, 421–426.
11 Y. Zhang, Y. Sun, Z. Liu, F. Xu, K. Cui, Y. Shi, Z. Wen and Z. Li, *J. Electroanal. Chem.*, 2011, **656**, 23–28.
12 R. Yuan, L. J. Bai, Y. Q. Chai, Y. L. Yuan, L. Mao and Y. Zhuo, *Analyst*, 2011, **136**, 1840–1845.
13 I. Lee, J. Lu, I. Do, L. T. Drzal and R. M. Worden, *ACS Nano*, 2008, **2**, 1825–1832.
14 A. A. Karyakin, *Electroanalysis*, 2001, **13**, 813–819.
15 A. A. Karyakin, E. E. Karyakina and L. Gorton, *Anal. Chem.*, 2000, **72**, 1720–1723.
16 A. A. Karyakin, E. E. Karyakina and L. Gorton, *Talanta*, 1996, **43**, 1597–1606.
17 F. Ricci and G. Palleschi, *Biosens. Bioelectron.*, 2005, **21**, 389–407.
18 R. Koncki, *Crit. Rev. Anal. Chem.*, 2002, **32**, 79–96.
19 R. Garjonyte and A. Malinauskas, *Sens. Actuators, B*, 2000, **63**, 122–128.
20 M. Ferreira, P. A. Fiorito, O. N. Oliveira and S. I. C. de Torresi, *Biosens. Bioelectron.*, 2004, **19**, 1611–1615.
21 J. J. Zhu, M. H. Xue, Q. Xu and M. Zhou, *Electrochem. Commun.*, 2006, **8**, 1468–1474.
22 D. Moscone, D. D'Ottavi, D. Compagnone, G. Palleschi and A. Amine, *Anal. Chem.*, 2001, **73**, 2529–2535.
23 F. Ricci, A. Amine, G. Palleschi and D. Moscone, *Biosens. Bioelectron.*, 2003, **18**, 165–174.
24 X. Y. Zou, X. C. Tan, M. J. Ll, P. X. Cai and L. J. Luo, *Anal. Biochem.*, 2005, **337**, 111–120.
25 A. Karyakin, E. Karyakina and L. Gorton, *Talanta*, 1996, **43**, 1597–1606.
26 Y. T. Wang, J. Z. Zhu, R. J. Zhu, Z. Q. Zhu, Z. S. Lai and Z. Y. Chen, *Meas. Sci. Technol.*, 2003, **14**, 831–836.
27 S. Varma, Y. Yigzaw and L. Gorton, *Anal. Chim. Acta*, 2006, **556**, 319–325.
28 R. Garjonyte, Y. Yigzaw, R. Meskys, A. Malinauskas and L. Gorton, *Sens. Actuators, B*, 2001, **79**, 33–38.
29 F. Ricci, A. Amine, C. S. Tuta, A. A. Ciucu, F. Lucarelli, G. Palleschi and D. Moscone, *Anal. Chim. Acta*, 2003, **485**, 111–120.
30 F. Ricci, C. Goncalves, A. Amine, L. Gorton, G. Palleschi and D. Moscone, *Electroanalysis*, 2003, **15**, 1204–1211.
31 P. A. Fiorito and S. I. C. de Torresi, *Talanta*, 2004, **62**, 649–654.
32 Y. J. Liu, L. H. Nie, W. Y. Tao and S. Z. Yao, *Electroanalysis*, 2004, **16**, 1271–1278.
33 M. P. O'Halloran, M. Pravda and G. G. Guilbault, *Talanta*, 2001, **55**, 605–611.
34 I. L. de Mattos, L. Gorton and T. Ruzgas, *Biosens. Bioelectron.*, 2003, **18**, 193–200.
35 J. Li, J. D. Qiu, J. J. Xu, H. Y. Chen and X. H. Xia, *Adv. Funct. Mater.*, 2007, **17**, 1574–1580.
36 J. H. Chen, Z. F. Li, W. Li, K. Chen, L. H. Nie and S. Z. Yao, *J. Electroanal. Chem.*, 2007, **603**, 59–66.
37 S. J. Dong, J. F. Zhai, Y. M. Zhai and D. Wen, *Electroanalysis*, 2009, **21**, 2207–2212.
38 B. Fang, W. Zhang, L. L. Wang, N. Zhang and G. F. Wang, *Electroanalysis*, 2009, **21**, 2325–2330.
39 D. Du, M. Wang, Y. Qin and Y. Lin, *J. Mater. Chem.*, 2010, **20**, 1532–1537.
40 N. Q. Jia, Y. Z. Zhang, X. M. Sun, L. Z. Zhu and H. B. Shen, *Electrochim. Acta*, 2011, **56**, 1239–1245.
41 L. Cao, Y. Liu, B. Zhang and L. Lu, *ACS Appl. Mater. Interfaces*, 2010, **2**, 2339–2346.
42 S. Q. Liu, J. J. Xu and H. Y. Chen, *Electrochem. Commun.*, 2002, **4**, 421–425.
43 D. Zhang, K. Zhang, Y. L. Yao, X. H. Xia and H. Y. Chen, *Langmuir*, 2004, **20**, 7303–7307.
44 W. Zhao, J. J. Xu, C. G. Shi and H. Y. Chen, *Langmuir*, 2005, **21**, 9630–9634.

45 A. A. Karyakin, E. A. Puganova, I. A. Budashov, I. N. Kurochkin, E. E. Karyakina, V. A. Levchenko, V. N. Matveyenko and S. D. Varfolomeyev, *Anal. Chem.*, 2004, **76**, 474–478.
46 L. T. Jin, Y. Z. Xian, Y. Hu, F. Liu, Y. Xian and L. J. Feng, *Biosens. Bioelectron.*, 2007, **22**, 2827–2833.
47 U. Scharf, *Electrochim. Acta*, 1996, **41**, 233–239.
48 R. Vittal, M. Jayalakshmi, H. Gomathi and G. P. Rao, *J. Electrochem. Soc.*, 1999, **146**, 786–793.
49 R. Vittal, H. Gomathi and G. P. Rao, *Electrochim. Acta*, 2000, **45**, 2083–2093.
50 S. M. S. Kumar and K. C. Pillai, *Electrochem. Commun.*, 2006, **8**, 621–626.
51 I. Dekany and V. Hornok, *J. Colloid Interface Sci.*, 2007, **309**, 176–182.
52 S. M. S. Kumar and K. C. Pillai, *J. Electroanal. Chem.*, 2006, **589**, 167–175.
53 R. Vittal and H. Gomathi, *J. Phys. Chem. B*, 2002, **106**, 10135–10143.
54 R. Vittal, K. J. Kim, H. Gomathi and V. Yegnaraman, *J. Phys. Chem. B*, 2008, **112**, 1149–1156.
55 S. Q. Liu, H. Li, W. H. Sun, X. M. Wang, Z. G. Chen, J. J. Xu, H. X. Ju and H. Y. Chen, *Electrochim. Acta*, 2011, **56**, 4007–4014.
56 B. Haghighi, S. Varma, F. M. Alizadeh, Y. Yigzaw and L. Gorton, *Talanta*, 2004, **64**, 3–12.
57 R. Garjonyte and A. Malinauskas, *Sens. Actuators, B*, 1999, **56**, 93–97.
58 A. Schwake, B. Ross and K. Cammann, *Sens. Actuators, B*, 1998, **46**, 242–248.
59 J. Wang, X. J. Zhang and M. Prakash, *Anal. Chim. Acta*, 1999, **395**, 11–16.
60 I. L. de Mattos, L. Gorton, T. Laurell, A. Malinauskas and A. A. Karyakin, *Talanta*, 2000, **52**, 791–799.
61 P. A. Fiorito, C. M. A. Brett and S. I. C. de Torresi, *Talanta*, 2006, **69**, 403–408.
62 M. H. Pournaghi-Azar and H. Razmi-Nerbin, *Electroanalysis*, 2000, **12**, 209–215.
63 C. X. Cai, K. H. Xue, Y. M. Zhou and H. Yang, *Talanta*, 1997, **44**, 339–347.
64 S. Milardovic, I. Kruhak, D. Ivekovic, V. Rumenjak, M. Tkalcec and B. S. Grabaric, *Anal. Chim. Acta*, 1997, **350**, 91–96.
65 P. A. Fiorito and S. I. C. de Torresi, *J. Electroanal. Chem.*, 2005, **581**, 31–37.
66 M. S. Lin, Y. C. Wu and B. I. Jan, *Biotechnol. Bioeng.*, 1999, **62**, 56–61.
67 S. M. Chen, *J. Electroanal. Chem.*, 2002, **521**, 29–52.
68 A. Eftekhari, *Microchim. Acta*, 2003, **141**, 15–21.
69 G. L. Shen, S. P. Wang, L. M. Lu, M. H. Yang, Y. Lei and R. Q. Yu, *Anal. Chim. Acta*, 2009, **651**, 220–226.
70 M. S. Lin, T. F. Tseng and W. C. Shih, *Analyst*, 1998, **123**, 159–163.
71 M. S. Lin and W. C. Shih, *Anal. Chim. Acta*, 1999, **381**, 183–189.
72 N. Dale, F. Tian and E. Llaudet, *Anal. Chem.*, 2007, **79**, 6760–6766.
73 J. M. Zen, A. S. Kumar and C. R. Chung, *Anal. Chem.*, 2003, **75**, 2703–2709.
74 A. Eftekhari, *Talanta*, 2001, **55**, 395–402.
75 J. Bácskai, K. Martinusz, E. Czirók, G. Inzelt, P. J. Kulesza and M. A. Malik, *J. Electroanal. Chem.*, 1995, **385**, 241–248.
76 S. Sinha, B. D. Humphrey and A. B. Bocarsly, *Inorg. Chem.*, 1984, **23**, 203–212.
77 S. Zamponi, M. Berrettoni, P. J. Kulesza, K. Miecznikowski, M. A. Malik, O. Makowski and R. Marassi, *Electrochim. Acta*, 2003, **48**, 4261–4269.
78 M. A. Malik, K. Miecznikowski and P. J. Kulesza, *Electrochim. Acta*, 2000, **45**, 3777–3784.
79 M. C. Rodriguez and G. A. Rivas, *Anal. Lett.*, 2001, **34**, 1829–1840.
80 S. A. Miscoria, G. D. Barrera and G. A. Rivas, *Sens. Actuators, B*, 2006, **115**, 205–211.
81 L. Gorton, *Electroanalysis*, 1995, **7**, 23–45.
82 L. Gorton, A. Lindgren, T. Larsson, F. D. Munteanu, T. Ruzgas and I. Gazaryan, *Anal. Chim. Acta*, 1999, **400**, 91–108.
83 R. S. Freire, C. A. Pessoa, L. D. Mello and L. T. Kubota, *J. Braz. Chem. Soc.*, 2003, **14**, 230–243.
84 S. P. Bi, J. W. Di, M. Zhang and K. A. Yao, *Biosens. Bioelectron.*, 2006, **22**, 247–252.
85 Y. T. Kong, M. Boopathi and Y. B. Shim, *Biosens. Bioelectron.*, 2003, **19**, 227–232.
86 P. R. Solanki, A. Kaushik, A. A. Ansari, G. Sumana and B. D. Malhotra, *Polym. Adv. Technol.*, 2011, **22**, 903–908.
87 A. Safavi, N. Maleki, O. Moradlou and M. Sorouri, *Electrochem. Commun.*, 2008, **10**, 420–423.
88 B. Z. Zeng, R. Yan, F. Q. Zhao, J. W. Li, F. Mao and S. S. Fan, *Electrochim. Acta*, 2007, **52**, 7425–7431.
89 X. Shangguan, J. Zheng and Q. Sheng, *Electroanalysis*, 2009, **21**, 1469–1474.
90 K. M. Razeeb, J. Xu, F. J. Shang, J. H. T. Luong and J. D. Glennon, *Biosens. Bioelectron.*, 2010, **25**, 1313–1318.
91 H. Y. Chen, J. J. Feng and J. J. Xu, *Biosens. Bioelectron.*, 2007, **22**, 1618–1624.
92 G. Y. Shi, Z. Y. Sun, M. C. Liu, L. Zhang, Y. Liu, Y. H. Qu and L. T. Jin, *Anal. Chem.*, 2007, **79**, 3581–3588.
93 Y. Wang, X. Ma, Y. Wen, Y. Xing, Z. Zhang and H. Yang, *Biosens. Bioelectron.*, 2010, **25**, 2442–2446.
94 B. Tang, F. Li, Y. Feng, Z. Wang, L. M. Yang and L. H. Zhuo, *Biosens. Bioelectron.*, 2010, **25**, 2244–2248.
95 L. X. Sun, C. Xiang, Y. Zou and F. Xu, *Sens. Actuators, B*, 2009, **136**, 158–162.
96 J. Xu, F. Shang, J. H. T. Luong, K. M. Razeeb and J. D. Glennon, *Biosens. Bioelectron.*, 2010, **25**, 1313–1318.
97 Y. Z. Xian, F. H. Wu, J. J. Xu, Y. Tian, Z. C. Hu, L. W. Wang and L. T. Jin, *Biosens. Bioelectron.*, 2008, **24**, 198–203.
98 H. Zhou, Q. A. Zhang, Y. Qiao, L. Zhang, S. Y. Wu, J. W. Xu and X. M. Song, *Electroanalysis*, 2011, **23**, 900–906.
99 M. Li, S. Xu, M. Tang, L. Liu, F. Gao and Y. Wang, *Electrochim. Acta*, 2011, **56**, 1144–1149.
100 S. L. Luo, X. D. Zeng, X. F. Li, X. Y. Liu, Y. Liu, B. Kong, S. L. Yang and W. Z. Wei, *Biosens. Bioelectron.*, 2009, **25**, 896–900.
101 S. F. Wang, F. Xie and G. D. Liu, *Talanta*, 2009, **77**, 1343–1350.
102 Q. J. Xie, Z. J. Cao, X. Q. Jiang and S. Z. Yao, *Biosens. Bioelectron.*, 2008, **24**, 222–227.
103 M.-Y. Hua, Y.-C. Lin, R.-Y. Tsai, H.-C. Chen and Y.-C. Liu, *Electrochim. Acta*, 2011, **56**, 9488–9495.
104 A. Salimi, L. Miranzadeh, R. Hallaj and H. Mamkhezri, *Electroanalysis*, 2008, **20**, 1760–1768.
105 A. Salimi, A. Noorbakhsh and M. Ghadermarz, *Anal. Biochem.*, 2005, **344**, 16–24.
106 K. H. Huang, K. J. Huang, D. J. Niu, X. Liu, Z. W. Wu, Y. Fan, Y. F. Chang and Y. Y. Wu, *Electrochim. Acta*, 2011, **56**, 2947–2953.
107 Y. N. Tian, B. J. Zhou, J. W. Wang and X. L. Gao, *Anal. Lett.*, 2008, **41**, 1832–1849.
108 A. Salimi, E. Sharifi, A. Noorbakhsh and S. Soltanian, *Biophys. Chem.*, 2007, **125**, 540–548.
109 H. Y. Chen, J. J. Feng, G. Zhao and J. J. Xu, *Anal. Biochem.*, 2005, **342**, 280–286.
110 L. X. Sun, C. L. Xiang, Y. J. Zou and F. Xu, *Electrochem. Commun.*, 2008, **10**, 38–41.
111 A. Zhu, Y. Tian, H. Liu and Y. Luo, *Biomaterials*, 2009, **30**, 3183–3188.
112 J. B. Hu, S. Q. Li, J. Xia, C. Y. Liu, W. Cao and Q. L. Li, *J. Electroanal. Chem.*, 2009, **633**, 273–278.
113 Q. Rui, K. Komori, Y. Tian, H. Liu, Y. Luo and Y. Sakai, *Anal. Chim. Acta*, 2010, **670**, 57–62.
114 X. H. Xia, H. L. Guo, D. Y. Liu and X. D. Yu, *Sens. Actuators, B*, 2009, **139**, 598–603.
115 J. J. Fei, S. S. Jia, T. Tian and F. Q. Zhou, *Electroanalysis*, 2009, **21**, 1424–1431.
116 Y. D. Zhao, Q. Xu, J. H. Wang, Z. Wang, H. Q. Wang and Q. Yang, *Anal. Lett.*, 2009, **42**, 2496–2508.
117 X. Yao, X. L. Xiao and W. Lu, *Electroanalysis*, 2008, **20**, 2247–2252.
118 H. M. Zhang, W. T. Xie, L. L. Kong, M. X. Kan, D. M. Han and X. J. Wang, *J. Nanosci. Nanotechnol.*, 2010, **10**, 6720–6724.
119 G. Zhao, J. J. Xu and H. Y. Chen, *Anal. Biochem.*, 2006, **350**, 145–150.
120 T. Lotzbeyer, W. Schuhmann and H. L. Schmidt, *Bioelectrochem. Bioenerg.*, 1997, **42**, 1–6.
121 Y. H. Wu, Q. C. Shen and S. S. Hu, *Anal. Chim. Acta*, 2006, **558**, 179–186.
122 Y. M. Li, X. T. Chen, J. Li and H. H. Liu, *Electrochim. Acta*, 2004, **49**, 3195–3200.
123 H.-P. Peng, R.-P. Liang and J.-D. Qiu, *Biosens. Bioelectron.*, 2011, **26**, 3005–3011.


 

124 D. W. Pang, S. F. Wang, T. Chen, Z. L. Zhang and K. Y. Wong, *Electrochem. Commun.*, 2007, **9**, 1709–1714.
125 Y. L. Zhou, W. Wang, T. J. Zhang, D. W. Zhang, H. Y. Li, Y. R. Ma, L. M. Qi and X. X. Zhang, *Talanta*, 2011, **84**, 71–77.
126 J. Wang, G. D. Liu and M. R. Jan, *J. Am. Chem. Soc.*, 2004, **126**, 3010–3011.
127 F. Patolsky, Y. Weizmann and I. Willner, *Angew. Chem., Int. Ed.*, 2004, **43**, 2113–2117.
128 J. Wang, M. Musameh and Y. H. Lin, *J. Am. Chem. Soc.*, 2003, **125**, 2408–2409.
129 J. Wang and M. Musameh, *Anal. Chem.*, 2003, **75**, 2075–2079.
130 K. P. Lee, K. M. Manesh, H. T. Kim, P. Santhosh and A. I. Gopalan, *Biosens. Bioelectron.*, 2008, **23**, 771–779.
131 M. M. Musameh, R. T. Kachoosangi, I. Abu-Yousef, J. M. Yousef, S. M. Kanan, L. Xiao, S. G. Davies, A. Russell and R. G. Compton, *Anal. Chem.*, 2009, **81**, 435–442.
132 M. D. Rubianes and G. A. Rivas, *Electrochem. Commun.*, 2003, **5**, 689–694.
133 K. P. Lee, P. Santhosh, K. M. Manesh and A. Gopalan, *Anal. Chim. Acta*, 2006, **575**, 32–38.
134 F. L. Qu, M. H. Yang, J. H. Jiang, G. L. Shen and R. Q. Yu, *Anal. Biochem.*, 2005, **344**, 108–114.
135 T. Yu-Chen, L. Shih-Ci and L. Shang-Wei, *Biosens. Bioelectron.*, 2006, **22**, 495–500.
136 T. Yu-Chen and H. Jing-Dae, *J. Nanosci. Nanotechnol.*, 2007, **7**, 3227–3232.
137 B. Fang, N. Zhang, W. Zhang, A. X. Gu and G. F. Wang, *J. Appl. Polym. Sci.*, 2009, **112**, 3488–3493.
138 K. C. Lin, T. H. Tsai and S. M. Chen, *Biosens. Bioelectron.*, 2010, **26**, 608–614.
139 W. Feng, Z. G. Wu, Y. Y. Feng, Q. Liu, X. H. Xu, T. Sekino, A. Fujii and M. Ozaki, *Carbon*, 2007, **45**, 1212–1218.
140 D. Ragupathy, P. Gomathi, M. K. Kim, J. J. Park, A. Rajendran, S. C. Lee, J. C. Kim, S. H. Lee and H. D. Ghim, *Sens. Actuators, B*, 2011, **155**, 897–902.
141 J. Tkac and T. Ruzgas, *Electrochem. Commun.*, 2006, **8**, 899–903.
142 Z. G. Wu, W. Feng, Y. Y. Feng, Q. Liu, X. H. Xu, T. Sekino, A. Fujii and M. Ozaki, *Carbon*, 2007, **45**, 1212–1218.
143 G. Chen, S. Qu, J. Wang, J. L. Kong and P. Y. Yang, *Talanta*, 2007, **71**, 1096–1102.
144 P. Gomathi, M. K. Kim, J. J. Park, D. Ragupathy, A. Rajendran, S. C. Lee, J. C. Kim, S. H. Lee and H. D. Ghim, *Sens. Actuators, B*, 2011, **155**, 897–902.
145 M. D. Rubianes and G. A. Rivas, *Electrochem. Commun.*, 2007, **9**, 480–484.
146 Y. H. Lin, F. Lu, Y. Tu and Z. F. Ren, *Nano Lett.*, 2004, **4**, 191–195.
147 S. Q. Liu, X. A. Xu, S. J. Jiang and Z. Hu, *ACS Nano*, 2010, **4**, 4292–4298.
148 L. M. Dai, K. P. Gong, F. Du, Z. H. Xia and M. Durstock, *Science*, 2009, **323**, 760–764.
149 R. G. Compton, B. Sljukic and C. E. Banks, *Nano Lett.*, 2006, **6**, 1556–1558.
150 Y. H. Lin, Y. Y. Shao, J. Wang, H. Wu, J. Liu and I. A. Aksay, *Electroanalysis*, 2010, **22**, 1027–1036.
151 M. Segal, *Nat. Nanotechnol.*, 2009, **4**, 611–613.
152 S. J. Dong, M. Zhou and Y. M. Zhai, *Anal. Chem.*, 2009, **81**, 5603–5613.
153 C. E. Banks and R. G. Compton, *Analyst*, 2005, **130**, 1232–1239.
154 C. E. Banks, T. J. Davies, G. G. Wildgoose and R. G. Compton, *Chem. Commun.*, 2005, 829–841.
155 C. E. Banks, R. R. Moore, T. J. Davies and R. G. Compton, *Chem. Commun.*, 2004, 1804–1805.
156 C. S. Shan, H. F. Yang, J. F. Song, D. X. Han, A. Ivaska and L. Niu, *Anal. Chem.*, 2009, **81**, 2378–2382.
157 L. Niu, C. S. Shan, H. F. Yang, D. X. Han, Q. X. Zhang and A. Ivaska, *Biosens. Bioelectron.*, 2010, **25**, 1070–1074.
158 X. H. Xia, J. Li, J. D. Qiu, J. J. Xu and H. Y. Chen, *Adv. Funct. Mater.*, 2007, **17**, 1574–1580.
159 J. H. T. Luong, S. Hrapovic, Y. L. Liu and K. B. Male, *Anal. Chem.*, 2004, **76**, 1083–1088.
160 S. A. Miscoria, G. D. Barrera and G. A. Rivas, *Electroanalysis*, 2002, **14**, 981–987.
161 M. C. Rodriguez and G. A. Rivas, *Anal. Lett.*, 2000, **33**, 2373–2389.
162 M. C. Rodriguez and G. A. Rivas, *Electroanalysis*, 2001, **13**, 1179–1184.
163 G. L. Luque, N. F. Ferreyra and G. A. Rivas, *Microchim. Acta*, 2006, **152**, 277–283.
164 G. A. Rivas and B. Maestroni, *Anal. Lett.*, 1997, **30**, 489–501.
165 M. C. Rodriguez and G. A. Rivas, *Electroanalysis*, 1999, **11**, 558–564.
166 F. N. Comba, M. D. Rubianes, P. Herrasti and G. A. Rivas, *Sens. Actuators, B*, 2010, **149**, 306–309.
167 S. Guo, D. Wen, S. Dong and E. Wang, *Talanta*, 2009, **77**, 1510–1517.
168 J. G. Liu, F. H. Meng, X. L. Yan, J. Gu and Z. G. Zou, *Electrochim. Acta*, 2011, **56**, 4657–4662.
169 R. Ramaraj and G. Maduralveeran, *J. Electroanal. Chem.*, 2007, **608**, 52–58.
170 G. L. Shen, M. H. Yang, Y. H. Yang, Y. L. Liu and R. Q. Yu, *Biosens. Bioelectron.*, 2006, **21**, 1125–1131.
171 G. L. Shen, M. H. Yang, Y. Yang, H. F. Yang and R. Q. Yu, *Biomaterials*, 2006, **27**, 246–255.
172 X. Y. Zou, X. H. Kang, Z. B. Mai, P. X. Cai and J. Y. Mo, *Talanta*, 2008, **74**, 879–886.
173 Y. H. Zhu, L. H. Xu, L. H. Tang, X. L. Yang and C. Z. Li, *Electroanalysis*, 2007, **19**, 717–722.
174 X. Y. Zou, X. H. Kang, Z. B. Mai, P. X. Cai and J. Y. Mo, *Anal. Biochem.*, 2007, **369**, 71–79.
175 G. L. Shen, F. L. Qu, M. H. Yang and R. Q. Yu, *Biosens. Bioelectron.*, 2007, **22**, 1749–1755.
176 S. Jeon, J. M. You, Y. N. Jeong, M. S. Ahmed, S. K. Kim and H. C. Choi, *Biosens. Bioelectron.*, 2011, **26**, 2287–2291.
177 Z. Li, Y. Shi, Z. L. Liu, B. Zhao, Y. J. Sun, F. G. Xu, Y. Zhang, Z. W. Wen and H. B. Yang, *J. Electroanal. Chem.*, 2011, **656**, 29–33.
178 Q. Chen, W. Zhao, H. C. Wang, X. Qin, X. S. Wang, Z. X. Zhao, Z. Y. Miao, L. L. Chen, M. M. Shan and Y. X. Fang, *Talanta*, 2009, **80**, 1029–1033.
179 T. J. Park, M. H. Yang, B. G. Choi, H. Park, W. H. Hong and S. Y. Lee, *Electroanalysis*, 2011, **23**, 850–857.
180 J. H. Jiang, Q. Zeng, J. S. Cheng, X. F. Liu and H. T. Bai, *Biosens. Bioelectron.*, 2011, **26**, 3456–3463.
181 Y. Liu, D. Wang, L. Xu, H. Hou and T. You, *Biosens. Bioelectron.*, 2011, **26**, 4585–4590.
182 J. S. Huang, D. W. Wang, H. Q. Hou and T. Y. You, *Adv. Funct. Mater.*, 2008, **18**, 441–448.
183 L. W. Yang, J. J. Yin, X. Qi, G. L. Hao, J. Li and J. X. Zhong, *Electrochim. Acta*, 2011, **56**, 3884–3889.
184 M. Jamal, J. Xu and K. M. Razeeb, *Biosens. Bioelectron.*, 2010, **26**, 1420–1424.
185 F. Q. Zhao, F. Xiao, Y. F. Zhang, G. P. Guo and B. Z. Zeng, *J. Phys. Chem. C*, 2009, **113**, 849–855.
186 P. Hernandez-Fernandez, S. Rojas, P. Ocon, J. L. GomezdelaFuente, J. SanFabian, J. Sanza, M. A. Pena, F. J. Garcia-Garcia, P. Terreros and J. L. G. Fierro, *J. Phys. Chem. C*, 2007, **111**, 2913–2923.
187 S. J. Dong, S. J. Guo and E. Wang, *J. Phys. Chem. C*, 2008, **112**, 2389–2393.
188 A. Safavi and F. Farjami, *Biosens. Bioelectron.*, 2011, **26**, 2547–2552.
189 Y. Li, R. Yuan, Y. Chai and Z. Song, *Electrochim. Acta*, 2011, **56**, 6715–6721.
190 Y. Tian, H. G. Liu, M. Wen, F. Zhang and D. Liu, *Anal. Methods*, 2010, **2**, 143–148.
191 Y. H. Lin, X. L. Cui and L. Y. Li, *Electrochem. Commun.*, 2005, **7**, 166–172.
192 S. J. Yao, J. H. Xu, Y. Wang, X. X. Chen, Y. X. Xu and S. S. Hu, *Anal. Chim. Acta*, 2006, **557**, 78–84.
193 Y.-H. Bai, H. Zhang, J.-J. Xu and H.-Y. Chen, *J. Phys. Chem. C*, 2008, **112**, 18984–18990.
194 X. Chen, X. Zhang, W. Yang and D. G. Evans, *Mater. Sci. Eng., C: Biomimetic Supramol. Syst.*, 2009, **29**, 284–287.
195 B. Sljukic and R. G. Compton, *Electroanalysis*, 2007, **19**, 1275–1280.
196 X. Cui, G. Liu and Y. Lin, *Nanomed.: Nanotechnol., Biol. Med.*, 2005, **1**, 130–135.
197 C. E. Langley, B. Sljukic, C. E. Banks and R. G. Compton, *Anal. Sci.*, 2007, **23**, 165–170.
198 B. Xu, M.-L. Ye, Y.-X. Yu and W.-D. Zhang, *Anal. Chim. Acta*, 2010, **674**, 20–26.

199 A. Salimi, R. Hallaj, S. Soltanian and H. Mamkhezri, *Anal. Chim. Acta*, 2007, **594**, 24–31.
200 L.-C. Jiang and W.-D. Zhang, *Electroanalysis*, 2009, **21**, 988–993.
201 R. Yuan, X. M. Miao, Y. Q. Chai, Y. T. Shi and Y. Y. Yuan, *J. Electroanal. Chem.*, 2008, **612**, 157–163.
202 G. L. Luque, M. C. Rodriguez and G. A. Rivas, *Talanta*, 2005, **66**, 467–471.
203 H. Elzanowska, E. Abu-Irhayem, B. Skrzynecka and V. I. Birss, *Electroanalysis*, 2004, **16**, 478–490.
204 J. J. Xu, Y. H. Bai, Y. Du and H. Y. Chen, *Electrochem. Commun.*, 2007, **9**, 2611–2616.
205 M. S. Lin and H. J. Len, *Electroanalysis*, 2005, **17**, 2068–2073.
206 F. N. Comba, M. D. Rubianes, L. Cabrera, S. Gutierrez, P. Herrasti and G. A. Rivas, *Electroanalysis*, 2010, **22**, 1566–1572.
207 K. Wang, J.-J. Xu and H.-Y. Chen, *Biosens. Bioelectron.*, 2005, **20**, 1388–1396.
208 K. I. Ozoemena, P. N. Mashazi and T. Nyokong, *Electrochim. Acta*, 2006, **52**, 177–186.
209 M. S. M. Quintino, H. Winnischofer, K. Araki, H. E. Toma and L. Angnes, *Analyst*, 2005, **130**, 221–226.
210 K. Ozoemena and T. Nyokong, *Electrochim. Acta*, 2006, **51**, 5131–5136.
211 J. S. Ye, Y. Wen, W. D. Zhang, H. F. Cui, G. Q. Xu and F. S. Sheu, *Electroanalysis*, 2005, **17**, 89–96.
212 Y. Shimizu, H. Komatsu, S. Michishita, N. Miura and N. Yamazo, *Sens. Actuators, B*, 1996, **34**, 493–498.
213 G. L. Luque, N. F. Ferreyra, A. Gabriela Leyva and G. A. Rivas, *Sens. Actuators, B*, 2009, **142**, 331–336.
214 M. Y. Hua, H. C. Chen, C. K. Chuang, R. Y. Tsai, J. L. Jeng, H. W. Yang and Y. T. Chern, *Biomaterials*, 2011, **32**, 4885–4895.
215 S. S. Narayanan and D. R. S. Jeykumari, *Biosens. Bioelectron.*, 2008, **23**, 1404–1411.
216 J. W. Choi, A. K. Yagati, T. Lee and J. Min, *Bioelectrochemistry*, 2011, **80**, 169–174.
217 P. Salazar, M. Martin, R. Roche, R. D. O'Neill and J. L. Gonzalez-Mora, *Electrochim. Acta*, 2010, **55**, 6476–6484.
218 P. Salazar, R. D. O'Neill, M. Martin, R. Roche and J. L. Gonzalez-Mora, *Sens. Actuators, B*, 2011, **152**, 137–143.
219 N. V. Kulagina and A. C. Michael, *Anal. Chem.*, 2003, **75**, 4875–4881.
220 L. A. Sombers, A. L. Sanford, S. W. Morton, K. L. Whitehouse, H. M. Oara, L. Z. Lugo-Morales and J. G. Roberts, *Anal. Chem.*, 2010, **82**, 5205–5210.
221 R. G. Cooks, Z. Ouyang, Z. Takats and J. M. Wiseman, *Science*, 2006, **311**, 1566–1570.
222 H. Chen, Q. Xu, S. Y. Liu, Q. J. Zou, X. L. Guo, X. Y. Dong, P. W. Li, D. Y. Song and Y. D. Zhao, *Anal. Chim. Acta*, 2009, **632**, 21–25.
223 Y. D. Zhao, Q. Xu, F. Wei, Z. Wang, Q. Yang and H. Chen, *Sens. Actuators, B*, 2009, **141**, 599–603.
224 Q. Xu, F. Wei, Z. Wang, Q. Yang, Y.-D. Zhao and H. Chen, *Phytochem. Anal.*, 2010, **21**, 192–196.
225 B. J. Day, *Biochem. Pharmacol.*, 2009, **77**, 285–296.
226 U. Rauen, T. Kettler-Thiel, H. De Groot, H.-G. Korth and R. Sustmann, *Chem. Biol. Drug Des.*, 2009, **73**, 494–501.
227 M. U. Triller, W. Y. Hsieh, V. L. Pecoraro, A. Rompel and B. Krebs, *Inorg. Chem.*, 2002, **41**, 5544–5554.




 