**Review**

# Recent Updates of Chemically Modified Electrodes in Analytical Chemistry

*Jyh-Myng Zen,* Annamalai Senthil Kumar, Dong-Mung Tsai*

Department of Chemistry, National Chung Hsing University, Taichung 402, Taiwan
* e-mail: jmzen@dragon.nchu.edu.tw

Received: January 21, 2003
Final version: February 20, 2003

**Abstract**

This review article updates recent developments in chemically modified electrodes (CMEs) towards analytical applications for the year of 2000 – 2002 with 179 references. The broad topics are subdivided into four main categories: i) physisorption/chemisorption, ii) covalently linked, iii) homogenous (uniform) multilayer and iv) heterogeneous (non-uniform) multilayer CMEs. The criteria for the preparation of CMEs in elecrocatalytic systems are clearly described in Section 1. Some of the encouraging results related to Au-nanoparticles for DNA detection and new ceramic carbon, carbon nanotubes, copper-plated screen-printed and Nafion/lead ruthenate pyrochlore CMEs for catalytic application were especially discussed in this review.

**Keywords:** Chemically modified electrode, Electrocatalysis, Sensor, Review

## 1. Introduction

The beauty of electrochemical (EC) techniques is to utilize a tailor made chemically modified electrode (CME) for sensitive and selective analytical applications. The electrode itself can act as a reactant to pump (reduction)/withdraw (oxidation) electron in the reaction, which cannot be expected in spectroscopic characterization methods. In combination with CMEs, the EC techniques can also be turned into important applications in electrosynthetic organic chemistry and material characterization. To prepare the CME, most often a thin film of selected chemical is either bound or coated onto the electrode surface to endow desirable properties of the film in rationally and chemically designed manners. Electrocatalytic property is one of the distinguishable features of CME to be utilized in electroanalytical chemistry. Figure 1 illustrates a typical example of electrocatalytic process at a CME with decrease in overpotential ($\eta$). The reversible redox mediator P/Q with a standard potential of $E^0_{P/Q}$ was modified on a functionalized electrode to promote the irreversible oxidation reaction of $A \rightarrow B^+ + e$. A relatively high $\eta$ was observed at a bare

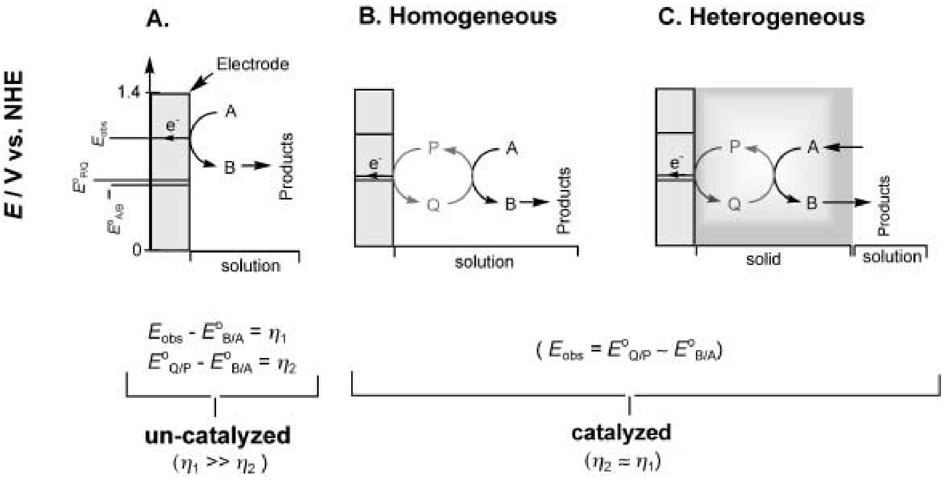


Fig. 1. Schematic representation for the oxidation reaction of $A \rightarrow B$ on bare (A) and mediated conditions (B, C). The terms P and Q correspond to the reversible mediator of reduced and oxidized states, respectively. The $E_{obs}$, $E^0_{P/Q}$, $E^0_{A/B}$ and $\eta$ correspond to uncatalyzed, P/Q mediated, standard and over potentials, respectively, for the above mentioned reaction. In homogenous catalyzed reaction, the P/Q mediator and reactant are in solution phase; while for heterogeneous catalyzed reaction, the P/Q is bonded on the electrode surface.

1040-0397/03/1307-1073 $ 17.50+.50/0

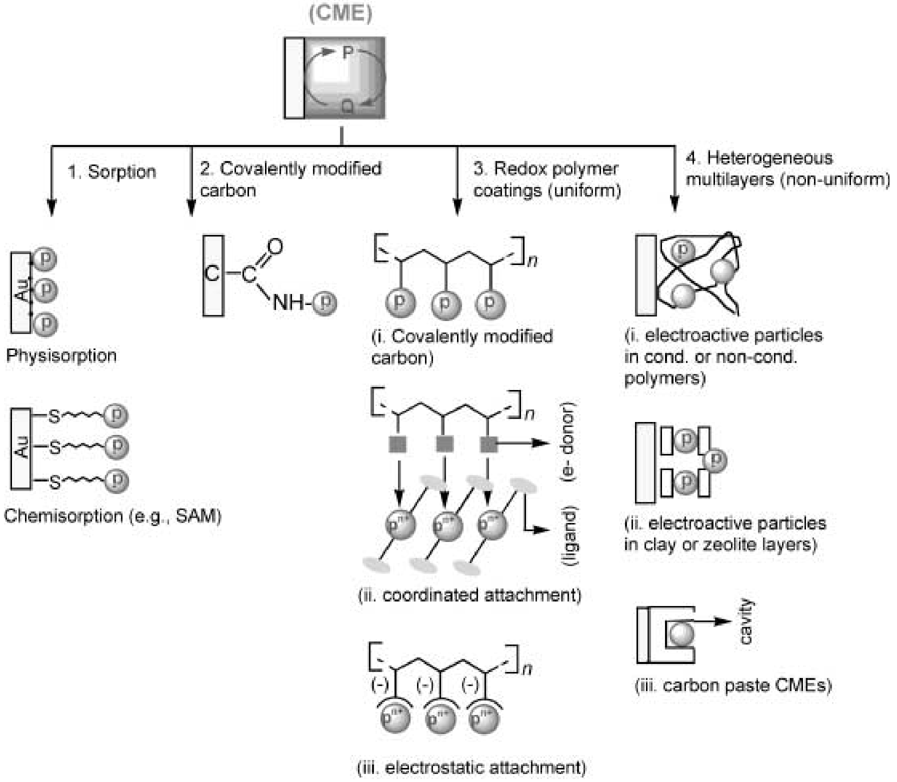


Fig. 2. Schematic representation for various kinds of CME preparation routes.

electrode while in the presence of P/Q the reaction was promoted by redox mediation at $E^0_{P/Q}$ with a low $\eta$. This type of heterogeneous CMEs is not only selective and sensitive but also fast and reusable in analytical measurements.

Before mid 1970's, electrochemistry was confined with electrode materials like C, Au, Hg and Pt. Murray and coworkers initiated the field of CMEs by taking the functional group transformation to $SnO_2$ and Pt–OH [1–3]. Nowadays the application of EC techniques with CMEs is quite ordinary and literature survey denotes that ca. 63% is contributed particularly in the past five years. To stimulate wide research fields for new inventions, this review article updates the applications of CMEs in analytical chemistry in the past three years (2000–2002).

The topics are divided into four main categories based on the nature of modifying process per Murray's assignment [2]. Figure 2 sketched the four possible routes for the preparation of CMEs. For the case of sorption-based CMEs, physical and chemical interaction properties are utilized as modified procedures to form monolayer structures. Thiols self-assembled monolayer (SAM) of Au-chemisorbed surface is a well-known example in sorption studies [4–7]. Easy surface modification and functional group attachment are the chief advantages of this approach. Covalent modification of the electrode surface that uses as a specific functional group is also of particular interest in the preparation of CME. For example, the $>C{=}O$ and $>C{-}O^-$ functional group formed on glassy carbon electrodes (GCEs) and –OH group from oxide electrodes are often utilized in various applications [8, 9]. Nevertheless, the limitation of monolayer coverage sometimes can restrict the amount of active component in the electrode surface. Alternatively, polymer-based multilayer CMEs provided an attractive route to resolve the above problem. Such CMEs can be prepared under homogeneous (uniform) or integrated heterogeneous (non-uniform) conditions. The uniform multilayer preparation includes ionomers, redox polymers, inorganic polymers, electrochemically deposition of mediators (metals or simple metal complexes) and mediator bearing monomers (pyrrole and amine containing complexes), etc. [3]. In the case of integrated non-uniform systems, the CMEs are constructed in heterogeneous supports like clay, zeolite, $SiO_2$ (sol-gel), phosphomolybdic acid ($PMo_{12}$), carbon paste, epoxy resin and other polymeric systems [10–18]. Some of the unique characteristic like ion exchange property and intrinsic catalytic activity of clay and zeolite as supporting materials are well exploited for analytical applications. Considering the broad scope of CME field with so many publications in the past three years, the present articles are restricted to new and interesting topics with key issues related to analytical chemistry. Detailed information and preparation route are also not included in this report.

## 2. CMEs in Analytical Applications

### 2.1. Sorption Based CMEs

### *2.1.1. Physisorption Methods*

To prepare sorption-based CMEs, pure organic or organometallic complexes can be physisorbed on porous carbon bases like vitreous carbon (VCE), graphite (GE), ordinary pyrolytic graphite (OPG) and basal plane pyrolytic graphite (BPG) by simple coating with nonaqueous solution followed by droplet evaporation. Table 1 lists some important advances in CME using this approach in a variety of analytical utilities. For example, Karayannis and co-workers reported physisorbed lanthanum 2,6-dichlorophenolindophenol and hexadecylpyridinum-bis(chloranilato)-antimony screen printed electrodes (SPEs) for ascorbic acid (AA) and sulfide sensing, respectively, to eliminate the matrix or host effect [19, 20]. In another case, phenothiazine (PH) derivatives-modified graphite rod prepared by dip coating with DMF solution was used for NADH oxidation [21]. The main concept behind was that a perfect reversible mediating system with remarkable stability could be achieved by increasing the aromaticity of the thiazine base. Zagal's group used pyridine solvent to modify cobalt phthalocyanine (CoPc) on VCE with a surface coverage ($\Gamma$) of ca. $3.1 \times 10^{-11}$ mol cm$^{-2}$ for nitrite oxidative detection [22].

Carbon nanotubes (CNT), a fast developing material having branches of single wall (SWNT) and multi-wall (MWNT), are also modified in the same way by simple casting with acetone, DMF and diluted $HNO_3$ sonicated solutions on GCE for NO, DA and AA oxidation [23–26]. The CNT has a peculiar and different chemical nature over the classical graphite and carbon structures. It has regular hexagonal honeycomb like nano-lattice structures with cylindrical type of closed topology. Due to the hollow like cylindrical structures, the CNT has appreciable adsorption ability for unique applications in diverse fields of capacitor, catalysis, sensor, etc. [27–29]. The electrochemical sensor application of the CNT was reviewed by Zhang et al. [30]. Two more recent important sensor application of the CNT are NADH and DNA sensors [31, 32].

Simple activation of GCE (designated as GCE*) also works well for the adsorption of soluble mediators. Recently, the cobaloxime complex was adsorbed at the GCE* for oxygen reduction reaction (ORR) [33, 34]. Prior to the adsorption, the GCE was electrochemically treated in the potential range of $-0.5$ – $1.8$ V (vs. Ag/AgCl) in 0.5 M $H_2SO_4$. However, the exact cause for the process was not discussed. Zen et al. investigated a similar type of GCE* for $Pb^{2+}$ accumulation and quantification [35]. It was concluded that the anodization leads to quinolic and phenonic functional groups on the GCE surface, which further help for the attractive interaction with $Pb^{2+}$.

Clay modified electrodes are other CMEs often prepared by dip coating of the aqueous colloidal solution [36]. It can be stabilized depending on the nature of the underlying surface. It was believed that bare GCE is quite unsuitable for the coating due to the non-porous and polished nature of the surface. Hence, additional polymeric systems are required to improve the stability [37]. Alternatively, Zen's group utilized porous SPEs as a base material to improve the clay

Table 1. Physisorbed and chemisorbed CMEs in analytical applications.

| *CME* | *Analyte* | *References* |
|---|---|---|
| 2,6-dichlrophenolindophenol-La ($[DCP]_3La$)-SPE | AA | [19] |
| $[Sb^VO(chloranilato)_2]$ Hex-SPE | Sulfide | [20] |
| Phenothiazine derivative (PH)-graphite | NADH | [21] |
| CoPc-VCE | $NO_2^-$ | [22] |
| C-MWNT-GCE | NO | [23] |
| C-SWNT-GCE | DA | [24] |
| C-MWNT-1-GE | DA and AA | [25] |
| C-MWNT-GCE and C-SWNT-GCE | NADH | [31] |
| HOOC-C-MWNT-GCE | DNA | [32] |
| Cobaloxime-GCE* | $O_2$ | [33, 34] |
| GCE* | $Pb^{2+}$ | [35] |
| Nontronite-clay-SPE | Arbutin, amitrole, xanthine, hypoxanthine and uric acid | [38–40] |
| Hemin P-lipid ($2C_{18}N^+Br^-$) -BPG (P: Imidazole polymer) | Organohalides | [43] |
| Rutin-lipid-GCE | NADH and AA | [44, 45] |
| ssDNA-$H_2N/SiO_2$-ITO | ssDNA in couple with aq. $Co(phen)_3^{3+}$ | [46] |
| Dendrimer-$PMo_{12}$-(4-ATP)-Au | Arsenite | [47] |
| Gly-Gly-His-Au | Cu (sub-ppt detection) | [50] |
| TNF-Au | NADH oxidation | [51] |
| Au colloid-CySH (SAM)-Pt | CO | [52] |
| Metallothioneine (MT)-Au (SAM) | DA | [53] |
| Vitamin $B_{12}$ disulfide derivative-Au (SAM) | $O_2$ | [54] |
| $C_{60}$-GSH-Au (SAM) | NADH | [55] |
| Dithiobishexaneamine-Au (SAM) | DA in the presence of AA | [56] |
| (3-Mercaptopropyl)-TMOS (MPS)-Hydrazine-Au (SAM) | $H_2O_2$ | [57] |
| DNA-Au nanoparticle (SAM) | Pathogen (Anthrax) | [58] |

stability and used in amperometric determination of arbutin (cosmetic agent), amitrole (insecticide) and some biochemical compounds [38–40].

Bilayer integral films of water-soluble mediator together with insoluble natural or synthetic lipids ($R{-}N^+X^-$, X = halides) are another interesting topics for stable surface modifications. Both Nakashima's and Rusling's groups initiated such works in early 1990's [41, 42]. Recently, Nakashima et al. reported hemin (iron protoporphyrin)-lipid (in $CH_2Cl_2$) and hemin (by soaking) on GCE surface for the catalytic reduction of organic halides at $-0.2$ V (vs. Ag/AgCl) in 0.1 M $Na_2SO_4$ [43]. Similarly, rutin (a flavornoid glycoside) was modified on the diapalmitoylphosphatidylcholine (DPPC) lipid for electrocatalytic oxidation of NADH and AA at physiological pHs [44, 45]. In another case, a silanized ITO modified electrode together with $Co(phen)_3^{3+}$ complex was used for the adsorption of single strand DNA (ssDNA) to detect its complimentary strand [46]. The amine functional group attached in the silaized ITO was found to play a key role for such modification.

### *2.1.2. Chemisorption Methods*

Even though the physisorbed systems are useful for analytical applications, stability is always a critical problem for such electrodes. The stability problem, however, can be solved by a chemisorbed route. Due to the easy procedures in preparing the self assembly monolayer (SAM)/Au-oriented system by simple soaking of the Au electrode (≡Au) in thiol ($-SH$) and ethanol solutions, this kind of system is still the Holy Grail in the chemisorbed studies. Several recent reviews cover salient features in diverse fields of applications about the SAM/Au [4–6]. Cox and co-workers reported a phosphomolybdate ($PMo_{12}$)/polyamidoamine dendrimer modified SAM/Au for arsenite oxidative detection [47]. Dendrimer is a branched polymer (Scheme 1) that has attracted significant attention over the last ten years and has been subjected to numerous reviews [48, 49]. In the preparation route, 4-aminothiol was first modified on the ≡Au, then $PMo_{12}O_{40}^{3-}$ was coated on the surface under acidic condition to protonate the amines. Finally, the dendrimer was modified as outer layer coatings. Amino acids and peptides, which contain free thiol ends, often couple with SAM for useful applications. Yang et al. reported Gly-Gly-His modified SAM for sub-ppt detection of $Cu^{2+}$ in physiological pH [50]. The four electron donating sites from N-terminals act as a chelating ligand for specific binding of $Cu^{2+}$. Following are some of the SAM/Au recently reported in the analytical assays: (2,4,7-trinitro-9-flurorenylidene)-malononitrile (TNF) (with π-π interaction with ≡Au) for NADH oxidation [51], cysteine (CySH) for CO oxidation [52], metallothioneins (CySH-containing protein) for DA oxidation [53], disulfide derivatives of vitamin $B_{12}$ for ORR [54], $C_{60}$-glutathione for NADH oxidation [55] dithiobishexaneamine acid for DOPAC oxidation [56] and (3-mercaptopropyl) trimethoysilane (MPS) for $H_2O_2$ reduction [57] reactions. Among the above cases, the MPS adsorbate has an additional advantage of stabilizing the SAM by polymerizing with trimetholysilane (TMEOS).

Recently, Mirkin's group has coupled the SAM approach with electronic chip for quick detection of pathogen [58]. In this approach, pair of Au microelectrode was first arranged in the non-conducting $SiO_2$ base, which was then modified with 4-(malemidophenyl)-butyrate (SMPB). Depending on the target pathogen's DNA sequence, an oligonucleotide (part 1) was suitably modified on the SMPB and the target DNA was captured by manual pipetting (ca. 10 nM). Finally, a complimentary oligonucleotide (part 2) in coupling with Au nanoparticles is spiked on the chip to make the detectable electrical signals. Figure 3 shows the possible route for the detection. The group planned to commercialize their scheme to market as a hand-held device [59].

## 2.2. Covalently Bonded CMEs

The surface functional group of base electrodes can be derivatized either by synthetic route or by controlling the oxidation/reduction potentials in a suitable medium. First example of the ≡Sn−OH and ≡Pt−OH functional group transformation on the electrode leads to new opening in the CMEs [1, 2]. Carbon surface is found to be efficient for the covalent modifications due to its alterable functionalities and hence numerous investigations are made on variety of carbon surfaces [9]. Among, amino ($-NH_2$) [60], aryl

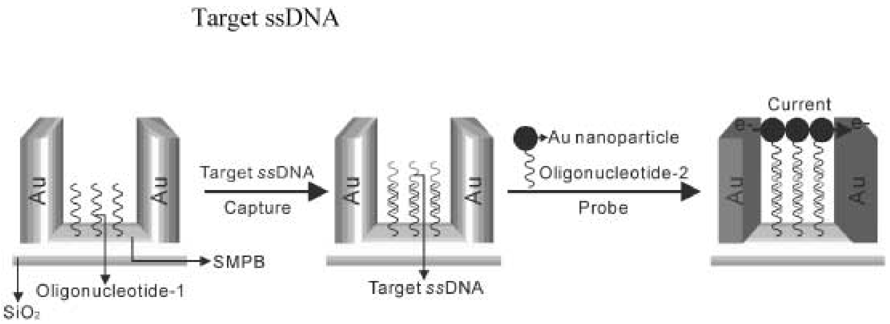


Fig. 3. Conceptional representation for the detection of pathogen's DNA using Au nanoparticle-based electrochemical chip systems [58].

diazonium (Ph-$N_2^+$) [61, 62] and arylacetate [63] compounds were found to be more viable for covalent modification (Fig. 4). The compounds are suitably coupled with redox active groups for further electroanalytical applications, as shown in Table 2.

Tammeveski et al. investigated anthraquinone (AQ)-grafted GCE surface (GC-AQ) in coupling with Au ring disk electrode for the ORR [64]. In the preparation route, AQ and diazonium salts were taken in the modifying solution under electroreductive conditions. The GC-AQ yielded a defined redox couple at $-0.9$ V (vs. SCE) in 0.1 M KOH with $\Gamma_{AQ} = 2.5 \times 10^{-10}$ mol cm$^{-2}$. Similarly, Zhang et al. prepared rhein (4,5-dihydroxyAQ-2-carboxylic acid)-modified GCE ($\Gamma_{AQ} = 1.9 \times 10^{-10}$ mol cm$^{-2}$) by simple potential electrochemical cycling method in pH 3 solution and used it for reductive detection of hemoglobin at $-0.2$ V (vs. Ag/AgCl) [65]. Even though such modified electrodes resulted in profound electrocatalytic activity, the exact chemical nature of the underlying modified surface was not clearly identified. Ramesh and Sampath improved the modification procedure with a step-by-step solution phase synthetic method from exfoliated graphite (≡EC) powder to covalently modified AQ-EC, through monitoring the functionalities with FT-IR and XPS [66]. The AQ-EC powder sample was further modified as a pressed-pellet and utilized for AA detection with surface renewable characteristics.

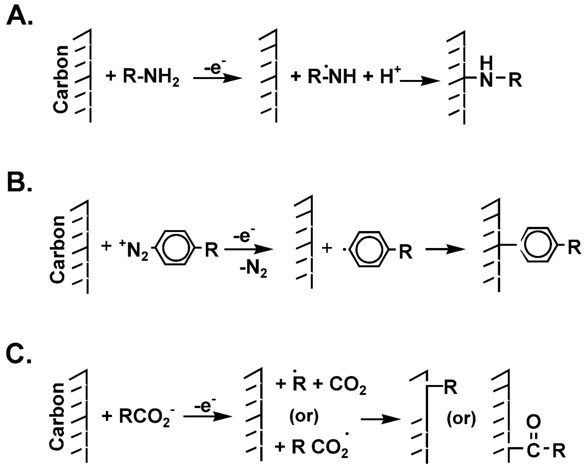


Fig. 4. Some possible routes for the covalent modification of carbon surface using A) amino, B) diazonium and C) acrylacetate-based compounds.

Zhang and Lin prepared glutamic acid (GA, $H_2NCH(COOH)CH_2CH_2COOH$) and glycine (Gly, $H_2N{-}CH_2{-}COOH$) covalently grafted-GCEs through formation of amine cation radical in the intermediate steps by simple electrochemical potential cycling treatment (0–1.6 V vs. SCE) with acetonitrile and $TBABF_4$ solution [67, 68]. X-ray photoelectron spectroscopy (XPS) was used to monitor the surface functional groups. The modification procedures resulted in an irreversible anodic wave with $E_{1/2}$ = ca. 0.3 V (vs. SCE) in pH 6 PBS and further extended to the catalysis of DA, AA and UA at low detecting potentials.

Dong and co-workers reported amino-derivatives grafted-GCE for multilayer assembling of Pd nanoparticles in combination with a polycation of $[Os(bpy)_2Cl]^{2+}$-quaternized poly(4-vinypyridine) (QPVP-Os) [69]. A four-step procedure was adopted in the preparation. In the first step, 4-aminobenoic acid was grafted in the ethanolic solution followed by ion exchange of QPVP-Qs (2nd step) and then to cationic $PdCl_4^{2-}$ (3rd step). Finally, the $PdCl_4^{2-}$ sandwich was deposited in situ as nanoparticle by electrochemical reduction method. The group further extended a similar procedure to ion-exchange the heteropolymetalate anions ($ZnW_{11}M(H_2O)O_{39}^{n-}$, M = Cr, Mn, Fe, Co, Ni, Cu and Zn)

Table 2. Covalently modified CMEs in analytical applications.

| *CME* | *Preparation procedure* | *Analyte* | *References* |
|---|---|---|---|
| AQ grafted-GCE | Potential cycling (0.65 to $-0.45$ V vs. SCE) of GCE with 10 mM diazonium salt + TBAP + acetronitrile + anthroquinone (AQ) | DO reduction | [64] |
| Rhein-GCE | Nucleophilic attack of GCE E-cycling ($-0.8$ to 0.4 V) in pH 3 on Rhein's quinone | Hemoglobin | [65] |
| AQ-CO-EG | Exfoliated graphite (≡EG) powder + $H_2SO_4$-$HNO_3$ (3:1) → ≡EG−C=O + $NaBH_4$ + EtOH (reduction) → ≡EG−C−OH + HOOC-AQ → AQ−CO-EG≡ + binder → pellet | AA | [66] |
| Glycine-grafted GCE | Potential cycling (0.0 to 1.6 V) the GCE with Gly in acetonitrile + TBTA | Separation of DA from AA | [67] |
| Glutamic acid modified GCE | Similar to the above case [67] but with glutamic acid | UA and AA | [68] |
| Pd nanoparticle matrix-GCE | GCE + 4-aminobenoic acid (ABA) + EtOH (grafting) → + (QPVP-Os-bpy)$_{ads}$-GCE → $PdCl_4^{2-}$ ion-exchange → in situ deposition | | [69] |
| Polyoxometalate (POM)-ABA-GCE | (QPVP-Os-bpy)$_{ads}$-GCE → ion-exchanged the POM ($ZnW_{11}M(H_2O)O_{39}^{n-}$ | $BrO_3^-$ and $H_2O_2$ | [70] |
| Ru$^{II}$Den-PSS-QPVP-sulfanilic acid (SAA)-GCE | GCE grafted by SAA → QPVP ion-exchange → soak in polystyrene sulfonic acid (PSS) → soak in cationic Ru$^{II}$Den (dendrimer of Ru$^{II}$terpyridine units). | Methionine and insulin | [71] |

Table 3. Homogenous multilayer (uniform) CMEs in analytical applications.

| *CME* | *Analyte* | *References* |
|---|---|---|
| Tosflex-$Fe(CN)_6^{3-}$-GCE | AA in pH 7 | [75] |
| $SiO_2$-Tosflex-$Fe(CN)_6^{3-}$-SPE | AA in pH 7/FIA | [76] |
| Cytochrome c (Cyt-c) doped polyestersulfonated ionomer-GCE | $Fe(CN)_6^{-3}$ and ascorbate, stabilization effect by catalysis | [77] |
| $Co(phen)_2^{2+}$-Nafion(Nf)-Pt | NO | [78] |
| Co-calix[8]-derivative-Nf-PG | Halogenated acid (reduction) | [79] |
| $C_{60}$-[β-CD]-Nf-GCE | Chloroacetic acid (reduction) | [80] |
| $C_{60}$-[β-CD]-Nf-GCE | AA in alkaline condition | [81] |
| $C_{60}$-(dimethyl[β-CD])-Nf-GCE | Norepinephrine (NE) | [82] |
| pH glass membrane modified sensor | $Cl^-$ and $Na^+$ | [84] |
| PVP-$Ru(bpy)_2$-GCE | Guanine moieties in DNA | [85] |
| PPy-metalloporphyrin-GCE | $O_2$ | [87] |
| Polyamino-FeNPc-GCE | Hydrazine | [88] |
| Polyaniline-Ni | AA | [89] |
| PolyNB and PolyTB-GE | NADH | [90] |
| PNB-GCE | $O_2$ | [91] |
| Poly-Caffeic acid (CFA)-CME | NADH | [92] |
| Poly(2-picolinic acid)-GCE | DA | [93] |
| Poly-eugenol-GCE or -Pt | NADH, Pt support is good | [94] |
| Poly-pABA-GCE | Monoamines | [95] |
| PPy-PQQ (co-enzyme)-C | Thiols (cystine-CySH, N-acetyl-CySH, GSH) by capillary electrophoresis (CE) | [96] |
| PPy-$Fe(CN)_6^{3-}$-GCE | AA | [97] |
| PPy-oABA-Pt | Phenol | [98] |
| PNAANI-β-CD-GCE | Thymine | [99] |
| PANI-$PW_{12}O_{40}^{3-}$-Pt/EQCM | $Na^+$ | [100] |
| PANI-$P_2W_{18}O_{62}^{6-}$-GCE | $H_2O_2$ | [101] |
| PPy-$P_2W_{18}O_{62}^{6-}$-PVP-GCE | $NO_2^-$ | [102] |
| Cu-SPE | $H_2O_2$ | [103] |
|  | Glucose (with GOx reactor) | [104] |
|  | Glucose (GOx-casted) | [105] |
|  | o-diphenol selective sensing | [106] |
|  | DO | [108] |
| Cu-GCE | Sulfide compounds | [109] |
| NiOOH-Au or -Pt | Carbohydrate | [110] |
| $IrO_2$/Pd-GCE | CySH and GSH | [111] |
| MHCF (M = Fe, Co, Ni, In) | $SO_3^{2-}$ and $S_2O_3^{2-}$ | [114] |
| CoHCF | AA | [115] |
| $[NiFe(CN)_6NO]^{0/-1}$ | AA and hydrazine | [116, 117] |
| NiHCF-GCE | Thiopurine detection and interaction study with BSA | [118] |
| InHCF-GCE | NO | [119] |
| InHCF-Nf-GCE | Alkali metal and $NH_4^+$ | [120] |
| CoCuHCF (hybrid)-GCE | AA | [121] |
| OxlOx-RuFeNiHCF | Urinary oxalate | [122] |
| $CuPtX_6$-GCE (X = Cl and Br) | $NO_2^-$, AA, $S_2O_3^{2-}$, NO, $H_2O_2$, X (with XOx enzyme) | [123–125] |

for the mediated reduction reaction of $BrO_3^-$ and $H_2O_2$ [70]. Meanwhile, Cox and co-workers prepared GCE-modified ruthenium metallodendrimer ($Ru^{II}$-Den) multiplayer for the mediated oxidation of methionine and insulin under physiological pH [71]. The basic route is similar to that reported by Dong's group except that poly(styrene sulfonate) anions and $Ru^{II}$-Den cations were used in the modification procedures.

## 2.3. Homogeneous Multilayer (Uniform) CMEs

Modification of specific ion-exchange polymers or membranes on the electrode surface is a fascinating branch in electroanalytical chemistry, where the systems allow the ionic species to incorporate as counter ions inside their galleries. Oyama and Anson first used the strategy to modify poly(4-vinyl pyridine) (PVP) on the carbon surface for ion exchange of $Fe(CN)_6^{4-}$ in acidic conditions [72, 73]. Other polymers such as partially quaternized PVP (QPVP) and Nafion were then extensively utilized for sensor applications [3, 11]. The cationic exchanging membrane Tosflex, having analogue backbone like Nafion, was also applied in analytical applications recently [74]. Zen and co-workers prepared thin layer of Tosflex-coated GCE to load $Fe(CN)_6^{3-}$ for AA mediated oxidation reactions [75]. The advantage over classical PVP film is that Tosflex can load $Fe(CN)_6^{3-}$ in a pH window of 2 – 12 while the PVP is restricted up to pH 4

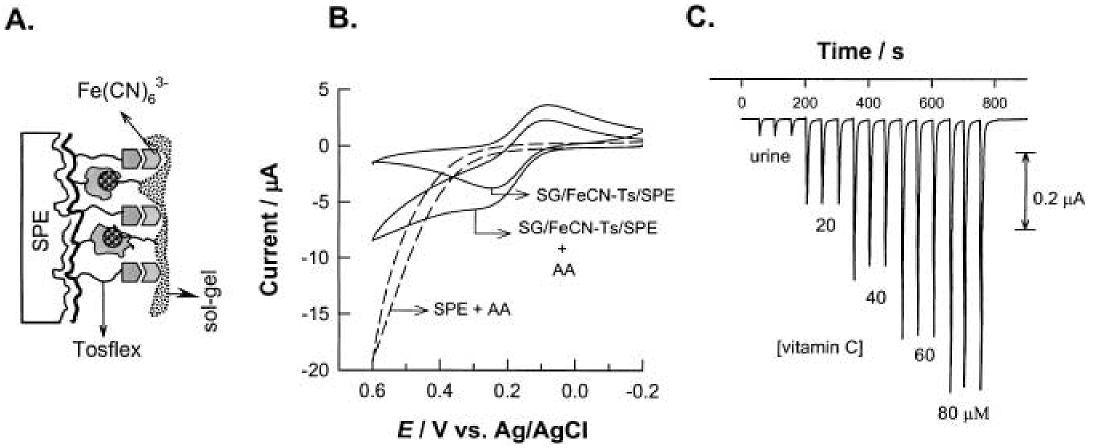


Fig. 5. A) Model structure for the SG/FeCN-Ts/SPE chemically modified system. B) CV response of 1 mM AA at a bare SPE and the SG/FeCN-Ts/SPE at a scan rate of 50 mV/s in pH 7 PBS. C) Typical FIA response of human urine real sample (100 times diluted) under optimized conditions ($E = 0.03$ V (vs. Ag/AgCl), flow rate = 0.5 mL/min). The [AA] detected was 631 μM [76].

only. However, such a thin-layer film was not suitable for the sensing under hydrodynamic conditions. Very recently, coating of a sol-gel film on the Tosflex-$Fe(CN)_6^{3-}$ modified system (SG/FeCN-Ts/SPE) was reported to solve the problem [76]. The procedure was further extended to the disposable SPE. As shown in Figure 5, analytical utilities towards the AA detection in urine and tea were demonstrated using hydrodynamic flow injection analysis (FIA) at an applied potential of 0.3 V (vs. Ag/AgCl) under physiological conditions. In a similar fashion, Ugo et al. investigated polyestersulfonated ionomer modified-GCE for cytochrome C detection [77]. He and Mo reported a $Co(phen)_2^{2+}$ ion-exchanged Nafion/Pt electrode for the sensing of NO [78]. On the other hand, Nafion was used as a matrix to prepare $C_{60}$-L and $C_{70}$-L (L: β-cyclodextrin (β-CD) and calix[8]-derivaties)-modified electrodes towards halogenated acid reduction and AA oxidation reactions [79–82]. Note that β-CD has a basket or trashcan like polysaccharide-host matrix (Scheme 1) and is able to trap bulky molecules inside its gallery [83].

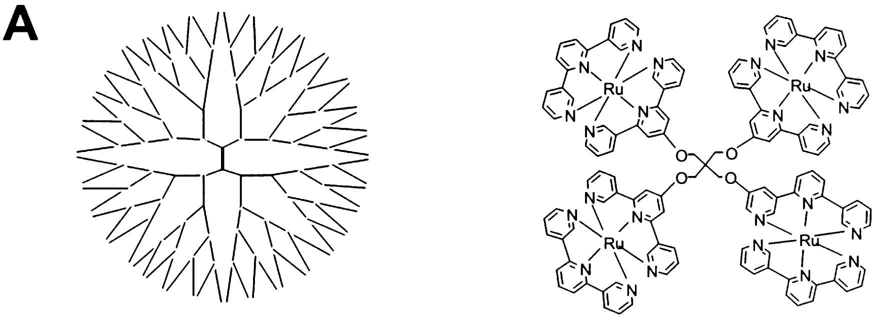
Other than catalytic applications, the ionomeric systems can also be used for the sensing of charged species. Nonetheless, selectivity is an important criterion for such studies and always limits the applications. Kimura et al. rationalized the pH-sensing electrode using a sol gel-based ionomeric system (tretradecyldimethyl(3-rimethoxysilylproyl)ammonium chloride) and crown ether derivative (bis(12-crown-4-methyl)dodecylmethylmalonate) for simultaneous potentiometric sensing of $Na^+$ and $Cl^-$ ions [84].

Rusling and co-workers introduce polymer pendant type of modified electrode by coating PVP as the underlying support to anchor $Ru(bpy)_2Cl_2$ complex [85]. Such studies were well established in polymer supported solution phase catalytic system [86]. The redox potential of the modified electrode was close to the solution phase $Ru(bpy)_3^{3+/2+}$ and was further extended to detect guanine in DNA source. Electrochemical depositions of monomeric units under potential cyclic conditions or by potentiostatic/galvanostatic methods gave another elegant way of preparing electrodes. Cosnier's group reported a polymeric system based on electropolymerization of metelloporphyrin-bearing pyrrole monomeric moieties (redox polymer) in acetonitrile as biomimetic devices for the sensing of dissolved oxygen [87]. In a similar fashion, amino-derivatized FePc was reported for hydrazine oxidation [88].

In some cases, a bare polymeric system itself can act as a catalytic surface towards organic compounds. Prasad and Munichandraiah reported a polyaniline modified Ni (PANI/Ni) electrode for effective AA oxidation at high concentration in 0.1 M $H_2SO_4$ [89]. At [AA] < 1 mM, the leucoemeraldine to emeraldine redox pair (at ca. 0.2 V vs. SCE) strongly interferes the detection through strong AA adsorption complications. Nevertheless, by holding the PANI/Ni electrode at 0.2 V (vs. SCE) for 300 s, the above complication was eliminated. The interference due to other electroactive compounds like dopamine and uric acid commonly present in real samples, however, is unknown. Moreover, the catalytic behavior in physiological conditions is questionable.

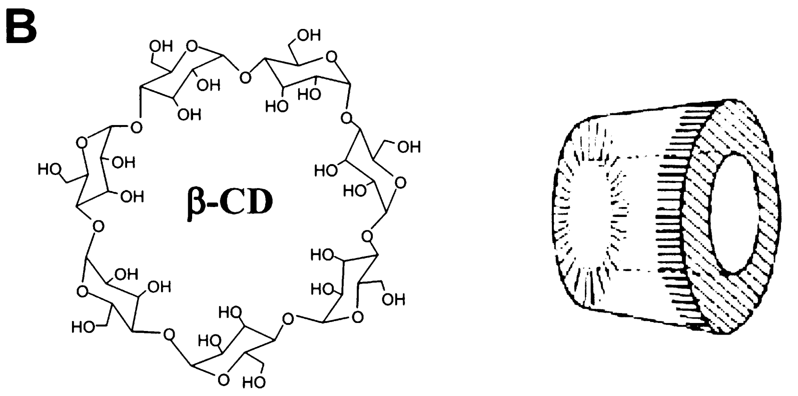
Similar to the above case, pure organic polymers without any metal and metal complex can also participate in the electron transfer reactions. Formation of nitronium or oxonium radicals is a typical example of these cases. In this category, Nile blue (for NADH oxidation and ORR) [90, 91], caffeic acid (for NADH oxidative detection) [92], 2-picolinic acid (for DA sensing) [93], eugenol (for NADH oxidation in alkaline condition) [94] and *p*-aminobenzoic acid (for monoamine detections) [95] based monomeric systems were reported for polymerization and redox reactions.

Utilization of electrochemical co-deposition technique is another popular area to form uniform multi-component films. Inoue and Kirchoff reported an electrochemical co-deposition method for the trapment of coenzyme pyrroloquiline quinone (PQQ) in polypyrrole (PPy) matrix in weak alkaline conditions [96]. The electrode was found to be very



Polyamidoamine dendrimer (G4-PAMAM) unit

Metallodendrimer with $Ru^{II}$-terpyridine units



Structure of β-Cyclodextrin

Shape of β-Cyclodextrin

Scheme 1. Structures of Dendrimers and β-Cyclodextrin

efficient for thiols oxidation (CySH, GSH and *N*-acetyl CySH). Similarly, $Fe(CN)_6^{3-}$ (for AA oxidation) and *o*-amionbenzesulfonic acid (for phenol oxidation) co-deposited PPy systems [97, 98], β-CD co-deposited poly-*n*-acetyl aniline film (PNAANI) (for thymine oxidation) [99], polyaniline (PANI)-modified Keggin, $PW_{12}O_{40}^{3-}$ (for $Na^+$) [100] and Dawson, $P_2W_{18}O_{62}^{6-}$ ($H_2O_2$) [101] type of heteropolyanions and PPy-modified Dawson (for $NO_2^-$) [102] were also recently reported for analytical purposes.

In addition to organic sources as modifiers, simple metal-plated electrodes can also be used for analytical applications. Zen and co-workers demonstrated a disposable copper plated SPE (designated as CuSPE) for $H_2O_2$ detection [103]. The CuSPE was further coupled with glucose oxidase for glucose sensing under physiological condition [104–106]. High stability of the deposited copper in neutral PBS ($K_{sp} = 1.39 \times 10^{-37}$) is a chief advantage of the CuSPE. The electrode was further utilized for the selective sensing of *o*-diphonolic neurotransmitter (e.g., catechol and dopamine) at ca. 0.0 V (vs. Ag/AgCl) in physiological conditions with no interference from AA, mono- and ortho- and para-di-phenolic systems (Fig. 6) [106]. Formation of a five membered intermediate Cu(II)-quinolate complex was found to play a key role for this operation. The practical utility was demonstrated by assaying with FIA technique. Recently, a copper dipyridyl ion-exchanged Nafion film was studied as a biomimetic catalytic electrode for the amperometric detection of phenols [107]. The selectivity in the detection, however, is not much appreciable like the CuSPE. The CuSPE is also utilized for the sensitive photoelectrochemical sensing of dissolve oxygen with excellent sensitivity [108]. Casella's group prepared Cu/GCE for the determination of organic sulfur containing compounds (i.e., CySH, CySSCy, GSH, $S^{2-}$, $S_2O_8^{2-}$, etc) in alkaline conditions and Pt or Au-supported Ni hydroxide (NiOOH) electrodes for carbohydrates oxidation [109, 110]. Xu et al. described an electrochemically deposited $IrO_2$/Pd-GCE, prepared from the precursor solution of $IrCl_6^{3-}$ and $PdCl_2$, for CySH and GSH detections [111].

Inorganic polymers have been given equal interest in analytical chemistry towards potentiometric and/or amperometric sensing. Prussian blue (PB) is a typical matrix known for more than 250 years. Neff first opened the PB electrochemistry in the year of 1978 [112]. Nowadays variety

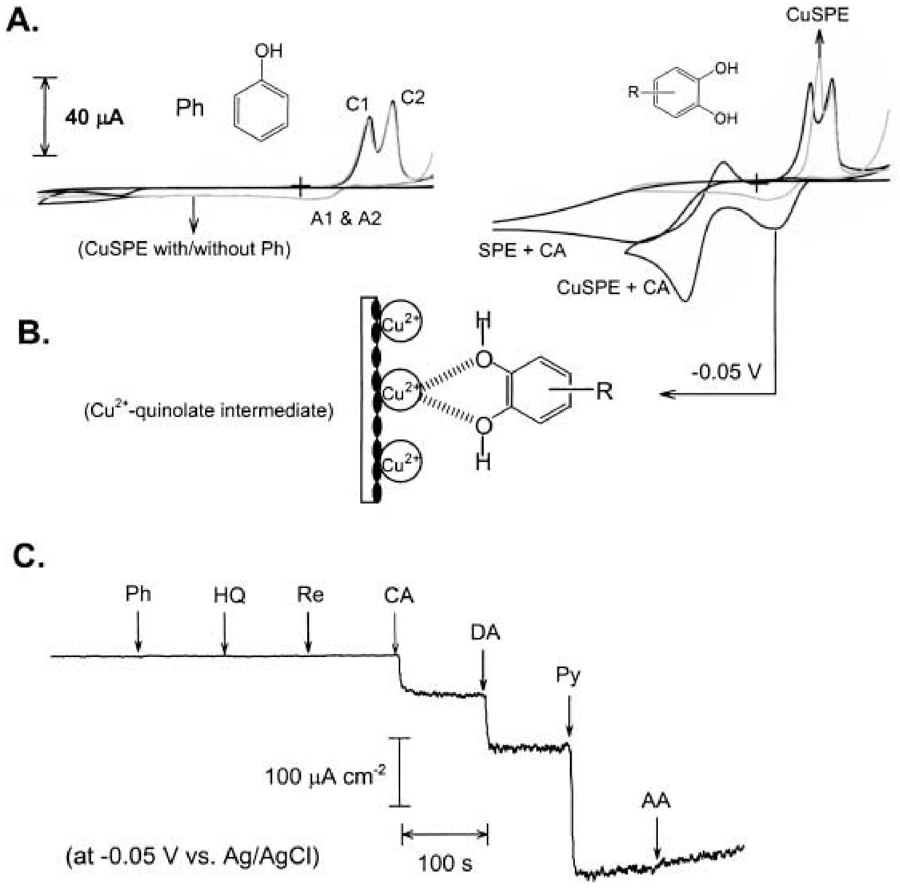


Fig. 6. A) CV response of phenol (Ph) and dihydroxy phenol derivative (catechol, CA) on the CuSPE and SPE in pH 7.4 PBS at a scan rate of 5 mV/s. B) Conceptional structure for the $Cu^{2+}$-quinolate intermediate on the CuSPE. C) Typical $i-t$ response of the CuSPE spiked with 2 mM monophenol (Ph), di-phenols of *para-* (HQ), *meta-* (Re) and *ortho-* (CA, DA, Pyrrogallol; Py) in pH 7.4 PBS.

of similar complexes is prepared by electrochemical methods for analytical applications [113]. For example, metal hexacayno-ferrate (MHCF, M = Fe, Co, Ni and In) complexes for $SO_3^{2-}$ and $S_2O_3^{2-}$ oxidation in the presence of various supporting electrolytes [114], CoHCF for hydrazine, NiHCF-NO complexes for AA [115–117], NiHCF for thiopurine (as well as bovine albumin serum (BSA) interactions studies) [118], InHCF for NO oxidative detection [119], Nafion-coated InHCF for alkali metal ion and $NH_4^+$ [120], hybrid CoCuHCF for hydroxylamine [121] and oxalate oxidase (OxlOx)-coupled RuFeNiHCF for urinary oxalate [122] detections. In a similar way, $CuPtX_6$ (X = Cl and Br) mixed valence compounds are also prepared simply by potential cycling of $CuCl_2$ and $K_2PtX_6$ in KCl solution for oxidation studies of $NO_2^-$, AA, $S_2O_3^{2-}$, NO and reduction reaction of $H_2O_2$ [123, 124]. The complexes are also suitable for the enzymatic detection of xanthine (X) in couple with xanthine oxidase enzyme (XOx) and BSA [125].

## 2.4. Heterogeneous Multilayer (Non-Uniform) CMEs

In the heterogeneous multilayer CMEs, the solid supports are deliberately combined with the mediator system under a non-uniform way (Table 4). Carbon paste electrode (CPE) is one of the convenient matrixes to prepare the CME by simple mixing of graphite/binder paste and redox mediator [12]. Enzymatic clay and zeolite modified electrodes can also be prepared by this procedure. Following are recent examples of simple mediators used in CPE for electroanalytical applications: MB, methyl viologen (MV) and benzyl viologen (BV) modified zirconium phosphate for NADH oxidation [126, 127], HgO for metal detection [128], ruthenium-diphenyldithoacarbamate ($Ru^{III}$-DDC) for AA oxidation [129], 1,2-bis(pro-2′-enyloxy)-9-10-anthraquinone (AQ-L) for $Pb^{2+}$ detection [130], picolinic acid *N*-oxide for selective determination of $Hg_2^{2+}$ [131], montmorillonite (SWy-1) clay for Au [132] and CoPc for amitrole detection [133]. Such an approach is also suitable for preparing multiple integrated systems. For example, Ferreira et al. reported MB immobilized $SiO_2/TiO_2$-based CPE for hydrazine oxidation [134]. Prior to the modification, the binary metal oxide $SiO_2/TiO_2$ composite was first washed in phosphoric acid and then dissolved in HF. It was precipitated in $NH_4OH$ solution followed by heating at 1073 K. The material was agitated with MB solution and finally filtered to use. Such a procedure resulted in good dispersion of the electroactive species in the surface with great improvement

Table 4. Heterogenous (non-uniform) CMEs in analytical applications.

| *CME* | *Analyte* | *References* |
|---|---|---|
| Nile Blue, MV and BV in ZrP-CPE | NADH | [126, 127] |
| HgO-CPE | Metals | [128] |
| $Ru^{III}$-DDC-CPE | AA | [129] |
| AQ-L-CPE | Pb(II) | [130] |
| Picolinic acid N-oxide-CPE | $Hg_2^{2+}$ | [131] |
| SWy-1/clay-CPE | Au | [132] |
| CoPc-CPE | Amitrole | [133] |
| $SiO_2/TiO_2$/phosphate-MB-CPE | Hydrazine | [134] |
| $Sb_2O_5/SiO_2/ZrO_2$-MB-CPE | NADH | [135] |
| $PMo_{12}$-sieve MCM-41-CPE | $ClO_3^-$ and $BrO_3^-$ | [136] |
| Fc doped β-CD-CPE | AA | [137] |
| Ag/zeolite (AgY)-ITO | $Cl^-$ and $Br^-$ | [138] |
| NAD-GIDH-CPE | Glycerol | [139] |
| $[Ru(NH_3)_6^{3+}]_4/[Ru(CN)_6^{4-}]_3$-GOx-CPE | Glucose | [140] |
| GDH-$NAD^+$ /NADH-$Ca^{2+}$- -HOOC-ϕ$NO_2$-GCE | Glucose | [141] |
| r-$MnO_2$ (enzyme)-AMB-DMFc-CPE | Glucose | [142] |
| GOx-clay-MV-CPE | Xanthine | [143] |
| $PMo_{12}$-CCE | $BrO_3^-$, nitrite, AA, $H_2O_2$ | [147–151] |
| $SiO_2$-PVA-g-PVP-α-$K_6P_2W_{18}O_{62}$-GCE | $BrO_3^-$ and $NO_2^-$ | [152] |
| $GeMo_{12}$-CCE | $BrO_3^-$, $NO_2^-$ and $H_2O_2$ | [153] |
| PB-CCE | $N_2H_4$ | [154] |
| MnHCF-CCE | L-Cysteine | [155] |
| NiHCF-CCE, CoHCF-CCE, InHCF | Thiosulfate | [156–158] |
| PQ-CCE | Iodate | [159] |
| ZrP-MB-CCE | NO | [160] |
| $Ru^{II}$terpyridine dendrimer-CPE | 5-hydroxytrptophan | [161] |
| Co di-quinolyl-diamine-BHPG | $O_2$ reduction | [162] |
| AOx-CoPc-NCA-SPE | Alcohol in beer | [164] |
| PVA-g-PVP-$SiO_2$-HRP-$MG^+$-Nf-GCE | $H_2O_2$ | [165] |
| Bacteria (Pseudomonas)-CA-Fc (or Q)-Pt-GCE | Phenol | [166] |
| HgO-SPE | Heavy metals | [167] |
| Pt/PANI-Au | Glycerol | [168] |
| Pt-mvRuOx-$WO_3$-GCE | $CH_3OH$ | [169] |
| NPyCME | CySH, DTT, $NO_2$ and NO | [170–172] |
| Clay-Py-CA-GCE | DA | [173] |
| Hybrid-PB-cinder-CPE | Guanine and $NO_2^-$ | [175, 177] |
| Hybrid-PB-cinder-SPE | $H_2O_2$ (in pH 2) | [176] |
| Hybrid-PB-cinder-SPE | $H_2O_2$ (in pH 7 with CTAB) | [178] |
| Hybrid-Co$(CN)_6$-cinder-SPE | Sulfide | [179] |

in stability and catalytic activity. Other examples are MB-immobilized silica-zirconia-antimonia mixed oxides (low temperature prepared)-CPE for NADH oxidation reaction [135], $PMo_{12}$ encapsulated molecular sieve MCM-41-CPE for $ClO_3^-$ and $BrO_3^-$ [136], β-CD-ferrocene-CPE for AA [137] and Ag/zeolite for $Cl^-$ and $Br^-$ [138] detections. On the other hand, the CPE-based enzymatic systems also provide an easy approach to construct biosensors. Some of the recent examples are $NAD^+$ coupled dehydrogenous (GIDH) for glycerol [139], $[Ru(NH_3)_6^{3+}]_4/[Ru(CN)_6^{4-}]_3$ coupled glucose oxidase (GOx) [140], nitrofluorenone CPE-(HOOC-ϕ-$NO_2$)-$Ca^{2+}$-NADH-GIDH configuration [141] and *microdochium nivale* carbohydrate oxidase (*r*-$MnO_2$) coupled 1-(*N*-*N*-dimethylamine)-4-(4-morpholine) benzene-1,1′-dimethylferrocene [142] systems for glucose and MV/SWy-1 coupled XOx for xanthine [143] detections.

Carbon ceramic composite electrode (CCE) introduced by Lev's group is a modern technique to prepare stable multilayers [144]. Wang and co-workers later tuned the CCE system extensively to analytical purpose [145, 146]. In the CCE preparation route, mediator was first mixed with $SiO_2$ precursors (like methoxysilanes) in a proper ratio with alcohol + diluted HCl and then sonicated for couple of minutes, followed by mixing with carbon powder. The composite was converted into a suitable electrode either by filling in a glass-tube or by coating on a conducting support. Finally, the configuration was allowed to sit for ca. 24 h to form a rigid structure. Such electrodes offer renewable surface characteristics. Some of the mediator reported recently for CCE are phosphomolybdic acid ($PMo_{12}$) for amperometric sensing of $BrO_3^-$, $ClO_3^-$, nitrite, AA and $H_2O_2$ [147–151], heteropolyanion of Dawson-type, $K_6P_2W_{18}O_{62}$ ($P_2W_{18}$) and Keggin-type-α-germanomolybdic acid, $GeMo_{12}$ for $BrO_3^-$, $NO_2^-$ and $H_2O_2$ [152, 153], PB for hydrazine [154], MnHCF for L-cysteine [155], NiHCF, CoHCF and InHCF for thiosulfate [156–158], 9, 10-phenanthrequinone for $IO_4^-$ [159], MB for NO [160] and metallodendrimer with $Ru^{II}$terpyridine ($Ru^{II}$Den) (Scheme 1) for 5-hydroxytryphtophan [161] detections.

Apart from the basic techniques mentioned above, sequential coating or dispersion of active centers on the conducting support also provide a way of making integrated CMEs. Okada et al. prepared an efficient catalyst for the ORR by simply mixing cobalt di-quinolydiamine with graphite and Nafion and coated on a BPG (high density) support [162]. Before mixing with Nafion, the composite was annealed in a furnace at ca. 400–800 °C. Walcarius et al. used zeolite dispersed siloprene polymer membrane in couple with urease enzyme to prepare a urea biosensor [163].

Other applications include an ethanol sensor made of alcohol oxidase enzyme (AOx) sandwiched by CoPc and nitrocellulose acetate (NCA) [164], a $H_2O_2$ sensor by PVA grafted PVP-horseradish peroxidase (HRP)-methylene green ($MG^+$)-$SiO_2$-Nafion film [165], a phenol sensor by mixture of graphite, acetyl cellulose acetate (ACA) with ferrocene (Fc) and *pseudomonas* bacteria [166]. Moreover, based on the same strategy, a HgO/graphite composite-coated SPE was reported for heavy metals detection [167], a successive electrodeposited PANI and Pt film on Au electrode for glycerol oxidation [168] and a $WO_3$ and polynuclear oxocyanoruthenium microcenter electrodeposited GCE for methanol oxidation [169].

Zen's group introduced a Nafion/lead ruthenate pyrochlore (*Py*) chemically modified electrode (N*Py*CME) for chemical sensor applications [13], where the *Py* units are in situ precipitated in the Nafion film. By tuning the solution pH and square wave voltammetric (SWV) parameters, the N*Py*CME can sense a variety of biological, pharmaceutical and environmental oriented compounds [13]. The basic active site surrounded by Nafion macro-polymeric units in the N*Py*CME resembles an enzyme analogue and was thus very effective in chemical sensor applications. Meanwhile, the electrocatalytic pathway on the N*Py*CME obeys Michaleis-Menten type of key-lock mechanism. The electrode

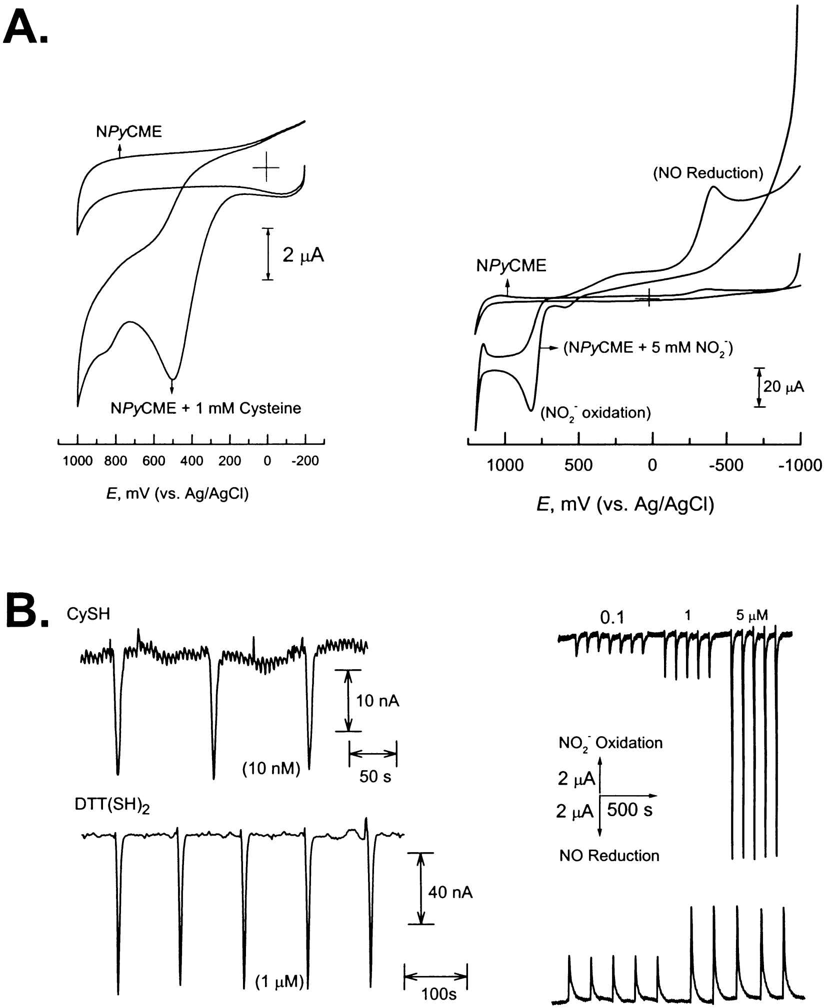


Fig. 7. Sensitive determination of thiols (CySH, $DTT(SH)_2$), $NO_2$ and NO at the N*Py*CME. A) CV responses for cysteine ($v = 50$ mV/s) in pH 7.4 PBS and for $NO_2^-$ oxidation and NO reduction ($v = 5$ mV/s) in pH 1.65 KCl solution. B) FIA responses for cysteine (flow rate = 0.3 mL/min at 1.0 V (vs. Ag/AgCl)), $DTT(SH)_2$ (flow rate = 0.7 mL/min at 0.9 V in pH 4 PBS), $NO_2^-$ (flow rate = 0.3 mL/min at 1.1 V (vs. Ag/AgCl)) and NO (flow rate = 0.5 mL/min at −0.8 V (vs. Ag/AgCl)).

was recently used for the sensitive detection of CySH, dithiotrinitol (DTT(SH)$_2$) and $NO_2^-$ and $NO^-$ (dual sensor) with nM detection limit by FIA [170–172]. Figure 7 shows typical FIA responses for the above detections based on the N*Py*CME. The preparation route was also extended to nontronite matrix for sensitive detection of DA [173] and Nafion membrane-based units in couple with $Ru(bpy)_3^{2+}$ for organic synthetic applications [174].

Industrially iron enriched waste cinder (CFe*) was also reported by Zen's group as a useful host to form stable PB hybrid (CFe*-Fe(CN)) derivatives directly inside the matrix by potential cycling with cyanometallate in pH 2 KC/HCl solutions (Fig. 8) [175]. The formation of PB was characterized by XPS and FT-IR as a typical example of electrostatic self-assembling of $Fe(CN)_6^{3-}$ with $Fe^{3+/2+}$ of the cinder material in a mixture of calcium silicate [176]. The free iron ions existing in the non-bridging terminal of the silicate oxygen (i.e., $\equiv SiO^{n-} \cdot Fe^{3+/2+}$) are essential for the hybrid PB, which cannot be expected for the $Fe_2O_3$ modified electrodes (Fig. 8) [176]. Prime advantage of such hybrid PB analogues is their stability and workability. The cinder/PB film is highly stable under hydrodynamic stress and can be operatable even in neutral PBS, which is impossible with classical PB films. Some of the recent applications include the PB/CFe*-CPE for guanine and $NO_2^-$ [175, 177], PB/CFe*-SPE for $H_2O_2$ [176, 178] and Co(CN)$_6$-CFe*/SPE for sulfide detections [179].

## 3. Conclusions and Future Prospects

This collective survey denotes solid improvement in the CMEs towards new analytical systems, especially for biological applications. Some of the results based on the selective DNA detection using Au-nanoparticles and pendant type of modified systems and electrode systems based on carbon nanotubes, *Mirodochium nivale* carbohydrate oxidase (good alternative to GOx enzyme with less $O_2$ interference), ceramic carbon (stable CME configuration in desire sizes), copper (selective detection of neurotransmitters at ca. 0 V (vs. Ag/AgCl)), Nafion/lead ruthenate pyrochlore and industrially waste cinder were found to be very positive for new openings. However, demonstration of practical applications for real samples is very limited. There are many invitations for extension to new applications. For example, the N*Py*CME can be applicable for the redox-based protein-folding studies. Since the electrochemical technique is quite sensitive for the thiols functional groups, it is easy to quantify folded and unfolded proteins and in turn to its kinetics. Similarly, other examples are the Au-nanoparticles to new virus, pendant systems to chip-based DNA detections, and cinder matrix for dirt-cheap electrode bases, etc. We hope that these CMEs can play a key role for new inventions in the near future.

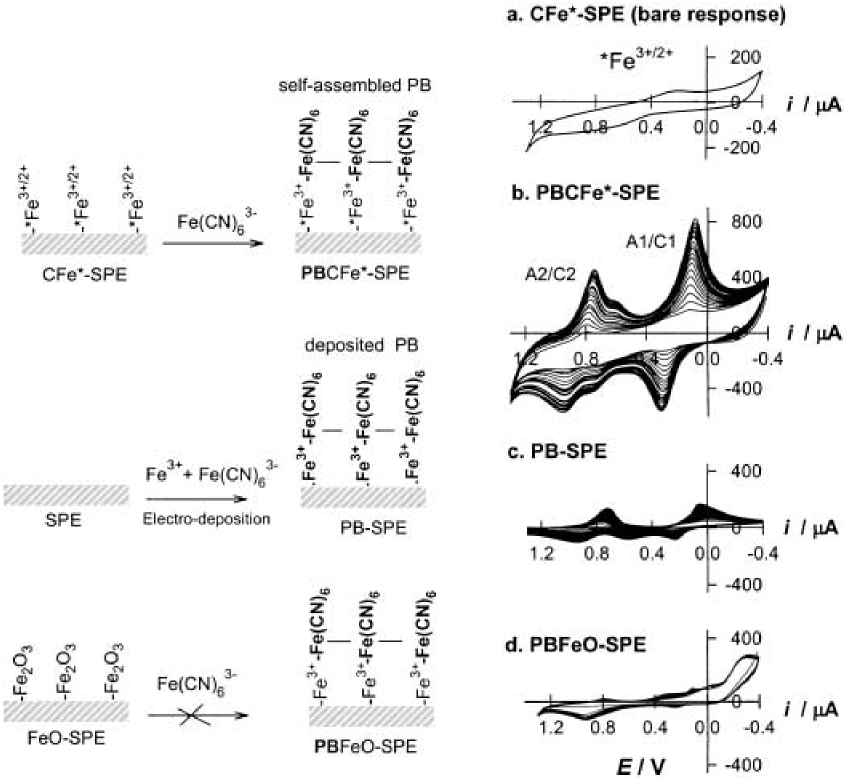


Fig. 8. CV response of various modified SPEs at 50 mV/s in pH 2 KCl/HCl ($I = 0.1$ M) solution. Except (a), other systems are in the presence of 2 mM $Fe(CN)_6^{3-}$. In (c) 2 mM each of $Fe(CN)_6^{3-}$ and $Fe^{3+}$ was used. The items at left side corresponds to the conceptional representation of the $Fe(CN)_6^{3-}$ self-assembling as hybrid PBCFe*-SPE, conventional PB-SPE and PBFeO-SPE. No PB formation with FeO-SPE indicates the unique behavior of cinder towards the PB self-assembling [176].

## 4. Acknowledgement

The authors gratefully acknowledge financial supports from the National Science Council of the Republic of China.

## 5. References

[1] R. W. Murray, *Acc. Chem. Res.* **1980**, *13*, 135.
[2] R. W. Murray, *Anal. Chem.* **1987**, *59*, 379A.
[3] *Molecular Design of Electrode Surfaces* (Ed: R. W. Murray), Wiley, New York **1992** and references therein.
[4] S. Flink, F. C. J. M. van Veggel, D. N. Reinhoudt, *Adv. Mat.* **2000**, *12*, 1315.
[5] D. Mandler, I. Turyan, *Electroanalysis*, **1996**, *8*, 207 and references therein.
[6] A. Ulmann, *Ultrathin Organic Films*, Academic Press, New York **1991** and references therein.
[7] N. K. Chaki, K. Vijayamohanan, *Biosen. Bioelect.*, **2002**, *17*, 1 and references therein.
[8] L. Kavan, *Chem. Rev.* **1997**, *97*, 3061.
[9] A. J. Downard, *Electroanalysis* **2000**, *12*, 1085.
[10] *Electrochemistry of Novel Materials, Frontiers of Electrochemistry* (Eds: J. Lipkowski, P. N. Ross), VCH, New York **1994**.
[11] *Advances in Chemical Physics, Polymeric Systems* (Eds: I. Prigogine, S. A. Rice), Wiley, New York **1996**.
[12] J. Wang, *Analytical Electrochemistry,* 2nd ed., Wiley, New York **2000**.
[13] J.-M. Zen, A. Senthil Kumar, *Acc. Chem. Res.* **2001**, *34*, 772.
[14] D. R. Rolison, C. A. Bessel, *Acc. Chem. Res.* **2000**, *33*, 737.
[15] A. Walcarius, *Chem. Mat.* **2001**, *13*, 3351.
[16] M. Sadakane, E. Steckhan, *Chem. Rev.* **1998**, *98*, 219.
[17] A. Walcarius, *Anal. Chim. Acta* **1999**, *384*, 1.
[18] A. Walcarius, *Electroanalysis* **2001**, *13*, 701.
[19] A. B. Florou, M. I. Prodromidis, S. M. T. Karayanni, M. I. Karayannis, *Anal. Chim. Acta* **2000**, *423*, 107.
[20] M. I. Prodromidis, P. G. Veltsistas, M. I. Karayannis, *Anal. Chem.* **2000**, *72*, 3995.
[21] D. Dicu, L. Muresan, I. C. Popescu, C. Cristea, I. A. Silberg, P. Brouant, *Electrochim. Acta* **2000**, *45*, 3951.
[22] C. A. Caro, F. Bedioui, J. H. Zagal, *Electrochim. Acta* **2002**, *47*, 1489.
[23] G.-C. Zhao, F.-H. Wu, X.-W. Wei, *Chem. Lett.* **2002**, 520.
[24] J. Wang, M. Li, Z. Shi, N. Li, Z. Gu, *Electroanalysis* **2002**, *14*, 225.
[25] Z. Wang, J. Liu, Q. Liang, Y. Wang, G. Luo, *Analyst* **2002**, *127*, 653.
[26] F.-H. Wu, G.-C. Zhao, X.-W. Wei, *Electrochem. Commun.* **2002**, *4*, 690.
[27] J. Kong, M. G. Chapline, H. Dai, *Adv. Mater.* **2001**, *13*, 1384.
[28] R. H. Baughman, A. A. Zakhidov, W. A. de Heer, *Science* **2002**, *297*, 787.
[29] R. C. Haddon, *Carbon Nanotube, Acc. Chem. Res.* **2002**, *35*, 997.
[30] Q. Zhao, Z. Gan, Q. Zhang, *Electroanalysis* **2002**, *14*, 1609.
[31] M. Musameh, J. Wang, A. Merkoci, Y. Lin, *Electrochem. Commun.* **2002**, *4*, 743.
[32] H. Cai, X. Cao, Y. Jiang, P. He, Y. Fang, *Anal. Bioanal. Chem.* **2003**, *375*, 287.
[33] M. Shamsipur, A. Salimi, H. Haddadzadeh, M. F. Mousavi, *J. Electroanal. Chem.* **2001**, *517*, 37.
[34] A. Salimi, M. Ghadermazi, *Anal. Sci.* **2001**, *17*, 1165.
[35] J.-M. Zen, H.-H. Chung, G. Ilangovan, A. Senthil Kumar, *Analyst* **2000**, *125*, 1139.
[36] J.-M. Zen, S.-H. Jeng, H.-J. Chen,. *Anal. Chem.* **1996**, *68*, 498.
[37] J.-M. Zen, S.-F. Wang, A. Senthil Kumar, Y. Yang, V. Dharuman, *Electroanalysis* **2002**, 14, 99.
[38] Y. Shih, J.-M. Zen *Anal. Chim. Acta* **2000**, *412*, 63.
[39] J.-M. Zen, H.-P. Chen, A. Senthil Kumar, *Anal. Chim. Acta* **2001**, *449*, 95.
[40] J.-M. Zen, Y.-Y. Lai, H.-H. Yang, A. Senthil Kumar, *Sen. Actuat. B: Chemical* **2002**, *84*, 237.
[41] N. Nakashima, K. Masuyama, M. Mochida, M. Kunitake, O. Manabe, *J. Electroanal. Chem.* **1991**, *319*, 355.
[42] J. F. Rusling, H. Zhang, *Langmuir* **1991**, *7*, 1991.
[43] N. Nakashima, T. Tokunaga, H. Owaki, H. Murakami, T. Sagara, *Colloids and Surfaces A: Physicochem. Eng. Aspects* **2000**, *169*, 163.
[44] J. Tang, Z. Wu, J. Wang, E. Wang, *Electrochem. Commun.* **2000**, *2*, 796.
[45] J. Tang, Z. Wu, J. Wang, E. Wang, *Electroanalysis* **2001**, *13*, 1315.
[46] J. Xu, J.-J. Zhu, Q. Huang, H.-Y. Chen, *Electrochem. Commun.* **2001**, *3*, 665.
[47] L. Cheng, G. E. Pacey, J. A. Cox, *Electrochim. Acta* **2001**, *46*, 4223.
[48] D. Astruc, F. Chardac, *Chem. Rev.* **2001**, *101*, 2991.
[49] E. E. Simanek, S. O. Gonzalez, *J. Chem. Edu.* **2002**, *79*, 1222 and references therein.
[50] W. Yang, D. Jaramillo, J. J. Gooding, D. B. Hibbert, R. Zhang, G. D. Willett, K. J. Fisher. *Chem. Comm.* **2001**, 1982.
[51] N. Mano, A. Thienpont, A. Kuhn, *Electrochem. Commun.* **2001**, *3*, 585.
[52] G. Shi, M. Luo, J. Xue, F. Xu, L. Jin, J. Jin, *Frensius J. Anal. Chem.* **2001**, *370*, 878.
[53] Q. Wang, N. Li, W. Wang, *Anal. Sci.* **2002**, *18*, 635.
[54] A. S. Viana, M. Kalaji, L. M. Abrantes, *Electrochim. Acta* **2002**, *47*, 1587.
[55] C. Fang, Z. Zhou, *Electroanalysis* **2001**, *13*, 949.
[56] C. Retna Raj, T. Ohsaka, *Electroanalysis* **2002**, *14*, 679.
[57] D. R. Shankaran, Y.-B. Shim, *Electroanalysis* **2002**, *14*, 704.
[58] S.-J. Park, T. A. Taton, C. A. Mirkin, *Science* **2002**, *295*, 1503.
[59] R. F. Service, News of the Week, *Nature* **2002**, *295*, 1447.
[60] R. S. Deinhammer, M. Ho, J. W. Anderegg, M. D. Porter, *Langmuir* **1995**, *10*, 1306.
[61] P. Allongue, M. Delamar, B. Desbat, O. Fagebaume, R. Hitmi, K. Pinson, J.-M. Savéant, *J. Am. Chem. Soc.* **1997**, *119*, 201.
[62] M. Delamar, G. Désarmot, O. Fagebaume, R. Hitmi, J. Pinson, J.-M. Savéant, *Carbon* **1997**, *35*, 801.
[63] C. P. Andrieux, F. Gonzalez, J.-M. Savéant, *J. Am. Chem. Soc.* **1997**, *119*, 4292.
[64] K. Tammeveski, K. Kontturi, R. J. Nichols, R. J. Potter, D. J. Schiffrin, *J. Electroanal. Chem.* **2001**, *515*, 101.
[65] Y. Z. Zhang, H. Zhao, Z. B. Yuan, *Electroanalysis* **2002**, *14*, 382.
[66] P. Ramesh, S. Sampath, *Analyst* **2001**, *126*, 1872.
[67] L. Zhang, X. Lin, *Frensius J. Anal. Chem.* **2001**, *370*, 956.
[68] L. Zhang, X. Lin, *Analyst* **2001**, *126*, 367.
[69] J. Liu, L. Cheng, Y. Song, S. Dong, *Langmuir* **2001**, *17*, 6747.
[70] J. Liu, L. Cheng, S. Dong, *Electroanalysis* **2002**, *14*, 569.
[71] L. Cheng, G. E. Pacey, J. A. Cox, *Anal. Chem.* **2001**, *73*, 5607.
[72] N. Oyama, F. C. Anson, *Anal. Chem.* **1980**, *52*, 1196.
[73] N. Oyama, F. C. Anson, *J. Electrochem. Soc.* **1980**, *127*, 640.
[74] L. Dunsch, J. Kavan, J. Weber, *J. Electroanal. Chem.* **1990**, *280*, 313.
[75] J.-M. Zen, D.-M. Tsai, A. Senthil Kumar, V. Dharuman, *Electrochem. Commun.* **2000**, *2*, 782.

[76] J.-M. Zen, D.-M. Tsai, A. Senthil Kumar, *Electranalysis* in press.
[77] P. Ugo, V. Zangrando, L. M. Moretto, B. Brunetti, *Biosen. Bioelectr.* **2002**, *17*, 479.
[78] X. C. He, J.-Y. Mo, *Analyst* **2000**, *125*, 793.
[79] T. Liu, M. Li, N. Li, Z. Gu, X. Zhou, *Electrochim. Acta* **2000**, *45*, 4457.
[80] M. Wei, M. Li, N. Li, Z. Gu, X. Zu, *Talanta* **2001**, *53*, 1045.
[81] M. Wei, M. Li, Z. Gu, X. Zu, *Electroanalysis* **2002**, *14*, 135.
[82] M. Wei, M. Li, N. Li, Z. Gu, X. Duan, *Electrochim. Acta* **2002**, *47*, 2673.
[83] N. J. Crane, R. C. Mayrhofer, T. A. Betts, G. A. Baker, *J. Chem. Ed.* **2002**, *79*, 1261.
[84] K. Kimura, S. Yajima, H. Takase, M. Yokoyama, Y. Sakurai, *Anal. Chem.* **2001**, *73*, 1605.
[85] A. Mugweru, J. Rusling, *Electrochem. Commun.* **2001**, *3*, 406; *Anal. Chem.* **2002**, *74*, 4044.
[86] U. Siemeling, *Chem. Rev.* **2000**, *100*, 1495; J. S. Higgins, *Chem. Soc. Rev.* **1997**, *26*, 247.
[87] S. Cosnier, C. Gondran, R. Wessel, F.-P. Montforts, M. Wedel, *J. Electroanal. Chem.* **2000**, *488*, 83.
[88] P. Ardiles, E. Trollund, M. Isaacs, F. Armijo, J. C. Canales, M. J. Aguirre, M. J. Canales, *J. Mol. Catal. A.* **2001**, *165*, 169.
[89] K. Rajendra Prasad, N. Munichandraiah, *Anal. Chem.* **2002**, *74*, 5531.
[90] A. Malinauskas, G. Niaura, S. Bloxham, T. Ruzgas, L. Gorton, *J. Colloids Interface Sci.* **2000**, *230*, 122.
[91] H. Ju, C. Shen, *Electroanalysis* **2001**, *13*, 789.
[92] H. R. Zare, S. M. Golabi, *J. Solid State Electrochem.* **2000**, *4*, 87.
[93] H. Zhao, Y. Zhang, Z. Yuan, *Analyst* **2001**, *126*, 358.
[94] A. Ciszewski, G. Milczarek, *Electroanalysis* **2001**, *13*, 860.
[95] F. Xu, M. Gao, L. Wang, L. Jin, *Anal. Biochem.* **2002**, *307*, 33.
[96] T. Inoue, J. R. Kirchhoff, *Anal. Chem.* **2002**, *74*, 1349.
[97] M. H. Pournaghi Azar, R. Ojani, *J. Solid State Electrochem.* **2000**, *4*, 75
[98] W. Lu, G. G. Wallace, M. D. Imisides, *Electroanalysis* **2002**, *14*, 325.
[99] S. Wu, Z. Zheng, L. Rui, X. Lin, *Electroanalysis* **2001**, *13*, 967.
[100] L. M. Abrantes, C. M. Cordas, E. Vieil, *Electrochim. Acta* **2002**, *47*, 1481.
[101] D. G. Shchukin, D. V. Sviridov, *Electrochem. Commun.* **2002**, *4*, 402.
[102] T. McCormac, D. Farrell, D. Drennan, G. Bidan, *Electroanalysis* **2001**, *13*, 836.
[103] J.-M. Zen, H.-H. Chung, A. Senthil Kumar, *Analyst* **2000**, *125*, 1633.
[104] J.-M. Zen, H.-H. Chung, A. Senthil Kumar, *Anal. Sci.* **2001**, *17*, i287.
[105] A. Senthil Kumar, J.-M. Zen, *Electroanalysis* **2002**, *14*, 671.
[106] J.-M. Zen, H.-H. Chung, *Anal. Chem.* **2002**, *74*, 1202.
[107] M. D. P. T. Sotomayor, A. A. Tanaka, L. T. Kubota, *J.Electroanal. Chem.* **2002**, *536*, 71.
[108] J.-M. Zen, Y.-S. Song, H.-H. Chung, C.-T. Hsu, A. Senthil Kumar, *Anal. Chem.* **2002**, *74*, 6126.
[109] I. G. Casella, M. Contursi, E. Desimoni, *Analyst* **2002**, *127*, 647.
[110] I. Casella, M. Gatta, *Anal. Chem.* **2000**, *72*, 2969.
[111] F. Xu, L. Wang, M. Gao, L. Jin, J. Jin, *Anal. Bioanal. Chem.* **2002**, *372*, 791.
[112] V. D. Neff, *J. Electrochem. Soc.* **1978,** *125*, 887.
[113] A. Karyakin, *Electroanalysis* **2001**, *13*, 813.
[114] S.-M. Chen, *J. Electroanal. Chem.* **2002**, *521*, 29.
[115] C.-X. Cai, K.-H. Xue, S.-M. Xu, *J. Electroanal. Chem.* **2000**, *486*, 111.
[116] M. H. Pournaghi Azar, H. R. Nerbin, *J. Electroanal. Chem.* **2000**, *488*, 17.
[117] H. R. Nerbin, M. H. Pournaghi Azar, *J. Solid State Electrochem.* **2002**, *6*, 126.
[118] S. Zhang, F. Huang, X. Cao, P. Yang, W. Zhang, L. Jin, *Analyst* **2002**, *127*, 485.
[119] E. Casero, F. Pariente, E. Lorenzo, *Anal. Bioanal. Chem.* **2003**, *375*, 294.
[120] Q. Xu, S. Zhang, W. Zhang, L. Jin, K. Tanaka, H. Haraguchi, A. Itoh, *Frensius J. Anal. Chem.* **2000**, *367*, 241.
[121] X. Cui, L. Hong, X. Lin, *Anal. Sci.* **2002**, *18*, 543.
[122] S. Milardovic, Z. Grabaric, V. Rumenjak, N. Blau, D. Miloševic, *JAOAC Int.* **2001**, *84*, 1927.
[123] J. Pei, X.-Y. Li, *Talanta* **2000**, *51*, 1107.
[124] J. Pei, X.-Y. Li, J. Buffle, *Electrochim. Acta* **2000**, *45*, 1581.
[125] J. Pei, X.-Y. Li, *Anal. Chim. Acta* **2000**, *414*, 205.
[126] A. Malinauskas, T. Ruzgas, L. Gorton, *J. Coll. Intef. Sci.* **2000**, *224*, 325.
[127] F. D. Munteau, L. T. Kubota, L. Gorton, *J. Electroanal. Chem.* **2001**, *509*, 2.
[128] R. Metelka, K. Vytras, A. Bobrowski, *J. Solid State Electrochem.* **2000**, *4*, 348.
[129] B. Nalini, S. S. Narayanan, *Anal. Chim. Acta* **2000**, *405*, 93.
[130] M. F. Mousavi, A. Rahmani, S. M. Golabi, M. Shamsipur, H. Sharghi, *Talanta* **2001**, *55*, 305.
[131] Y.-T. Kong, G.-H. Choi, M.-S. Won, Y.-B. Shim, *Chem. Lett.* **2002**, 54.
[132] P. Kula, Z. Navrátilová, *Electroanalysis* **2001**, *13*, 795.
[133] M. Chicarro, A. Zapardiel, E. Bermejo, M. Moreno, E. Madrid, *Anal. Bioanal. Chem.* **2002**, *373*, 277.
[134] C. U. Ferreira, Y. Gushikem, L. T. Kubota, *J. Solid State Electrochem.* **2000**, *4*, 298.
[135] G. Zaitseva, Y. Gushikem, E. S. Ribeiro, S. S. Rosatto, *Electrochim. Acta* **2002**, *47*, 1469.
[136] L. Li, W. Li, C. Sun, L. Li, *Electroanalysis* **2002**, *14*, 368.
[137] Z. G. Rong, W. X. Lei, S. X. Wang, S. T. Ling, *Talanta* **2000**, *51*, 1019.
[138] Y.-J. Li, C.-Y. Li, *J. Electroanal. Chem.* **2001**, *517*, 117.
[139] M. I. A. González, S. B. Saidman, M. J. L. Castañón, A. J. M. Ordierer, P. T. Blanco, *Anal. Chem.* **2000**, *72*, 520.
[140] L. Chen, W. Gorski, *Electroanalysis* **2002**, *14*, 78.
[141] N. Mano, A. Kuhn, *Biosen. Bioelect.* **2001**, *16*, 653.
[142] J. Kulys, L. Tetianec, P. Schneider, *Biosen. Bioelect.* **2001**, *16*, 319.
[143] S. Hu, C. Xu, J. Luo, J. Luo, D. Cui, *Anal. Chim. Acta* **2000**, *412*, 55.
[144] M. Tsionsky, J. Gun, V. Glezer, O. Lev, *Anal. Chem.* **1994**, *66*, 1747.
[145] J. Wang, V. A. Prasad, D. S. Park, *Electroanalysis* **1997**, *9*, 52.
[146] J. Wang, V. A. Pamidi, D. S. Park, *Anal. Chem.* **1996**, *68*, 2705.
[147] P. Wang, X. Wang, G. Zhu, *Electroanalysis* **2000**, *12*, 1498.
[148] P. Wang, X. Wang, G. Zhu, *Electrochim. Acta* **2000**, *46*, 637.
[149] P. Wang, X. Wang, X. Jing, G. Zhu, *Anal. Chim. Acta* **2000**, *424*, 51.
[150] P. Wang, X. Wang, G. Zhu, *New J. Chem.* **2000**, *24*, 481.
[151] W. Song, Y. Liu, N. Lu, H. Xu, C. Sun, *Electrochim. Acta* **2000**, *45*, 1639.
[152] B. Wang, L. Cheng, S. Dong, *J. Electroanal. Chem.* **2001**, *516*, 17.
[153] P. Wang, Y. Yuan, Z. Han, G. Zhu, *J. Mater. Sci.* **2001**, *11*, 549.
[154] P. Wang, Y. Yuan, X. Wang, G. Zhu, *J. Electroanal. Chem.* **2000**, *293*, 130.
[155] P. Wang, X. Jing, W. Zhang, G. Zhu, *J. Solid State Electrochem.* **2001**, *5*, 369.
[156] P. Wang, Y. Yuan, X. Jing, G. Zhu, *Talanta* **2001**, *53*, 863.

[157] P. Wang, Y. Yuan, G. Zhu, *Frensius J. Anal. Chem.* **2001**, *369*, 153.

[158] P. Wang, X. Wang, C. Ren, G. Zhu, *J. Mater. Chem.* **2000**, *10*, 2863.

[159] Z. Yang, P. Wang, W. Zhang, G. Zhu, *Frensius J. Anal. Chem.* **2001**, *371*, 337.

[160] Y. Yuan, P. Wang, G. Zhu, *Anal. Bioanal. Chem.* **2002**, *372*, 712.

[161] J. L. Cohen, J. Widera, J. A. Cox, *Electroanalysis* **2002**, *14*, 231.

[162] T. Okada, M. Yoshida, T. Hirose, K. Kasuga, T. Yu, M. Yuasa, I. Sekine, *Electrochim. Acta* **2000**, *45*, 4419.

[163] M. L. Hamlaui, K. Reybier, M. Marrakchi, N. Jaffrezic-Renault, C. Martelet, R. Kherrat, A. Walcarius, *Anal. Chim. Acta* **2002**, *466*, 39.

[164] M. Boujtita, J. P. Hart, R. Pittson, *Biosen. Bioelect.* **2000**, *15*, 257.

[165] B. Wang, S. Dong, *Talanta* **2000**, *51*, 565.

[166] P. Skládal, N. O. Morozova, A. N. Reshetilov, *Biosen. Bioelectr.* **2002**, *17*, 867.

[167] J.-Y. Choi, K. Seo, S.-R. Cho, J.-R. Oh, *Anal. Chim. Acta* **2001**, *443*,241.

[168] E. C. Venancio, W. T. Napporn, A. J. Motheo, *Electrochim. Acta* **2002**, *47*, 1495.

[169] P. J. Kulesza, B. Grzybowska, M. A. Malik, M. Chojak, K. Miecznikowski, *J. Electroanal. Chem.* **2001**, *512*, 110.

[170] J.-M. Zen, A. Senthil Kumar, J.-C. Chen, *Anal. Chem.* **2001**, *73*, 1169.

[171] J.-M. Zen, A. Senthil Kumar, J.-C. Chen, K. Jayachitra, K. Balamurugan, D.-H. Chin, *Analyst* **2001**, *126*, 1409.

[172] J.-M. Zen, A. Senthil Kumar, H.-F. Wang, *Analyst* **2000**, *125*, 2169.

[173] J.-M. Zen, A. Senthil Kumar, H.-P. Chen, *Electroanalysis* in press.

[174] J.-M. Zen, S.-L. Liou, A. Senthil Kumar, M.-S. Hsia, *Angew. Chem. Int. Ed.* **2003**, *42*, 577.

[175] J.-M. Zen, A. Senthil Kumar, H.-W. Chen, *Electroanalysis* **2000**, *12*, 542.

[176] A. Senthil Kumar, P.-Y. Chen, J.-M. Zen, *Electroanalysis* in press.

[177] J.-M. Zen, A. Senthil Kumar, H.-W. Chen, *Electroanalysis* **2001**, *13*, 1171.

[178] J.-M. Zen, P.-Y. Chen, A. Senthil Kumar, *J. Chin. Chem. Soc.* **2002**, *49*, 915.

[179] J.-M. Zen, P.-Y. Chen, A. Senthil Kumar, *Electroanalysis* **2002**, *14*, 513.