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3D origami electrochemical device for sensitive Pb^{2+} testing based on DNA functionalized iron-porphyrinic metal-organic framework

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ABSTRACT

A highly sensitive electrochemical (EC) biosensor combined with a 3D origami device for detection of Pb^{2+} was developed based on novel Au nanoparticles modified paper working electrode (Au-PWE) as sensor platform and DNA functionalized iron-porphyrinic metal-organic framework ((Fe-P)n-MOF-Au-GR) hybrids as signal probes. In the presence of Pb^{2+}, GR could be specifically cleaved at the ribonucleotide (rA) site, which produced the short $(Fe\text{-}P)_n$-MOF-linked oligonucleotide fragment to hybridize with hairpin DNA immobilized on the surface of Au-PWE. Because of the mimic peroxidase property of $(Fe\text{-}P)_n$-MOF, enzymatically amplified electrochemical signal was obtained to offer the sensitive detection of Pb^{2+}. In addition, benefiting from the Pb^{2+} dependent GR, the proposed assay could selectively detect Pb^{2+} in the presence of other metal ions. This method showed a good linear relationship between the current response and the Pb^{2+} concentration ranging from 0.03 to 1000 nmol L^{-1} with a detection limit of 0.02 nmol L^{-1}. The Au-PWE based electrochemical sensor along with the $(Fe\text{-}P)_n$-MOF-Au-GR probe exhibited the advantages of low-cost, simple fabrication, high sensitivity and selectivity, providing potential application of real-time Pb^{2+} detection both in environmental and biological samples.

1. Introduction

Paper is a biocompatible porous cellulose fiber web with large surface area, and the porous nature fulfills the primary tasks such as diagnostic tests using body fluids and fluid transport. Since microfluidic paper-based analytical devices (μ-PADs) were first reported by White sides' group (Martinez et al., 2010) which offered excellent properties (Abe et al., 2008), including low sample and reagent consumption, low cost, small size, portable and easy-to-operate (Martinez et al., 2007), μ-PADs were considered as ideal platforms designed for point-of-care (POC) detection (Manz et al., 1990; Martinez et al., 2008), To make real POC device, not only the production of low-cost and portable devices were required but also the instrument to measure the signal should be portable (Delaney et al., 2011), Efforts have been made to improve the immobilization of bio-recognition substance in paper (Wu et al., 2013) as well as the signal amplification for paper-based assays (Li et al., 2008). Gold nanoparticles (AuNPs) have attracted much attention in different bio-affinity assays due to their unique physical and chemical properties, such as easily controllable size distribution, long-term stability, superior conductivity, large surface area, and biocompatibility (Dai et al., 2010). Taking into consideration the above advantages, a novel porous Au-paper working electrode (Au-PWE) was developed on a compatibly designed microfluidic origami electrochemical (EC) device through the growth of an interconnected AuNPs layer on the surfaces of cellulose fibers in the paper sample zone to enhance the conductivity of the paper sample zone (Wang et al., 2014a, 2014b).

As an emerging class of highly ordered porous materials, metal-organic frameworks (MOFs) have attracted great attention in the last two decades (Li et al., 1999; Mattos et al., 2012). They have great potential applications in many fields, especially in gas storage/separation, sensing, and catalysis. Recently, prominent progress has been made in the application of luminescent MOF for sensing important targets such as cations, anions, small molecules, gas, and vapors (Corma et al., 2010) (Furukawa et al., 2013; Suh et al., 2012). Linker modification is one of the most direct methods for MOF functionalization (Liu et al., 2012; Jiang et al., 2010; Zou et al., 2012; Jin et al., 2014). Porphyrinic ligands are such a category of versatile linkers that have been extensively explored. These porphyrin derivatives play key roles in many chemical and biological processes (Li et al., 2012). For example, MOF created with porphyrin or porphyrin derivatives have been used to catalyze organic reactions (Lu et al., 2014), including olefin epoxidation (Gao et al., 2014) and CO_2/propylene oxide coupling reactions (Ling et al., 2015a, 2015b). Fe(III)-based MOF have been reported to

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exhibit peroxidase-like catalytic activity and used to construct colorimetric biosensing methods for detection of H_2O_2 and ascorbic acid (Feng et al., 2013). Recently, a porous iron-porphyrinic MOF has been synthesized to show peroxidase activity similar to horse radish peroxidase in an organic solvent (Liu et al., 2013). When MOFs work as platforms to immobilize porphyrin groups, their rigid structures with high surface area and porosity can not only make each porphyrin accessible by substrates but also prevent the dimerization of reaction centers, which will block the catalysis pathway (Mckinlay et al., 2010). Because of the versatility of porphyrin and its promising combination with MOFs, extensive synthetic studies have been reported (Kreno et al., 2012).

Recent study also proves that MOFs could be as a promising candidate for the catalyst of the hydrogen evolution reaction (Hu et al., 2014). In particular, MOF possess intrinsic catalytic activity, and were found to catalyze the reduction reaction procedure of hydrogen peroxide (H_2O_2) (Sugikawa et al., 2013). Gold nanoparticles (AuNPs) are the most useful metal nanoparticles in electrochemical biosensors due to their good biocompatibility and easy functionalization with –SH and $–NH_2$, and large specific surface area, good stability and optical properties (Sugikawa et al., 2011). More importantly, AuNPs provided a good pathway of electron transfer and enhanced the immobilized amount of biomolecules. Hereon, the AuNPs can immobilize on the surface of MOF through animation of silicon dioxide, which can linked with much sensor probs. As a consequence, gold nanoparticles functionalized MOF (MOF-Au) was applied in our work.

As a well-known and nondegradable environmental pollutant, lead cation (Pb^{2+}) can accumulate in human body through the food chain and lead to adverse effects on the immune, central nervous, and reproductive systems, particularly in children (He et al., 2006; Lu et al., 2013). Therefore, different Pb^{2+} sensors have been proposed for sensitive detection of Pb^{2+} by using cost-effective Pb^{2+}-dependent DNAzyme (Wang et al., 2013; Wang and Irudayaraj, 2011) This enzyme is quite stable and can remain its activity or binding ability after repeated denaturation and renaturation (Wei et al., 2008). The detection sensitivity of electrochemical sensors (Cao et al., 2013) for Pb^{2+} can be improved by replacing small redox molecules with signal amplification strategies by employing inorganic nanoparticles combined with additional amplification processes, such as surface preconcentration (Lin et al., 2011) or enzymatic recycling (Tang et al., 2013; Zhang et al., 2015). However, these amplification ways usually need long detection time, and the native enzymes suffer from the certain disadvantages of time-consuming separation and purification, high cost, easy denaturation, and being susceptible to environmental conditions (Chad et al., 2003). Thus, a new detection strategy to produce more signal products with cost efficient and stable enzyme mimic has been considered as another opportunity for electrochemical detection of Pb^{2+} (Gilad et al., 2012; Xiang et al., 2009; Cui et al., 2015).

In the present work, a highly sensitive and selective electrochemical sensor for Pb^{2+} was proposed with a newly designed DNA functionalized iron-porphyrinic MOF. The stable $(Fe\text{-}P)_n$-MOF could produce multisignal species to achieve the high sensitivity, while the GR which was linked to $(Fe\text{-}P)_n$-MOF via the Au nanoparticles (AuNPs), achieved the high selectivity of this method. The good performance showed its potential application for the detection of Pb^{2+} in different environments.

2. Experimental methods

2.1. Preparation of the 3D origami EC device and Au-PWE

The preparation of the 3D origami EC device was similar to our previous work (Martinez et al., 2008) and a detailed procedure was described in Supporting Information. As shown in Scheme 1A, the Au-PWE was fabricated through growth of an Au NPs layer on the surfaces of cellulose fibers in the paper sample zone of PWE to enhance the conductivity and enlarge the effective surface area of bare PWE. The fabrication procedures of the porous Au-PWE were described as follows: First, The suspension of AuNP seeds was prepared by using $NH_4OH \cdot HCl$ as reductant and stabilized with sodium citrate according to the literature. (Busbee et al., 2003) Then, 15.0 μL as-prepared AuNP seeds solution were dropped into the paper sample zone of bare PWE (Scheme 1A), respectively. Then the origami device was equilibrated at room temperature for 1 h to optimize the surface immobilization of AuNP seeds on cellulose fibers. After rinsing with water thoroughly to remove loosely bound AuNP seeds, 15 μL freshly prepared growth aqueous solution of 0.01 mol L^{-1} PBS (pH 7.0) containing 1.2 mmol L^{-1} $HAuCl_4$, 2.0 mmol L^{-1} cetyltrimethylammonium chloride and 7.2 mmol L^{-1} H_2O_2 for seeds growth were applied into the AuNP seeded PWE, and incubated at room temperature for 10 min. Subsequently, the resulting porous Au-PWE was washed with water thoroughly. Thus a layer of interconnected AuNPs on cellulose fibers with good conductivity were obtained (Scheme 1A), which were dried at room temperature for 20 min

2.2. Preparation of (Fe-P)n-MOF and $(Fe\text{-}P)_n$-MOF-Au-GR

The $(Fe\text{-}P)_n$-MOF and $(Fe\text{-}P)_n$-MOF-Au-GR were prepared according to the literature with slight modification: (Jahan et al., 2012; Cui et al., 2015) TMPP (30.22 mg), $FeCl_3 \cdot 6H_2O$ (35.45 mg) and HCl (0.8 mL, 0.1 mol L^{-1} in ethanol) were homogeneously dissolved in a mixture of 3 mL of DMF and 6 mL of ethanol with assistance of sonication treatment. The final mixture was placed into a 40 mL Teflon stainless vessel and was then thermally treated at 150 °C in an oven for 36 h, followed by slow cooling to room temperature. The crystals were collected via filtration and washed with DMF and ethanol, then dried at 60 °C in a vacuum oven.

First, $(Fe\text{-}P)_n$-MOF (4.0 mg) was dispersed in 1 mL of ethanol. This dispersion was added to a mixture of 0.20 mL of ammonium hydroxide (1.00 mol L^{-1}) and 11.3 mL ethanol, and then TEOS (1.5 mL, 6.0 mmol L^{-1}) was added. After the mixture was stirred for reaction at room temperature for 2 h, the products were harvested by centrifuging and washing three times with ethanol and dried under vacuum overnight to get the SiO_2 coated $(Fe\text{-}P)_n$-MOF composite. Then, 4 mg of SiO_2 coated $(Fe\text{-}P)_n$-MOF was added into 4 mL of 20 mmol L^{-1} MPTS ethanol solution and refluxed at 65 °C for 3 h. After centrifugation and washing several times with ultrapure water, the $(Fe\text{-}P)_n$-MOF modified with MPTS was dried at 50 °C for 12 h. The MPTS modified $(Fe\text{-}P)_n$-MOF was further modified with AuNPs by mixing 4 mL of AuNPs (13 nm diameter) solution with 2 mL of MPTS modified $(Fe\text{-}P)_n$-MOF (1 mg mL^{-1}) and shaking vigorously for 2 h. The formed $(Fe\text{-}P)_n$-MOF-Au composite was collected by centrifugation, washed with ultrapure water three times, and dispersed in 6 mL of 50 mmol L^{-1} Tris-acetate buffer (pH 7.0).

A volume of 100 μL of GR (10 μmol L^{-1}, in 50 mmol L^{-1} pH 8.2 Trisacetate buffer containing 300 mmol L^{-1} NaCl) was heated at 95 °C for 10 min and then cooled to room temperature. After the treated GR was activated with 5 μL of 10 mmol L^{-1} TCEP to reduce disulfide bond, it was mixed with 500 μL of $(Fe\text{-}P)_n$-MOF-Au suspension to incubated for 24 h at room temperature to obtain $(Fe\text{-}P)_n$-MOF-Au-GR probe, which was blocked with 1% BSA for 1 h and dispersed in 500 μL of 50 mmol L^{-1} Tris-acetate buffer (containing 300 mmol L^{-1} NaCl, pH 7.0) to store at 4 °C before use (as shown in Scheme 1B).