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Bimetallic NiFe oxide structures derived from hollow NiFe Prussian blue nanobox for label-free electrochemical biosensing adenosine triphosphate

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ABSTRACT

We designed and constructed a novel aptasensor based on the porous nanostructured bimetallic NiFe-oxides embedded with the mesoporous carbon (represented by NiO_xFeO_y@mC) for sensitively detecting adenosine triphosphate (ATP), of which the porous NiO_xFeO_y@mC was derived from the hollow NiFe Prussian blue analogue (hollow NiFe PBA) by calcinating under high temperature. Owning to the excellent electrochemical activity originated from the metal oxides and mesoporous carbon and the strong binding interaction between the aptamer strands and the nanostructure hybrid, the formed porous NiO_xFeO_y@mC composite calcinated at 900 °C exhibited superior sensitivity toward ATP determination in comparison with other porous nanocubes obtained at 500 and 700 °C. The proposed aptasensor not only revealed a wide linear range from 5.0 fg·mL^{-1} to 5.0 ng mL^{-1} with a extremely low detection limit of 0.98 fg·mL^{-1} (1.62 fM) (S/N = 3), but also displayed high selectivity towards other interferences, good stability and reproducibility, and acceptable applicability. Therefore, this proposed approach provides a promising platform for ultra-sensitive detection of ATP, further having the potential applications on diagnosis of ATP-related diseases.

1. Introduction

Adenosine triphosphate (ATP), the primary energy currency, dominates the cellular energy state and regulates cellular metabolism, which can be as an indicator for cell injury, tumors and many diseases (Peng et al., 2018). Early detection of ATP is extremely important in clinical diagnosis, and much attention has been paid to the development of new technologies to determine early signs of various diseases (Berg et al., 2015; Dong et al., 2016; Lai et al., 2017; Wei et al., 2015; Zhang et al., 2016a). Normally, a complex hairpin aptamer probe (AP) was designed by integrating the ATP aptamer to determine ATP by fluorescence spectroscopy (Shrivastava et al., 2017; Wang et al., 2017), electrochemical methods (Xie et al., 2017), ratiometric surface-enhanced Raman spectroscopy (Wu et al., 2017), and colorimetric approaches (Gao et al., 2017). Notwithstanding many efforts were done to fabricate the sensitive AP-based ATP biosensor, it still remains challenges owning to their disadvantages, such as the complicated aptamer strands design and fussy determination procedure.

Recently, owing to the large surface area, tunable porosity, organic functionality, and high thermal stability, metal-organic frameworks (MOFs) composed of metal ions or clusters linked by organic ligands have received increased scientific and technological interest, such as energy, environment, material and biology (Cui et al., 2016; Li and Huo, 2015). MOFs can also be thermally transformed into metals, metal oxides, carbon materials and other components with the desired structure in a facile manner (Zhao et al., 2017). It is clear for MOFs-derived composites that they exhibit good electrochemical performances because of the rich content of mesoporous carbon, metal oxides and porous structure. For example, the cobalt oxide hollow nanododecahedra synthesized by a facile thermal transformation of Co-MOF template exhibited high activity and showed an outstanding performance for determining glucose (Zhang et al., 2016b). Ni/NiO/C composites prepared by successively thermal annealing Ni-MOFs was employed as the matrix of myoglobin/hemoglobin immobilization to fabricate enzyme-based biosensor for the detection of nitrite (NO_2^-) (Liu et al., 2017b). Fe_3O_4@mC derived from an Fe(II)-MOF was developed as a scaffold for oxytetracycline aptamer strands (Song et al., 2017). Despite the progress achieved to date, research on the facile

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synthesis of bimetallic nanostructured inorganic functional materials derived from MOFs is still in its very early stage. As one kind of MOFs, Prussian blue (PB) or Prussian blue analogue (PBA) can easily form a nanocube morphology in the preparation process and composed of transition metals as metallic nodes and CN^- groups as linkers, provides an ideal template or precursor to prepare composite materials with well-defined structure and highly nitrogen-doped carbon (Ye et al., 2014). Earlier oxidative thermal decomposition studies of PB and PBAs showed potential applications in the field of electrocatalysts (Du et al., 2017; Guo et al., 2017; Li et al., 2017). Although various PBAs were employed to fabricate the electrochemical biosensors (Azadbakht et al., 2016; Chu et al., 2017; Zhang et al., 2017), to the best of our knowledge, studies on hollow PBA-derived bimetallic oxides embedded within the mesoporous carbon composites for detecting ATP applications have not been reported.

The motivation of our work is to construct a novel ATP aptasensor based on a hollow bimetallic NiFe oxides with various nanostructures by simple annealing the hollow NiFe PBA nanoboxes. Owning to high surface area, mesoporous three dimensional structure, and exposure of electrochemically active sites, NiFe Prussian blue analogue (NiFe-PBA) MOF was employed to develop mesoporous NiFe-oxide nanocube or bimetallic phosphide catalyst, and further explored as bifunctional and stable electrocatalysts for splitting water or oxygen evolution reaction (Kumar and Bhattacharyya, 2017; Zou et al., 2017). As illustrated in Scheme 1, the FeFe@NiFe PBA nanocubes were prepared by using the FeFe PB as template. When removing the FeFe template, the hollow NiFe PBA nanoboxes were produced following by being calcinated under different high temperatures. As anticipated, the formed hollow bimetallic NiFe oxides nanoparticles were embedded within the mesoporous carbon matrix (porous NiO_xFeO_y@mC), which not only exhibited excellent electrochemical activity but also possessed strong binding interaction toward the oligonucleotide strands. Due to the porous nanostructure of the as-prepared NiO_xFeO_y@mC, the aptamer strands can be immobilized both in the interior of the composite and onto the surface. As reported by Liu et al., aptamer strands immobilization can be achieved mainly via π–π stacking interactions between DNA nucleobases and nucleosides and mesoporous carbon (Liu et al., 2011). Additionally, aptamer strands also can be adsorbed onto the metal oxide nanoparticles via the phosphate backbone (Liu and Liu, 2015). Subsequently, the aptamer strands would reconfigure their conformation to G-quadruplex structure to recognize ATP molecules. As compared with the routine platform nanomaterials, the fabricated aptasensor based on hollow NiO_xFeO_y@mC nanoboxes showed excellent sensitivity, selectivity and stability for detecting trace analyte, due to the combined advantages of synergistic effect originated from the multiple components and the hollow nanostructure. The present strategy can not only provide a promising platform for ultra-sensitive detection of ATP but also broaden the applications of MOFs in diagnosis of ATP-related diseases, monitoring of diseases progression and evaluation of prognosis.

2. Experimental section

All of the reagents were of analytical purity grade and used as received. FeFe PB seeds, NiFe PBA seeds and FeFe@NiFe PBA nanocubes were synthesized according to the literature (Cai et al., 2016). The preparation procedures of these samples were shown in **Experimental section** of Supporting Information.

2.1. Synthesis of hollow NiFe PBA nanoboxes

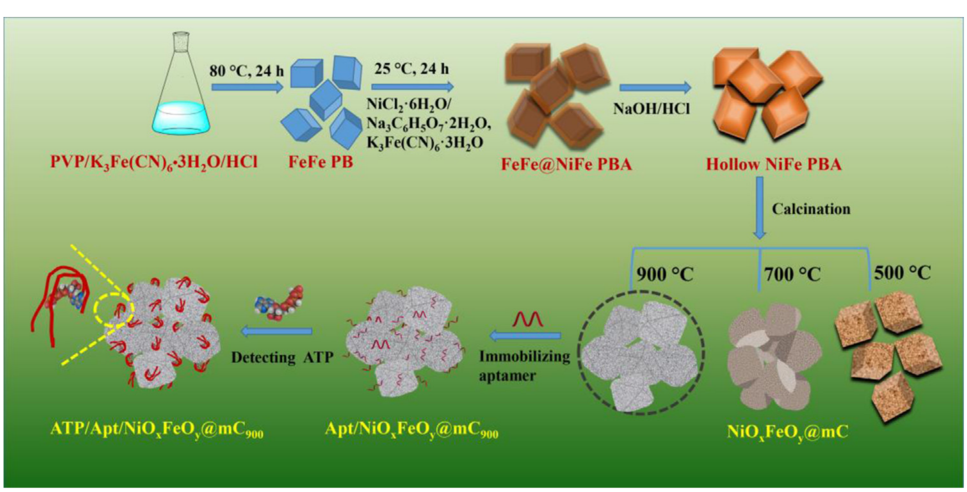
Firstly, 15 mL of the FeFe@NiFe PBA nanocubes suspension in ethanol was mixed with NaOH solution (15 mL, 0.1 M). Afterward, the mixture was shaken by hand for 5 min until the mixture color turned yellow. The as-prepared product was collected by centrifugation and washed with distilled water and ethanol for several times. Secondly, the as-prepared $Fe(OH)_3$@NiFe PBA composites were dispersed into 30 mL of Milli-Q water, following by the addition of 2.5 mL of concentrated hydrochloric acid. The $Fe(OH)_3$ core of the $Fe(OH)_3$@NiFe PBA was removed, leading to the formation of the hollow NiFe PBA nanobox. After stirring for 20 min, the obtained product was collected by centrifugation and washed with distilled water and ethanol for several times.

2.2. Synthesis of the series of NiO_xFeO_y@mC composites

In typical, a series of NiO_xFeO_y@mC composites were obtained by annealing hollow NiFe PBA nanoboxes in a tube furnace under Ar flow at 500, 700, and 900 °C for 2 h with the heating rate of 5 °C min^{-1}. In this step, the samples were cooled down to room temperature in Ar atmosphere and are denoted as porous NiO_xFeO_y@mC_{500}, NiO_xFeO_y@mC_{700}, and NiO_xFeO_y @mC_{900} in according to the pyrolysis temperature of 500, 700, and 900 °C, respectively. The basic characterizations for chemical and crystal structures of all samples are shown in the part of S2 (see Supporting Information).

2.3. Fabrication of ATP aptasensors based on the as-prepared samples

As for the fabrication of NiO_xFeO_y@mC_{900}-based aptasensor, the NiO_xFeO_y@mC_{900} powder (0.5 mg) was dispersed in 1.0 mL of Milli-Q water and thoroughly mixed using ultrasound until the homogeneous NiO_xFeO_y@mC_{900} suspension was obtained. Then, NiO_xFeO_y@mC_{900}



Scheme 1. The schematic diagram of the construction of the NiO_xFeO_y@mC-based aptasensor for detecting ATP.