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A ratiometric electrochemical deoxyribonucleic acid sensing strategy based on self-signal of highly stable reduced graphene oxide-flavin mononucleotide aqueous dispersion modified nanointerface

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ABSTRACT

A label-free ratiometric electrochemical DNA sensing strategy was established by simultaneously adopting the self-redox signal of electrode interface and signal of electrochemical indicator as ratiometric signals together. The sodium salt of flavin mononucleotide (FMNs)/reduced graphene oxide(rGO) nanocomposite was prepared by simple ultrasonication method. The obtained FMNs/rGO possesses high water dispersion and good electrochemical redox signal. FMNs/rGO was further applied as the electrode modification material to immobilize DNA probe and provide the self-redox signal for DNA detection, while the electrochemical indicator Meldola's Blue (MDB) was served as another detection signal. With the increase of target DNA concentration, the self-redox signal of the FMNs/rGO would decrease due to the formation of more DNA duplex, while more MDB would combine with the DNA duplex and resulted in higher signal of MDB. By measuring the ratios of the two signals, this novel ratiometric strategy effectively improved the reproducibility and reliability while avoided using expensive and complicated redox labels on DNA.

1. Introduction

Ratiometric electrochemical sensors (E-sensors) obviously improved the performance of classic electrochemical sensors. Based on this technique, more excellent detection performances, such as higher reproducibility, better selectivity, lower detection limit and wider linear range were realized [1,2]. For example, Sessler et al. designed a ratiometric DNA E-sensor by simultaneously labeling the methylene blue (MB) and ferrocene (Fc) as two redox tags on hairpin DNA. With the application of ratiometric technique, the reproducibility and credibility of electrochemical sensors were obviously improved [3]. Gao et al. reported a ratiometric DNA E-sensor based on the labeling technique and circular strand displacement strategy, which exhibited more excellent selectivity compared with single signal E-sensors [4]. Chen et al. designed a ratiometric DNA E-sensor by using MB and Fc labeled hairpin DNA capture probe and Exo III-assisted signal amplification strategy and realized lower detection limit and wider linear range [5]. These label-based ratiometric DNA E-sensors have successfully proved that the application of ratiometry could yield better detection properties compared with classic E-sensors. But what must be pointed out is that due to the application of labeling technique, the fabrication of these sensors is usually expensive, complex and time-consuming, which negated some advantages of E-sensor such as simple, chap and point of care [6]. Thus, these shortages may limit the applications of these ratiometric DNA E-sensors.

Due to advantages such as label-free, direct, cheap, simple, the redox signal of sensing interfaces is also frequently applied in fabricating E-sensors. For example, Ma et al. employed the oxide peaks of gold-decorated polyaniline derivatives to construct a label-free electrochemical immunosensor for simultaneous detection of three lung cancer biomarkers [7]. Chen et al. designed an electrochemical tumor marker sensor based on the self-signal of different redox substrates for label-free and reagentless detection of two biomarkers [8]. The self-redox signal of electrode interface also has been applied in ratiometric E-sensors. For DNA E-sensor, Zhang et al. applied poly(xanthurenic acid) functional-

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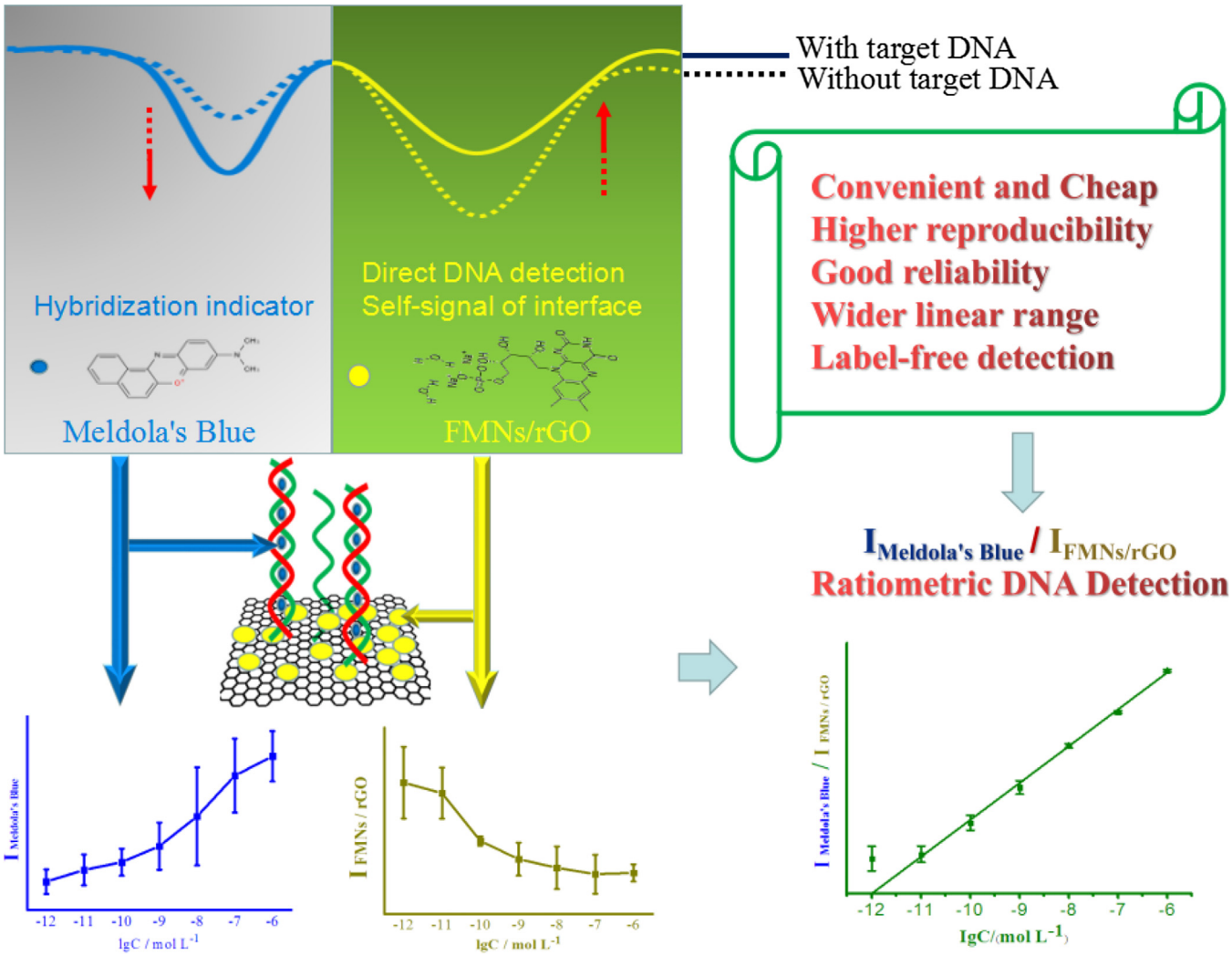

Fig. 1. The schematic illustration of the label-free ratiometric electrochemical strategy.

ized FePt/reduced graphene oxide to construct a DNA monitoring platform. Accompanied with the self-signal of poly(xanthurenic acid) functionalized FePt/reduced graphene oxide nanocomposite, sensitive detection performance was realized [9]. Our group also fabricated a novel DNA E-sensor based on reduced graphene oxide-poly(m-aminobenzenesulfonic acid) for direct and freely switchable detection of target DNA [10]. For the ratiometric E-sensors, Wei et al. fabricated a ratiometric ascorbic acid E-sensor by adopting the self-redox signal of thionine/Ketjen black nanocomposite [11] So, we can infer that the self-redox signal of nanointerface could be successful applied in fabricating ratiometric ratiometric DNA E-sensors which is label-free. To our best knowledge, none ratiometric DNA E-sensors based on self-signal have been reported up to now.

The sodium salt of flavin mononucleotide (FMNs) was proved as an efficient dispersant and stabilizer for dispersing concentrated aqueous dispersion of graphene flakes [12]. Besides, the FMNs/Graphene nanocomposite also possesses excellent inherent electrochemical activities. In this work, the reduced graphene oxide (rGO) was applied to replace the Graphene to prepare a novel FMNs/rGO nanocomposite and further construct a label-free ratiometric DNA E-sensor with the assistance of the electrochemical hybridization indicator, Meldola's Blue (MDB) [13,14]. While the probe DNA immobilized on electrode surface hybridized with target DNA, the self-signal of FMNs/rGO was reduced due to the formation of DNA duplex which obstructed the effective electron transfer channel [10]. Besides, MDB could combine with the duplex, which was typical behavior for this mediator [14]. Thus, more DNA duplex would cause the signal increase of MDB. By measuring the ratio of the two signals, direct and label-free DNA detection was realized with high reproducibility (Fig. 1).

2. Experimental section

2.1. Apparatus and reagents

All electrochemical measurements were carried out with a CHI 840D electrochemical workstation (Shanghai CH Instrument Company, China) with a conventional three-electrode cell: A carbon paste electrode (CPE) or modified CPE was used as the working electrode. A saturated calomel electrode and a platinum wire were separately used as the reference and auxiliary electrodes. The pH values of all solutions were determined by a pHS-25 digital acidimeter (Shanghai Leici Factory, China). The morphologies of the resulted materials were characterized by a scanning electron microscopy (SEM, JSM-6700F, JEOL, Japan) and a transmission electron microscopy (TEM, JEM 2100, JEOL, Japan). Fourier transform infrared spectroscopy (FT-IR) was obtained from a Tensor 27 FT-IR spectrophotometer (Bruker, Germany).