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# Hybridization biosensor using 2,9-dimethyl-1,10-phenantroline cobalt as electrochemical indicator for detection of hepatitis B virus DNA

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**Abstract**

A label-free biosensor for the detection of oligonucleotides related to hepatitis B virus sequence via the interactions of DNA with redox-active complex, 2,9-dimethyl-1,10-phenantroline cobalt [Co(dmp)($H_2O$)($NO_3$)$_2$] is described. The study was carried out by the hybridization of 21-mer probe DNA modified on glassy carbon electrode (GCE) with target DNA, and [Co(dmp)($H_2O$)($NO_3$)$_2$] whose sizes are comparable to those of the small groove of native double-helix DNA was used as an electrochemical indicator. Electrochemical detection was performed by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) over the potential range where the [Co(dmp)($H_2O$)($NO_3$)$_2$] was active. Under the optimum conditions, the electrical signal had a linear relationship with the concentration of target DNA ranging from $3.96\times10^{-7}$ to $1.32\times10^{-6}$ M, and the detection limit was $1.94\times10^{-8}$ M (S/N=3). The biosensor has good selectivity by detecting the three-base mismatch sequence ssDNA.


*Keywords:* Hepatitis B virus; 2,9-Dimethyl-1,10-phenanthroline cobalt; Electrochemical indicator; DNA biosensor

## 1. Introdution

DNA biosensor for the detection of short sequence DNA makes it possible for people to study organism in molecular level, so it has become an important topic in the fields of gene mutation, disease diagnosis, drug screening, and forensic activation analysis [1–6]. Compared with nearly all other analytical techniques, electrochemical detection assays have the advantage of being inexpensive, robust and relatively simple to operate. On this basis alone, electrochemical biosensors for DNA hybridization present attractive prospects for real-world clinical applications which represent a substantial driver to achieve reliable, sensitive, quantitative detection of DNA hybridization [7]. Electrochemical sensors based on impedance [8–10] or voltammetry [11,12] have been reported. And in recent years, conducting copolymer [13–17] and metal nanoparticles [18–20] have been applied for electrochemical DNA sensors with high sensitivities.

Electrochemical DNA biosensors commonly rely on the conversion of the hybridization event into useful electrical signals. Barton and co-workers had developed an electrochemical DNA detector that can detect single-base pair mismatches without requiring any stringent washings. The concept relies on long-range charge transfer through DNA helix [21–23]. Electrons have been shown to transfer through DNA helix, but not through single stranded DNA, to the intercalator at the distal end of the DNA [24]. The recognition capabilities of DNA through hybridization reactions are well established, but adequate transducers are needed to generate a physically measurable signal from the hybridization events. For this purpose, various electroactive metal complexes with rigid bidentate ligands, such as 1,10-phenanthroline or 2,2′-bipyridyl were often investigated because the mode of the interaction between these complexes and DNA are intercalative or electrostatic which could make more stable biosensors due to their potential application in the molecular recognition of nucleic acids [25–31]. Transition metal complexes using 1,10-phenanthroline as ligands are capable of selectively binding DNA through intercalation [32–34]. Cobalt complexes have the interesting characteristics of metallointercalation and

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DNA cleaving properties [35]. The interactions between the complexes and DNA were studied via electrochemical methods [36,37].

One recent focus in our group has been the searching for more efficient and sensitive electroactive indicators for the direct monitoring of DNA hybridization/recognition events [38–41]. In present work, an electrochemical transducers have been developed for monitoring the hybridization event of HBV DNA fragments in connection with electroactive hybridization indicators, $[Co(dmp)(H_2O)(NO_3)_2]$. We attempted to determine the nature of the interaction between DNA and the complex, because the planar aromatic ring of the ligand may enhance the interaction with DNA via intercalation and hydrogen-bonding interaction. Under the optimal conditions, the HBV DNA could be quantified over the range from $3.96\times10^{-7}$ M to $1.32\times10^{-6}$ M, and a detection limit of $1.94\times10^{-8}$ M.

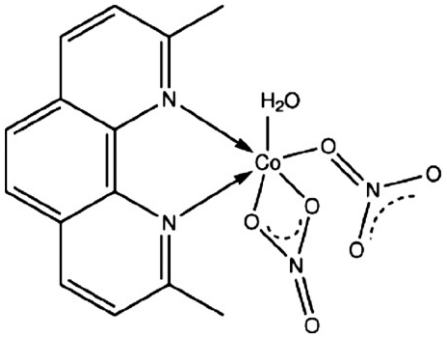
## 2. Experimental

### 2.1. Materials

The complex of $[Co(dmp)(H_2O)(NO_3)_2]$ (Scheme 1) was prepared as described in the literature [42]. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide solution (EDC) and *N*-hydroxysuccinimide solution (NHS) were purchased from Sigma and used without further purification. Double-stranded salmon sperm DNA (dsDNA) were purchased from Shanghai Huashun Biological Engineering Company ($A_{260}/A_{280}>1.8$). The 21-mer synthetic oligonucleotided for the HBV were purchased from the SBS Genetech company (Beijing, China), with the following base sequences:

- immobilized probe sequence ($S_1$): 5′-GAG-GAG-TTG-GGG-GAG-CAC-ATT-3′.
- target sequence ($S_2$): 5′-AAT-GTG-CTC-CCC-CAA-CTC-CTC-3′.
- three-base mismatch sequence ($S_3$): 5′-AAT-GTG-CTC-*T*CC-*GG*A-CTC-CTC-3′.

All stock solutions of the 21-base oligonucleotides ($100\ \mu g\cdot mL^{-1}$) and salmon sperm DNA were dissolved in Tris-EDTA buffer (TE, pH 8.00). The concentration of dsDNA was determined by the ultraviolet absorption at 260 nm ($\varepsilon=6600\ L\cdot mol^{-1}\cdot cm^{-1}$). 0.10 M NaOAc–HOAc buffer solution (pH 4.60), 50 mM $Na_2HPO_4$–$NaH_2PO_4$ buffer solution (pH 7.40), and 20 mM Tris–HCl buffer solution (pH 7.00) were used in this work. Other chemicals were all of analytical grade. All solutions were prepared with doubly distilled water throughout.




Scheme 1. The molecular structure of $[Co(NO_3)_2(C_{14}H_{12}N_2)(H_2O)]$.

### 2.2. Apparatus

All electrochemical experiments were performed by using CHI 832B and 660C electrochemical analyzer (ChenHua Instruments, China) with a three-electrode system consisted of a platinum wire that served as an auxiliary electrode, an Ag/AgCl electrode as reference electrode, and a GCE (a geometric area of 0.071 $cm^2$) as working electrode. All potentials are reported versus Ag/AgCl reference at room temperature.

### 2.3. Electrochemical studies of the interaction between $[Co(dmp)(H_2O)(NO_3)_2]$ and dsDNA

Appropriate amount of $[Co(dmp)(H_2O)(NO_3)_2]$ solution were added to 2 mL of 0.10 M NaOAc–HOAc buffer solution (pH 4.60), and then different quantities of dsDNA were added to the solution followed by recording the cyclic voltammetry (CV) and differential pulse voltammetry (DPV) curves. For CV scanning, the potential scanning range was from −0.20 V to 0.40 V, the scanning rate was $0.10\ V\cdot s^{-1}$. For DPV, the initial potential was −0.20 V, the final potential was 0.40 V, amplitude was 0.05 V.

### 2.4. The fabrication of biosensor

#### 2.4.1. Covalent immobilization of probe DNA

The GCE was polished with 1.0, 0.3 and 0.05 μm alumina, respectively, sonicated in doubly distilled water, ethanol, and oxidized at +0.50 V for 1 min in 50 mM phosphate buffer (PBS, pH 7.40) followed by thorough rinse with DDW. The electrode was inverted and activated by evaporation to dryness of 20 μL of a solution containing 5 mM DEC and 8 mM NHS in 50 mM phosphate buffer (pH 7.00). After rinsing, ssDNA ($S_1$) was then coupled to the surface by evaporating to dryness 20 μL of $1\ mg\cdot mL^{-1}$ ssDNA in the TE buffer. The electrode was rinsed with water to eliminate the absorbed ssDNA. Electrodes thus modified was rinsed and stored in 20 mM Tris–HCl buffer (pH 7.00) at 4 °C.

#### 2.4.2. Hybridization reaction

Hybridizations were performed at 42 °C by immersing the ssDNA-immobilized electrode to 2 mL of 20 mM Tris–HCl buffer solution (pH 7.00) containing the complementary ssDNA ($S_2$), or three-base mismatched ssDNA ($S_3$). And the dsDNA-immobilized electrode was washed with Tris–HCl buffer and then water to remove ssDNA bound nonspecifically.

#### 2.4.3. Indicator binding to the hybrid

The $[Co(dmp)(H_2O)(NO_3)_2]$ was accumulated onto the hybrid by immersing the electrode into the stirred 0.10 M NaOAc–HOAc buffer solution (pH 4.60) containing $4.0\times10^{-4}$ M $[Co(dmp)(H_2O)(NO_3)_2]$ for 20 min.

### 2.5. Electrochemical detection

After the modified electrode was rinsed with the Tris–HCl buffer to eliminate the [Co(dmp)($H_2O$)($NO_3$)$_2$] adsorbed on the electrode surface, the accumulated [Co(dmp)($H_2O$)($NO_3$)$_2$] was measured by CV and DPV using electrochemical analyzer in the 0.10 M NaOAc–HOAc buffer solution.

Electrochemical impedance measurements were perform in a solution of 0.1 M KCl containing 10 mM $Fe(CN)_6^{-3}$/$Fe(CN)_6^{-4}$ with the frequencies ranging from $10^5$ to $10^{-2}$ Hz.

## 3. Results and discussion

### 3.1. Electrochemical study on the interaction between [Co(dmp)($H_2O$)($NO_3$)$_2$] and dsDNA

To explore the application of [Co(dmp)($H_2O$)($NO_3$)$_2$] in electrochemical DNA biosensors, an electrochemical study on [Co(dmp)($H_2O$)($NO_3$)$_2$] and its interaction with dsDNA was performed at room temperature. Typical CVs of [Co(dmp)($H_2O$)($NO_3$)$_2$] in the absence and presence of dsDNA are showed in Fig. 1. There was a reversible redox peak in the range of −0.2–0.4 V. The anodic peak potential $E_{pa}$ and the cathodic peak potential $E_{pc}$ were 0.155 and 0.119 V (curve a), respectively, then the separation of the anodic and the cathodic peak potentials ($\Delta E_p$) was 36 mV, and its formal potential $E^0$, take as the average of $E_{pa}$ and $E_{pc}$, was 0.137 V. It was observed that the peak current of complex was greatly decreased with addition of dsDNA and no new redox peaks appeared after adding dsDNA (curve b). The peak potential shifted positively a little, so the initial conclusion can be drawn that [Co(dmp)($H_2O$)($NO_3$)$_2$] was interacted with the dsDNA in solution.

The phenomena mentioned above were further studied by DPV, as shown in Fig. 2. The curve a is the voltammogram of the [Co(dmp)($H_2O$)($NO_3$)$_2$] solution in the absence of dsDNA, while the curves b, c and d were the results when [Co(dmp)($H_2O$)($NO_3$)$_2$] interact with different concentrations of dsDNA for 20 min. It was can be seen from the figure that the peak current

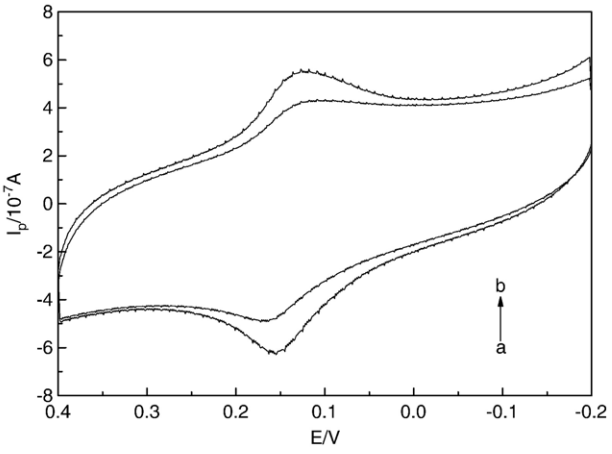



Fig. 1. The cyclic voltammograms of $3.27\times10^{-4}$ M [Co(dmp)($H_2O$)($NO_3$)$_2$] before and after the addition of dsDNA in a 0.10 M NaOAc–HOAc buffer (pH 4.60) at 200 mV·s$^{-1}$. $C_{dsDNA}$: (a) 0, (b) $8.75\times10^{-6}$ M.

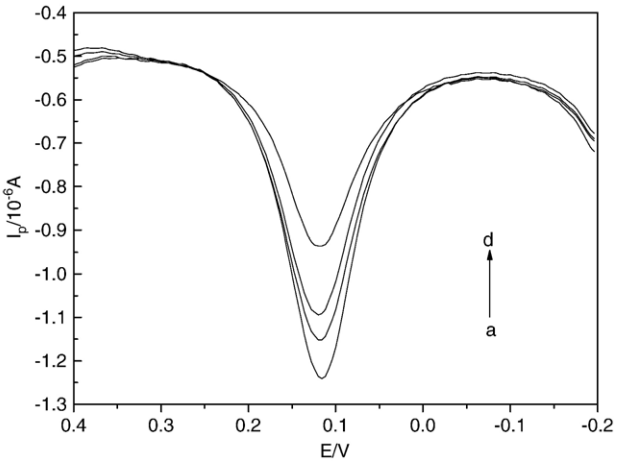



Fig. 2. The DPV of $2.02\times10^{-4}$ M [Co(dmp)($H_2O$)($NO_3$)$_2$] with different concentrations of dsDNA ($10^{-5}$ M) in a 0.10 M NaOAc–HOAc buffer (pH 4.60): (a) 0, (b) 0.84, (c) 1.68, (d) 3.36.

decreased with the increasing of the concentration of dsDNA. This strongly demonstrated that the interaction of [Co(dmp)($H_2O$)($NO_3$)$_2$] with dsDNA occurred. When the concentration of dsDNA came to some extent, the anodic peak of [Co(dmp)($H_2O$)($NO_3$)$_2$] would reach a constant value, indicating that [Co(dmp)($H_2O$)($NO_3$)$_2$] in the 0.10 M NaOAc–HOAc buffer solution interacted completely with dsDNA. The anodic peak potential also shifted positively a little.

### 3.2. Optimization of experimental parameters

The influence of experimental parameters including the pH value of NaOAc–HOAc buffer solution and the [Co(dmp)($H_2O$)($NO_3$)$_2$] accumulation time on the sensitivity of the present method were explored for optimum analytical performance. PH 4.60 and an incubation time of 20 min were adopted with the maximum peak current.

### 3.3. Characterizaton of the biosensor fabrication

The CV (A) and DPV (B) curves for [Co(dmp)($H_2O$)($NO_3$)$_2$] at a concentration of $6.02\times10^{-4}$ M were shown in Fig. 3. The peak currents decreased in the order of bare GCE (curve a), ssDNA/GCE (curve b) and dsDNA/GCE (curve c) with the potentials shifted positively a little. The changes in the current signal were more pronounced for the dsDNA than for the single ssDNA. The decreases were attributed to the accumulation of the indicators at the electrode surface as a result of the different interaction of the planar ring between the ssDNA and dsDNA. The electrochemically active metal centers of [Co(dmp)($H_2O$)($NO_3$)$_2$] were enveloped by the bulky DNA molecule on the GCE surface and the signal of [Co(dmp)($H_2O$)($NO_3$)$_2$] was thus reduced. Because of the dsDNA helix, the [Co(dmp)($H_2O$)($NO_3$)$_2$] intercalated only into the dsDNA but not into the ssDNA. In addition, this proved that ssDNA or dsDNA could be immobilized on the GCE surface, and the target ssDNA was hybridized with the probe ssDNA. The peak current for [Co(dmp)

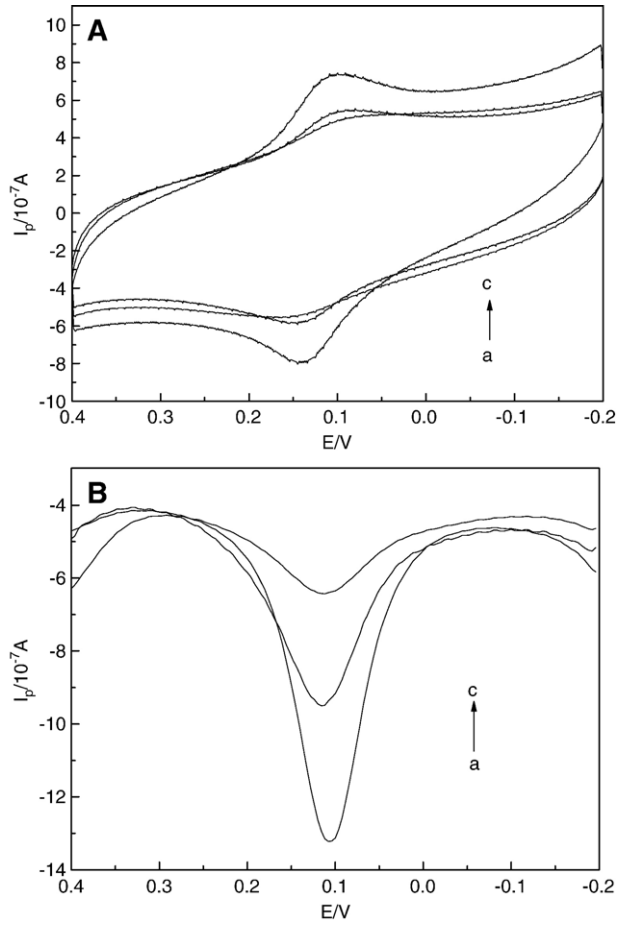



Fig. 3. The cyclic voltammograms (A) and the differential pulse voltammograms (B)of bare GCE (a), ssDNA/GCE (b) and dsDNA/GCE (c) in a 0.10 M NaOAc–HOAc buffer (pH 4.60) containing $6.02\times10^{-3}$ M $[Co(dmp)(H_2O)(NO_3)_2]$.

$(H_2O)(NO_3)_2]$ would come to a constant value at ssDNA/GCE or dsDNA/GCE soak for more than 20 min.

Electrochemical impedance spectroscopy (EIS) was also applied to monitor the whole procedure in preparing modified

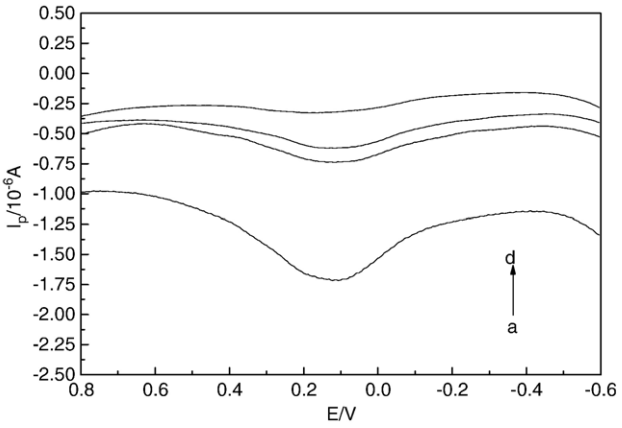



Fig. 5. The differential pulse voltammograms of $[Co(dmp)(H_2O)(NO_3)_2]$ on $S_1$–$S_2$/GCE (a); $S_1$–$S_3$/GCE (b); $S_1$/GCE (c) and bare GCE (d) in a 0.10 M NaOAc–HOAc buffer (pH 4.60).

electrodes, which could provide useful information for probing the changes of the surface modification in the modification process. The curve of the EIS includes a semicircular part and a linear part. The semicircular part at higher frequencies corresponds to the electron-transfer-limited process and its diameter is equal to the electron transfer resistance (Ret), which controls the electron transfer kinetics of the redox probe at the electrode interface. Meanwhile, the linear part at lower frequencies corresponds to the diffusion process. By using $Fe(CN)_6^{3-/4-}$ redox couples as the electrochemical probe, Fig. 4 showed the typical results of EIS curves of the bare GCE (curve a), ssDNA/GCE (curve b), dsDNA/GCE (curve c), respectively. Significant differences in EIS were observed. When ssDNA was modified on the GCE, the diameter of semicircle greatly increased, suggesting the ssDNA obstructed the electron transfer of the redox-prode. While the diameter of semicircle for dsDNA/GCE further increased. The highest electron-transfer resistance ($R_{ct}$) was attributed to the bad conductivity of dsDNA double helix structure, which slowed down the redox reaction of $Fe(CN)_6^{3-/4-}$. This also proved that ssDNA was immobilized on the GCE

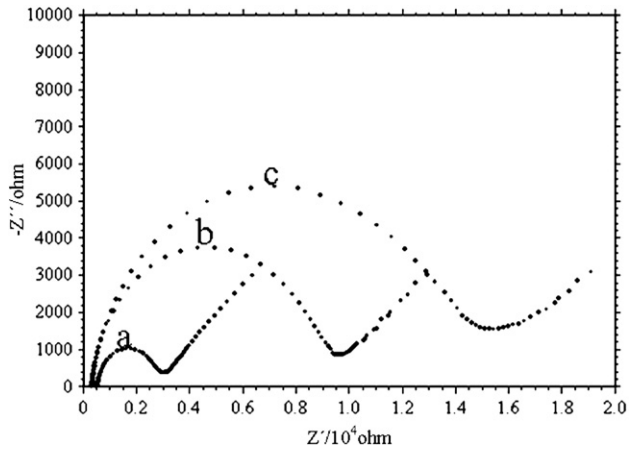



Fig. 4. Electrochemical impedance spectroscopy for bare GCE (a), ssDNA/GCE (b), dsDNA/GCE (c) in a solution of 0.1 M KCl containing 10 mM $Fe(CN)_6^{-3}$/$Fe(CN)_6^{-4}$.

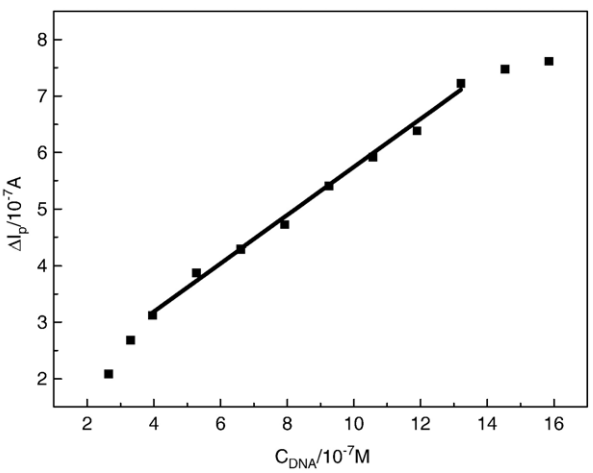



Fig. 6. Plot of the peak current vs. the concentration of complementary target from $3.96\times10^{-7}$ M to $1.32\times10^{-6}$ M in a 0.10 M NaOAc–HOAc buffer (pH 4.60).

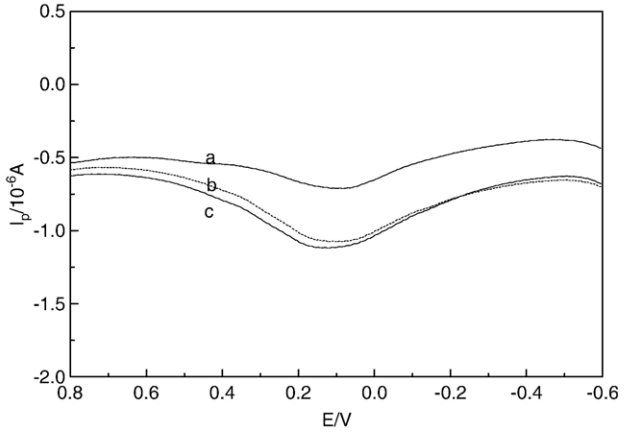



Fig. 7. Differential pulse voltammograms of $[Co(dmp)(H_2O)(NO_3)_2]$ on a DNA probe denaturation/regeneration working cycle. The original ssDNA probe (a), regeneration of the dsDNA probe (b), and hybridization (c).

surface, and target ssDNA was hybridizated with the probe ssDNA.

### 3.4. Recognition of the target sequence by HBV DNA sensor

The DNA biosensor using $[Co(dmp)(H_2O)(NO_3)_2]$ as electrochemical hybridization label for detection of a synthetic 21-mer sequence of hepatitis B virus was studied, as shown in Fig. 5. Curves a, b and c were the representative DPV curves obtained in NaOAc–HOAc buffer solution using $S_1$-modified GCE, $S_1$–$S_3$ hybridized GCE and $S_1$–$S_2$ hybridized GCE as working electrode respectively. Each measurement was performed after $[Co(dmp)(H_2O)(NO_3)_2]$ accumulation. It was found that the electrochemical response of $S_1$-modified GCE or $S_1$–$S_3$ hybridized GCE was very little. Significant increases in the voltammetric signal were observed in curve a, indicating that $[Co(dmp)(H_2O)(NO_3)_2]$ intercalated within the hybrid on the surface. These results suggested that $[Co(dmp)(H_2O)(NO_3)_2]$ can be used as an electrochemical indicator for recognizing the HBV target sequence. The interaction of $[Co(dmp)(H_2O)(NO_3)_2]$ and dsDNA was mainly the intercalative process.

### 3.5. Quantitative analysis of target ssDNA

The analytical performance of the DNA biosensor was assessed using different concentrations of target ssDNA ranging from $2.64\times10^{-7}$ to $1.58\times10^{-6}$ M. The target ssDNA calibration curve, measured using background subtracted ssDNA/GCE, was shown in Fig. 6. The different current value obtained in the DPV of $[Co(dmp)(H_2O)(NO_3)_2]$ after hybridization of probe with target DNA was recorded with three repetitive measurements. Results showed that different current obtained in DPV measurement increased with the increasing of the concentration of target DNA. The current responses had a linear relationship with the concentration of the complementary DNA ($S_2$) ranging from $3.96\times10^{-7}$ to $1.32\times10^{-6}$ M. The regression equation was $y=0.4209x-0.1619$ ($x$ was the concentration of the target DNA, $10^{-7}$ M; y was the DPV peak current of $[Co(dmp)(H_2O)(NO_3)_2]$) with a coefficient of 0.9951. The detection limit of $1.94\times10^{-8}$ M of target DNA could be estimated using $3\sigma$ ($n=11$).

### 3.6. Regeneration of modified electrode

The regeneration of the modified electrode was studied as shown in Fig. 7. In present study, the hybridized electrode was reproduced by washing the electrode with preheated 100 °C water for 3 min. The electrode response returned to its original signal (curve a), indicating that the dsDNA hybrid was dissociated into single strands and that the signal of the immobilized probe ssDNA was not destroyed after the regeneration. The regenerated sensor (curve b) produced a similar decrease of the DPV when hybridized with the target DNA, demonstrating the regeneration and stability of the DNA biosensor. This feature of the biosensor was useful for continuous monitoring of the target DNA in the future research.

## 4. Conclusions

Interaction between $[Co(dmp)(H_2O)(NO_3)_2]$ and salmon sperm DNA was studied using CV and DPV. Results showed that $[Co(dmp)(H_2O)(NO_3)_2]$ could intercalate into the base pairs of the dsDNA. With $[Co(dmp)(H_2O)(NO_3)_2]$ used as a new electroactive indicator, selectively detection of the short DNA segments related to HBV was performed. The current respond had a linear relationship with the concentration of target DNA ranging from $3.96\times10^{-7}$ to $1.32\times10^{-6}$ M, and the detection limit was $1.94\times10^{-8}$ M of target DNA was obtained. The successful discrimination between the complementary ssDNA and three-base mismatched ssDNA displayed a good selectivity for the biosensor. So the utility of the new electrochemical hybridization indicator and developed electrochemical DNA sensor might have promising utilities in real-world clinical applications such as drug designing and diagnosis of diseases.

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## References

[1] D. Leslie, D. Logan, R. Laura, A.M. Elizabeth, D. Sapna, D. Sylvia, Bioluminescence DNA hybridization assay for plasmodium falciparum based on the photoprotein aequorin, Anal. Chem. 79 (2007) 4149–4153.
[2] M.C. Rebeca, S.Á. Patricia, L.C. Jesús, J.M.O. Arturo, T.B. Paulino, Hairpin-DNA probe for enzyme-amplified electrochemical detection of legionella pneumophila, Anal. Chem. 79 (2007) 4050–4055.
[3] J. Wang, Survey and summary from DNA Biosensors to gene chips, Nucleic Acids Res. 28 (2000) 3011–3016.
[4] D. Frank, A.H. Margaret, R.C. Andrew, P.J.H. Séamus, Single gene differentiation by DNA-modified carbon electrodes using an AC impedimetric approach, Anal. Chem. 79 (2007) 1153–1157.
[5] F.C. Abreu, M.O.F. Goulart, B.A. Oliveira, Detection of the damage caused to DNA by niclosamide using an electrochemical DNA biosensor, Biosens. Bioelectron. 17 (2002) 9139.
[6] M.O.B. Ana, C.D. Victor, Electrochemical study of quercetin-DNA interactions Part II. In situ sensing with DNA biosensors, Bioelectrochemistry 64 (2004) 143–150.

[7] D. Xue, C.M. Elliott, P. Gong, D.W. Grainger, C.A. Bignozzi, S. Caramori, Indirect electrochemical sensing of DNA hybridization based on the catalytic oxidation of cobalt (II), J. Am. Chem. Soc. 129 (2007) 1854–1855.
[8] E. Katz, I. Willner, Probing biomolecular interactions at conductive and semiconductive surfaces by impedance spectroscopy: routes to impedimetric immunosensors, DNA-sensors, and enzyme biosensors, Electroanalysis 15 (2003) 913–947.
[9] S. Pan, L. Rothberg, Chemical control of electrode functionalization for detection of DNA hybridization by electrochemical impedance spectroscopy, Langmuir 21 (2005) 1022–1027.
[10] G. Huiru, S. Xiao, P.L. Kian, Electrochemical impedance sensing of DNA hybridization on conducting polymer film-modified diamond, J. Phys. Chem., B 109 (2005) 13611–13618.
[11] A. Anne, A. Bouchardon, J. Moiroux, 3′-ferrocene-labeled oligonucleotide chains end-tethered to gold electrode surfaces: novel model systems for exploring flexibility of short DNA using cyclic voltammetry, J. Am. Chem. Soc. 125 (2003) 1112–1113.
[12] L. Alfonta, A. Singh, I. Willner, Liposomes labeled with biotin and horseradish peroxidase: a probe for the enhanced amplification of antigen-antibody or oligonucleotide-DNA sensing processes by the precipitation of an insoluble product on electrodes, Anal. Chem. 73 (2001) 91–102.
[13] P. Hui, S. Christian, V. Nickolas, A.K. Paul, B.C. Mark, A.B. Graham, P.C. Ralph, T.S. Jadranka, Label-free electrochemical DNA sensor based on functionalized conducting copolymer, Biosens. Bioelectron. 20 (2005) 1821–1828.
[14] C.S. Riccardi, H. Yamanaka, M. Josowicz, J. Kowalik, B. Mizaikoff, C. Kranz, Label-free DNA detection based on modified conducting polypyrrole films at microelectrodes, Anal. Chem 78 (2006) 1139–1145.
[15] P. Hui, S. Christian, V. Nickolas, A.K. Paul, B.C. Mark, A.B. Graham, P.C. Ralph, T.S. Jadranka, Label-free electrochemical DNA sensor based on functionalized conducting copolymer, Biosens. Bioelectron. 20 (2005) 1821–1828.
[16] L.A. Thompson, J. Kowalik, M. Josowicz, Ji. Janata, Label-free DNA hybridization probe based on a conducting polymer, J. Am. Chem. Soc. 125 (2003) 324–325.
[17] R. Steeve, P. Benoît, N. Vincent, C.P. Minh, DNA electrochemical sensor based on conducting polymer: dependence of the "signal-on" detection on the probe sequence localization, Anal. Chem. 77 (2005) 3351–3356.
[18] J. Wang, G. Liu, A. Merkocüi, Electrochemical coding technology for simultaneous detection of multiple dna targets, J. Am. Chem. Soc. 125 (2003) 3214–3215.
[19] J.A. Hansen, R. Mukhopadhyay, J. Hansen, K.V. Gothelf, Femtomolar electrochemical detection of DNA targets using metal sulfide nanoparticles, J. Am. Chem. Soc. 128 (2006) 3860–3861.
[20] H. Cai, N. Zhu, Y. Jiang, P. He, Y. Fang, Cu@Au alloy nanoparticle as oligonucleotides labels for electrochemical stripping detection of DNA hybridization, Biosens. Bioelectron. 18 (2003) 1311–1319.
[21] S.O. Kelley, J.K. Barton, N.M. Jackson, M.G. Hill, Electrochemistry of methylene blue bound to a DNA-modified electrode, Bioconjug. Chem. 8 (1997) 31–37.
[22] S.O. Kelley, E.M. Boon, J.K. Barton, N.M. Jackson, M.G. Hill, Single-base mismatch detection based on charge transduction through DNA, Nucleic Acids Res. 27 (1999) 4830–4837.
[23] S.O. Kelley, N.M. Jackson, M.G. Hill, J.K. Barton, Long-range electron transfer through DNA films, Angew. Chem., Int. Ed. Engl. 38 (1999) 941–945.
[24] E.M. Boon, D.M. Ceres, T.G. Drummond, M.G. Hill, J.K. Barton, Mutation detection by electrocatalysis at DNA-modified electrodes, Nat. Biotechnol. 18 (2000) 1096–1100.
[25] K. O'Donoghue, J.C. Penedo, J.M. Kelly, P.E. Kruger, Photophysical study of a family of $[Ru(phen)^2(Me_ndpq)]^{2+}$complexes in different solvents and DNA: a specific water effect promoted by methyl substitution, J. Chem. Soc., Dalton Trans. 11 (2005) 1123.
[26] S.J. Moon, J.M. Kim, J.Y. Choi, S.K. Kim, J.S. Lee, H.G. Jang, $[Ru(phen)_2DPPZ]^{2+}$ is in contact with DNA bases when it forms a luminescent complex with single-stranded oligonucleotides, J. Inorg. Biochem. 99 (2005) 994.
[27] J. Olofsson, L.M. Wilhelmsson, P. Lincoln, Effects of methyl substitution on radiative and solvent quenching rate constants of $[Ru(phen)_2dppz]^{2+}$ in polyol solvents and bound to DNA, J. Am. Chem. Soc. 126 (2004) 15458–15465.
[28] T. Urathamakul, J.L. Beck, M.M. Sheil, J.R. Aldrich-Wright, S.F. Ralph, A mass spectrometric investigation of non-covalent interactions between ruthenium complexes and DNA, J. Chem. Soc., Dalton Trans. 126 (2004) 2683.
[29] R. Caspar, L. Musatkina, A. Tatosyan, H. Amouri, M. Gruselle, C. Guyard-Duhayon, R. Duval, C. Cordier, Efficient DNA binding by optically pure ruthenium Tris(bipyridyl) complexes incorporating carboxylic functionalities. Solution and structural analysis, Inorg. Chem. 43 (2004) 7986.
[30] L. Havran, M. Fojta, E. Palecek, Voltammetric behavior of DNA modified with osmium tetroxide 2,2′-bipyridine at mercury electrodes, Bioelectrochemistry 63 (2004) 239–243.
[31] M. Fojta, L. Havran, M. Vojtiskova, E. Palecek, Electrochemical detection of DNA triplet repeat expansion, J. Am. Chem. Soc. 126 (2004) 6532–6533.
[32] A. Pasini, F. Zunino, New cisplatin analogues-on the way to better antitumor agents, Angew. Chem., Int. Ed. Engl. 26 (1987) 615.
[33] J.K. Barton, Metals and DNA: molecular left-handed complements, Science 233 (1986) 727–734.
[34] Y. Ni, D. Lin, S. Kokot, Synchronous fluorescence, UV–visible spectrophotometric, and voltammetric studies of the competitive interaction of bis (1,10-phenanthroline)copper(II) complex and neutral red with DNA, Anal. Biochem. 352 (2006) 231–242.
[35] M.T. Carter, M. Rodriguez, A.J. Bard, Voltammetric studies of the interaction of metal chelates with DNA. 2. Tris-chelated complexes of cobalt(III) and iron(II) with 1,10-phenanthroline and 2,2′-bipyridine, voltammetric studies of the interaction of metal chelates with DNA. 2. Tris-chelated complexes of cobalt(III) and iron(II) with 1,10-phenanthroline and 2,2′-bipyridine, J. Am. Chem. Soc. 111 (1989) 8901–8911.
[36] J. Wang, X. Cai, G. Rivas, H. Shiraishi, P.A.M. Farias, N. Dontha, DNA electrochemical biosensor for the detection of short DNA sequences related to the human immunodeficiency virus, Anal. Chem. 68 (1996) 2629–2634.
[37] M.T. Carter, A.J. Bard, Voltammetric studies of the interaction of tris(1,10-phenanthroline)cobalt(III) with DNA, J. Am. Chem. Soc. 109 (1987) 7528–7530.
[38] X.M. Li, H.Q. Ju, L.P. Du, S.S. Zhang, A nucleic acid biosensor for the detection of a short sequence related to the hepatitis B virus using bis (benzimidazole)cadmium(II) dinitrate as an electrochemical indicator, J. Inorg. Biochem. 101 (2007) 1165–1171.
[39] X.M. Li, H.Q. Ju, C.F. Ding, S.S. Zhang, Nucleic acid biosensor for detection of hepatitis B virus using 2,9-dimethyl-1,10-phenanthroline copper complex as electrochemical indicator, Anal. Chim. Acta 582 (2007) 158–163.
[40] S.S. Zhang, S.Y. Niu, B. Qu, G.F. Jie, H. Xu, C.F. Ding, Studies on the interaction mechanism between hexakis(imidazole) manganese(II) terephthalate and DNA and preparation of DNA electrochemical sensor, J. Inorg. Biochem. 99 (2005) 2340.
[41] S.Y. Niu, S.S. Zhang, L. Wang, X.M. Li, Hybridization biosensor using di (1,10-phenanthroline) (imidazo[f]1,10-phenanthroline)cobalt(II) as electrochemical indicator for detection of human immunodeficiency virus DNA, J. Electroanal. Chem. 597 (2006) 111–118.
[42] C.F. Ding, M.L. Zhang, X.M. Li, Aqua(2,9-dimethyl-1,10-phenanthroline-$\acute{K}^2$N, N′) dinitratocobalt(II), Acta Crystallogr. 62 (2006) 2540–2542.