

Hybrids of Nickel-histidine Functionalized Graphene Quantum Dots: Fabrication and Non-enzymatic Glucose Sensing

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Abstract. In this work, a method of in-situ recombination of Ni²⁺ with histidine functionalized graphene quantum dots (His-GQDs) was constructed a three-dimensional network porous structure. The collected precipitate complex precursor was oxidized and the NiO-His-GODs were obtained. The NiO-His-GQDs compound was subjected to high-temperature thermal reduction by inert gas to form Ni-His-GQDs. On the one hand, the intimate contact between Ni nanoparticles and His-GQD greatly shortens the gap between the two complexes, resulting in faster electron migration speed; On the other hand, the conductive (Ni)/semiconductor (His-GQDs) catalytic interface can produce Stokes diode-like structures, accelerate the migration rate of holes carriers in the semiconductor, and exhibit good electrocatalytic activity. A Ni-His-GQDs modified electrode as non-enzymatic glucose electrochemical sensor was shown good electrocatalytic activity and anti-interference property. The concentration of glucose was detected by amperometric analysis, and showed a good linear relation in the concentration range of 5.0×10^{-6} ~ 2.0×10^{-3} M. The detection limit (S/N = 3) is 1.7×10^{-6} M. In addition, interference of sodium chloride (NaCl), uric acid (UA), dopamine (DA) and ascorbic acid (AA) was less than 5.0 % in the same conditions indicating that the hybrids modified electrode sensor could be used for the sensitive and selective detection of glucose.

1. Introduction

Glucose is widely distributed in nature and played an important position as the main functional materials of biology. So the detection of glucose is also important in lots of field, especially in medical treatment field. [1-4] Up to now, the biosensor technology was often used for the detection of glucose, especially obtained the information of glucose by glucose oxidase (GOD). Because GOD can quickly catalyze glucose to gluconic acid and H₂O₂, thereby further identify the information of glucose. [5, 6] However, the GOD activity often is influenced by temperature, humidity, etc. [7, 8] Hence, there are interest to fabricated glucose biosensor which can detect glucose through the direct oxidation of glucose. At present, a part of metallic, metal oxide and alloy nanoparticles have found the ability as



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electrocatalyst materials, especially the Ni-based materials. [1, 9-17] Because the Ni-based materials could form a high-valent, oxyhydroxide species [NiOOH] in the oxidation processes, and could be obtained in large numbers at low cost. [14, 17]

Graphene, a single atomic layer that consisted of sp² carbon atoms covalently bonded in a hexagonal manner, has excellent electrical, thermal, mechanical and other physical and chemical properties.[14-18] Moreover, graphene has a large surface which afforded the place to disperse metal nanoparticles and obtained nanocomposites. The graphene materials could enhance the electron transport and keep the active of metals nanoparticles in the composites, which is beneficial to the composites as electrochemical sensing materials for the detection of glucose.[13-17] Different from common graphene, graphene quantum dots (GQDs) is less than 100 nm in lateral sizes, have several unique properties besides properties of graphene materials.[19-20] The studies have revealed that GQDs as better electron transporter and acceptor could be an all-right candidate for electrochemical sensing materials.[20, 21]

In this work, the hybrids of Ni-His-GQDs were obtained and served as electrochemical electrode material for glucose electrochemical detection. As electrochemical electrode, Ni-His-GQD hybrids modified electrodes exhibited high sensitivity, low detection limit, and excellent selectivity in non-enzymatic glucose electrochemical detection.

2. Experimental

2.1. Materials

D-glucose, citric acid, histidine and nickel chloride hexahydrate (NiCl₂·6H₂O) were bought from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). His-GQD was generated as described in Ref. [22] Phosphate-buffered saline (PBS, pH 7.0, 0.01 M) was used as the supporting electrolyte. Ultrapure water (18.2 MΩ cm) generated by a Milli-Q purification system was used for all the experiment. All other reagents were analytical purity grade and were bought from Shanghai Chemical Company (Shanghai, China).

2.2. Synthesis of Ni-His-GQDs hybrids

A NiCl₂·6H₂O aqueous solution (0.25 M, 40 mL) was added into the His-GQDs dispersion (50 mg mL⁻¹, 20 mL, pH 7) with stirring. The precipitate was collected and then further oxidized at 300 °C for 3 h in air and the NiO-His-GQD was obtained. Finally, Ni-His-GQDs hybrids were obtained after thermal reduction processing at 600 °C for 0.5 h in N₂ atmosphere. Meanwhile, for comparison, NiO-His-GQD and His-GQD were also treated using the same processing.

2.3. Electrochemical Characterization

The electrochemical experiments were performed with a CHI660D electrochemical workstation (Shanghai, China) using a three electrode system. The Ni-His-GQD, NiO-His-GQD and His-GQD modified or bare GCEs (Φ = 1.0 mm) were employed as work electrode, an Ag/AgCl electrode (saturated KCl) as reference electrode, a platinum wire as counter electrode. The GCEs were modified with different materials to obtain different sensors by the same procedure: Ni-His-GQD, NiO-His-GQD and His-GQD dispersing in the chitosan solution (5 mg mL⁻¹) and the suspension (2 mg mL⁻¹) was obtained, respectively. Then these suspensions (10 mL) were dropwise on the GCEs surface, and were dried in air for using, respectively. All measurements experimental solution was degassed by nitrogen for at least 15 min under room temperature.

3. Results and Discussion

3.1. Synthesis and Characterization of Material

Because His-GQDs contains multiple imidazole groups, which can coordinate with Ni²⁺ and rapidly extend outward with Ni-N bonds to form the three-dimensional network precursor. So, first, His-GQDs reacted with Ni²⁺ to form Ni-His-GQD precursor. Second, the precursor was further oxidized at 300 °C in air atmosphere; thereby gain NiO-His-GQDs hybrids. In order to reduce the NiO and

improve the crystallinity of the His-GODs, the NiO-His-GQDs hybrids were further treated at 600 °C in N₂ atmosphere. Finally, Ni-His-GQDs hybrids were obtained.

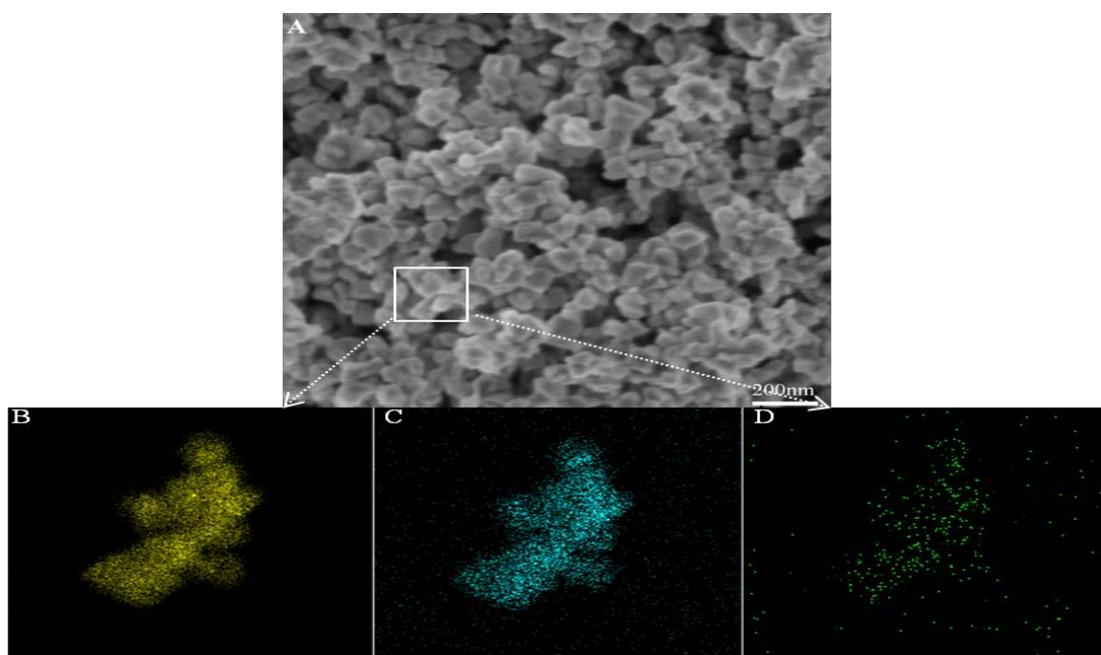


Figure 1. The SEM (A), Nickel Element (B), Carbon Element (C), Nitrogen Element (D) Mapping of the Ni-His-GQDs Hybrids

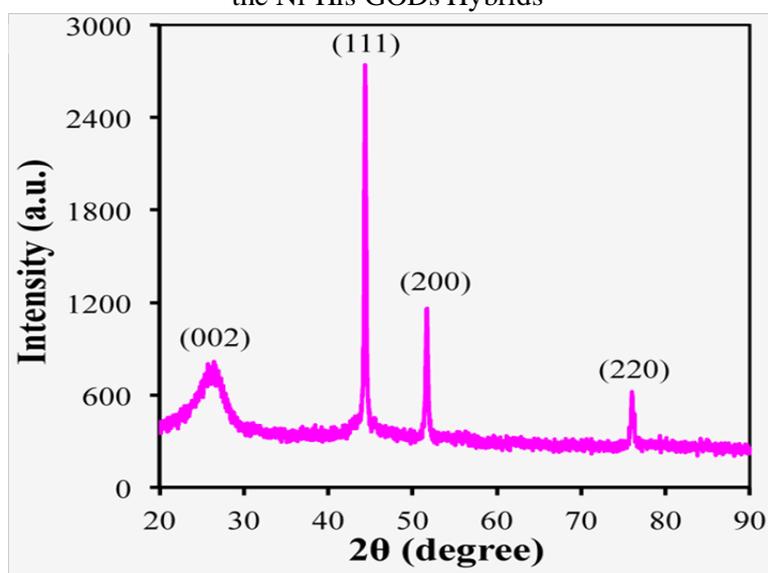


Figure 2. The XRD Spectrum of the Ni-His-GQDs Hybrids

The morphology and chemical composition of Ni-His-GQD hybrids were examined by SEM and EDX, and the results were shown in Figure 1. The Ni-His-GQD hybrids show hierarchical architecture (Figure 1A). Nevertheless, the architecture morphologies of the hybrid was preserved properly after the annealing process when the NiO-His-GQD complex converting to Ni-His-GQD hybrids. Moreover, the size dimension of the Ni-His-GQD hybrids particles were about 50 nm. The results of EDX analysis revealed that the hybrids contained of nickel (Ni), carbon (C) and nitrogen (N) elements (Figure 1C). The nitrogen element could only come from the imidazole groups of His-GODs.

In the Ni-His-GQD hybrids XRD pattern (Figure 2), the diffraction peaks corresponding to the diffractions of (111), (200), (220) of the Ni (fcc), respectively (JCPDS 04-0805). A broad diffraction peaks at $\sim 26.0^\circ$ is corresponding to the diffraction of (002) of His-GQDs materials, suggesting the His-GQD successful reduction in thermal reduction processing.

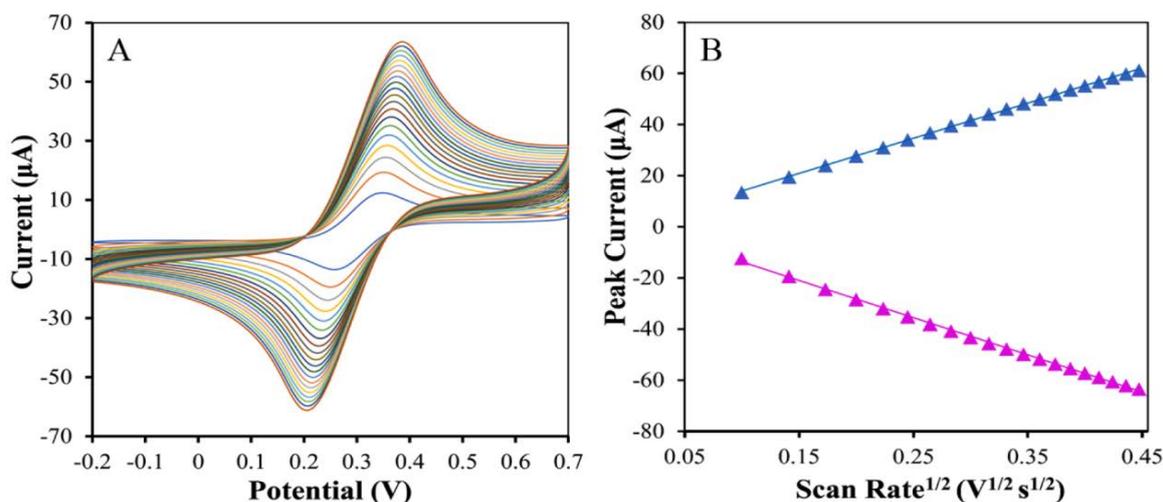


Figure 3. A: CV Curve of Ni -His-GQDs Hybrids Modified Electrode in a PBS (pH 7.0, 1.0 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$) at Various Scan Rates. B: I_p vs. Square Root of Scan Rate

To investigate the electrocatalytic activity of Ni-His-GQDs hybrids modified electrode, the cyclic voltammograms (CV) were measured at different scan rates (Figure 3). The results revealed that the anodic peak occur a significantly positive shift and the cathodic peak occur a negatively shift with the increase of scan rates. This phenomenon indicated that the Ni-His-GQD hybrids-modified GCE is rapid and reversible. Furthermore, Figure 3B reveals anodic and cathodic peak currents of Ni-His-GQDs hybrids modified electrode is linearly scale with the square root of scan rates, suggesting that the redox reaction of $\text{K}_3[\text{Fe}(\text{CN})_6]$ is a typical diffusion-controlled electrochemical process at the electrode surface.[13,14]

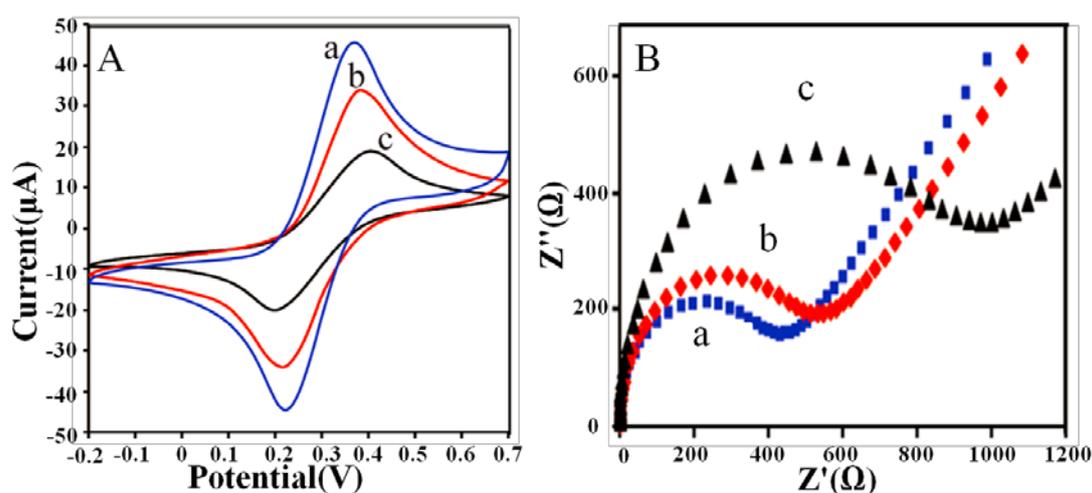


Figure 4. CV (A) and EIS (B) Curve of Ni -His-GQDs (a), NiO-His-GQDs (b) and His-GQDs (c) Hybrids Modified Electrode in a PBS (pH=7, 1.0 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$) at the Scan Rate of 100 mV s^{-1}

To compare the electrocatalytic activity, their CV behaviours of NiO-His-GQDs, His-GQDs and Ni-His-GQDs hybrids modified electrodes were studied in PBS (pH 7.0, 1.0 mM $K_2Fe(CN)_6$) at the scan rate of 100 mV s^{-1} (Figure 4A). All CV curves of the hybrids electrode shown obvious redox peak, displaying the oxidation and reduction reactions of $K_2Fe(CN)_6$ in electrodes surface. Moreover, the Ni-His-GQDs hybrids modified electrode exhibited the highest peak currents. This is mainly due to the Ni crystals nanoparticles in hybrids have better the electrical conductivity and electrochemical properties compared with NiO crystals nanoparticles, resulting to an evidently improved electrocatalytic activity.

EIS is used to investigate the charge transfer ability of the different electrodes surface (Figure 4B). The Nyquist complex plane impedance plots included a semicircle and a linear portion. The high-frequencies semicircle region corresponds to the electron transfer limited process, and the low-frequencies region linear portion is assigned to the diffusion process. The electron transfer resistance (R_{ct}) of the electrodes surface can be quantified through the diameter of the semicircle diameter. The R_{ct} of Ni-His-GQDs hybrids sensor was much smaller than that of His-GQDs and Ni-His-GQDs hybrids sensors, indicating Ni nanoparticles are beneficial for electron transfers in the hybrids and probably generate synergistic effects. Therefore, Ni-His-GQDs hybrids could dramatically improve the electron transfer efficiency between the electrolyte and electrode interface.

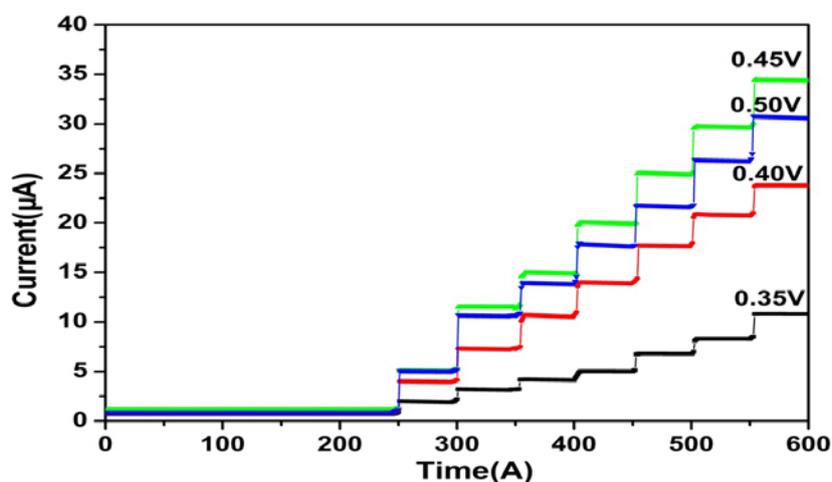


Figure 5. Amperometric Current Response of Ni-His-GQDs Hybrids Sensor at Different Applied Potentials with a Dropwise Addition of 2 mM Glucose into the 0.1 M NaOH

To obtain better detection potential on amperometric current response of sensors, the effect of the applied potential was further investigated from +0.35 V to +0.50 V. The result revealed that the current response is gradually increase from 0.35 V to 0.45 V, and then begin to decrease (Figure 5). It indicated that the applied potential of +0.45 V has the maximum current response and is the optimized suitable working potential in the subsequent studies. It is mainly because of the high potential activated interfering substances and generated many intermediates, which would interact with the electrode, thereby leading to the lowered current. In the meanwhile, the irreversible absorption of intermediates could further harm the electrode and hindered the glucose oxidation. [1]

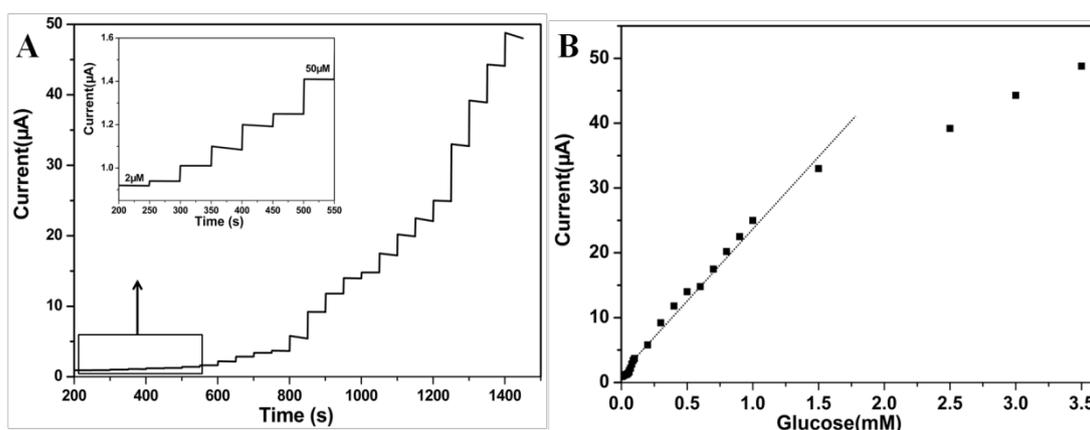


Figure 6. A: Amperometric current response of Ni-His-GQDs hybrids modified electrode on the successive addition of glucose into NaOH (0.1 M) at 0.45 V. The inset shows a magnification of the current response in a low concentration of glucose; B: Current response versus glucose concentration

To confirm the amperometric responses steady state of the Ni-His-GQDs hybrids modified electrode, the dynamic steady state current response of the interface was measured through successive additions of glucose. Figure 6A displayed a current-time plot of the Ni-His-GQDs hybrids modified electrode interface on successive additions of glucose at the +0.45 V potential. The result shows a very quickly response to glucose. The inset results revealed that the current response could begin to the addition of 2 μM glucose (inset in Figure 6A). In addition, the sensor exhibits a broad linear detection range of $5.0 \times 10^{-6} \sim 2.0 \times 10^{-3}$ M (Figure 6B). The linear regression equation is $I_P (\mu\text{A}) = 20.89 C (\text{mM}) + 1.7713$. Based on a signal-to-noise ratio of 3, the detection limit is 1.7×10^{-6} M, suggesting the extremely fast and high sensitivity of the electrochemical electrode.

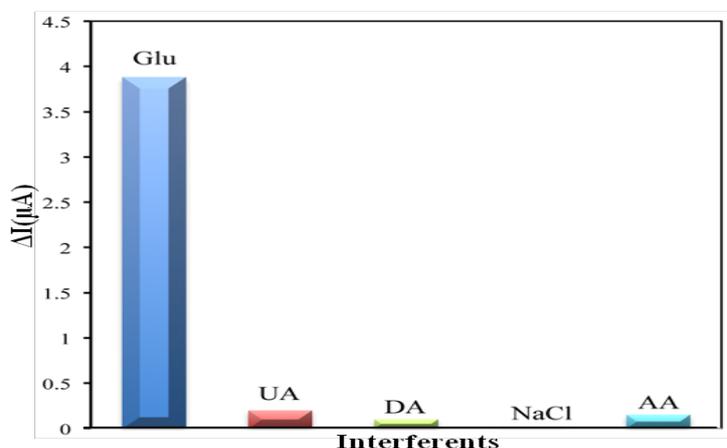


Figure 7. The Bar Diagram of Normalized Amperometric Current against Interferents

Besides the above factors, other substances probably simultaneous oxidize at the same applied potential which is also one challenge in detection field of glucose. In addition, chloride ions could also poison electrodes in some cases. So, the effect of other four kinds of interferential compounds, NaCl, UA, DA and AA were investigated. The result presented in Figure 7, the current response of these four kinds interferential were all less than 5.0%, suggesting that the Ni-His-GQDs hybrids modified electrode can be used in the sensitive and selective detection of glucose, and could neglect the interference of NaCl, UA, DA and AA, etc.

4. Conclusions

In summary, the Ni-His-GQDs hybrids were obtained through coordination between Ni²⁺ and His-GQDs, oxidation and reduction processing. The good electrical contacts between Ni and reduced His-GQD afford synergistically exceptional electrochemical properties in the Ni-His-GQDs hybrids which could obviously enhance catalytic activity. The Ni-His-GQDs hybrids modified electrode exhibited high sensitivity, quickly response and excellent stability for glucose detection. It will be the most promising composites for fabricating Ni-His-GQD hybrids for practical nonenzymatic glucose sensors in biotechnology and clinical diagnosis.

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6. References

- [1] S. Fu, G. Fan, L. Yang, F. Li, *Electrochim. Acta*, 2015, 152 146–154
- [2] C. Chen, Q. Xie, D. Yang, H. Xiao, Y. Fu, Y. Tan, S. Yao, *RSC Adv.*, 2013, 3(14): 4473-4491
- [3] K. J. Chen, C. F. Lee, J. Rick, S. H. Wang, C. C. Liu, B. J. Hwang, *Biosens. Bioelectron.*, 2012, 33 (1): 75-81
- [4] A. Heller, B. Feldman, *Chem. Rev.*, 2008, 108, 2482-2505
- [5] Y. Liu, M. K. Wang, F. Zhao, Z. Xu, S. J. Dong, *Biosens. Bioelectron.*, 2005, 21, 984-988.
- [6] P. Si, S. J. Ding, J. Yuan, X. W. Lou, D. H. Kim. *ACS Nano*, 2011, 5, 7617-7626.
- [7] T. W. Tsai, G. Heckert, L. F. Neves, Y. Tan, D. Y. Kao, R. G. Harrison, D. E. Resasco, D. W. Schmidtke, *Anal. Chem.*, 2009, 81(19): 7917-7925
- [8] Z. G. Zhu, L. Garcia-Gancedo, A. J. Flewitt, H. Q. Xie, F. Moussy, W. I. Milne, *Sensors*, 2012, 12, 5996.
- [9] J. Zhang, X. Zhu, H. Dong, X. Zhang, W. Wang, Z. Chen, *Electrochim. Acta* 105 (2013) 433–438.
- [10] K. Li, G. Fan, L. Yang, F. Li, *Sensor. Actuat. B-Chem.*, 199 (2014) 175–182.
- [11] S. Liu, B. Yu, T. Zhang, *Electrochim. Acta*, 102 (2013) 104–107.
- [12] A. Ciszewski, I. Stepniak, *Electrochim. Acta*, 111 (2013) 185–191.
- [13] A. Zhan, C. Liu, H. Chen, H. Shi, L. Wang, P. Chen, W. Huang, X. Dong, *Nanoscale*, 2014, 6(13): 7424-7429
- [14] P. Subramanian, J. Niedziolka-Jonsson, A. Lesniewski, Q. Wang, M. Li, R. Boukherroub, S. Szunerits, *J. Mater. Chem. A*, 2014, 2, 5525-5533
- [15] G. Li, H. Huo, C. Xu, *J. Mater. Chem. A*, 2015, 3, 4922-4930
- [16] Z. Wang, Y. Hu, W. Yang, M. Zhou, X. Hu. *Sensors*, 2012, 12, 4860-4869
- [17] J. Yang, J. H. Yu, J. R. Strickler, W. J. Chang, S. Gunasekaran, *Biosens. Bioelectron.*, 2013, 47, 530–538
- [18] Y. Yang, R. Pang, X. Zhou, Y. Zhang, H. Wu, S. Guo, *J. Materi. Chem.*, 2012, 22, 23194-23200
- [19] Y. Yang, Q. Wang, Z. Liu, W. Liu, Y. Wen, L. Jin, Y. Liu, B. Ou, *Adv. Eng. Res.*, 2018, 120, 1611-1615
- [20] W. Chen, R. Li, Z. Li, Y. Yang, H. Zhu, J. Liu, *J. Alloy. Compd.*, 2019, 777, 1001-1009
- [21] H. Chu, J. Hu, Z. Li, R. Li, Y. Yang, X. Sun, *Sensor. Actuat. B-Chem.*, 2019, 298, 126866
- [22] X.Y. Zhou, R.Y. Li, Z.J. Li, G.Z. Gu, G.L. Wang, *RSC Adv.*, 2016, 6, 42751-42755
- [23] Z. Chen, Y. Zhang, J. Zhang, J. Zhou, *J. Electrochem. Soc.*, 166 (2019) B787-B792.