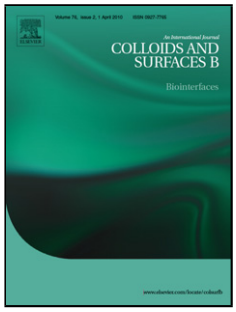


One-step electrodeposition of poly(*m*-aminobenzoic acid) membrane decorated with peptide for antifouling biosensing of Immunoglobulin E

Shuai Wang (Methodology)<ce:contributor-role>Writing- original draft), Yihui Ma (Data curation), Yu Wang (Investigation), Mingxia Jiao (Software), Xiliang Luo (Conceptualization), Min Cui (Supervision)<ce:contributor-role>Writing- review and editing)

PII: S0927-7765(19)30850-1

DOI: https://doi.org/10.1016/j.colsurfb.2019.110706

Reference: COLSUB 110706

To appear in: *Colloids and Surfaces B: Biointerfaces*

Received Date: 11 October 2019

Revised Date: 28 November 2019

Accepted Date: 2 December 2019

Please cite this article as: Wang S, Ma Y, Wang Y, Jiao M, Luo X, Cui M, One-step electrodeposition of poly(*m*-aminobenzoic acid) membrane decorated with peptide for antifouling biosensing of Immunoglobulin E, *Colloids and Surfaces B: Biointerfaces* (2019), doi: https://doi.org/10.1016/j.colsurfb.2019.110706

One-step electrodeposition of poly(*m*-aminobenzoic acid) membrane decorated with peptide for antifouling biosensing of Immunoglobulin E

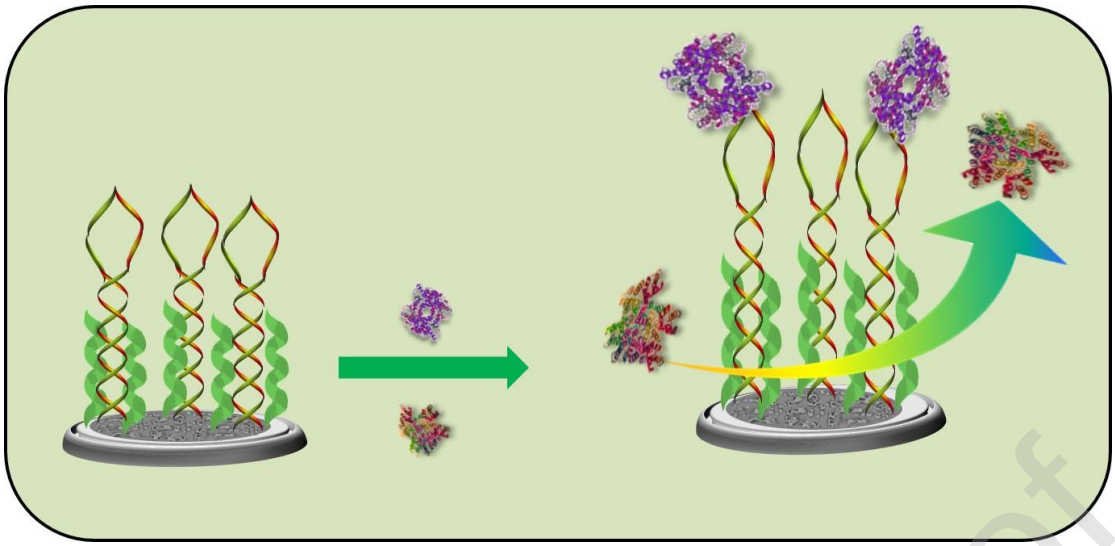
Shuai Wang[a], Yihui Ma[b], YuWang[b], Mingxia Jiao[b], XiliangLuo[b], Min Cui[a,*]

[a] Shandong Provincial Key Laboratory of Molecular Engineering, School of Chemistry and Pharmaceutical Engineering, Qilu University of Technology (Shandong Academy of Sciences), Jinan 250353, P. R. China.

[b] Key Laboratory of Sensor Analysis of Tumor Marker, Ministry of Education; Shandong Key Laboratory of Biochemical Analysis; Key Laboratory of Analytical Chemistry for Life Science in Universities of Shandong; College of Chemistry and Molecular Engineering, Qingdao University of Science & Technology, Qingdao 266042, P. R. China.

*Corresponding author, E-mail: ujn_cm@126.com (M. Cui).

Graphical abstract



Highlights

- PABA membrane was electrodeposited onto electrode surface by a one-step CV method;
- Aptamer and peptide were immobilized onto PABA to form an antifouling biosensor;
- The biosensor supported the quantification of IgE in serum with low fouling.

Abstract

m-Aminobenzoic acid (ABA) is one popular derivative of highly conductive monomer of aniline, which contains a carboxyl (-COOH) group in its skeleton that is beneficial to various bio-interface and bio-analysis. Hence, Poly(*m*-aminobenzoic acid) (PABA) membrane was firstly electrochemical deposited onto bare electrode surface using a straightforward cyclic voltammetry (CV) method. PABA membrane exhibited excellent electrochemical stability and apparent wrinkle morphology that could effectively enhance response signal and immensely increase specific surface area of electrode. Next, PABA membrane was decorated with well-designed hairpin aptamer

and preferred antifouling peptide in sequence to construct a two-layer architectural bio-interface that could present both sensitive target recognition capability and excellent antifouling ability. Benefiting from the electrodeposited PABA membrane to enhance electrochemical response signal, the developed biosensor performed excellent sensitivity toward target protein, meanwhile, associated with good selectivity and reproducibility attributing to the favored peptide that was able to decline nonspecific protein adsorption and improve target recognition.

Keywords: Electrodeposition, Poly(*m*-Aminobenzoic acid), Antifouling, Peptide, Immunoglobulin E

1. Introduction

Among the range of available analytical assays, electrochemical methods manifest highly effective manner of cheap, sensitive, selective, portable and multiplexed in reporting protein recognitions at suitable as-prepared interfaces based on electrochemical current and impedance techniques, respectively [1-3]. Conductive polymers, such as poly(3,4-ethylenedioxythiophene) (PEDOT), polypyrrole (PPY) and polyaniline (PANI), have been widely utilized to enhance the electrochemical signal response in a variety of electrochemical fields especially for biosensors, batteries, supercapacitors, etc., due to their large surface area, low cost consumption, benign synthesis environment, high mechanical flexibility, outstanding physical and chemical stability [4-6]. As the most promising candidate, various PANI polymers have

won enormous interest [7-8]. For instance, PANI nanofibers with considerable surface area and conductivity have been synthesized through a simply electrochemical procedure, and further successfully utilized in fabricating biosensor for DNA sensing [8]. And as we know, *m*-Aminobenzoic acid (ABA) is one popular derivative of aniline, therefore, poly(*m*-aminobenzoic acid) (PABA) is considerably becoming a class of attractive material in electrochemical biosensing field [9-10], because of, except its high conductivity and large surface area, the inherent presence of carboxyl (-COOH) groups in its backbone that is particularly convenient for the immobilizations of diverse biomolecules. Nevertheless, through simple electrochemical polymerization to obtain PABA still remains a lack of study so far, as well as the promising application based on PABA polymer in bio-analysis field. Therefore, in this work, the straightforward electrodeposition of PABA through an electrochemical method was explored, including of its powerful support in construction of biosensing platform toward protein.

Human immunoglobulin E (IgE) plays a crucial role in pathological states, such as allergic reactions, anti-tumour defence and autoimmune diseases [11-12]. For healthy individual, IgE presents in extremely low concentration (~ 1 nM) in serum [13-16]. As a glycoprotein, IgE can bind to mast cells to trigger the release of some chemical components like leukotrienes and histamine, resulting in observable allergic symptoms. Hence, the concentration of IgE in human serum has been demonstrated to be elevated following the event occurrences of atopic dermatitis, allergic asthma and immune deficiency diseases like AIDS. Therefore, the realization of accurate

assessment of IgE in complex serum sample will undoubtedly underpin future advances in the improvements of diagnosis and treatment of allergy/immune-mediated diseases. Nowadays, many IgE bio-analytical platforms such as fluorescence analysis [17-19] and electrochemical methods [15, 20], which mainly based on the specific binding between antibody/antigen and/or aptamer/protein, have been successfully established. As we know, aptamer, as synthetic DNA or RNA oligonucleotides, selected through systematic evolution of ligands by exponential enrichment (SELEX) technique [21], with the remarkable advantages of low cost, high stability and reversible denaturation, can specifically interact with their preselected targets including nucleic acids, proteins and cells with powerful affinity [22-23, 1]. Here, a well-designed DNA aptamer with hairpin structure [24] was preselected and synthesized as the specific recognition probe to develop biosensing platform for the electrochemical analysis of IgE.

It is noteworthy that, many biosensing interfaces may suffer from severe signal influence coming from nonspecific protein adsorption when they are seeking to detect specific targets in real biological media [25-26]. The nonspecific protein adsorption eventually could severely hinder the analytical performance of constructed biosensing interface. So presently, to address this issue, some high hydrophilic and charge neutral peptides with particular amino acid sequences had been certified to be of remarkable capability in resisting nonspecific protein adsorption when adopted in the establishment of biosensing surfaces [1, 27-30]. Such type of peptide, coupled with its inherently superior biocompatibility and flexible coordinability, is becoming a

prospective candidate in biomedical field. We presented here an electrochemical antifouling biosensor for IgE analysis, based on the electrodeposited PABA membrane that was decorated with well-designed hairpin aptamer and preferred antifouling peptide in sequence. Initially, we have sought to prepare PABA membrane on bare glassy carbon electrode (GCE) surface using a very simply electrochemical manner and investigated the electrochemical stability of PABA covered GCE. The particular peptide was designed with the amino acid sequence of CHHHDDD, because a similar peptide only carrying the amino acid of H and D had been verified of ultralow fouling ability in crude serum [30].The aptamer and peptide were successively immobilized onto PABA membrane through the covalent binding between its carboxyl (-COOH) groups and amino ($-NH_2$) groups of biomolecules to form a two-layer architectural interface that was envisaged to present both high recognition ability (from strong interaction between aptamer and its target protein) and famous antifouling characteristic (from excellent capability in preventing nonspecific protein adsorption of peptide). Different electrochemical techniques were adopted to survey the fabrication procedure and analytical performance, mainly including the identification ability toward target protein, antifouling property in resisting nonspecific protein adsorption, reproducibility and specificity of the constructed biosensor.

2. Materials and Methods

2.1. Reagents and apparatus

ABA, Fetal bovine serum (FBS), alpha fetoprotein (AFP), human serum albumin

(HSA), lysozyme (Lys), human IgE and immunoglobulin G (IgG) were purchased from Sangon Biotech Co., Ltd. N-hydroxysuccinimide (NHS) and 1-ethyl-3-3-(dimethylaminopropyl) carbodiimide (EDC) were obtained by Sangon Biotech Co., Ltd. Peptide was synthesized, purified and provided by Bankpeptide biological technology Co., Ltd. Specific hairpin aptamer for IgE purified by liquid chromatography was supplied by Sangon Biotech Co., Ltd. The related DNA sequences were as follows: 5' NH_2-GCG CGG GGC ACG TTT ATC CGT CCC TCC TAG TGG CGT GCC CCG CGC 3'. Synthetic oligonucleotides with the DNA sequence of 5' GAT TTT CTT CCT TTT GTT C 3' for specificity study were also purchased from Sangon Biotech Co., Ltd. The stock solutions of oligonucleotides were prepared by phosphate buffered saline (PBS, 0.2 M, pH 7.4). All solutions used in this work were prepared with ultrapure water produced from a Milli-Q water purifying system. All other reagents used were of analytical grade.

Electrochemical determinations were conducted with a CHI 660E electrochemical workstation (Shanghai Chenhua Instrument Co. Ltd., China). A three electrode system was employed in all electrochemical experiments, where a bare or modified GCE, a saturated calomel electrode and a platinum wire were adopted as working electrode, reference electrode and counter electrode, respectively. A scanning electron microscope (SEM) with the model of JEOL JSM-7500F (Hitachi High-Technology Co., Ltd., Japan) was used to characterize the surface morphology of as-prepared PABA membrane. X-ray photoelectron spectroscopy (XPS) tests were performed using an ESCALAB 250Xi spectrometer (Thermo Fisher Scientific, UK)

with a monochromatic Al Kα X-ray source. Static water contact angle (CA) measurements of different modified surfaces were carried out with the JC2000 Instrument (Shanghai Zhongchen Instrument Co., China).

2.2. Electrochemical deposition of PABA membrane

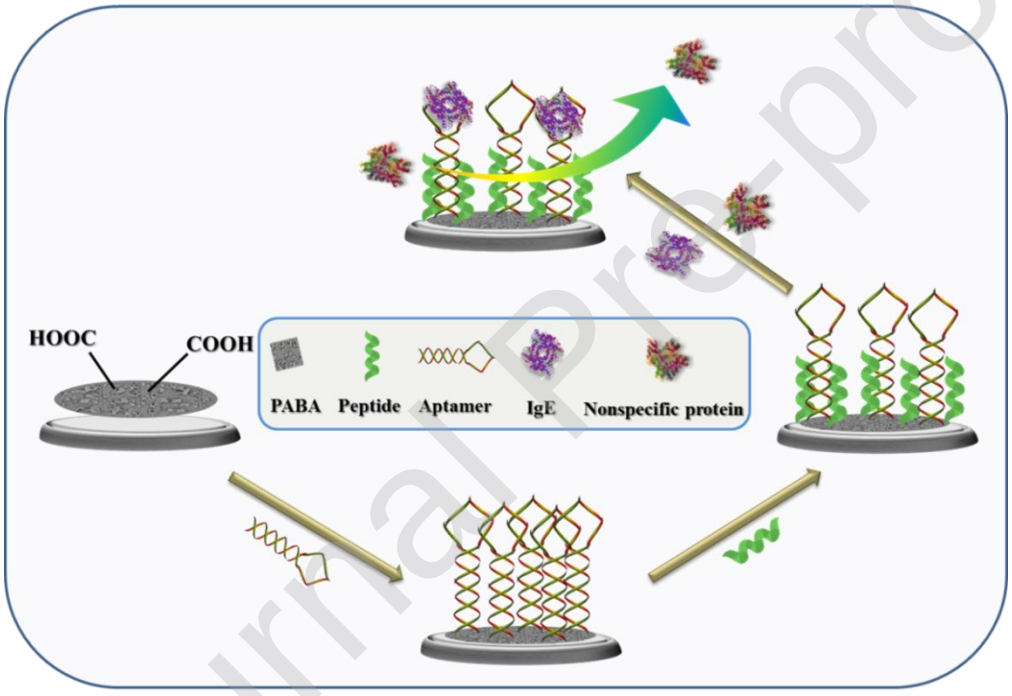
Bare GCE was polished, cleaned and electrochemically pretreated according to a previous method [31]. PABA membrane was electrochemically deposited onto pretreated GCE surface from an aqueous $HClO_4$ solution (1.0 M) containing 0.5 M ABA using CV method from -0.6 V to 1.2 V at the scan rate of 100 mV/s for 20 cycles. As expected, the PABA membrane was obtained on bare GCE surface (PABA/GCE).

2.3. Electrochemical stability investigation of PABA covered GCE

The electrochemical stability of PABA membrane covered electrode (PABA/GCE), which is a crucial factor directly influencing the development and performance of biosensor, was investigated through electrochemical CV method in 0.5 M $HClO_4$ solution for uninterrupted 5 000 cycle scans. Afterwards, the current values of a pair of oxidation and reduction peaks in different CV curves were recorded, respectively, to compare the decline levels of peak currents and further to inquire the electrochemical stability of PABA/GCE.

2.4. Biosensor surface fabrication

The fabrication process is schematically stated as **Scheme 1**. Based on the abundant carboxyl (-COOH) group present on PABA membrane, the capture probe of aptamer (1.0 μM) was firstly attached through covalent binding under the assistance of NHS and EDC, subsequently, the preferred peptide was compactly immobilized onto PABA surface with the same manner to form a two-layer architecture. Here, the PABA membrane densely decorated with aptamer and peptide would present the capability of sensitive signal response, specific target recognition, and effective antifouling property.



Scheme 1. Fabrication of a two-layer architecture biosensor based on PABA membrane decorated with well-designed aptamer and favored peptide in sequence.

2.5. Antifouling capability measurement

Different dilution ratios (V/V) of FBS solutions that had been adopted as typical antifouling assay sample [32] in PBS solutions (0.2 M, pH 7.4) were selected to assess the antifouling ability of constructed biosensing surface based on preferred peptide.

Electrochemical impedance spectroscopy (EIS), a sensitive, powerful and facile technique measured in PBS (0.2 M, pH 7.4) solution containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$ and 0.1 M KCl, was employed to sensitively monitor the change happened at so-prepared electrode surface. For EIS test, the direct current potential was set at 0.23 V associated with the frequency range from 0.1 Hz to 1 000 KHz and the amplitude of applied sine wave of 5 mV. For the antifouling evaluation, the fabricated different surfaces were continuously immersed into different ratios (V/V) of FBS solutions for 30 min, after that, EIS responses were recorded and analyzed.

3. Results and discussion

3.1. Synthesis and characterization of PABA on GCE surface

The straightforward electrochemical synthesis with only one step CV curve of PABA on bare GCE surface is shown in **Fig. 1**A, which covered the first, second, tenth, fifteenth and twentieth cycle, respectively. A big oxidation peak (at about 1.0 V) occurred in the first cycle from **Fig. 1**A, ascribing to the occurrence of oxidation reaction of ABA monomer to form PABA polymer. With the continued scan, the peak at 1.0 V dropped clearly. From the second cycle, two pairs of oxidation and reduction peaks derived from PABA polymer were observed obviously, and along with the CV scan, both the oxidation and reduction peak currents increased until reached equilibrium, declaring the polymerization reaction accomplished.

The electrochemical stability of PABA covered electrode (PABA/GCE) was explored using uninterrupted CV scan for 5 000 cycles (**Fig. 1**B). Encouragingly, after

5 000 cycles, the current values corresponding to a pair of oxidation and reduction peaks did not clearly decline, which still reserved about 93.5% (Oxidation peak) and 91.5% (Reduction peak) of initial currents, respectively, certainly declaring the approving charge storage capability and also the pleasing electrochemical stability that would to be the vital foundation for biosensor construction.

Typical SEM photographs of PABA modified GCE (PABA/GCE) surface with different magnifications are distinctly exhibited in **Fig. 1**C and D. Clearly, from **Fig. 1**C and D, the PABA membrane as-deposited on GCE surface revealed a very apparent wrinkle structure, which could offer larger specific surface area and more binding sites for biomolecule immobilizations to further improve the signal response of biosensor.

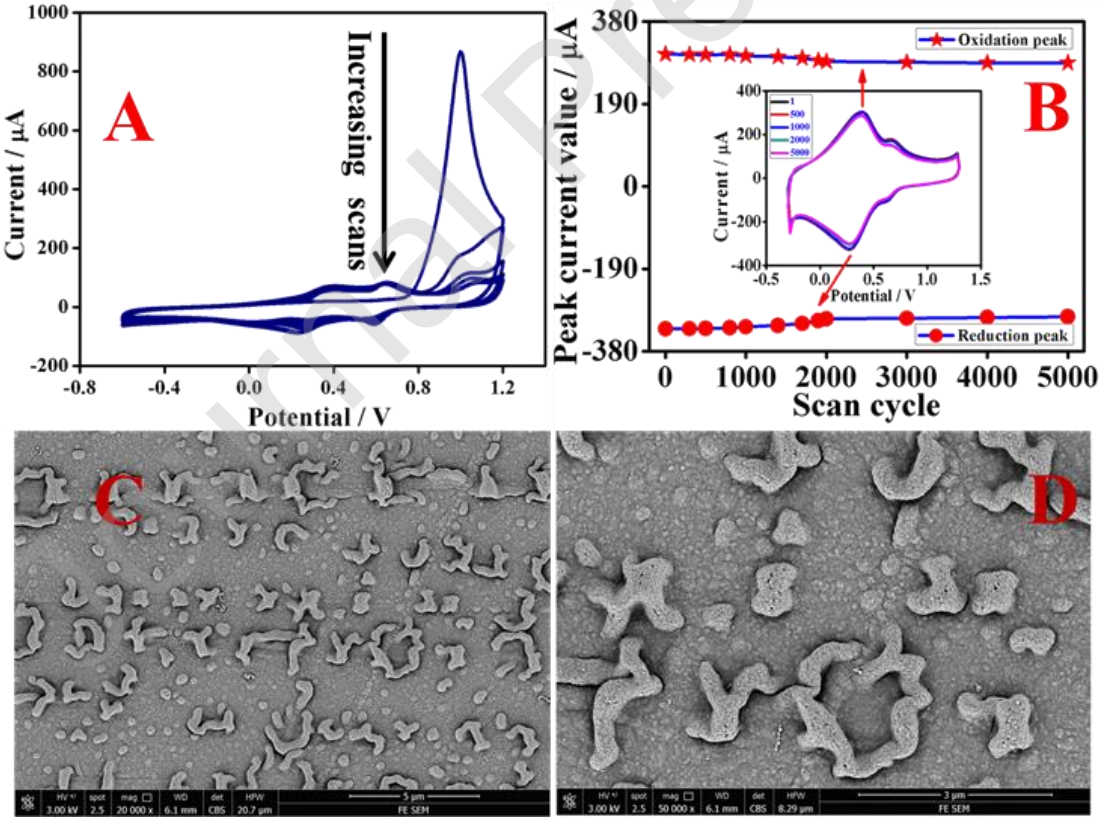


Fig. 1. (A) Electrochemical polymerization CV curves of PABA, including the first, second, tenth, fifteenth and twentieth cycle, respectively. (B)The electrochemical stability of PABA modified

GCE (PABA/GCE) with different CV scan cycles, tested in 0.5 M $HClO_4$ solution.
SEM images of PABA covered GCE surface at low (C) and high (D) magnifications, respectively.

3.2. Fabrication characterization of biosensor

3.2.1. Electrochemical characterization

Electrochemical methods of CV and EIS are adopted to characterize the stepwise fabrication process of a modified electrode (shown in **Fig. 2**A and B). After PABA was electrochemically deposited onto bare GCE surface (**Fig. 2**A), the current signal dramatically enhanced (curve b) compared with that of bare GCE (curve a), due to the excellent conductivity of PABA membrane that could significantly accelerate the electron transfer. Interestingly, accompanied by the sequential attachments of aptamer and peptide, the current responses accordingly decreased associated with the migration of peak potential (curve c and d), certifying the successful combinations of biomolecular aptamer and peptide. The insulating biomolecules prevented the electron transfer to some degree. As expected, when the fabricated electrode was incubated in IgE solution, the obtained current (curve e) signal further decreased, resulting from the binding between specific aptamer and its target protein that declined the electron transfer.

Fig. 2B shows the EIS Bode plots of different fabrication steps of a modified electrode. In contrast with bare GCE (curve a), the highly conductive PABA membrane decreased impedance signal and boosted electron transfer (curve b). After the covalent assembly of aptamer and peptide and the specific binding between target protein and aptamer, the impedance responses of modified electrode kept increasing

correspondingly, indicating improved impedance in electron transfer. The EIS results in accordance with CV response are proof of successful development and sensitive targetrecognition of such fabricated biosensor based on PABA platform.

3.2.2. XPS characterization

To further verify the deposition of PABA, and the attachments of aptamer and peptide on PABA covered electrode surface, XPS analysis was performed after several modification steps. As shown in **Fig. 2**C, for PABA coated surface, C 1s, N 1s and O 1s peaks derived from PABA were obviously observed. **Fig. 2**D confirmed the sequentially covalent bindings of aptamer and peptide, because of the appearances of P 2p (from aptamer) and S 2p (from peptide) peaks, due to the compactly coverage of aptamer and peptide on PABA membrane. The XPS signals verified the successful deposition of PABA on electrode surface and approving decoration of aptamer and peptide on PABA surface.

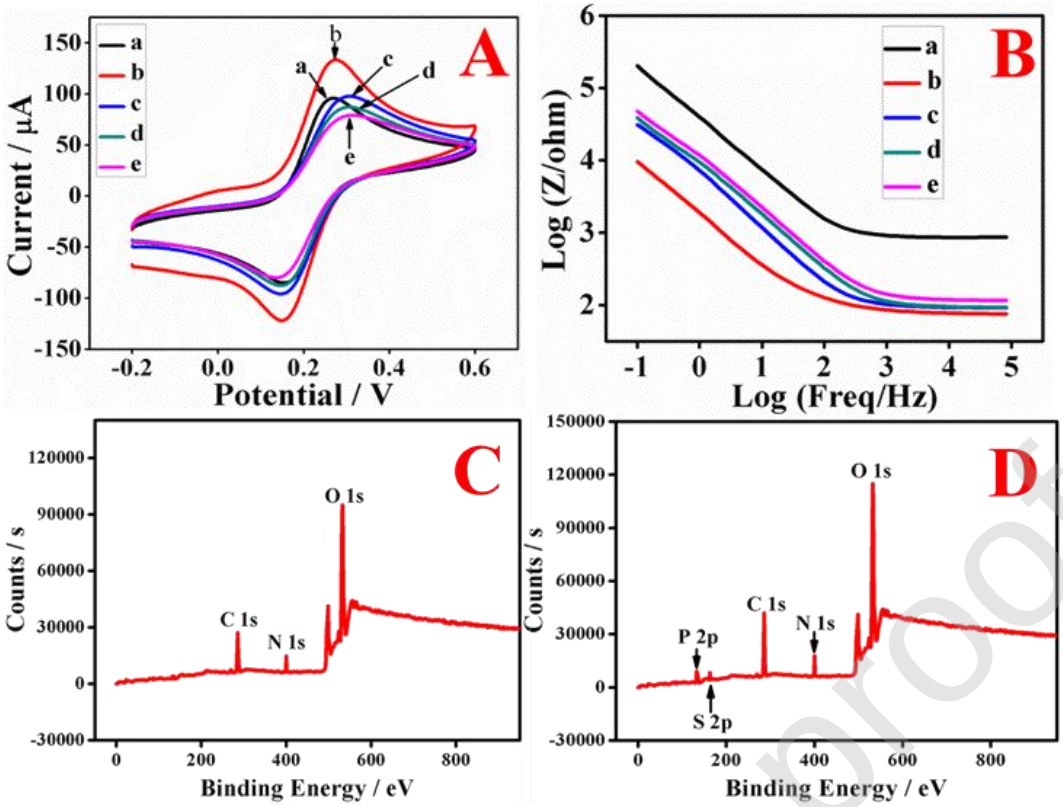


Fig. 2. (A) CV curves of (a)bare GCE, (b) PABA/GCE, (c) Aptamer/PABA/GCE, (d) Peptide/Aptamer/PABA/GCE and (e) Peptide/Aptamer/PABA/GCE bound with target protein, recorded in PBS (0.2 M, pH 7.4) containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$and 0.1 M KCl.
(B) EIS Bode plots of (a) bare GCE, (b) PABA/GCE, (c) Aptamer/PABA/GCE, (d) Peptide/Aptamer/PABA/GCE and (e) Peptide/Aptamer/PABA/GCE bound with target protein, measured in PBS (0.2 M, pH 7.4) containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$and 0.1 M KCl.
XPS spectra of electrode modified with (C) PABA membrane and (D) Peptide/Aptamer/PABA, respectively.

3.3. Hydrophilicity characterization

CA measurement was conducted to evaluate the hydrophilicity property of different surfaces, which would be extremely important in resisting nonspecific protein adsorption, because enough hydrophilicity could eliminate/decline the protein interaction with surface through hydrophobicity effect. As clearly shown in **Fig. 3**, after being coated with PABA membrane, the CA of PABA/GCE surface decreased from 69 ° (A) to 63 ° (B), indicating moderate hydrophilicity of PABA membrane,

which may be ascribed to the abundant present of carboxyl (-COOH) groups in PABA membrane. The covalent attachment of aptamer with PABA caused further decrease (C), showing the successful immobilization of biomolecule aptamer. As expected, the modified electrode surface became more hydrophilic (D) after the densely package of peptide, suggesting the excellent hydrophilic property of such preferred peptide-based surface that would make it capable of eliminating/decline nonspecific protein adsorption.

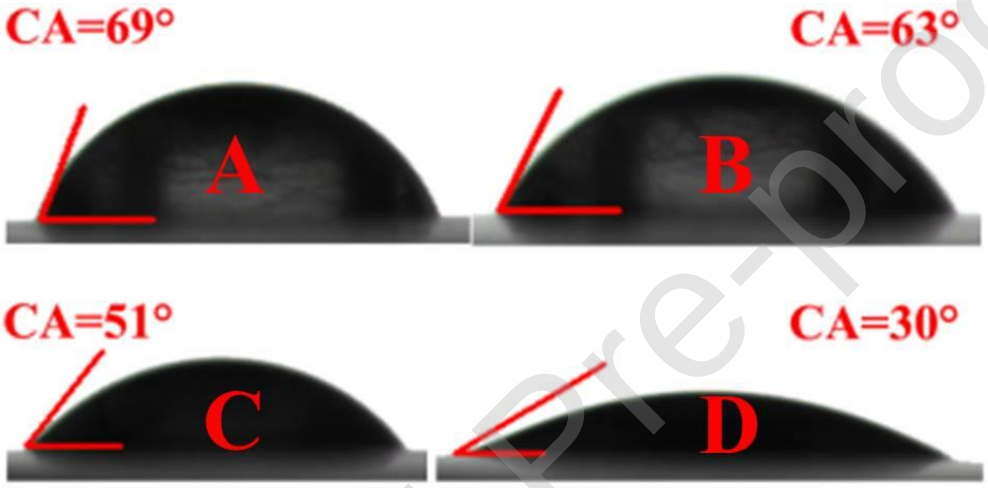


Fig. 3. Water CA images of (A) bare GCE, (B) PABA/GCE, (C) Aptamer/PABA/GCE and (D) Peptide/Aptamer/PABA/GCE surfaces.

3.4. Antifouling property investigation

As noted, the direct and sensitive detection of disease biomarker in complex biological sample especially when in the presence of plenty of nonspecific protein is exceedingly demanding. To assess the performance of peptide-based biosensing interface in preventing nonspecific protein adsorption, EIS was used to monitor superficial changes before and after the soaking of biosensor in different dilution ratios (V/V) of FBS solutions. As clearly shown in **Fig. 4**A, for the fabricated

interface, a very small EIS signal increase was observed until the immersion in 20% FBS solution (no observed change when the FBS concentration was below 10%), and the signal slightly increased when the FBS concentrations were above 20% (100% FBS led to only 35% increase, as presented in **Fig. S1**). However, for the control interface without peptide introduction, only 10% FBS soaking caused significant signal augment (more than 35%) and a greater enlargement (more than 180%) occurred by 100% FBS soaking (**Fig. 4**B and **Fig. S1**). These results manifested such peptide-based interface admirable capability in preventing nonspecific protein adsorption even in complex serum sample, which principally derived from remarkable hydrophilicity and favourable charge neutrality of the preferred peptide.

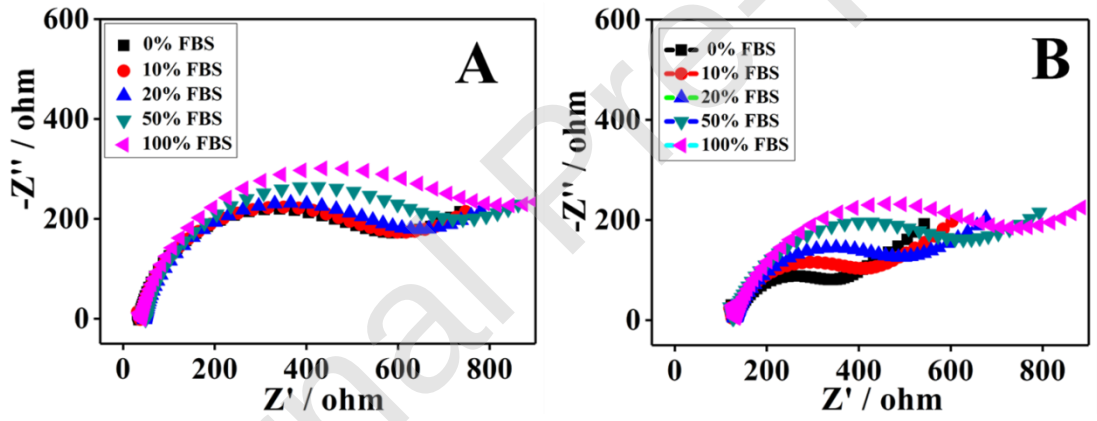


Fig. 4. Nonspecific protein adsorption measurements of electrodes modified (A) with and (B) without peptide using EIS. EIS plots were recorded before and after soaking in different ratios (V/V) of FBS solutions. EIS measurements wereperformed in PBS (0.2 M, pH 7.4) solution containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$ and 0.1 M KCl.

3.5. Analytical biosensing performance

The analytical performance of developed biosensor toward target protein IgE was surveyed using differential pulse voltammetry (DPV) method performed in PBS (0.2 M, pH 7.4) solution containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$ and 0.1 M KCl. The

specific target binding led to a DPV response decrease until reaching equilibrium along with IgE concentration increasing from 0.001 ng/mL to 100.0 ng/mL (**Fig. S2**). The detailed analysis of such biosensor response to target IgE was shown in **Fig. 5**, from which the DPV response change ($-\Delta I_p/ I_{p0}$) behaved as a good linear correlation ($R^2 = 0.998$) with the logarithmic value of IgE concentration within the range from 0.001 ng/mL to 50.0 ng/mL, and the limit of detection (LOD) was calculated to be 0.52 pg/mL (S/N = 3). Besides, the signal response change ($-\Delta I_p/ I_{p0}$) of constructed biosensor to different concentrations of IgE in the presence of 10% (V/V) FBS was also tested as shown in **Fig. S3**, and the same linearity range from 0.001 ng/mL to 50.0 ng/mL was obtained. All results were evident that the biosensor exhibited pleased binding efficiency and delighted detecting sensitivity that was sufficient for such biosensing surface to be detectably responsive to its target IgE across its clinically relevant range, primarily attributing to the incorporation of favourable conductivity of synthesized PABA, admirable antifouling characteristic of preferred peptide and superior binding capability between aptamer and target.

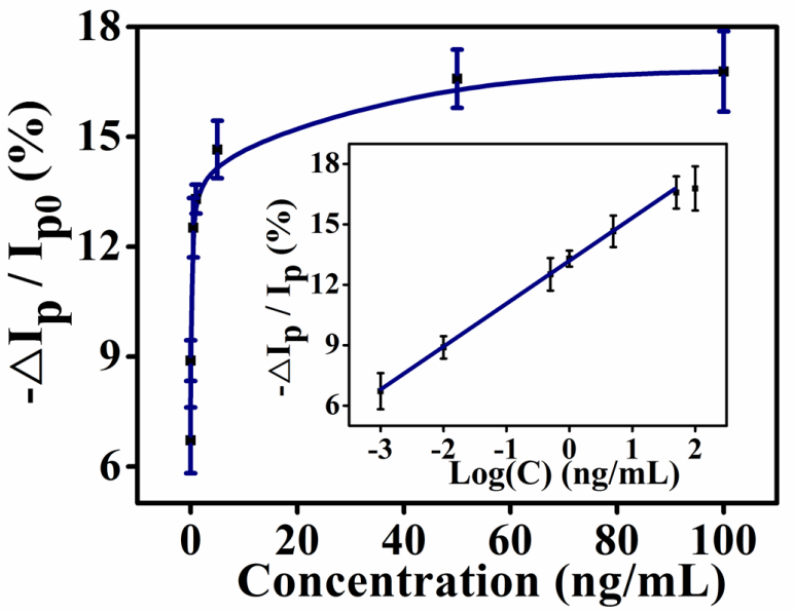


Fig. 5. Dynamic response range and calibration curve (inset) of prepared biosensor toward target IgE concentration.

For numerous biosensing systems, the specific and accurate detection of target with the presence of a great deal of nonspecific ingredients, such as proteins and DNA, is especially demanded. To evaluate the interfacial specificity toward its target IgE, the current response change ($-\Delta I_p/ I_{p0}$) was tested in different PBS solutions containing HSA, AFP, Lys, IgG, single-stranded DNA or target IgE, separately. Strikingly, as shown in **Fig. 6**, such interface displayed satisfying specificity to target IgE because interfacial responses behaved rather weak toward other ingredients even in artificial higher concentration. Hence, the fabricated biosensor performed outstanding specificity toward target protein IgE, which was ascribed to the superior target binding ability and advanced antifouling property of such biosensor.

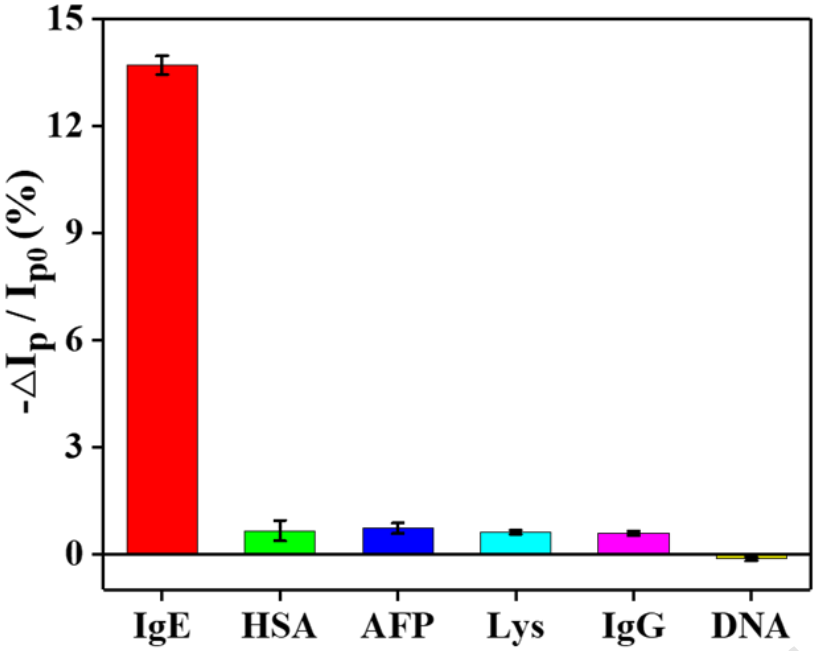


Fig. 6. Responses of the IgE biosensor to 1.0 ng/mL of IgE, 100.0 ng/mL of HSA, AFP, IgG, Lys and 100.0 nM DNA, respectively.

Ten biosensors were prepared independently, and then used to measure 1.0 ng/mL target IgE, respectively. Encouragingly, the received result showed benign reproducibility of the established biosensor, because a small relative standard deviation (RSD) of about 4.9% was obtained.

To survey the accuracy of the constructed biosensor in real serum samples, different concentrations of IgE were added into 10% (V/V) FBS solutions, and then measured by prepared biosensor. The results were listed in **Table ~~S~~1**, from which satisfying recoveries (from 97.81% to 100.02 %) with the RSD between 0.52% and 3.58% were obtained, manifesting a promising practical application potential of such biosensor.

Table 1 Analytical results for IgE in 10% (V/V) fetal bovine serum (FBS).

Sample	Add (ng/mL)	Found (ng/mL)	Recovery (%)	RSD (%)
1	0.50	0.496±0.012	99.21	2.42
2	1.00	0.978±0.035	97.81	3.58
3	50.00	50.01±0.262	100.02	0.52

4. Conclusion

In summary, a highly conductive PABA membrane was successfully deposited onto electrode surface using a straightforward electrochemical method of CV. As expected, the PABA membrane expressed both excellent electrochemical stability and apparent wrinkle morphology that could effectively increase response signal and specific surface area of electrode. Next, well-designed aptamer and favored antifouling peptide were covalently and successively assembled onto the as-prepared PABA membrane that bears abundant carboxyl (-COOH) groups to build a two-layer architectural bio-interface with target recognition ability and antifouling capability for the accurate detection of disease biomarker IgE. The biosensor performed well in testing target IgE across its clinically relevant range associated with high specificity, sensitivity and reproducibility, due to the incorporation of highly conductive PABA membrane, specific aptamer for target and preferred antifouling peptide. It is believed that, the simple electrochemical deposition method of PABA widely broadens the application area, especially in bio-analysis, of conductive ABA, in view of its inherent carboxyl (-COOH) group. And also the assembly procedure of two-layer architecture biosensing platform will bring more conveniences to bio-analysis of human disease

biomarker.

Shuai Wang: Methodology, Writing- Original draft preparation;
Yihui Ma: Data curation;
Yu Wang: Investigation;
Mingxia Jiao: Software;
Xiliang Luo: Conceptualization;
Min Cui: Supervision; Writing- Reviewing and Editing.

Notes

The authors declare that there is no conflict of interest regarding this manuscript.

Acknowledgment

This research was supported by the National Natural Science Foundation of China (21804051), the Natural Science Foundation of Shandong Province of China (ZR2019BB042 and ZR2019BB077), the Doctor Foundation of University of Jinan (XBS160100311), and the Open Foundation of Key Laboratory of Sensor Analysis of Tumor Marker of Ministry of Education of Qingdao University of Science &Technology (SATM201809).

References

[1] L.L. Lu, L. Zhou, J. Chen, F. Yan, J.Y. Liu, X.P. Dong, F.N. Xi, P. Chen, Nanochannel-Confined graphene quantumdots for ultrasensitive electrochemicalanalysis of complex samples, ACS Nano12 (2018)12673-12681.

[2] S. Somasundaram, C.J. Easley, A nucleic acid nanostructure built through On-Electrode ligationfor electrochemical detection of a broad range of analytes, J. Am. Chem. Soc. 141 (2019) 11721-11726.

[3] D. Wang, Y.Q. Chai, Y.L. Yuan, R. Yuan, Precise Regulation of Enzyme Cascade Catalytic Efficiency with DNA Tetrahedron as Scaffold for Ultrasensitive Electrochemical Detection of DNA, Anal. Chem. 91 (2019) 3561-3566.

[4] A. Weathers, Z.U. Khan, R. Brooke, D. Evans, M.T. Pettes, J.W. Andreasen, X. Crispin, L. Shi, Significant electronic thermal transport in the conducting polymer poly(3,4-ethylenedioxythiophene), Adv. Mater. 27 (2015) 2101-2106.

[5] Z.S. Wu, K. Parvez, S. Li, S. Yang, Z.Y. Liu, S.H. Liu, X.L. Feng, K. Müllen, Alternating stacked graphene-conducting polymer compact films with ultrahigh areal and volumetric capacitances for High-Energy Micro-Supercapacitors, Adv. Mater. 27 (2015) 4054-4061.

[6] T. Wang, M. Farajollahi, S. Henke, T.T. Zhu, S.R. Bajpe, S.J. Sun, J.S. Barnard, J.S. Lee, J.D.W. Madden, A.K. Cheetham, S.K. Smoukov, Functional conductive nanomaterials via polymerisation in nano-channels: PEDOT in a MOF, Mater. Horiz. 4 (2017) 64-71.

[7] N. Hui, F.L. Chai, P.P. Lin, Z.L. Song, X.T. Sun, Y.N. Li, S.Y. Niu, X.L. Luo, Electrodeposited conducting polyaniline nanowire arrays aligned on carbon nanotubes network for high performance supercapacitors and sensors, Electrochim. Acta 199 (2016) 234-241.

[8] N. Hui, X.T. Sun, S.Y. Niu, X.L. Luo, PEGylated polyaniline nanofibers:

Antifouling and conducting biomaterial for electrochemical DNA sensing, ACS Appl. Mater. Interfaces 9 (2017) 2914-2923.

[9] R.X. Wang, X.F. Wang, Y.M. Sun, One-step synthesis of self-doped carbon dots with highly photoluminescence as multifunctional biosensors for detection of iron ions and pH, Sens. Actuators, B 241 (2017) 73-79.

[10] J.P. Wang, X.X. Tan, X.J. Pang, L. Liu, F.P. Tan, N. Li, MoS_2 Quantum Dot@PolyanilineInorganic-Organic nanohybrids for in vivo Dual-Modal imaging guided synergistic Photothermal/Radiation therapy, ACS Appl. Mater. Interfaces 8 (2016) 24331-24338.

[11] H.J. Gould, B.J. Sutton, IgE in allergy and asthma today, Nat. Rev. Immunol. 8 (2008) 205-217.

[12] N. Drinkwater,B.P. Cossins, A.H. Keeble, M. Wright, K. Cain, H.H. Amanda Oxbrow, J. Delgado, L.K. Shuttleworth, M.W.P. Kao, J.M. McDonnell, A.J. Beavil1, A.J. Henry, B.J. Sutton, Human immunoglobulin E flexes between acutely bent and extended conformations, Nat. Struct. Mol. Boil. 21 (2014) 397-404.

[13] E.S. Gusareva, I. Kurey, I. Grekov, M. Lipoldova, Genetic regulation of immunoglobulin E level in different pathological states: integration of mouse and human genetics, Biol. Rev. 89 (2014) 375-405.

[14] M.C. Alonso, L.T. Alfonso, J.M. Costa Fernándezn, R. Pereiron, A.S.Medel, Functionalized gold nanoclusters as fluorescent labels for immunoassays: Application to human serum immunoglobulin E determination, Biosens. Bioelectron.77 (2016) 1055-1061.

[15] B.Y. Jiang, F.Z. Li, C.Y. Yang, J.Q. Xie, Y. Xiang, R. Yuan, Aptamer Pseudoknot-Functionalized electronic sensor for reagentlessand Single-Step detection of immunoglobulin E in human serum, Anal. Chem.87 (2015) 3094-3098.

[16] K. Maehashi, T. Katsura, K. Kerman, Y. Takamura, K. Matsumoto, E. Tamiya, Label-free protein biosensor based on aptamer-modified carbon nanotube field-effect transistors, Anal. Chem. 79 (2007) 782-787.

[17] J.J. Yao, X.G. Han, S. Zeng, W.W. Zhong, Detection of Femtomolar Proteins by Nonfluorescent ZnS Nanocrystal Clusters, Anal. Chem. 84 (2012) 1645-1652.

[18] J.J. Yao, S. Schachermeyer, Y.D. Yin, W.W. Zhong, Cation exchange in Zn Senanocrystals for signal amplification in bioassays, Anal. Chem. 83 (2011) 402-408.

[19] H. Li, C.Y. Chen, X. Wei, W.B. Qiang, Z.H. Li, Q. Cheng, D.K. Xu, Highly sensitive detection of proteins based on metal-enhanced fluorescence with novel silver nanostructures, Anal. Chem. 84 (2012) 8656-8662.

[20] A. Salimi, S. Khezrian, R. Hallaj, A. Vaziry, Highly sensitive electrochemical aptasensor for immunoglobulin E detection based on sandwich assay using enzyme linked aptamer, Anal. Biochem. 466 (2014) 89-97.

[21] C. Tuerk, L. Gold, Systematic evolution of ligands by exponential enrichment: RNA ligands to bacteriophage T4 DNA polymerase, Science 249 (1990) 505-510.

[22] G. Bozokalfa, H. Akbulut, B. Demir, E. Guler, Z.P. Gumus, D.O. Demirkol, E. Aldemir, S. Yamada, T. Endo, H. Coskunol, S. Timur, Y. Yagci, Polypeptide functional surface for the aptamer immobilization: lectrochemical Cocaine Biosensing, Anal. Chem. 88 (2016) 4161-4167

[23] D. Roncancio, H.X. Yu, X.W. Xu, S. Wu, R. Liu, J. Debord, X.H. Lou, Y. Xiao, A label-free aptamer-fluorophore assembly for rapid and specific detection of cocaine in biofluids, Anal. Chem.86 (2014)11100-11106.

[24] Y.H. Kim, J.P. Kim, S.J. Han, S.J. Sim, Aptamer biosensor for lable-free detection of human immunoglobulin E based on surface plasmon resonance, Sens. Actuators, B 139 (2009) 471-475.

[25] B. Li, P. Jain, J. Ma, J.K. Smith, Z. Yuan, H.-Ch. Hung, Y. He, X. Lin, K. Wu, J. Pfaendtner, S.Y. Jiang, Trimethylamine N-oxide-derived zwitterionic polymers: A new class of ultralow fouling bioinspired materials, Sci. Adv. 5(2019) 1-11.

[26] J.A. Callow, M.E. Callow, Trends in the development of environmentally friendly fouling-resistant marine coatings, Nat.Commun. (2011) 1-10.

[27] A.K. Nowinski, F. Sun, A.D. White, A.J. Keefe, S.Y. Jiang, Sequence, structure, and function of peptide Self-Assembled monolayers, J. Am. Chem. Soc.134 (2012) 6000-6005.

[28] P. Zhang,P. Jain, C. Tsao, K. Wu, S.Y. Jiang, Polypeptides with High Zwitterion Density for Safe and Effective Therapeutics, Angew Chem Int Edit 57 (2018) 7743-7747.

[29] H.J. Ye, L.B. Wang, R.L. Huang, R.X. Su, B.S. Liu, W. Qi, Z.M. He, Superior antifouling performance of a zwitterionic peptide compared to an amphiphilic, Non-Ionic peptide, ACS Appl Mater Interfaces 7 (2015) 22448-22457.

[30] O.R. Bolduc, J.N. Pelletier, J.F. Masson, SPR biosensing in crude serum using ultralow fouling binary patterned peptide SAM, Anal. Chem. 82(2010) 3699-3706.

[31] G.X. Wang, Q.J. Xu, L. Liu, X.L. Su, J.H. Lin, G.Y. Xu, X.L. Luo, Mixedself-assembly of polyethylene glycol and aptamer on polydopamine surface forhighly sensitive and low fouling detection of adenosine triphosphate in complexmedia, ACS Appl. Mater. Interfaces 9 (2017) 31153-31160.

[32] Z. Matharu, P. Daggumati, L. Wang, T.S. Dorofeeva, Z.D. Li, E. Seker, Nanoporous-Gold-Based electrode morphology libraries for investigating Structure-Property relationships in nucleic acid based electrochemical biosensors, ACS Appl. Mater. Interfaces 9(2017) 12959-12966.