Design and Fabrication of Nanostructured Flexible Devices for Biomarkers Detection

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Abstract

We developed flexible devices based on gold nanostructures obtained via photolithography on a flexible platinum surface.

Introdução

Biomarkers are biotransformation of substances or products of biochemical alterations that can be expressed in large amounts whenever there is an imbalance in the human body [1]. The detection of biomarkers, such as ascorbic acid, dopamine, glucose and salivary cortisol, it can be useful to prevent and other genetic diseases as well as for subsequent treatment [1]. Chemical sensors and biosensors have been used as an alternative to the analytical tools of large and expensive [2].

Thus, the motivation of this work was developed a nanostructured flexible device based on Pt/Au for biomarkers detection. We report the fabrication, characterization and applicability of the nanostructured flexible device. The electrochemical oxidation of the biomarkers was monitored by measuring the increase in oxidation current (ascorbic acid and dopamine) and by measuring the increase in the resistance of charge-transfer (cortisol) to the flexible surface, respectively.

Resultados e Discussão

Nanostructured interdigitated microelectrode array (IMA) of platinum/gold (Pt/Au) was fabricated by lift-off process photolithographic and [3] in transparent acetate sheets covered with a 5nm layer of chromium (Cr) and a 100 nm layer of platinum (Pt). The first step consists in depositing a layer of positive photoresist AZ4210 on slides transparent acetate covered with a layer of 5 nm of chromium and 100 nm Pt using a spin coater rotation speed of 3000 rpm for 30 s, followed by heat treatment at 90 ° C for 5 min and exposed to UV light for 40 seconds. Then, the surface was immersed in a developing solution (K400) for 15 seconds. After obtaining the interdigitated pattern in the photoresist film, it is metalized 100 nm gold. The removal of the excess photoresist and gold was done by immersing the substrate in acetone (lift-off).

Firstly, the nanostructured flexible device was applied to electrochemical oxidation of the biomarkers (ascorbic acid and dopamine) detection by differential pulse voltammetry in PBS solution. The results showed a good analytical performance.

Finally, the self-assembled monolayer (SAM) was immobilized by immersion of nanostructured flexible device in a solution containing 5 mM of 3mercaptoacetic acid (3-MAA) by 20 h. The anticortisol was immobilized on the nanostructured flexible surface with EDC/NHS. Then 25 µL of stock solutions containing $1.0 \times 10^{-12} - 1.0 \times 10^{-3}$ g mL⁻¹ of cortisol were dispensed on the flexible surface for the immobilization of the target (cortisol) in the flexible device for 20 min, subsequently Nyquist diagrams were performed in PBS solution containing 5.0 mmol L^{-1} the redox probes $K_3[Fe(CN_6)]/$ $K_4[Fe(CN)_6]$. Increased cortisol concentration in the immobilized on flexible device produced a significant increase in charge-transfer resistance (R_{ct}) of Nyquist plots suggesting that cortisol was efficiently adsorbed on flexible surface. The R_{ct} values produced a linear relationship with increasing concentration of cortisol on the flexible device in the range between 1.0 x 10^{-12} and 1.0 x 10^{-8} mg L⁻¹ (3.1 x 10^{-15} e 2.7 x 10^{-3} mol L⁻¹) represented by equation $(I (A) = 0.04 + 0.702 \pm 0.052 \ 0.004 \pm C_{\text{cortisol}} \ (\text{mg L}^{-1})$ with a coefficient of linear correlation (r) of 0.997.

Conclusões

The nanostructured flexible surface was developed successfully and it was applied in the biomarkers detection ascorbic acid, dopamine, glucose and cortisol salivary. The flexible device is promising to wearable devices development for non-invasive detection.

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¹ Lim, C. S.; Chua, C. K.; Pumera, M. Analyst. 2014, 139, 1072.

² Turner, A. Trends Biotechnol., **2013**, *31*, 119.

³Huanga, H.M.; Liua, C.H.; Leeb, V.; Leea, C. Sens. Act. B, 2010, 149, 59.