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**Electrodeposited Highly Porous Gold Microelectrodes for the Direct Electrocatalytic
Oxidation of Aqueous Glucose**

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Abstract

High-surface area electrode materials are particularly relevant for a vast range of applications, especially in the field of catalysis and electrochemical energy conversion (e.g. fuel cells).

5 In this work high surface area gold electrodes were produced by direct electrodeposition of highly porous gold (hPG) films onto gold electrodes via a very fast (15 sec), simple, and cost-effective methodology that involves a hydrogen bubble template. This methodology was also successfully applied to gold microelectrodes produced by lift-off lithography, thus paving the way for interesting lab-on-a-chip applications.

10 The hPG electrodes showed very high sensitivity towards glucose, with a detection limit of 5 μM . This reactivity was maintained when the electrodes were tested in artificial urine, thus encouraging their use in healthcare.

The hPG electrodes showed high sensitivity also towards other aldoses and other reducing sugars (maltose, lactose, galactose).

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Keywords: nanoporous gold, glucose sensor, lab-on-a-chip, nanostructure, electrocatalysis

1. Introduction

20 Glucose monitoring is essential for the effective treatment of diabetes. For the past three decades enzymatic glucose tests have been the prevailing technology [1]. Non-enzymatic glucose-sensitive electrodes, however, can potentially lead to sensors that are less affected by temperature and pH, and generally more stable than those dependent on immobilised enzymes [2].

25 In this context, considerable attention has recently been given to the development of glucose sensors based on highly porous gold (hPG) electrodes, such as nanoporous gold electrodes, due to the observed reactivity of these electrodes towards glucose [3]. The non-enzymatic aerobic oxidation of glucose to gluconic acid at neutral pH by nanoporous gold was reported as far back as 2008 [4]. Only much more recently the use of hPG electrodes as a glucose sensor has been
30 investigated [3, 5, 6].

Key features of hPG electrodes are: very large specific surface area, high electrocatalytic activity, conductivity, and biocompatibility [3, 7, 8].

35 The establishment of efficient, simple and low-cost processes for the manufacture of such electrodes is therefore key. The development of methodologies that could easily be transferred to the microscale is particularly attractive for the use of hPG electrodes in lab-on-a-chip sensors and microfluidic electrochemical devices.

40 The main techniques so far reported to produce hPG films required the selective etching of silver from thick layers of gold and silver alloys [9, 10]. Other more complicated templated methods have also been used [11, 12]. Only recently two simple and rapid methods that target the deposition of gold, and avoid the use of any harsh or expensive reagents were reported [3, 13]. Cherevko et al., in particular, developed a hydrogen template assisted electrodeposition of hPG onto a Pt/Ti/Si electrode in conjunction with a gold (III) electrolyte [13]. Yet, this technique has not been proven to
45 be transferable to lab-on-a-chip scale thin film gold electrodes.

This study reports a rapid, easy, cost-effective, and targeted direct electrodeposition method to produce hPG electrodes, which has been also applied for the first time to thin film electrodes produced by lift-off lithography. The resulting electrode was then tested for the amperometric
50 detection of aqueous glucose. The nature of the electrochemical reaction occurring at the electrode surface was then investigated by comparing the electrode response towards a selection of sugars.

Finally, the hPG electrodes were tested in artificial urine to explore their potential implementation in healthcare.

2. Experimental

2.1 Materials

AZ nLOF 2070 photoresist and AZ 326 MIF Developer were purchased from Microchemicals. All other reagents were of analytical grade and purchased from Sigma-Aldrich.

Gold disk electrodes (2 mm diameter), saturated calomel electrodes (SCE) and platinum counter electrodes were purchased from IJCambria Ltd.

The hPG film electrodeposition and all the electrochemical processes were conducted using the Autolab PGSTAT128N potentiostat. All potentials are referred to against SCE.

2.2 Patterning Electrodes onto Glass Slides

Gold electrodes (1 mm x 10 mm) were patterned onto glass slides by lift-off lithography as described in the supplementary data (Figure SS1).

2.3 Electro-deposition of Porous Gold Film and

Gold electrodeposition was performed in an aqueous electrolyte consisting of 0.1 M H₂AuCl₄ and 1 M NH₄Cl.

The morphology of the resulting electrodes was characterised using a Hitachi S-4300 field emission scanning electron microscope (FESEM).

2.4 Electrochemical Characterisation

The electrochemical characterisation regarded only the hPG electrodes fabricated on gold disks.

All the experiments were carried in phosphate buffered saline (PBS), prepared in distilled water with: 137 mM NaCl, 2.7 mM KCl, 10 mM Na₂HPO₄, 2 mM KH₂PO₄. The pH was adjusted to 7.

Artificial urine was prepared by adding urea (8 g l⁻¹) to PBS and by adjusting the pH of the resulting solution to 8.9 [14, 15].

Cyclic voltammetry (CV) and amperometric tests were performed in a three-electrode electrochemical cell with a SCE reference electrode and a platinum rod counter electrode.

CV scans were performed at the potential range of -0.8 V - 0.8 V (vs. SCE). The amperometric tests were performed at 0.15 V (vs. SCE). A concentration range of 0.005 - 50 mM was considered for all the sugars tested. During the addition of the target sugar the solution was agitated for 20 s. In

order to minimise the amperometric noise observed, the agitation was stopped and the solution was left for 270 s to allow for stabilisation of the amperometric response under natural convection. The

average response over a period of 10 s was then recorded. Three replicates were performed per experiment.

The electrochemically effective surface area (ESA) of the porous gold electrodes was determined using equation 1:

$$ESA = \Delta I_{porous} \times \frac{SA_{flat}}{\Delta I_{flat}} \quad (1)$$

Where SA_{flat} is the surface area of the bare electrode, and ΔI is the charging current, or capacitance, of the system measured at 0.5 V during a CV scan between 0.42 V and 0.6 V (vs. SCE) at 1 mV s⁻¹.

3. Results and Discussion

The electrodeposition of porous gold films *via* a hydrogen bubble template is a new technique to produce hPG electrodes which requires small amount of gold; is fast; does not involve harsh reagents; and is easy to perform [13].

In our group we observed, however, that the resulting gold structures were unstable, as pieces of black hPG film would easily flake off the surface of the gold disk. A better control of the evolution and removal of hydrogen gas during the electrodeposition process could improve the adhesion of

the porous gold film onto the electrode surface. A gradual potential step down process was therefore developed. Firstly, the working potential was set to -0.7 V vs. SCE (potential at which the evolution of hydrogen gas first occurs) for a period of 5 seconds. This first step (S1) would create an uneven gold surface for the adhesion of the hPG film. The set potential was then stepped down to -4.0 V (vs. SCE) for a period of 10 seconds (S2). This highly negative potential ensures intense hydrogen bubbling that is key for the final foam-shape of the electrode

After S1, a crystalline feather-like framework of gold developed on the surface of the gold disk electrode (Figure 1A), which would serve as an anchoring point for the subsequent electrodeposition of the porous gold film. At the end of the electro-deposition process, the electrode presented a 3D foam-like structure with a wide pore size distribution ranging from 10 nm to 30 μm (Figure 1B). The nano-structure inside the large pores was comparable with the structure of nanoporous gold films previously reported [13].

This large distribution in pore size is crucial for the high amperometric reactivity observed. The larger pores (lined with nano-pores) allow for the free movement of the electrolyte deep into the porous gold structure of the electrode resulting in an ESA of $29 \pm 5.3 \text{ cm}^2$, approximately 10^3 times higher than the ESA of the bare gold disk (0.031 cm^2).

The direct electrodeposition of hPG films was subsequently applied on thin-film gold electrodes patterned on glass slides by lift-off lithography.

Initial tests showed that these electrodes were more fragile than the commercial ones, as the rapid evolution of hydrogen gas at -4.0 V (vs. SCE), during S2, damaged the patterned electrodes (data not shown). It was, therefore, decided to reduce the hydrogen evolution by using a potential of only -2.5 V (vs. SCE) during this stage, for the same period of time (10 sec).

A much greater variance in the deposited gold morphology was observed in this case (Figure 1C). Inside the large pores, some feather-like structures, similar to those obtained on gold disks after S1, were observed, which might be a result of the weaker deposition potential adopted.

The electrodeposition methodology for these microelectrodes must be further optimised, and a further characterisation of the resulting structure is required. Nonetheless, this result demonstrates for the first time the direct electrodeposition of highly porous gold on thin film (100 nm thick) gold microelectrodes, paving the way for the easy and fast fabrication of high surface area gold microelectrodes for lab-on-a-chip sensors and microfluidic devices.

In future work electrodeposition times longer than 10 seconds, during S2, will be investigated to search for the time that optimises the hPG structure without damaging the microelectrode.

Long range CV scans conducted on freshly prepared porous gold disk electrodes in the presence of glucose and at a scan rate of 5 mV s^{-1} , revealed a clear glucose-dependent response. In particular, a strong current peak on the forward scan was observed at approximately 0.15 V (vs. SCE), as previously found [5]. The magnitude of the current peak changed with the concentration of glucose in the electrolyte (Figure 2).

The reactivity of the porous gold electrodes was also tested on other reducing sugars, such as maltose, lactose and galactose. A ketose (fructose), and a non-reducing sugar (sucrose) were also considered for comparison.

Figure 3 reports the cyclic voltammetry tests obtained with a concentration of 5 g l^{-1} for each sugar. In the case of fructose and sucrose, no relevant peak currents were observed when compared to blank scans conducted in PBS (Figure 3D). On the other hand, for each aldose the forward peak at approximately 0.15 V (vs. SCE) was confirmed. The electro-oxidation of each sugar tested might involve the dehydrogenation of the aldehyde group, as for glucose [16]. The oxidation peak observed for all the aldoses tested might, in particular, refer to the hydrogen atom bounded to the carbon C1 atom of the aldehyde group of the sugars [16]. This justifies the inertness of sucrose and fructose that both lack the reactive hydrogen on the carbon C1 atom.

The shape of the cyclic voltammetry curves was generally different for each sugar. An exception was observed for maltose with a CV curve very similar to the one obtained with glucose (Figure 3A).

5 By considering the results from the CV scans, the potential of 0.15 V (vs. SCE) was chosen for the amperometric tests. Figures 4A and 4B show the increase in current observed by step-increasing the concentration of glucose. A very strong correlation between the current observed and the concentration of glucose in the solution was observed, with a detection limit of 5 μ M. This is concurrent with the sensitivity obtained when using similar porous gold electrodes and gold nano-composites produced in much more costly processes [5, 17]. The standard deviation in the current observed between three different electrodes was substantial at low concentrations of glucose (up to 80% for a 5 μ M glucose solution, Figure 4B). For the purpose of using these electrodes as sensors the data sets were therefore normalised. This was achieved by calibrating the electrodes between 0 and 50 mM glucose in PBS. The amperometric response in glucose free PBS, I_0 , and the amperometric response in a 50 mM glucose and PBS solution, I_{50} , was recorded and then used to calculate the normalised response, N , for any given amperometric response, I (Equation 2).

$$N = \frac{I - I_0}{I_{50} - I_0} \quad (2)$$

The resulting data (Figure 4C) shows a much lower percentage standard deviation for all data points, with a maximum standard deviation of 15% observed for a 5 μ M glucose solution.

20 The hPG electrodes showed the same sensitivity with the other reducing sugars tested (supplementary data, Figure SS2).

The range of sensitivity required by a sensor for glucose levels in the human body varies according to the type of test implemented. In urine the normal glucose concentration varies between 0.0 and 0.8 mM [18].

25 Following a positive urine test, further more invasive testing of blood or cerebrospinal fluid glucose levels are usually conducted. Currently, sweat glucose tests (glucose range: 0.5 μ M- 27 μ M) are considered as a potential valid alternative to invasive tests [19].

30 The reactivity of the hPG electrode towards glucose was consequently investigated in artificial urine (supplementary data, Figure SS3). The relationship between current observed and concentration of glucose was unaffected by the presence of urea and by the higher pH (from 7 to 8.9).

35 Future work will regard the analysis of the influence that other compounds present in biological fluids, such as uric and ascorbic acid, and catecholamine, might have on the hPG amperometric response. Due to the high sensitivity of hPG, its potential use to detect glucose in sweat will also be investigated.

4. Conclusions

40 A rapid method (15 seconds) for the direct electrodeposition of highly porous gold electrodes was developed, which is easily transferable to thin-film microelectrodes lithographically produced. The resulting electrodes have a wide pore size distribution and an electrochemically effective surface area 10^3 times greater than bare gold.

45 The porous gold electrodes showed high sensitivity towards glucose with a detection limit of 5 μ M, which was maintained when the electrodes were tested in artificial urine.

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Vitae

Hendrik du Toit is a PhD student in the Department of Chemical Engineering, University of Bath, UK. He received his MEng in Chemical Engineering from Imperial College London in 2011. He is currently conducting research into the production of biocompatible biosensors and biofuel cells.

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