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Enhanced Ion Sensing Stability with Nanotextured Biosensors

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***Abstract*— The rapidly growing market on healthcare wearable electronics has been witnessed and raised enormous research interest in biosensors for noninvasive health monitoring. Electrolytes are present as an essential in the human body, while properly maintaining the balance of the electrolytes in our bodies is critical to ensure the normal function of our body. Herein, in order to achieve reliable detection of the sodium (Na^+) concentrations in the body fluids, nanotextured biosensors were designed and fabricated. The ionic detection is realized by a Na^+ ion selective membrane assembled onto a nanotextured Au @ PEDOT: PSS layer. The sensor prepared on flexible substrate allows monitoring of Na^+ concentration levels through a highly selective and sensitive electrochemical process, and is capable to achieve long-term stability with significantly reduced signal drift, which has been rarely studied. The results proved that nanotextured biosensors can be a practical and effective method to enhance ion sensing stability.**

Keywords— nanotextured biosensor; ion sensing; noninvasive health monitoring; long-term stability

I. Introduction

The noninvasive health monitoring technique has gained increasing interest in clinical diagnosis and personalized health care in recent years because it is more convenient and more friendly compared with the traditional clinical procedures. Normally, it relies on sensors as the key component to monitor critical analytes through body fluids, and refer to an integrated product in clothing or accessories fashion, such as watches [1], sweatbands [2], shirts [3], gloves [4], glasses [5], patch [6, 7] and contact lenses [8], to fulfill the intelligent functions. Body fluids like sweat, saliva, tears and urine that can be acquired in noninvasive approaches contain a huge library of biomarkers as those can be invasively obtained by blood tests [4]. These biomarkers can serve as human health indicators. Human body normally has a well maintained and proportioned mixture of varies electrolyte ions and other components, such as proteins, glucose and lactate. Studies have showed that a disproportionate amount of specific ion could interfere with the ion equilibrium status inside human body and cause a corresponding variation in the sweat secretion composition. Sodium ion, for instance, is a key biomarker to indicate the balance state of the body fluids and reflect our health state. A massive loss of sodium ions in body fluid is a note of alarm for patients with cystic fibrosis, because it can cause hyponatremia, while a long term continues increasing on the concertation of sodium ion could be considered as a sign which relate to high blood pressure[9].

With the increasing demand for clinical diagnosis and heightened awareness of personalized healthcare, wearable biosensors are believed to provide ideal approaches to implement noninvasive health monitoring in real time, which is necessary for daily and personalized healthcare. Biosensors fabricated on flexible platforms can closely adhere to human skin and monitor the physiological signals of the human body without disturbing our daily life. In the real application of the wearable potentiometric ion sensors, selectivity, sensitivity and stability are crucial factors. While a large amount of research effort has been invested to achieve high selectivity and sensitivity, the long-term stability of noninvasive biosensing still requires much improvement.

In this work, we developed a nanotextured biosensor for selective Na^+ sensing. The sensor electrode is modified with Au nanodendritic structure and well controlled active materials mass loading. The largely increased electrode surface area could facilitate the ion diffusion and charge transfer. Thus, the potentiometric response of the as-fabricated sensor delivers significantly enhanced sensing stability and largely suppressed signal drift over 30 hours continuous ion sensing. Besides, its sensitivity is desirable for a relatively low concentration range, especially for noninvasive monitoring via sweat. The as-developed nanotextured biosensors fabrication strategy can be applied to a large library of biomarkers, including various electrolyte ions, for their promising applications in health monitoring.

II. Results and Discussions

For Na^+ sensing, a two-electrode system that contains a Ag/AgCl reference electrode and a functionalized working electrode was designed and fabricated on a flexible polyethylene terephthalate (PET) substrate to achieve noninvasive potentiometric detection in biofluids, as shown in Figure 1. The conductive electrode patterns were made through evaporation of Au on a thin and flexible PET. The working electrode was then nanotextured with Au dendritic nanostructures to enhance biosensing response and better adhesion of active materials. The dendritic nanostructure grown on the Au pattern by over-potential deposition via applying a periodic voltage wave with amplitude of -2 V, frequency of 50 Hz and duty cycle of 50% in gold planting solution (50 mM $HAuCl_4$ and 50 mM HCl) for 3000 cycles following previous reports [10]. Following that, a layer of conducting polymer Poly(3,4-ethylenedioxythiophene) modified with Poly(sodium-p-styrene-sulfonate) (PEDOT-PSS) was electrochemically deposited on the Au dendrites. PEDOT has the characteristics of high conductivity, simple molecular structure, and small energy gap. And it is widely used in the research of thin film materials, especially in the field of electronic devices due to its almost transparent thin layer. PEDOT is doped with a water-soluble polymer electrolyte PSS to obtain a PEDOT/PSS thin layer with high conductivity, high mechanical strength and good stability. This layer serves as an ion-to-electron transducer, and ensures stable electroactivity due to its low sensitivity to O_2 and pH to ensure reliable biosensing [11, 12]. The as-fabricated dendritic Au @ PEDOT: PSS nanostructures is shown in the SEM image in Figure 1. The selective

potentiometric sensing of Na^+ is achieved by assembling an ion selective membrane consisted of Na ionophore, lipophilic ion exchanger Na-TFPB, PVC as supporting polymer and DOS as plasticizer.

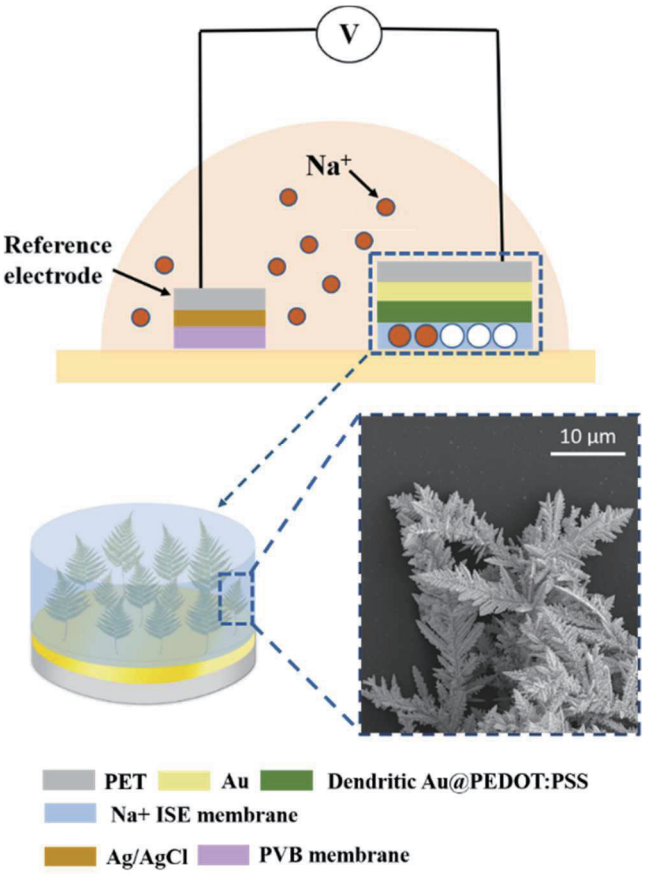

Figure 1. Schematic illustration of the Na^+ biosensor and SEM image of dendritic nanostructures.

The ion sensing performance of the as-fabricated sensor was tested by electrochemical methods, including instance open circuit voltage-time and electrochemical impedance. The electrochemical behavior of the as-fabricated Na^+ sensors were characterized in standard solutions with Na^+ concentrations from 15 mM to 120 mM, which is in the range as that in sweat. The corresponding results were studied systematically. As shown in Figure 2a, both the as-prepared sensors with thin film or nanotextured electrodes deliver potentiometric response to the Na^+ concentration variation, while the nanotextured one contributes to higher response signals. This is mainly due to the reduced intrinsic resistance with dendritic nanostructures, which can be proved with the electrochemical impedance spectrum (EIS) in Figure 2b. As demonstrated in Figure 2b, it is very clear that a smaller arc at higher frequencies was observed at nanotextured electrodes than thin film sensor, which indicates a reduced charge-transfer resistance at the nanotextured sensor interface. Besides, compared with the thin film sensor electrode, the nanotextured sensor delivers a superior sensing recovery with negligeable hysteresis in repeated response to the same ion concentration, as indicated by the dash line in Figure 2a. It is believed that the large surface area of dendritic Au@ PEDOT: PSS layer facilitates ion absorption and reduces the ion charge transport impedance, which contributes to the suppressed hysteresis.

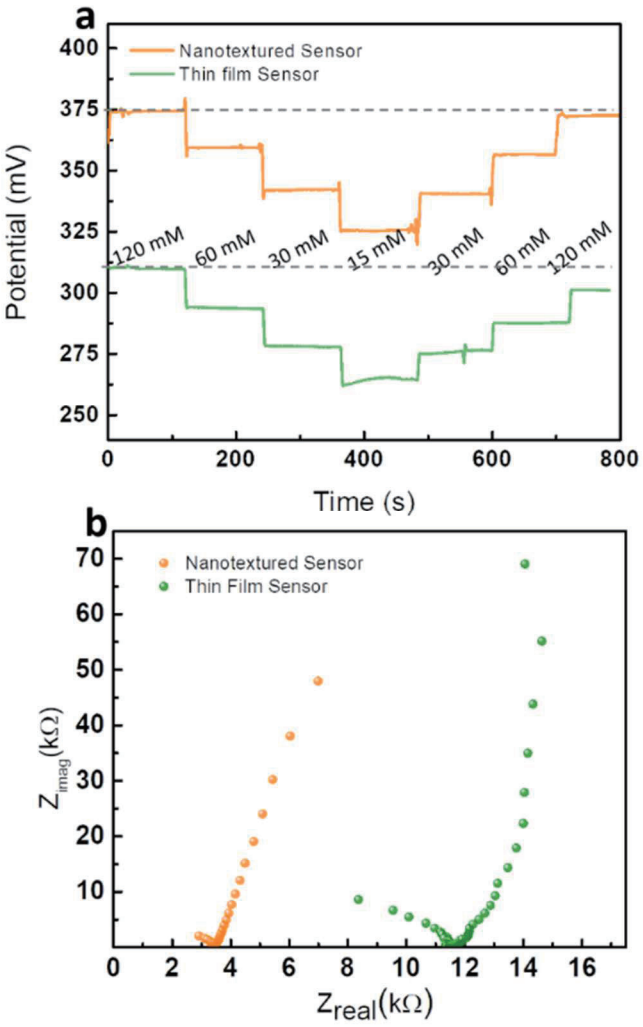

Figure 2. Electrochemical performance comparison of nanotextured and thin film sensors. (a) Potentiometric response in standard Na^+ solutions and (b) EIS curves.

Serving as the ion-to-electron layer, the optimization of PEDOT: PSS has a critical influence on the ion sensing performance without doubt. Compared with constant potential deposition, pulse deposition is easier to obtain a conformal coating layer. By using pulse deposition, the resulted mass loading and morphology of the active materials can be controlled by parameters such as waveform, frequency, duty cycle and average current density. By optimizing the parameters in this electrodeposition process, it is possible to obtain a uniform active material coating on the nanotextured electrode. During pulse deposition process, after applying a pulse potential, the electrolyte ions consumed at the electrode-electrolyte interface can be replenished within the pulse interval. Thus, the electrolyte concentration polarization at the interface is effectively reduced. Besides, it hinders the growth of large particles, so that it is not easy to form coarse particles.

To achieve conformal coating of PEDOT: PSS onto the nanodendritic Au electrode, pulse deposition under a periodic voltage wave with amplitude of 0.865 V, frequency of 1 Hz, duty cycle of 25 % was utilized [13]. Figure 3a shows the performance comparison between the sensor with conformal PEDOT: PSS layer deposited under pulse sensor and the one using a constant potential of 0.865 V for PEDOT: PSS

deposition. It can be seen that the pulse deposition strategy contributes to a larger response signal. This result proves that the pulse deposition realizes successful PEDOT: PSS mass loading, and indicates that a conformal layer coating can reduce the sensor resistance, and thus facilitate electron transfer.

Apart from providing a conformal material coating on complicated nanostructures, the layer thickness can be well controlled under pulse deposition method by adjusting the deposition time represented by the deposition cycle numbers. The ion sensing performance of sensors with different PEDOT: PSS thickness is displayed in Figure 3b and the corresponding sensitivities are plotted in Figure 3c. In this work, PEDOT: PSS was deposited with a cycle number of 630, 840 and 1050, respectively. The results indicate that the optimized performance was achieved with 840 cycles of pulse deposition, generating a high sensitivity of 55.5 mV/decade and eliminated hysteresis in varying ion concentrations. It can be concluded that inadequate mass loading of ion-to-electron transfer materials could result in relatively poor sensing recovery, while the sensitivity could be sacrificed when the layer thickness keeps increasing.

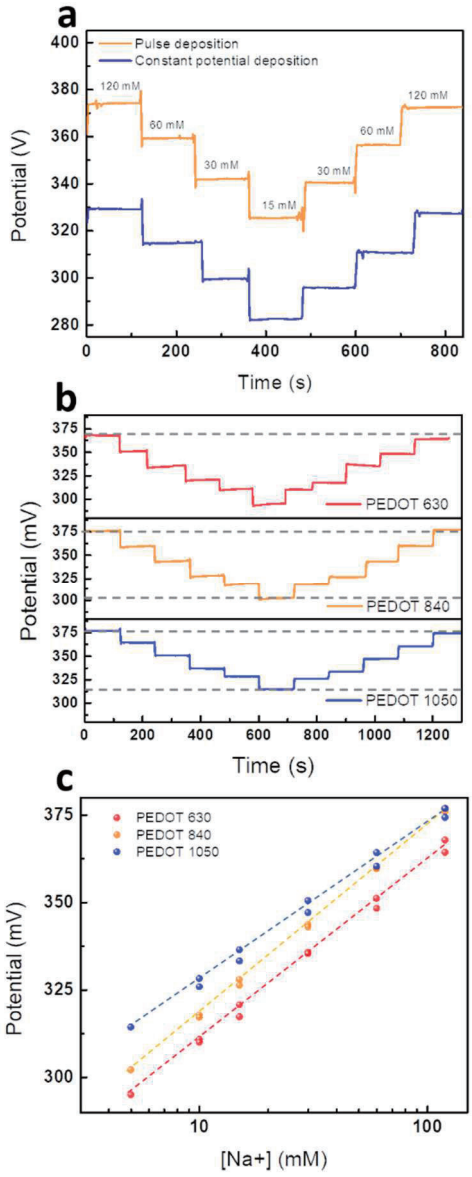

Figure 3. Optimization of deposition on PEDOT:PSS. Potentiometric response comparison between (a) different deposition methods and (b) different deposition cycle numbers and (c) the corresponding sentivities.

The as-fabricated nanotextured electrodes with optimized active material coating deliver remarkable enhancement on long-term ion sensing stability. It is worth mentioning that signal drift is one of the critical form factors for sensing performance evaluation, especially for wearable healthcare applications. Sensor drifting refers to the phenomenon that the output of the sensor changes with time when the input is unchanged. Reliable sensing is unlikely to be demonstrated without significant suppressed drift, simply because large errors will show up when the drift keeps accumulating over long-term using. There are two reasons for sensor drifting, one is the structural parameters of the sensor itself and another is the surrounding environment (such as temperature, humidity, etc). As shown in Figure 4a and b, the nanotextured sensor shows a largely reduced potential drift than thin film sensor in different concentrations over a long-term test of 35 hours. For non-invasive sensors, long-term stability is still a huge challenge, such long-term continuous monitoring of up to 35 hours has rarely been seen before. The nanotextured sensor has a potential drift of less than 1 mV hr^{-1}, while the thin film one shows a signal drift of over two times larger, as shown in Figure 4c. The results indicate that the nanotextured sensor with conformal active material coating can significantly enhance the long term sensing stability. This desirable form factor can be attributed to the suppressed capacitance on the nanotextured electrode with reduced charge accumulation. Besides, a robust adhesion between the ion selective membrane and the electrode can be achieved with the nanotextured morphology, so as to eliminate possible mechanical interference, such as a introduced undesirable capacitance due to the formation of hydration layer between layers of materials.

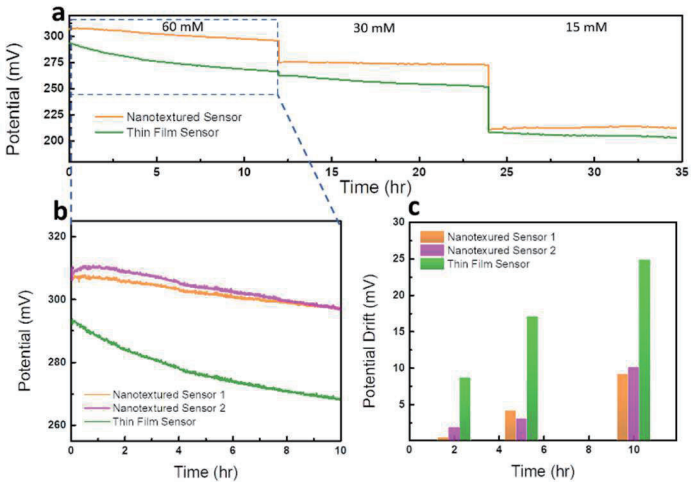

Figure 4. Ion sensing stability with nanotextured sensors. (a) 35 hours long-term testing and (b) repeatability with two nanotextured sensors compared with thin film sensor. (c) Potential drift of the sensors.

III. Conclution

In this work, nanotextured sensors for Na^+ ion sensing were fabricated and systematically characterized. Optimized fabrication approach was explored and the remarkable electrochemical performance enhancement was demonstrated. The as-fabricated nanotextured sensors achieve a superior

sensing stability with eliminated hysteresis and largely suppressed signal drift without sacrificing selectivity and sensitivity. The as-demonstrated enhanced ion sensing stability is desirable for long-term and real time noninvasive health monitoring via body fluids like sweat. The biosensor fabrication approach developed in this work can also be applied for sensitive and reliable monitoring of a variety of ions and other health relevant biomarkers, which is critical for wearable biosensors innovation.

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