

# A SELF-POWERED SENSOR PATCH FOR GLUCOSE MONITORING IN SWEAT

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## ABSTRACT

We developed a paper-based self-powered sensor patch for detecting glucose levels in sweat. This wearable, non-invasive biosensor made use of the integration of a vertically stacked paper-based glucose/oxygen enzymatic fuel cell into a standard Band-Aid patch. The paper-based device, attached directly to human skin, wicked sweat from human skin and monitored an electrochemical energy conversion as a transducing element for glucose monitoring in sweat, thus obviating the requirement of external power sources and sophisticated readout instrumentation. The device features (i) a 3-D origami paper-based fuel cell structure for easy system integration on paper, (ii) an electrically conducting paper microfluidic reservoir for high anode surface area and efficient mass transfer, and (iii) a direct electron transfer between enzymes and electrodes for enhanced electron discharge properties. The sensor showed a linear range of output current at 0.02-1.0mg/mL glucose ( $R^2=0.989$ ) with a high sensitivity.

## INTRODUCTION

A painless and non-invasive method for glucose monitoring from other tissue fluids, such as tears, saliva, skin interstitial fluid and sweat, is an attractive alternative to blood measurement [1]. Among them, sweat glucose monitoring offers considerable promise as a wearable platform that can provide continuous and real-time analysis [2, 3]. A glucose level in sweat is metabolically related to blood glucose [4]. Despite their vast potential and promise, however, further progress in the wearable glucose sensors has been hindered by (i) requirement for sophisticated external readout instrumentation, (ii) an insufficient on-chip electrical power, and (iii) a complicated device architecture with additional reference electrode integration. Recently, an innovative concept for glucose monitoring has been proposed by using electrochemical energy transformation in an enzymatic fuel cell as a transducing technique [2, 5, 6]. Their electron discharging properties from enzymes contributed to the development of self-powered glucose sensors, in which glucose is oxidized at the anode while oxygen is reduced at the cathode. Thus, the electrical output of the fuel cell as an analytical signal is proportional to the glucose concentration.

In this work, we report the first demonstration of the sensing concept for self-powered wearable glucose monitoring in sweat. A 3-D glucose/oxygen enzymatic fuel cell was assembled from a 2-D paper sheet by simply folding along pre-defined creases and gluing with adhesive spray (Figure 1). The fuel cell-based sensor substantially improved the device fabrication by simply patterning hydrophilic reservoirs in paper with hydrophobic wax boundaries and adding water-dispersed electrically

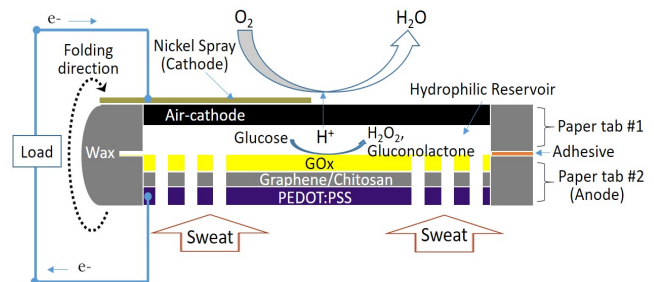


Figure 1: Schematic diagram of a cross section of the device. When sweat containing glucose is introduced into the hydrophilic reservoir of the paper tab #1, glucose oxidation is catalyzed by the glucose oxidase (GOx) immobilized on the paper tab #2. Then, the GOx transfers its electrons to the PEDOT:PSS anode through a direct electron transfer reaction. These electrons flow to the air-cathode through the external circuit. Protons released by the oxidation reaction travel through the paper reservoir toward the air-cathode. By using freely-available oxygen as the electron acceptor, the air-cathode completes the redox reaction. The current and power generated from the device are a function of glucose concentration in sweat, creating a self-powered glucose monitoring system.

conducting polymer mixture, poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS) to the reservoirs [7, 8]. In order to overcome the kinetic barrier for enzymatic electron transfer, graphene nanoparticles were introduced to the PEDOT:PSS reservoir. The microporous paper structure ensured a large surface area and efficient mass transfer to and from the electrodes while the conductive polymers and graphene nanoparticles enhanced electrocatalytic activity and the rate of electron transfer. This self-powered, non-invasive, disposable wearable sensor will be an alternative for real-time sweat glucose monitoring at any time.

## METHODS AND MATERIALS

The fuel cell consisted of three functional regions; (i) the anode layer with the conductive reservoir layer, (ii) the sweat reservoir and (iii) the air-cathode layer (Figure 1). The circular-shaped fuel cell were carefully aligned with a hole cut in the Band-Aid patch so that the cathode was exposed to the air for their cathodic reactions and the anodic reservoir was directly in contact with human skin (Figure 2).

### Reagents

Glucose oxidase (GOx) from *Aspergillus niger* (CAS 9001-37-0), chitosan (CAS 9012-76-4), acetic acid (CAS 64-19-7), Nafion® solution (CAS 31175-20-9), and D-glucose (CAS 50-99-7) were purchased from Sigma-Aldrich. Activated carbon (AC) was purchased

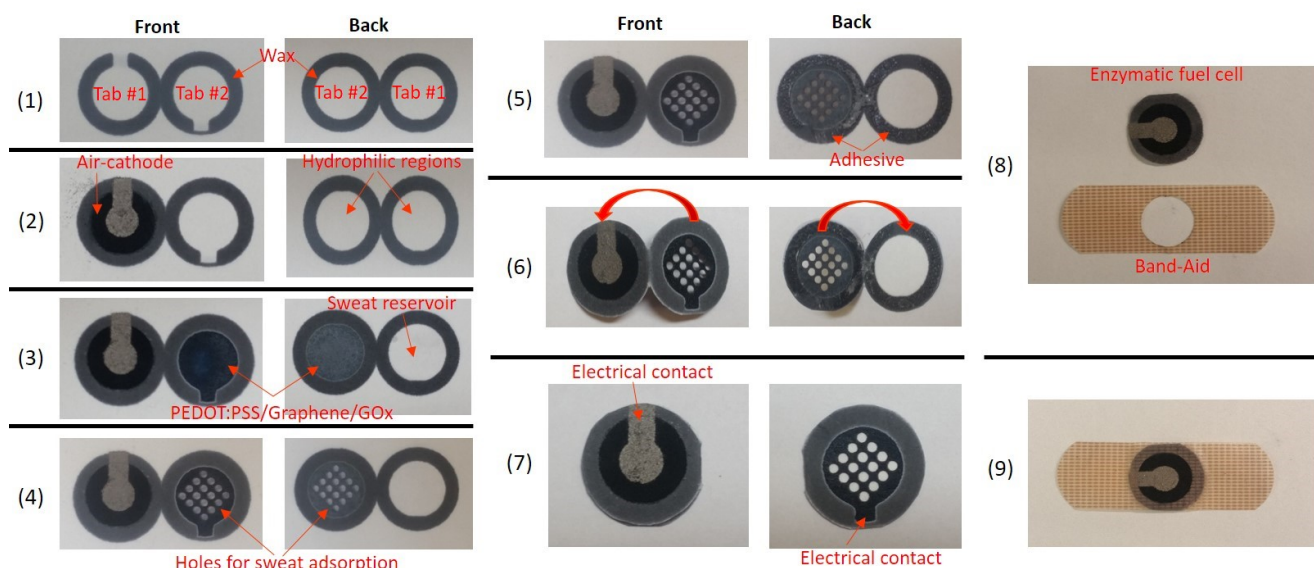


Figure 2: (1)-(9) Intermediate steps for fabrication process of the device. Step 1. wax-boundary formation; Step 2. Air-cathode fabrication; Step 3. Anode and GOx formation; Step 4. Cutting holes; Step 5. Spraying adhesive; Step 6. Folding tabs; Step 7. Assembled enzymatic fuel cell; Step 8. Cutting hole in the Band-Aid; Step 9. Assembled sensor patch.

from Cabot Corporation. We also used a nickel conductive spray purchased from MG Chemicals for the air-cathode.

### Device fabrication and operating principle

The 2-D sheet of paper was designed to have two folding tabs and patterned into hydrophilic regions defined by printed wax boundaries with controlled geometry using a commercially available solid-wax printer (Xerox Phaser 8570dn). The front side pattern was printed first and then heat treated at 150°C for 90 seconds. The back side pattern was printed after heat treatment of the front side and was also heat treated at 130 °C for 30 seconds so that complete penetration of wax from either side can be allowed through the paper. AutoCAD software was used to design the wax patterns on the paper sheet. One of the tabs incorporated an air-cathode with a hydrophilic reservoir for sample holding while the other tab included a conductive PEDOT:PSS treated reservoir for immobilization of GOx (Figure 1 & Figure 2). When a sample containing glucose was introduced into the paper reservoir, glucose oxidation was catalyzed by the GOx immobilized on the anode. The enzyme then transferred its electrons to the anode through a direct electron transfer reaction. These electrons flowed to the air-cathode through the external circuit. The device determined glucose concentration by measuring changes in current from the enzymatic oxidation, enabling the development of self-powered glucose sensors.

### Conductive anode reservoir

A mixture of PEDOT:PSS (Sigma-Aldrich), dimethyl sulfoxide (DMSO, Sigma-Aldrich), and deionized (DI) water was pipetted into the defined anode reservoir to make it conductive and porous and 3-glycidoxypoly-trimethoxysilane was added to improve hydrophilicity. GOx was immobilized on the conductive reservoir by using graphene/chitosan solution which had been applied on the anode reservoir before GOx was

introduced. Graphene/chitosan solution was prepared by sonicating 1mL of 0.05wt% chitosan solution prepared in 2% acetic acid for 15 minutes and adding 1mg of graphene powder. GOx solution was prepared by stirring 5 mg GOx dissolved in 0.5 mL 0.1 M pH 7.0 phosphate buffer solution [5, 9]. GOx was used in this work due to its extremely specific catalytic activity towards glucose. The graphene nanoparticles acted as mediator and helped the GOx transfer electrons to the anode through a direct electron transfer reaction. The bioanode was dried in air overnight at 4°C. 16 holes were cut on the anodic reservoir to allow for the introduction of sweat.

### Air-cathode

An AC-based air-cathode was constructed on one side of the paper tab with nickel spray to provide structural support and to function as a current collector. Our group previously constructed the air-cathode on paper successfully by layering deposited Ni with AC catalyst (15 mg/cm<sup>2</sup>) in a binder solution [10, 11]. The AC catalysts with a binder solution were applied, which was subsequently air-dried for 24h. The binder solution was prepared by adding a mixture of (i) 1200μL of 5 wt% Nafion solution, (ii) 150μL of DI water, and (iii) 600μL of isopropanol into a conical tube and mixed well in a vortex machine. Since oxygen is readily accessible, sustainable, and environmentally friendly, the air-cathode based device offers the best promise for this application. Moreover, the proton exchange membrane can be removed from the system to reduce production cost and increase power generation with better proton travel efficiency through the hydrophilic reservoir.

### Test Setup

We measured the potentials between the anodes and the cathodes with a data acquisition system (National Instrument, USB-6212), and recorded the readings via a

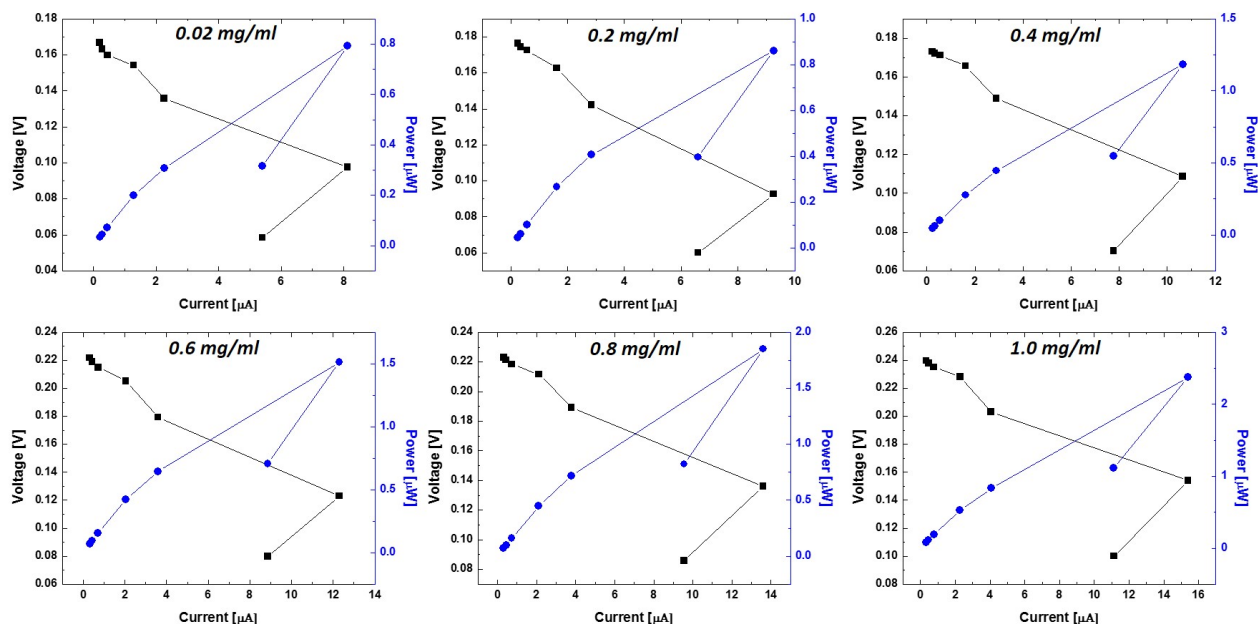


Figure 3: Power outputs and polarization curves with varying concentration of glucose.

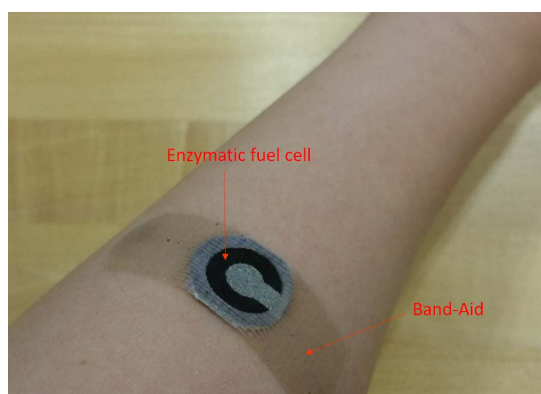


Figure 4: Glucose sensor patch attached to human skin

customized LabView interface. An external resistor connected between the anode and the cathode closed the circuit. The current through this resistor was calculated using Ohm's law.

## RESULTS AND DISCUSSION

### Sample introduction

When the device was assembled, various artificial sweat samples with different glucose concentrations were introduced into the device. The solution wicked through both the conductive and hydrophilic reservoirs without the need for any external pumps and electrical power. This adsorption promoted attachment of the glucose in the sample to the anodic reservoir and immediate electron transfer from GOx. The large pore sized filter paper ( $\sim 10\mu\text{m}$ ) allowed a higher volume of sample to be absorbed into the reservoir and consequently a longer duration of stable current generation [12]. To maximize the cathodic reactions, the air-cathode part was exposed to the air. The hydrophilic reservoir was necessary to electrically separate the anode and the cathode.

### Glucose monitoring from artificial sweat

Figure 3 shows polarization curves and power outputs

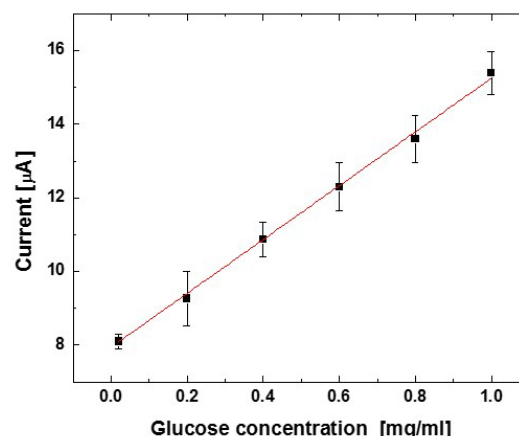


Figure 5: Calibration curve of the sensor (Output current vs. concentration of glucose in artificial sweat)

of the devices with varying concentration of glucose in artificial sweat (0.02mg/ml, 0.2mg/ml, 0.4mg/ml, 0.6mg/ml, 0.8mg/ml, and 1mg/ml). The data were derived and calculated based on the maximum current value at a given external resistance (700k $\Omega$ , 500k $\Omega$ , 300k $\Omega$ , 100k $\Omega$ , 50k $\Omega$ , 10k $\Omega$ , and 1k $\Omega$ ). Using the polarization curve, we estimated device internal resistances from the point where the polarization curve showed a near-linear drop (i.e. the ohmic loss region). These values agree well with the external resistor values where the maximum power density is obtained in Figure 3 [13]. The maximum power outputs were obtained under a 10k $\Omega$  resistor indicating that the internal resistance of the devices was approximately 10k $\Omega$ , which was significantly lower than that of our recent paper-based enzymatic fuel cell (1M $\Omega$ ) [5]. The reduced internal resistance observed in this work is most likely due to the efficient electron transfer through the graphene nanoparticles and the enhanced anodic surface area in the 3-D conductive paper reservoir. This paper-based enzymatic fuel cell developed in this work showed a remarkable potential as a self-powered glucose sensor because it generated enough current and power to



Table 1: Glucose levels of human sweat and blood

	Sweat		Blood glucose level
	Current at 10k $\Omega$	Glucose level estimation from the calibration curve	
Subject #1	8.26 $\mu$ A	0.044mg/ml	0.96 mg/ml
Subject #2	8.10 $\mu$ A	0.021mg/ml	0.85 mg/ml

sensitively resolve varying glucose concentrations in the artificial sweat samples (Figure 5). The calibration curve of the device with a 10k $\Omega$  resistor shows a high linearity ( $R^2=0.989$ ).

### Glucose monitoring from human sweat

The Band-aid sensor patch was applied to two healthy human subjects (Figure 4) and the glucose levels in sweat were monitored (Table 1). Also the sweat glucose were compared with the results obtained with a blood glucose meter (OneTouch Ultra Mini Meter Blue, Lifescan). The results indicate a strong correlation between sweat glucose and blood glucose [14-16].

## CONCLUSION

In this work, we reported a paper-based self-powered sensor patch that allowed for the non-invasive detection of glucose in human sweat. This device used (i) a screen printed graphene/chitosan/GOx anode, (ii) an air-cathode, and (iii) a PEDOT:PSS treated conductive anode reservoir for higher device performance and practical applications. The device was based on glucose/oxygen enzymatic fuel cell using an electrochemical energy conversion as a transducing element for glucose monitoring in sweat, establishing a self-powered, low-cost, and disposable glucose sensing platform. Furthermore, the sensor bandage patch allowed intimate contact with human skin. The device did not require external power sources nor sophisticated external transducers.

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