A self-powered glucose monitor

Tanmay Kulkarni, Naomi Mburu and Gymama Slaughter

Bioelectronics Laboratory, Department of Computer science and Electrical engineering,
University of Maryland Baltimore County,
1000 Hilltop circle,
Baltimore MD 21250, USA

ABSTRACT

Glucose substrates are successfully harnessed to generate electricity in a membraneless biofuel cell with a mesh network of carbon nanotubes pyroquinoline quinone glucose dehydrogenase-modified anode and a laccase-modified cathode. Using glucose as a substrate, this glucose-oxygen biofuel cell is able to produce a steady current density of 337.5 μA/cm² and an open circuit voltage of 524 mV in 360 mg/dL glucose solution. Interestingly, the fuel cell in combination with a capacitor as the transducer element can also be utilized as a glucose monitor while generating electricity simultaneously to power small electronic devices, such as light emitting diode (LED). Moreover, the self-powered glucose monitor exhibited a linear dynamic range of 9 mg/dL to 630 mg/dL glucose. These results and device demonstrations suggest that further research into self-powered glucose monitors can provide major benefit in developing a novel autonomous implantable glucose monitor platform to greatly improve the quality of life for individuals living with diabetes..

Keywords: glucose monitor, diabetes, biofuel cell, voltage boosting

1 INTRODUCTION

The current epidemic of diabetes and its potential growth is a public health risk that is unsustainable and must be addressed. According to the Center for disease control (CDC) 2014 report, 29.1 million people in the U.S. suffer from the disease diabetes, which is the seventh leading cause of death. The cost incurred to keep diabetes under control was 245 billion US dollars [1]. This cost is attributed to the complications that arise due to poor maintenance of blood glucose levels. Some of the complications include retinopathy, neuropathy, gastroparesis, foot complications, ketoacidosis, kidney disease, etc [2]. Diabetes is a metabolic disorder caused by abnormal blood glucose level and is a result of either insufficient production of hormone insulin by the pancreas or the cells in the body do not respond correctly to the insulin produced. There is a significant growth in the number of people suffering from Type 2 diabetes due to the unhealthy lifestyle and stress in their daily life. Normal blood glucose levels for a healthy individual as well as an individual suffering from diabetes is provide in Table I.

Table I: Normal blood sugar levels for non-diabetic as well as diabetic people.

Non-diabetic people		**Diabetic people**	
Test	**Blood glucose (mg/dL)**	**Test**	**Blood glucose (mg/dL)**
Normal	79.2-110	**Pre-meal**	90-130
Fasting	70-100	**Post-meal**	< 180

Current technology for monitoring blood glucose levels involves the use of invasive devices, such as the finger prick test using a glucometer as illustrated in Figure 1A. However, this device is bulky and at times, depending on different batches of the test strips, the meter must be recalibrated. The blood glucose reading can drift by as large as 72 mg/dL. This drift in the blood glucose level can be fatal at times. In addition, tight glucose monitoring may involve pricking the finger multiple times per day, which may prove painful and tedious. Continuous glucose monitoring (CGM) devices (Figure 1B) is another invasive technique used to monitor blood glucose level.

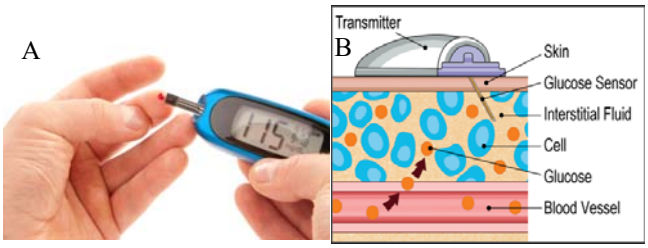

Figure 1 Blood glucose monitoring devices. (A) Glucometer and (B) Conitnuous glucose monitor (CGM)

This device consist of a disposable needle that acts as an *in-vivo* sensor and an external transmitter and receiver. The receiver at the receiving end displays the blood glucose level information. The receiver section consist of a potentiostat circuit, which makes the entire device bulky. This sensor can be used for up to 7 days before replacement. There have been several attempts made to design a noninvasive glucose monitoring device. Of all the attempts, the only device that was approved by U.S. Food and Drug administration (FDA) was the "GlucoWatch G2 Biographer" (Figure 2), which was designed by Cygnus Inc. However, the inconsistencies in the measurement of glucose levels as a result of perspiration

made this device a fad on the market. The above shortcomings of the current glucose monitoring technology must be addressed by developing a closed loop system that would be minimally invasive and flexible and easy to use.

Figure 2. A GlucoWatch G2 Biographer designed by Cygnus Inc.

Glucose selective enzyme, such as glucose oxidase have been used to oxidize glucose to form Gluconolactone. However, the oxidation reaction produces harmful hydrogen peroxide [3] which affects the sensor's stability and life. On the contrary, many glucose monitors strive to use glucose dehydrogenase enzyme because they do not produce any byproducts. Moreover, glucose dehydrogenase enzyme have also been used to fabricate a glucose biofuel cell in prior works [4, 5]. Here we use glucose dehydrogenase enzyme to build a glucose monitor assembly consisting of glucose biofuel cell and a capacitor transducing element acting as a glucose sensor. We also show improved stability of our system compared to the previous work done [5]. This device has the potential to overcome the shortcomings of the existing glucose monitors

2 EXPERIMENTAL SECTION

2.1 Materials and method

180 mg/dL x 2 mm strips of Buckypaper were prepared according to previously established protocols [5]. Briefly, the cleaned buckypaper strips (anodic and cathodic electrodes) were incubated with 1-Pyrenebtanoic acid, succinimidyl ester (PBSE) in 180 mg/dL DMSO solution, where noncovalent π- π stacking occurred between the aromatic ring on the PBSE molecule and the series of aromatic rings that compose buckypaper. The excess PBSE were removed by rinsing the electrodes in 180 mg/dL PBS (pH 7.0), followed by DMSO rinse. Pyroquinoline quinone glucose dehydrogenase (PQQ-GDH) was immobilized at the anode and laccase was immobilized at the cathode. The immobilized electrodes were preserved by coating the active surface with 2 µL of Nafion. Finally, the enzyme modified electrodes were stored in their respective buffer

2.2 Voltage amplification circuit

The anode and cathode electrodes were assembled together to realize a biofuel cell. The electrical current and voltage produced by this single biofuel cell is not sufficient of powering any device (i.e., a transducer). To improve the electrical output, multiple biofuel cells have been stacked together [6] at the expense of complexity and the bulkiness of the circuit. Here we use a charge pump integrated circuit (IC) to excite the low input voltage from 300 mV to 1.8-2.4 V depending on the current and voltage requirements of the electronic device. This excited voltage is sufficient to provide the drive strength for an LED [7]. A capacitor was incorporated in our circuit to function as the transducing element, wherein the charging/ discharging frequency of the capacitor can be correlated to the changes in glucose concentration.

3 RESULTS AND DISCUSSION

The biofuel cell system was tested in 180 mg/dL and 360 mg/dL glucose standard solutions at a neutral pH and 37 °C. The assembly produced an open circuit voltage and short circuit current density of 339.2 mV and 524 mV in 180 mg/dL and 360 mg/dL glucose solution and 228.75 µA/cm² and 337.5 µA/cm², respectively (Figure 3). The peak power density produced by the biofuel cell was 22.74 µW/cm² and 43.41 µW/cm² in 180 mg/dL and 360 mg/dL glucose solution, respectively which is greater than the previously reported [8-10].

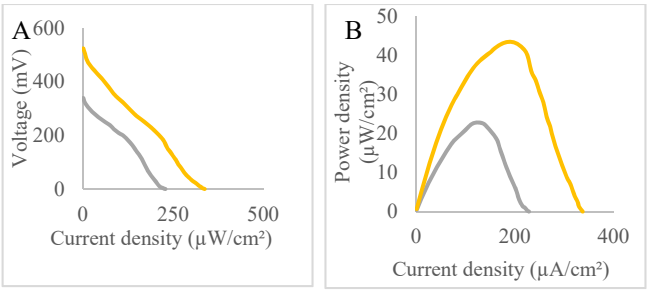

Figure 3: Glucose biofuel cell characterization. (A) Polarization curve and (B) corresponding power curves (gray) performed in 180 mg/dL glucose solution and (yellow) in 360 mg/dL glucose solution in 0.1 M PBS (37 °C, pH 7).

An increase in the peak power density was observed compared to our previous work [5] and this is attributed to decrease in internal resistance of the system thereby, allowing better electron transfer between the active sites and the buckypaper. Moreover, the system exhibited a stable peak power density for 96 days which improved from previously reported [5]. At the end of 96th day of operation, the overall drop in the peak power density was approximately 87% and 79% in 180 mg/dL and 360 mg/dL

glucose, respectively. This ascertains, the stability of enzymes even after over three months which surpasses all data previously reported [11-14]. The experiments were performed in triplicates and the standard deviation values of 4.69 and 5.68 in 180 mg/dL and 360 mg/dL glucose solution confirms the stable operation of this device after 96 days.

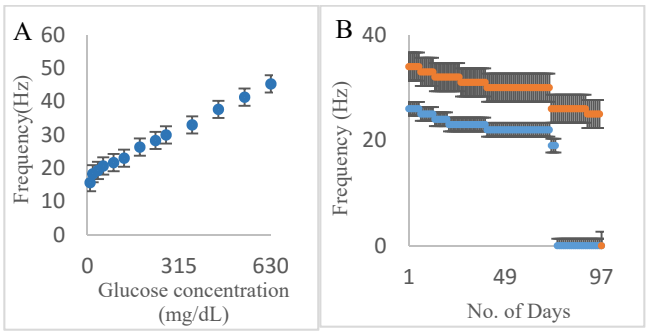

Figure 4: (A) A calibration curve for glucose monitor system (error bars indicate RSD). (B) 96 day stability profile in the presence of 180 mg/dL (blue) and 360 mg/dL (orange) Glucose (37 °C, pH 7; error bars indicated the RSD).

The power from the biofuel cell was supplied to the charge pump IC, which amplified the voltage to 1.8 V which was sufficient to power the LED and the charge cycle across the transducer element (capacitor) was monitored. Figure 4A shows a calibration curve in which the average frequency of charge/ discharge cycle of the capacitor was observed. The linear dynamic range observed is 1.8 – 630 mg/dl glucose with a regression coefficient of 0.993. The linear trend in the charge cycle with increase in glucose concentration confirms that this system can be used as a glucose monitoring system. This system is capable of detecting hypoglycemic, normal, and hyperglycemic glucose levels. In addition to detecting different glucose concentration via charge/ discharge cycle of the transducer, the system exhibited a stable operation for 96 days after which the voltage dropped below 300 mV for 360 mg/dL glucose (Figure 4B). The charge pump IC was no longer able to amplify the small voltage produced since the minimum voltage requirement of the charge pump IC was not satisfied. The charge cycle across the capacitor was also monitored in 180 mg/dL glucose solution for 74 days without recalibration which is still higher than the previously seen [5, 15]. In the presence of 180 mg/dL and 360 mg/dL glucose concentration, the overall drop in the performance of the system was approximately 15% and 24% at the end of 96th day indicating stable operation of the glucose monitor, which surpassed the previous known results without recalibration [16, 17]. The glucose monitoring system described here could greatly reduces the need to device recalibrate. The performance of the glucose monitor could be further improved by improving the performance of the glucose biofuel cell which will extend the life of the sensor. This sensing system's stability along with its stable operation at various pH and temperature demonstrated in our prior work [5] serves a strong candidate for a potential glucose monitoring system.

4 CONCLUSION

We successfully demonstrated the stable functioning of the glucose monitoring system. Our system demonstrated a stable operation in the presence of 360 mg/dL glucose solution for over 3 months which enabled effective functioning of the sensing circuit. The successful functioning of the charge pump IC enabled sufficient drive strength to light a LED. The system had an overall drop of 15.38% and 26.47% in the presence of 180 mg/dL and 360 mg/dL glucose concentration solution after 74 and 96 days of continuous operation, respectively. This glucose sensing microsystem has a potential to replace the currently available technology on the market if the durability of the system can be extended. Future work will focus on testing our system with human plasma.

REFERENCES

[1] Centers for Disease Control and Prevention. "National diabetes statistics report: estimates of diabetes and its burden in the United States, 2014."*Atlanta, GA: US Department of Health and Human Services* (2014). Forbes, Josephine M., and Mark E. Cooper. "Mechanisms of diabetic complications." *Physiological reviews* 93, no. 1 (2013): 137-188,

[2] Forbes, Josephine M., and Mark E. Cooper. "Mechanisms of diabetic complications." *Physiological reviews* 93, no. 1 (2013): 137-188.

[3] Chen, Chao, Qingji Xie, Dawei Yang, Hualing Xiao, Yingchun Fu, Yueming Tan, and Shouzhuo Yao. "Recent advances in electrochemical glucose biosensors: a review." *Rsc Advances* 3, no. 14 (2013): 4473-4491.

[4] Ravenna, Yehonatan, Lin Xia, Jenny Gun, Alexey A. Mikhaylov, Alexander G. Medvedev, Ovadia Lev, and Lital Alfonta. "Biocomposite Based on Reduced Graphene Oxide Film Modified with Phenothiazone and Flavin Adenine Dinucleotide-Dependent Glucose Dehydrogenase for Glucose Sensing and Biofuel Cell Applications." *Analytical chemistry* 87, no. 19 (2015): 9567-9571.

[5] Slaughter, Gymama, and Tanmay Kulkarni. "A self-powered glucose biosensing system." *Biosensors and Bioelectronics* 78 (2016): 45-50.

[6] Miyake, Takeo, Keigo Haneda, Syuhei Yoshino, and Matsuhiko Nishizawa. "Flexible, layered biofuel cells." *Biosensors and Bioelectronics* 40, no. 1 (2013): 45-49.

[7] Southcott, Mark, Kevin MacVittie, Jan Halámek, Lenka Halámková, William D. Jemison, Robert

Lobel, and Evgeny Katz. "A pacemaker powered by an implantable biofuel cell operating under conditions mimicking the human blood circulatory system–battery not included." *Physical chemistry chemical physics* 15, no. 17 (2013): 6278-6283.

[8] Halámková, Lenka, Jan Halámek, Vera Bocharova, Alon Szczupak, Lital Alfonta, and Evgeny Katz. "Implanted biofuel cell operating in a living snail."*Journal of the American Chemical Society* 134, no. 11 (2012): 5040-5043.

[9] Szczupak, Alon, Jan Halámek, Lenka Halámková, Vera Bocharova, Lital Alfonta, and Evgeny Katz. "Living battery–biofuel cells operating in vivo in clams." *Energy & Environmental Science* 5, no. 10 (2012): 8891-8895.

[10] Castorena-Gonzalez, Jorge A., Christopher Foote, Kevin MacVittie, Jan Halámek, Lenka Halámková, Luis A. Martinez-Lemus, and Evgeny Katz. "Biofuel cell operating in vivo in rat." *Electroanalysis* 25, no. 7 (2013): 1579-1584.

[11] Elouarzaki, K., M. Bourourou, M. Holzinger, A. Le Goff, R. S. Marks, and S. Cosnier. "Freestanding HRP–GOx redox buckypaper as an oxygen-reducing biocathode for biofuel cell applications." *Energy & Environmental Science* 8, no. 7 (2015): 2069-2074.

[12] Kizling, Michal, Krzysztof Stolarczyk, Petter Tammela, Zhaohui Wang, Leif Nyholm, Jerzy Golimowski, and Renata Bilewicz. "Bioelectrodes based on pseudocapacitive cellulose/polypyrrole composite improve performance of biofuel cell." *Bioelectrochemistry* (2016).

[13] MacAodha, Domhnall, Maria Luisa Ferrer, Peter Ó. Conghaile, Paul Kavanagh, and Dónal Leech. "Crosslinked redox polymer enzyme electrodes containing carbon nanotubes for high and stable glucose oxidation current."*Physical Chemistry Chemical Physics* 14, no. 42 (2012): 14667-14672.

[14] Tran, Tu O., Emily G. Lammert, Jie Chen, Stephen A. Merchant, Daniel B. Brunski, Joel C. Keay, Matthew B. Johnson, Daniel T. Glatzhofer, and David W. Schmidtke. "Incorporation of single-walled carbon nanotubes into ferrocene-modified linear polyethylenimine redox polymer films." *Langmuir*27, no. 10 (2011): 6201-6210.

[15] Falk, Magnus, Miguel Alcalde, Philip N. Bartlett, Antonio L. De Lacey, Lo Gorton, Cristina Gutierrez-Sanchez, Raoudha Haddad et al. "Self-powered wireless carbohydrate/oxygen sensitive biodevice based on radio signal transmission." *PloS one* 9, no. 10 (2014): e109104.

[16] Sode, Koji, Tomohiko Yamazaki, Inyoung Lee, Takuya Hanashi, and Wakako Tsugawa. "BioCapacitor: A novel principle for biosensors."*Biosensors and Bioelectronics* 76 (2016): 20-28.

[17] Updike, Stuart J., Mark C. Shults, Barbara J. Gilligan, and Rathbun K. Rhodes. "A subcutaneous glucose sensor with improved longevity, dynamic range, and stability of calibration." *Diabetes Care* 23, no. 2 (2000): 208-214.