Biochip with Graphene-based Nanosensor for Non-invasive Glucose Sensing

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Abstract

Diabetes has become a serious global health threat and glucose test is very important for diabetic patients on a daily basis. Traditional blood glucose test uses a lancet device to prick the patient's finger to get a drop of blood sample for testing. This invasive test causes pain to patient and increases the risk of cross-infection of blood-transmitted diseases. Non-invasive glucose monitoring has become very attractive alternative to blood glucose test. Research has found that other biological samples (e.g. saliva, tears, sweat, urine) also contains trace amount of glucose molecules and they may be used for diabetes diagnosis. However, glucose level in such biological samples is generally too low for traditional sensors. Nanotechnology offers new hope in high-resolution glucose sensing. In this research, we proposed a saliva glucose sensor that combines graphene-based glucose nanosensor with microfluidic biochip to develop a complete lab-on-a-chip (LoC) system for non-invasive glucose sensing. It is designed to collect, prepare and manipulate the microfluidic sample for glucose sensing using graphene-based glucose nanosensor. The key components of the lab-on-a-chip are designed and simulated with COMSOL. The LoC device may be used for non-invasive glucose sensing for diabetes diagnosis and self-monitoring.

Introduction

According to 2014 World Health Organization report, about 347 million people worldwide have diabetes. Diabetes is predicted to become the 7th leading cause of death in the world by the year 2030. US Center for Disease Control and Prevention (CDC) estimates more than 29 million people - or 9.3% of the US population - to have diagnosed or undiagnosed diabetes. More than 200,000 deaths occur each year among people with diabetes in the United States. Diabetes has become serious threat to public health and there is urgent need for diabetes prevention and health management worldwide.

Diabetic patients need to monitor their blood glucose level in daily basis to adjust medication or insulin usage. Traditional blood glucose test uses a lancet device to prick the patient's finger to get a drop of blood sample for testing. This invasive test causes pain to patient and increases the risk of cross-infection of blood-transmitted diseases. Non-invasive glucose monitoring has become very attractive alternative to blood glucose test. Research has found that saliva glucose is promising to be used as biological sample for diabetes diagnosis. However, the major challenging in the testing is that the glucose concentration in saliva is generally very low and many other ingredient in saliva may interfere with the measurement. To overcome this issue, graphene offers the opportunity to alternative saliva for non-invasive painless glucose sensing due to their extremely large surface area and improved catalytic activities even in the molecular level. In this research, we proposed a saliva glucose sensor that combine graphene-base glucose nanosensor with microfluidic biochip to develop a complete lab-on-chip (LoC) system for non-invasive glucose sensing using saliva sample. As shown in Figure 1, the proposed biochip takes the sample to be tested, performs necessary on-chip sample preparation and manipulation, and drives it toward the reacting chamber for electrochemical glucose sensing. The Cu nanoparticle and graphene sheets are pre-deposited on the working electrode to enable highly selective and sensitive detection of minute glucose concentration in the sample. The electrochemical current can be measured by a signal sensing circuitry, and converted into corresponding glucose concentration to be read on a LCD display.

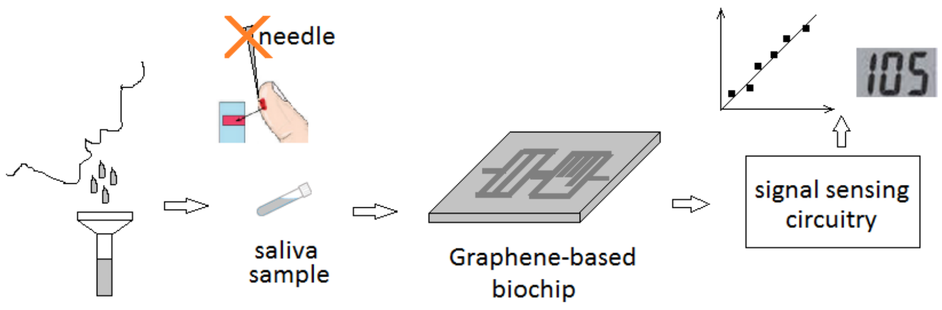


Figure 1. Non-invasive glucose sensing using saliva sample

The aimed device does not cause any wound to patient's body and avoids cross-infection of blood-transmitted diseases during the testing. It may allow continuous monitoring of glucose level, which is very important for diabetes patients in their disease self-monitoring. With the measured glucose level, diabetic patients can adjust their medication intake or insulin injection to achieve healthy control of the disease.

Design and Working Principle

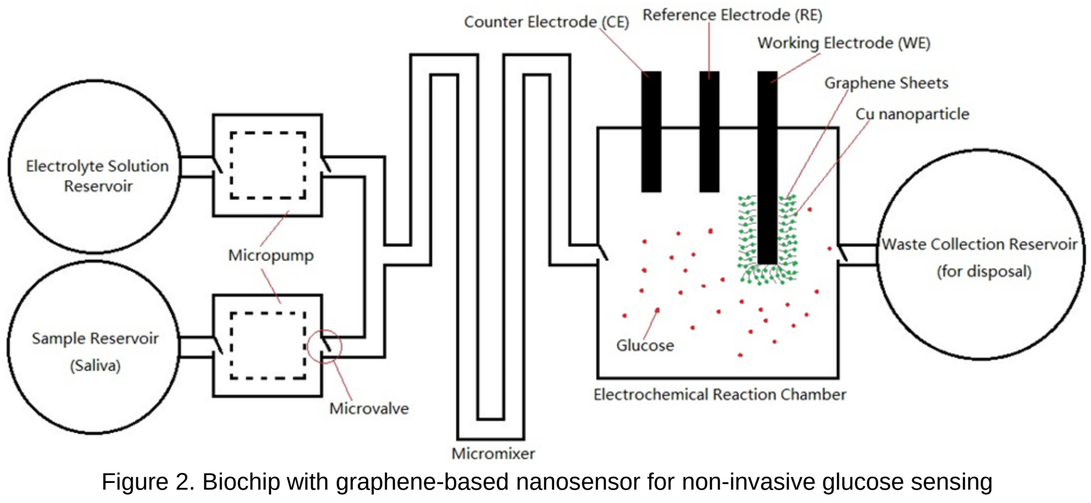


Figure 2. Biochip with graphene-based nanosensor for non-invasive glucose sensing

The proposed lab-on-a-chip with graphene-based nanosensor for non-invasive glucose sensing is shown in Figure 1. It consists of three functional stages: sample preparation, electrochemical sensing chamber, and waste disposal. It also consists of two electrolyte solution reservoirs for storing electrolyte solutions and saliva sample; two micropumps for pumping the electrolyte solution and saliva samples into the following micromixer; the microvalves for regulating the direction of the microfluidic flow; the micromixer for improving the mixing. Once electrolyte solution and saliva samples are thoroughly mixed, they are injected into the electrochemical reaction chamber. There are three electrodes pre-embedded in the chamber: Counter Electrode (CE), Reference Electrode (RE) and Working Electrode (WE) with graphene and Cu nanoparticles pre-deposited on its surface. The glucose concentration in the saliva sample can be derived by measuring the electrochemical current between the electrodes when glucose molecules in saliva interact with Cu nanoparticle in graphene sheets and changes the electrocatalytic activities. After the glucose level is identified, the mixed solution is pumped into waste collection reservoir for disposal.

Graphene will be prepared and purified with the Hummers method. The preparation of the Cu modified graphene (Cu-graphene) electrode mainly refers to Jing Luo's method [J. Luo, et al, Analytica Chimica Acta, 2012]. The working principle of the Working Electrode (WE) with graphene and Cu nanoparticles is explained as below. Free electrons are produced during the Reduction-Oxidation. Once chamber, the current is then converted into corresponding glucose concentration.

COMSOL Simulation Results

The key components (e.g. micropumps, microvavles, micromixer) are designed and simulated in COMSOL. The results are shown in Figure 3-8 respectively.

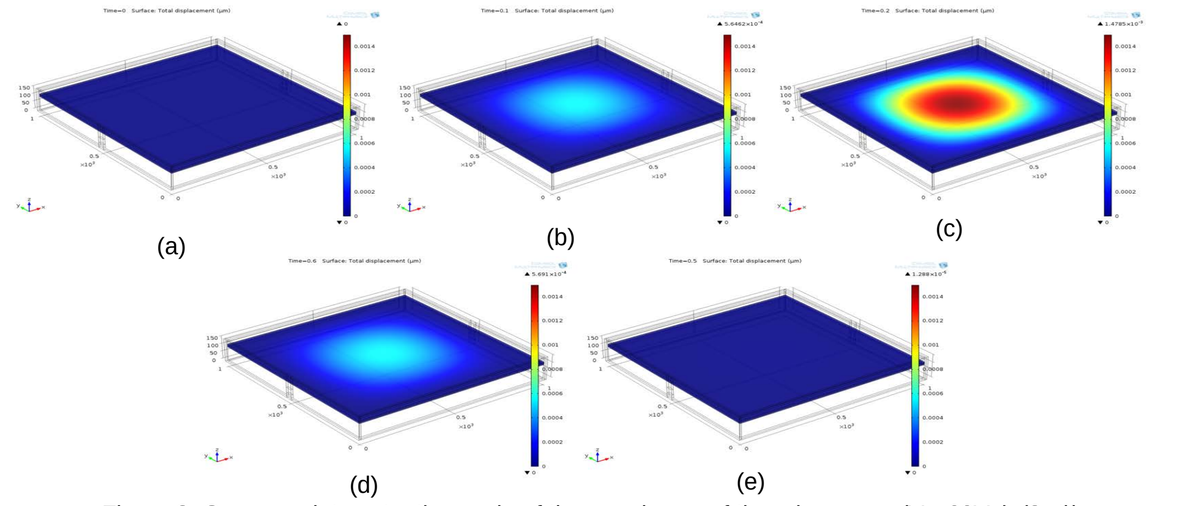


Figure 3. One complete actuation cycle of the membrane of the micropump (V_d=60Vsin(2πt))

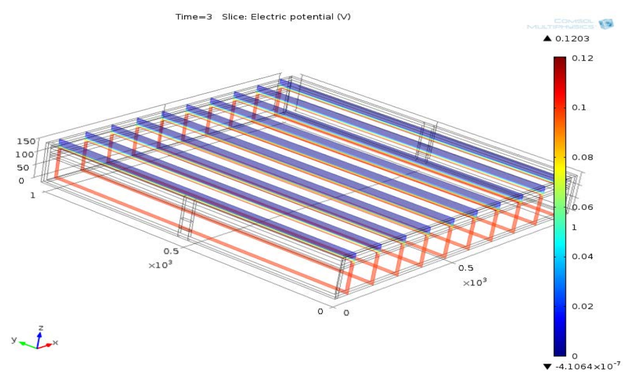


Figure 4. The electric potential distribution on the actuator

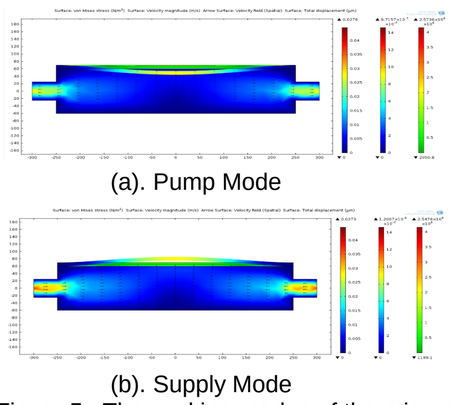


Figure 5. The working modes of the micropump

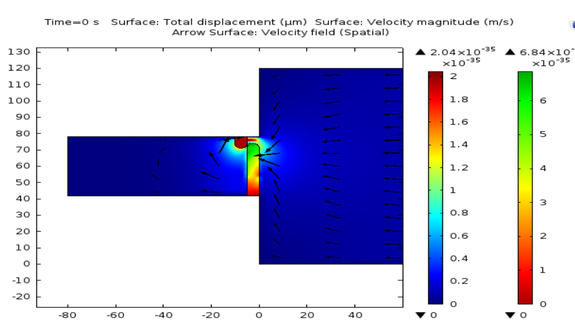


Figure 6. The microvalve prevents the backflow

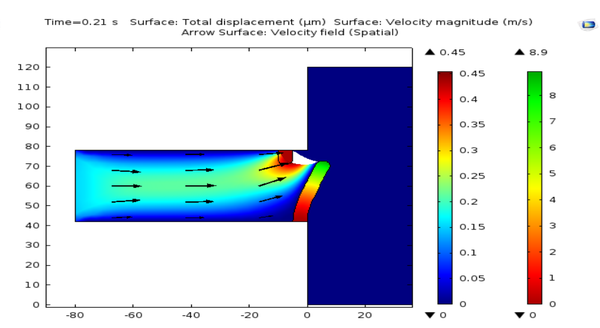
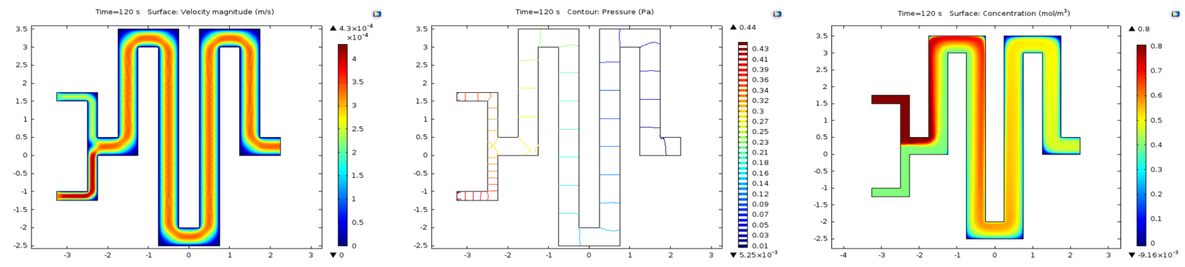


Figure 7. The microvalve in "ON" state



a. Velocity distribution b. Pressure distribution c. Concentration distribution

Figure 8. The simulation result of the micromixer (t=120s)

The two micropumps are actuated by electrostatic force. The simulation result of one working cycle of the actuator is shown in Figure 3. The maximum displacement is 1.478×10^{-3}μm. Figure 4 shows the electric potential distribution of the actuator and the driving voltage is 60V(AC). The two working modes of the micropump are shown in Figure 5. The "ON" and "OFF" modes of the microvalve is shown in Figures 6 and 7. The microvalve allows "one-way" flow of the microfluid. It consists of two parts: a cantilever beam and a stopper. When there is a backflow, the valve is pushed against the stopper, hence preventing the revers flow of the microfluid. Thus the valve is turned off. If there is a forward flow, due to the fluid pressure, the beam bends outwards so that the valve is open. The micromixer is also designed and simulated, as shown in Figure 8. According to the result of the concentration distribution, it takes the micromixer 2 minutes to complete the mixing of two microfluidic flows (0.4mol/m^3 and 0.8mol/m^3). The velocity distribution is layered along the outlet indicating it is a laminar flow. The pressure keeps decreasing from inlet to outlet and the minimum pressure (5.25×10^{-3} Pa) occurs at the outlet.

Conclusions and Further Work

In the poster, the architecture design of a lab-on-a-chip with graphene-based nanosensor for non-invasive glucose sensing is proposed. The key microfluidic components (*e.g.* micropump, micromixer, microvalve) of the lab-on-a-chip have been designed and simulated with COMSOL. The simulation results guide us to further optimize the design for the system. In the future, the signal sensing circuitry will be designed. We will also work on the fabrication of the graphene-based glucose nanosensor. Its electrochemical current in response to the glucose water solution will be measured. Based on the result of measurement and characterization of the graphene-based glucose nanosensor, its sensitivity will be improved. The proposed lab-on-a-chip with graphene-based nanosensor may be used for non-invasive glucose sensing application.

Acknowledgement

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