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# The development of an autonomous self-powered bio-sensing actuator

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ABSTRACT

The inherent low power supplies from biofuel cells limits their application as power sources in implantable devices. To overcome these limitations, we have previously developed a novel device designated as a "BioCapacitor" (Hanashi et al., 2009). The BioCapacitor generates sufficient stable power to operate biosensing devices and signal transducers. In this paper, we report an autonomous, self-powered, sensing actuator that employs the principle of BioCapacitor as the core technology. The device is composed of a BioCapacitor, which uses a direct electron transfer-type glucose enzyme fuel cell, connected to a stepper motor as the actuator. In the presence of glucose, the BioCapacitor was able to generate enough electricity to operate the actuator. The torque and rotational speed of the stepper motor was dependent on the capacitance of the capacitor used in the BioCapacitor, and on the glucose concentration. A higher glucose concentration provided the stepper motor with higher torque and speed, resulting from the charge/discharge frequency of the capacitor as a function of the enzyme reaction at the anode. The actuator was operated entirely by the energy derived from glucose oxidation, and its performance was regulated by the glucose concentration. We also present the performance of a liquid-pumping system that employs the autonomous, self-powered, sensing actuator, which demonstrates its potential for application as a drug delivery/pumping system.



## 1. Introduction

Advancements in medicine require the development of better therapeutic agents, as well as novel techniques that combine therapeutic agents with biomedical devices. In recent years, various implantable medical devices, especially drug delivery systems (DDSs), have demonstrated great potential in a vast number of applications for which the controlled and accurate delivery of critically prescribed drugs doses is required without direct medical intervention [2–9]. In particular, numerous drugs designed to target various cellular processes have emerged, creating a demand for the development of intelligent DDSs, which can sense and respond directly to the conditions of patients. Intelligent DDS-based therapeutics refers to novel DDSs that are designed to detect disease conditions and then release therapeutic agents for the treatment of these conditions. Currently, such systems play an important role in theranostic approaches. Some of the existing implantable biomedical devices are "active," in the sense that they require a power source for operation [2–6,8]. Actively controlled drug delivery devices provide advantages over passive release devices [6,8]. An intelligent DDS should contain biomedical sensing devices for monitoring the patient's health condition and an autonomously operating actuator to actively deliver the drug. Preferably, the device should operate as a stand-alone device that is implanted or mounted in the human/animal body. Moreover, the sensing devices and actuators should be self-powered, utilizing biological energy sources, such as glucose, like natural organs do.

Enzyme fuel cells that use blood glucose as their energy source are currently utilized in the operation of implantable devices [10–18]. However, the inherent low power supply of biofuel cells limits their application as power sources in implantable devices. These limitations inspired us to develop a novel device, designated a "BioCapacitor" [1]. The BioCapacitor generates sufficient stable power to operate biosensing devices and signal

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transducers. The biofuel cell is connected to a charge pump to increase the voltage, and a capacitor stores the potential generated by the charge pump to provide sufficient power and voltage for operating an electric device. Using the charge pump and the capacitor, high voltages with sufficient temporary current for operating an electric device can be generated without modifying the design and construction of the biofuel cell. The frequency of the charge/discharge cycle depends on the electric power generated by the cell, which in turn depends on the fuel concentration in the cell. The coefficient of variations of sensor signals corresponding to glucose concentration, which were measured with the same BioCapacitor repeatedly, was below 10% [1]. Thus, a BioCapacitor that uses an enzyme glucose fuel cell can serve as a glucose sensor. In our previous study, we reported 2 types of standalone, self-powered wireless glucose sensing systems based on the BioCapacitor principle, called "BioRadioTransmitter" [19] and "BioLC-Oscillator" [20]. Both systems generate sufficient power to operate an oscillator circuit that is used as a radio transmitter, and glucose concentration is determined from the transmission frequency of the radio wave (BioRadioTransmitter) or the resonance frequency of the radio wave (BioLC-Oscillator). Although in these systems, the electric power derived from the BioCapacitor was used only for signal transmission, the electric power generated is sufficient for both signal transmission and operation of an actuator.

In this paper, we report the development of an autonomous, self-powered, sensing actuator that uses the principle of the BioCapacitor as the core technology. The device is composed of a BioCapacitor that uses a direct transfer-type glucose enzyme fuel cell connected to a stepper motor as the actuator. In the presence of glucose, the BioCapacitor generates enough electricity to operate the actuator. Moreover, the torque and rotational speed of the stepper motor depend on the glucose concentration; a higher glucose concentration provides higher torque and speed to the stepper motor. This is because of the charge/discharge frequency of the capacitor as the function of the bioanodic reaction. The actuator is operated entirely and solely by the energy derived from glucose oxidation, and its performance is regulated by the glucose concentration. We also discuss the performance of a liquid-pumping system that employs the autonomous, self-powered, sensing actuator, which has potential application as an insulin pumping system.

## 2. Materials and methods

### 2.1. Materials for construction of enzyme fuel cell

Recombinant flavin adenine dinucleotide-dependent glucose dehydrogenase (FADGDH) complex was prepared using the expression vector pTrc99A, which contained the structural genes for the FADGDH complex, and pAYCYC184. The pAYCYC184 contained the structural genes for ccm (pEC86). The FADGDH complex was then introduced into an *Escherichia coli* strain, BL21(DE3), and cultivated as described in a previous study [21]. Bilirubin oxidase (BOD) was purchased from Amano Enzyme (Aichi, Japan). Ketjen black (KB), ECP600JD, was purchased from Mitsubishi Chemical Corp. (Tokyo, Japan). Platinum-supported carbon (Pt/C), TEC10E50E, (Pt wt% = 50) was purchased from Tanaka Kikinzoku Kogyo (Tokyo, Japan). Glutaraldehyde solution (25%, w/v) was purchased from Wako Pure Chemicals (Osaka, Japan). Nafion perfluorinated resin solution and poly(dimethyl-siloxane) (PDMS) were purchased from Sigma-Aldrich (St. Louis, MO). Triton X-100 was purchased from Kanto Chemical (Tokyo, Japan). All other chemicals were of reagent grade.

### 2.2. Construction of enzyme-immobilized electrode

The KB screen-printed electrode was constructed as follows: the underlayer electrode was formed by sputter depositing a Pt layer on a base film. Insulation printing was performed to form the enzyme-immobilizing area (2 mm × 2 mm). The area was coated with KB ink, which was prepared by mixing 15 mg of KB with 670 μL of ultrapure water and 30 μL of Triton X-100, using screen printing. This mixture was then sonicated for 20 min to disperse the KB throughout the solution.

For construction of the anode employing the KB screen-printed electrode, 2 μL of FADGDH solution (14 U/μL) was mixed with 3 μL of KB ink solution and 5 μL of 100 mM potassium phosphate buffer (PPB) (pH 7.0). Then 4 μL of the mixture was deposited onto a KB screen-printed electrode and air-dried at 4 °C for 1 h to allow the mixture to coat the KB screen-printed electrode. The KB screen-printed electrode was cross-linked in 25 (w/v)% glutaraldehyde vapor for 30 min and then washed with 10 mM of Tris–HCl buffer (pH 7.0). We also constructed an anode by using 0.07 $cm^2$ Au rod electrode (002421; BAS, Tokyo, Japan). 7 μL of the mixture contained 2.8 U/μL of FADGDH, 30% (v/v) of KB ink and 50 mM PPB (pH 7.0) was deposited onto the Au rod electrode. Then the electrode was air-dried and cross-linked in the same manner of the KB screen printing electrode.

To construct the cathode by using the KB screen-printed electrode, Pt/C ink was prepared by mixing 100 mg of Pt/C with 400 μL of ultrapure water and 1.08 mL of 5% (w/v) Nafion solution. The mixture was agitated at room temperature for 3 h using a vortex, and then incubated for 3 days at 4 °C. After incubation, 8 μL of the mixture of Pt/C ink (1 μL) and 0.12% Triton X-100 in 100 mM PPB (pH 7.0) (14 μL) was deposited on the KB screen-printed electrode and air-dried at 80 °C for 1 h. Next, 3 μL of 3% (v/v) PDMS was deposited on the electrode and air-dried, after which 8 μL of BOD solution (0.06 U/μL) was deposited on the electrode and air-dried at 4 °C for 1 h. The electrode was cross-linked in 25 (w/v)% glutaraldehyde vapor for 30 min and washed with 10 mM Tris–HCl buffer (pH 7.0). We also constructed a cathode by using 0.5 $cm^2$ carbon cloth (BT70-30; TORAY, Tokyo, Japan). 50 μL of the mixture contained 3.2 U/μL of BOD, 30% (v/v) of KB ink and 50 mM PPB (pH 7.0) was deposited onto the carbon cloth. Then the carbon cloth was air-dried and cross-linked in the same manner of the KB screen printing electrode. Both the anode and the cathode were stored in 100 mM of PPB at 4 °C until used.

### 2.3. Construction and operation of miniaturized direct electron transfer-type enzyme fuel cell

The anode and the cathode were attached to a 10 mL-water-jacket cell. In the cell, 100 mM PPB (pH 7.0) was stirred at 37 °C at 250 rpm with a magnetic stirrer. Glucose was then added to the cell for carrying out the measurements. The voltage generated by the cell in the presence of 20 mM glucose was measured by using a HZ3000 electrochemical analyzer (Hokuto Denko, Tokyo, Japan) after applying an external variable load resistance (model 278620; Yokogawa Electric Corporation, Tokyo, Japan).

### 2.4. Construction and operation of an autonomous self-powered bio-sensing actuator employing the principle of the BioCapacitor

Fig. 1(a) shows the designed circuit diagram of an an autonomous self-powered bio-sensing actuator that employed a BioCapacitor as the power source. The system was composed of a BioCapacitor connected to a stepper motor (CITIZEN, Tokyo, Japan) as the actuator. The BioCapacitor was composed of the enzyme fuel cell connected to a capacitor via an ultra-low voltage operation charge pump IC (S-882Z18-M5T1G Seiko Instruments, Chiba,