Very Important Paper

A Microelectronic Sensor Device Powered by a Small Implantable Biofuel Cell

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Biocatalytic buckypaper electrodes modified with pyrroloquinoline quinone (PQQ)-dependent glucose dehydrogenase and bilirubin oxidase for glucose oxidation and oxygen reduction, respectively, were prepared for their use in a biofuel cell. A small (millimeter-scale; $2 \times 3 \times 2$ mm$^3$) enzyme-based biofuel cell was tested in a model glucose-containing aqueous solution, in human serum, and as an implanted device in a living gray garden slug ($Deroceras reticulatum$), producing electrical power in the range of 2–10 μW (depending on the glucose source). A microelectronic temperature-sensing device equipped with a rechargeable supercapacitor, internal data memory and wireless data downloading capability was specifically designed for activation by the biofuel cell. The power management circuit in the device allowed the optimized use of the power provided by the biofuel cell dependent on the sensor operation activity. The whole system (power-producing biofuel cell and power-consuming sensor) operated autonomously by extracting electrical energy from the available environmental source, as exemplified by extracting power from the glucose-containing hemolymph (blood substituting biofluid) in the slug to power the complete temperature sensor system and read out data wirelessly. Other sensor systems operating autonomously in remote locations based on the concept illustrated here are envisaged for monitoring different environmental conditions or can be specially designed for homeland security applications, particularly in detecting bioterrorism threats.

1. Introduction

Enzyme-based biofuel cells,[1] extracting electrical power from abundant biomolecules have been studied for several decades[2] to resolve fundamental bioelectrochemical problems for efficient electron exchange between enzyme active centers and electrode conducting supports.[3] Engineering problems in constructing biofuel cells are mostly related to increasing the power density generated by electrochemical devices and extending their operational time.[4,5] While some scientific/engineering papers use “green energy,” “sustainable power sources,” “cheap electrical power” and other politically motivated wording as justification for biofuel cell research,[6] it should be clearly understood that biofuel cells, particularly those based on enzyme biocatalysis, will likely never produce sufficient power to contribute any meaningful amount of power to the national power grid. Also, the electrical power produced through biological reactions is unlikely to be cheap, particularly when using expensive enzymes with limited operational time. Therefore, the real motivation for the research in biofuel cells is their promise for powering implantable biomedical devices[7] or sensors/biosensors,[8] particularly in remote locations where locally produced electrical power extracted from environmentally available biological sources[9] can be beneficial. Since the amount of power produced is rather small,[10–12] the cost of this power is not critically important, while other parameters, like operation in a biological environment, are becoming more important. With a clear understanding of this motivation, the research focus has moved to implantable biofuel cells surgically introduced in biological tissue of living animals[13–16] (used as models for future use in humans) and wearable biofuel cells[17,18] located externally on a body, being easily replaced when the operational resource is exhausted. Differently constructed enzyme-based biofuel cells have been tested in vitro in human serum solution[19,20] or whole blood[21–23] and in vivo in various living species, such as insects,[24] snails[25] clams,[26] lobsters,[27] rats,[28,29] rabbits,[30,31] etc. Wearable biofuel cells have been reported that are placed on human skin and powered by sweat[32,33] or in an eye and powered by tears.[34,35]

The next highly important research direction is interfacing implantable or wearable biofuel cells with various electronic devices that consume power generated by the biofuel cells.[36–40]

While most of the studied bioelectronic systems have included only model devices, such as an electronic watch,[27] digital thermometer,[41] and light-emitting diode (LED),[42] some of the electronic devices powered by implantable biofuel cells, e.g., a pacemaker,[20] glucometer,[42] and smart contact lenses,[34,43] are close to the expected future biomedical applications. In designing integrated bioelectronic systems composed of a biofuel cell producing electrical power and an electronic device consuming this power, the major problem is the insufficiency of the power produced. When the connected electronic device needs continuously provided power, the problem can be solved by...
improving the efficiency of the connected biofuel cell (not easy) or by increasing the biofuel cell size (easy but not practical for implantable systems). The required power is often limited by the threshold needed for the operation of the DC-DC converter ("charge pump"), which increases the voltage generated by a biofuel cell to the level required by the power-consuming device. In most of the systems studied, the power required for continuous (without interruption) operation of any practically important electronic device was produced by relatively large (several cm²) biocatalytic electrodes, which are too big for implantable bioelectronic systems. Another much more practical solution has been suggested for systems that are activated periodically or "duty cycled". This approach uses the standby time intervals for accumulating electrical energy in a rechargeable battery or supercapacitor. The technical question remaining is how small can a biofuel cell be that provides sufficient power for activation of a microelectronic device that operates periodically. The answer depends mostly on the efficiency of the microelectronic device. The present paper offers an experimental answer to this question using a highly efficient microelectronic device, which includes a power management system equipped with a supercapacitor.

Rapid progress in microelectronics has resulted in small but very powerful computing and sensing systems. Nowadays, people are using centimeter-scale devices in their daily lives (e.g., smartphones), and millimeter/micrometer-scale systems are on the horizon. In such miniature systems, battery size and thus battery capacity are highly limited, and the available energy stored in a battery is a significant limitation. We developed a millimeter-scale custom designed system with low-power circuits that consumes current in the mA range in the active mode for time intervals of ca. 100 ms and current in the nA range while in standby mode for tens of seconds. Relying on a millimeter-size thin-film battery, the proposed system can operate for about a month. To extend this system lifetime, replacing a battery is difficult since the system needs to be fully encapsulated for physical protection and, in any case, replacing batteries in vivo is impractical. Thus, these millimeter-scale systems must include an energy-harvesting feature and a rechargeable battery. In this way, the microelectronic devices can become energy autonomous by recharging the battery using energy harvested from sources available in the operational environment. However, the system lifetime is still limited by the rechargeable battery degradation, as its capacity decreases and internal resistance increases with each cycle of charging/discharging. A supercapacitor is a good alternative to a battery since its performance degradation is negligible even after a large number of charging/discharging cycles compared with that of a miniature rechargeable battery. In this paper, we demonstrate a temperature-loggining millimeter-scale system that is based on a supercapacitor and is recharged with a millimeter-size biofuel cell. A supercapacitor typically suffers from limited energy density, but that challenge is overcome by an efficient biofuel cell and low-power circuits in this system. This integrated bioelectronic system composed of a power-producing biofuel cell and a power-consuming sensor device, both millimeter-scale, was studied and reported in this paper.

While many other implanted biofuel cells have been reported, the present work aims at demonstration of the implanted biofuel cell operation together with a microelectronic device. The size of the implanted biofuel cell matches the size of the microelectronic device and the use of a slug as a host organism is based on its availability in the natural environment in the season when the experimental work was done. Notably, the slug is only an example for the integrated biofuel cell – microelectronic device. It should be noted that the enzymes used in the present study, PQQ-dependent glucose dehydrogenase (PQQ-GDH) in the anode and bilirubin oxidase (BOx) in the cathode, are not the only possible enzymes for the use in the studied implantable biofuel cell. Some other enzymes, particularly those operating without redox mediators (through direct electron transfer), might be successfully used, but their application was outside the scope of the present study.

Experimental

Materials

PQQ-dependent glucose dehydrogenase (PQQ-GDH; E.C. 1.1.5.2) from a microorganism not specified by the company was purchased from Toyobo Co., Japan. Bilirubin oxidase (BOx; E.C. 1.3.3.5) from Myrothecium verrucaria was kindly donated by Amano Enzyme Inc., U.S.A. 3-Thiopheneacetic acid, 3-methoxythiophene, β-D-glucose, 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid (HEPES buffer), 2-(N-morpholino)ethanesulfonic acid (MES buffer), tris(hydroxymethyl)aminomethane (TRIS buffer), N-(3-dimethylaminopropyl)-N'-ethyl-carboimidide hydrochloride (EDC), N-hydroxy succinimide (NHS), sterile-filtered human serum from human male AB plasma USA origin, and other standard organic and inorganic chemicals and reactants were purchased from Millipore Sigma (formerly Sigma-Aldrich) and used as supplied. Ultrapure water (18.2±0.2 MΩ·cm) from a NANOpure Diamond (Barnstead) source was used in all of the experiments. The live specimens of the gray garden slug (Doroceras reticulum) used in this study were collected in the Clarkson University park (NY, USA). The specimens measured on average 3 cm in length when extended (1.5–2 cm when retracted), which is usual for adults of this species. The slugs were held in a box containing dirt with fruit and grass.

Electrode Preparation

Buckypaper composed of compressed multiwalled carbon nanotubes (MWCNTs; Buckeye Composites, NanoTechLabs, Yadkinville, NC) was used as the electrode material (2 mm×3 mm; geometric area = 0.06 cm²). Indium-tin oxide (ITO; 20±5 Ω/sq surface resistivity; Millipore Sigma) was used as the conducting support for the mechanical reinforcement of the buckypaper, which was attached to ITO using silver conductive epoxy glue (MG Chemicals, Surrey, Canada). First, the electrodes were modified with a thiophene-based polymer. Electropolymerization of thiophene monomers was performed by using a potentiostatic pulse method, adopting the following parameters: 1.4 V oxidation potential and 0.8 s oxidation pulse time, −0.3 V reduction potential, 0.1 s reduction pulse time, and 677 pulses, which means a total experiment time of 600 s. The solution used for the electropolymerization included two thiophene-derivative monomers, 3-thiopheneacetic acid (67 mM) and 3-methoxythiophene (33 mM), and supporting electrolyte KCl (100 mM) in aqueous solution containing 5% (v/v) acetonitrile. The electropolymerization procedure was optimized based on the
results reported in the literature. After the polythiophene electrodeposition, the modified electrode was repeatedly rinsed with water, and four cyclic voltammogram scans (100 mV s⁻¹, between −0.2 V and 0.5 V) in 5 mM MES buffer, pH 6.5, were performed to remove the monomer residues and acetonitrile from the polymer layer. Afterwards, the modified electrodes were incubated with a mixture of 25 mM NHS and 100 mM EDC (to activate −COOH groups of the polymer) under moderate shaking for 1 h at room temperature (23 ± 2°C) and subsequently rinsed with phosphate buffer (50 mM, pH 7.4, containing 100 mM Na₂SO₄). PQQ-GDH and BOx were used to modify the anode and cathode, respectively. The polymer-modified electrodes with the activated carboxylic groups were immediately incubated with enzyme solutions, 2.4 mg mL⁻¹ for PQQ-GDH (in 10 mM HEPES buffer, pH 6.0, containing 6 mM CaCl₂) and 3.7 mg mL⁻¹ for BOx (10 mM TRIS buffer, pH 7, containing 100 mM Na₂SO₄), for 1 h at room temperature under moderate shaking. The modified electrodes were stored (4°C) in phosphate buffer (50 mM, pH 7.4, containing 100 mM Na₂SO₄) until used in the biofuel cell.

**Microelectronic Device Operating as a Temperature Sensor**

The batteryless temperature sensor measures ambient temperature and saves the data in internal memory (8kByte SRAM), and a user can wirelessly download the results later using optical or radio frequency (RF) communication. All operations can be powered by energy from the biofuel cell with the help of a supercapacitor operating as an energy buffer. As shown in Figure 1, the microelectronic device consists of stacked chips (1.4 × 2.8 × 1.0 mm³) and a supercapacitor (3.2 × 2.5 × 0.9 mm³) packaged in a ceramic pin grid array (PGA) for ease of testing. The stack of chips includes 8 integrated circuit chips, including a ‘charge pump,’ ‘power management,’ ‘memory,’ ‘decoupling capacitors,’ ‘processor,’ ‘radio,’ ‘temperature sensor & timer,’ and ‘optical receiver.’ They are all fabricated in 180-nm CMOS technology and were custom designed to construct a millimeter-scale sensor system. The circuits on the chips are designed with the highest priority placed on low power consumption and operate with less power on average than what the biofuel cell can provide.

**Biofuel Cell Measurements**

In the preliminary experiments, polarization curves of the biofuel cell were recorded at different glucose concentrations (5 mM, 10 mM and 20 mM) in phosphate buffer (50 mM, pH 7.4, containing 100 mM Na₂SO₄ and oxygen under equilibrium with air). Then, the biofuel cell was also tested in a human serum solution. Finally, the implantable electrodes were inserted into the slugs through two holes cut with a small knife in a dorso-posterior part of the body and placed into the hemolymph between the body wall and heart, dorsal to the visceral mass with a distance between the electrodes of ca. 2 mm (varied in different specimens by ±1 mm). The geometrical area of the electrodes immersed in the hemolymph was 0.06 cm². The volume of the biofuel cell was ca. 0.012 cm³. The volume was calculated as the inner volume (operational volume inside the cell) based on the distance between the biocatalytic electrodes (the anode and cathode). The voltage and current generated by the biofuel cell were measured with a multimeter (Meterman 37XR) with a variable resistance used as an external load. All measurements were performed at ambient temperature (23 ± 2°C).
changes to maintain high efficiency in energy harvesting. Vbfc and thus Vcap vary depending on glucose concentration. Under such a varying Vcap, the circuits of other chips cannot operate properly. Hence, the ‘Power Management’ chip takes this varying Vcap and generates a set of three regulated voltages: 0.6 V, 1.2 V, and 3.6 V. The power management chip includes 3 up/down charge pumps, and their switching frequencies adapt to the amount of current draw from the load circuits. For example, the power management charge pumps change their configuration to significantly faster in active mode than in standby mode. A ‘Decoupling Capacitor’ chip provides decoupling capacitance in the nF range to further stabilize the three output voltages (0.6 V, 1.2 V, and 3.6 V) and to suppress high frequency noise due to the instantaneous current draw from the circuits in the supplied chips. The ‘Processor’ chip manages the temperature logging operation using an ARM Cortex-M0 processor and 8 kByte memory. The ‘Memory’ chip stores the measured temperature data up to 8k samples using 16 kByte memory. The ‘Temperature Sensor & Timer’ chip converts the temperature to a digital code with 0.05°C temperature inaccuracy from 0°C to 105°C using both a temperature-sensitive and temperature-insensitive clock generator. Finally, the timer on this chip accurately sets the period between two adjacent temperature measurements within 1% accuracy across temperatures. This sensor communicates with a user by optical and radio methods. For programming, a user sends an optical signal to a photovoltaic cell on the ‘Optical Receiver’ chip, and the signal is converted to a digital format in the ‘Processor’ chip.

Figure 2. The electronic block scheme of the microelectronic temperature-sensing device powered by the biofuel cell. A charge pump chip converts the low voltage of the biofuel cell to voltage acceptable for operating electronic circuits. The power management chip (also containing up/down charge pumps internally) generates three stabilized voltages for the different load circuits.

Figure 3. The experimental setup for studying the microelectronic device operation and characterizing its different components. The numbered parts of the experimental setup are as follows: (1) power supply (Agilent E3630A); (2) sourcemeter (Keithley 2401 Sourcemeter) used in preliminary experiments (data not reported) to mimic the real biofuel cell; (3) sourcemeter (Keithley 2400 Sourcemeter) needed to charge the supercapacitor (Seiko CPX3225A752D, 7.5 mF); (4) electrometer (Keithely 6514 System Electro- meter) to monitor voltages of the M3 sensor; (5) universal software radio peripheral (USRP) (Ettus, USRP X310); (6) laptop (Lenovo P51) equipped with custom programming software; (7) biofuel cell operating with a model aqueous solution, replaced with a live slug in the final system test; (8) anti-static wrist (ESD) strap used by an operator; (9) microelectronic sensor device; (10) custom light programing module; (11) custom printed circuit board (PCB) antenna for base station; (12) desktop computer using a LABVIEW program; (13) analog-to-digital converter module (National Instruments, NI-9292 & NI CDAQ-9171); (14) analog buffer PCB (Texas Instruments, OPA4354AIDR).

‘Processor’, ‘Memory’, and ‘Radio’ chips consume 11.2 nW, 0.36 nW, 6.8 nW, 1.3 nW and 0.37 nW, respectively. The ‘Power Management’ chip has a power conversion efficiency of 60%. Thus, the microelectronic device, except for the supercapacitor, consumes 34.0 nW.

Figure 3 shows the setup used to test the different components individually and also, when configured as a complete system, autonomous system operating without external power. The shown setup includes the biofuel cell operating with an aqueous model solution (phosphate buffer) containing glucose and O₂. A sourcemeter (Keithley 2401 Sourcemeter) is used to characterize the sensor by measuring current consumption at a given voltage and can also accelerate tests by pre-charging the supercapacitor. Another sourcemeter is used to characterize the energy harvesting of the sensor by mimicking a biofuel cell. An electrometer (Keithely 6514 System Electro- meter) is used to monitor 1.2 V from the ‘Power Management’ chip to confirm that the sensor works properly by providing voltage to the load circuits. To avoid impacting the low-power circuits, a high impedance electrometer is used. To monitor the voltage of the supercapacitor (Vcap), the node is connected to an analog buffer (Texas Instruments, OPA4354AIDR) powered by a power supply (Agilent E3630A) to avoid influence on this low-power circuit. Then, the voltage is converted to a digital format by an analog-to-digital converter module (National Instruments, NI-9292 & NI cDAQ-9171). The results are displayed on the monitor using a LABVIEW program. A laptop and a custom light programing module are used to generate an optical signal and program the sensor. A universal software radio peripheral (USRP) (Ettus, USRP X310), a custom antenna and the same laptop are used to wirelessly download the measured data from the sensor.
2. Results and Discussion

Both enzymes, PQQ-dependent glucose dehydrogenase (PQQ-GDH)\textsuperscript{[25,59]} and bilirubin oxidase (BOx)\textsuperscript{[60,61]} used for catalyzing the anodic and cathodic reactions in the biofuel cell, respectively, are known for direct (non-mediated) electron communication with electrodes, especially when using buckypaper as the conducting support.\textsuperscript{[62–65]} While PQQ-GDH and BOx can operate as electrocatalysts at modified electrodes without electron transfer mediators, the use of a polythiophene sub-layer can further promote electron transfer and enhance the anodic and cathodic currents catalyzed by PQQ-GDH and BOx.\textsuperscript{[53,54]} Figure 4 shows schematically the electropolymerization process for preparation of the polythiophene layer, further functionalized with the enzymes PQQ-GDH and BOx for preparing the anode and cathode, respectively. The enzymes were attached covalently to the carboxylic groups in the polymer film (note the use of 3-thiopheneacetic acid as a co-precursor in the polymerization process; see description of the preparation process).

Figure 4. The scheme showing preparation of the electropolymerized polythiophene sub-layer, further modified with covalently bound enzymes. Note the ratio of the original thiophene-monomers n : m = 2 : 1.

With the goal of power production by a small (millimeter-scale) implantable biofuel cell, we assembled a biofuel cell with 2 mm by 3 mm (0.06 cm\textsuperscript{2} geometrical area) enzyme-modified electrodes. Prior to implantation of the electrodes into living species, the biofuel cell performance was studied with a 20 mM glucose/O\textsubscript{2} aqueous solution (50 mM phosphate buffer, pH 7.4, containing 100 mM Na\textsubscript{2}SO\textsubscript{4}). Figure 6A–C. The biofuel cell demonstrated an OCV of 600 ± 10 mV (as expected), a short circuit current of 48 ± 2 μA (ca. 800 μA cm\textsuperscript{-2} short circuit current density vs. geometric area) and a maximum power release of 10.5 ± 0.5 μW at 25 kΩ load resistance and 0.39 V. Taking into account the electrode area of 0.06 cm\textsuperscript{2} and the distance between the biocatalytic electrodes of ca. 0.2 cm, the volume of the biofuel cell was ca. 0.012 cm\textsuperscript{3}, thus resulting in a maximum power density of 875 ± 5 μW cm\textsuperscript{-3}. The power output was dependent on the glucose concentration, Figure 7, decreasing as the glucose concentration decreased, as expected.

In the next preliminary experiment, the biofuel cell was tested with a human serum solution containing approximately 10 mM glucose. The power output was 30 μW, thus resulting in a maximum power density of 0.30 μW cm\textsuperscript{-3}. The glucose concentration decreased from 10 to 0.1 mM during operation of the biofuel cell, thus resulting in a maximum power density of 0.01 μW cm\textsuperscript{-3}. The power output was dependent on the glucose concentration, Figure 7, decreasing as the glucose concentration decreased, as expected.

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6 mM glucose.$^{20,66}$ The output voltage, current and power were smaller than those obtained with the buffer solution, Figure 6D–F, due to lower glucose concentration and much higher viscosity of the biofluid. Still the maximum power release was rather impressive, 660 ± 20 μW cm$^{-3}$, smaller only by factor of 1.3 compared to that obtained in the aqueous glucose solution. The biofuel cell operation with the human serum solution provides important information for future biomedical applications; however, in vivo testing is also desirable. Since the implantation of the biofuel cell into a human body is not possible at the present stage, particularly in a chemical lab, we performed our experiments using slugs (invertebrate terrestrial mollusks).$^{52}$

The biocatalytic electrodes were inserted in the living slug tissue, and the implanted biofuel cell operated with hemolymph (biofluid equivalent to blood in invertebrates) containing glucose and O$_2$. Figure 8. The glucose concentration in the hemolymph has seasonal variation, with a typical concentration of ca. 0.7 mM in summer,$^{67}$ when the experiments were performed. While the voltage, current and power release were further decreased, the maximum power was measured as 2.4 ±
0.1 μW (ca. 200 μW cm⁻³), only smaller by a factor of ca. 2.4 compared with the power produced in a buffer solution containing 5 mM glucose (Figure 7), which is expected due to the lower glucose concentration in the hemolymph. An important question is if the power produced by the small implanted biofuel cell is sufficient for activation of the microelectronic device. The answer will depend on the power demanded by the device. It should be noted that the slug was alive during the experiments and survived after them.

After the biofuel cell and microelectronic sensor were characterized in terms of current, voltage and power, the biofuel cell was connected to the microelectronic sensor and the sensor operated autonomously powered only from the biofuel cell. Figure 9A shows the measured voltage of the supercapacitor (Vcap in Figure 2) over time. In the beginning, the sensor starts to measure temperature every 11 seconds. However, since the biofuel cell is not yet activated and the sensor consumes energy from the supercapacitor, its voltage decreases gradually. During the higher current draw, when the sensor is in the active mode, there is a short downward spike in the voltage due to the internal resistance of the supercapacitor. When the biofuel cell is activated, as noted in the figure, the sensor ‘charge pump’ chip activates and start to recharge the supercapacitor using energy from the biofuel cell. The rising voltage indicates that the system is energy autonomous and can continue the operation using the power provided by the implanted biofuel cell. The supercapacitor supports the different active operations of the sensor, including programming of the sensor (at the very start of the curve) and wireless data downloading (at the end of the curve) without significant voltage decrease (<18 mV drop due to internal resistance), ensuring correct system operation. Figure 9B shows the temperature measurements recorded by the sensor, logged in its internal memory and readout wirelessly and saved in the laptop. The sensing device can operate autonomously as long as the biofuel cell is active and the energy source (glucose in the hemolymph) is available. The present biofuel cell was not studied for long-term operation, however, it demonstrated reproducible power production over several days. It should be noted that similar kinds of biofuel cells have been reported to successfully operate for over 1 year,[68] which is much longer than can be obtained with a battery of a comparable size. The microelectronic device, despite the fact that it is a very sophisticated system, can be produced in many copies with reproducible features. The manufacturing process is rather standard for the state-of-the-art in microelectronics.

3. Conclusions

Enzyme-based biofuel cells implanted in different living species (ranging from invertebrates[24–27] to mammals[28–31]) have been reported recently. The power produced by them was in the μW range depending on the bioelectrode size and the “biofuel” (e.g., glucose) concentration in the biofluid (see Table S1 in the Supporting Information). It should be noted that the power density (power normalized to the electrode surface, μW/cm², or to the biofuel cell volume, μW/cm³) is not the parameter that is
important for practical use of the biofuel cell. Indeed, even if the power density is high but the biofuel cell is very small, the total power produced might be insufficient for activating any connected electrical/electronic device. Therefore, the total power produced, particularly for small biofuel cells, is the critical parameter that should meet the power requirements of the connected electrical load.

Very small enzyme-based biofuel cells (micrometer-scale) have been reported previously,[9] however, there are not many examples of their operation with a connected electrical/electronic load consuming the produced power. Particularly, sophisticated “smart” microelectronic sensors with wireless data readout have never been powered by small biofuel cells. The present work combined two challenging research goals: designing a small size biofuel cell and assembling a “smart” microelectronic device with its harvesting ability and power consumption designed for the available power. The exemplified power source was a slug, but many other potential environmental sources of energy exist.[9] The process limiting power generation by an implanted biofuel cell, which could be at the biocathode or bioanode, depends on many parameters. Some of them can be controlled by preparing the electrodes (changing the activity/amount of the immobilized enzymes), but some are controlled by physiological processes in the living host species (i.e. slug in the present study).[25] It has been shown that feeding a snail (used in our previous study) increases the power production due to elevated glucose concentration produced physiologically. The physiological variation of glucose and oxygen concentrations may change the limiting process in the implanted biofuel cell.

Autonomously operating microelectronic devices continuously powered by small biofuel cells will be beneficial for various environment-monitoring functions, including biosensors designated specifically for homeland security and military applications. Further miniaturization of the sensor device and connected biofuel cell would allow their operation as implantable biomedical devices. The microelectronic device can accommodate the biocatalytic electrodes directly in the structure of the device, thus further reducing the device size and eliminating unnecessary wiring connecting the biofuel cell and the electronic device. For microelectronic production convenience, the biofuel cell can be prepared as an “abiotic” device[28] with the electrocatalytic electrodes modified with inorganic catalytic species (e.g., noble metal nanoparticles) instead of the enzymes used in the present study. “Abiotic” biofuel cells can extract electrical energy from biological sources, e.g., using glucose as the “fuel.”[27] Overall, the present first report of a biofuel cell combined with a microelectronic device has many different potential technological extensions for various applications.

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Conflict of Interest

The authors declare no conflict of interest.

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