

Muscle-Driven In Vivo Nanogenerator

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Harvesting energy from the environment is crucial for the independent, wireless, and sustainable operation of nanodevices. This is a key requirement for building self-powered nanosystems. The living environment of nanodevices is diverse ranging from natural to in vitro and in vivo. Mechanical energy is one of the most abundant and popular energies in the environment, which can range from wind energy to mechanical vibration, sonic/ultrasonic waves, noise, fluidics, biomotions, muscle stretching, and more.

Harvesting energy using piezoelectric materials has been demonstrated some time ago,^[1–3] but these structures are rather large and a tiny physical motion, such as the contraction of a blood vessel is not strong enough to drive the generator. More importantly, the demonstrated cantilever-based microelectromechanical systems (MEMS) work only under a specific driving resonance frequency that is determined by the cantilever. In a real biological system, the mechanical disturbance has a large frequency range and the mechanical vibration is time dependent.

We have demonstrated a few approaches for harvesting mechanical energy from several different sources,^[4–6] one of which was based on an alternating-current (AC) nanogenerator using a two-ends-bonded piezoelectric nanowire (NW).^[7] The NW is laterally bonded on a flexible substrate, and the physical deformation of the NW is directly driven by the shape change of the substrate that is induced by external dynamic mechanical sources. When a ZnO NW is subject to a periodic mechanical stretching and releasing, the mechanical-electric coupling effect of the NW, combined with the gate effect of the Schottky contact at the interface, results in an alternating flow of the charge in the external circuit. The single-wire generator (SWG) acts as a “charging pump” that drives the electron motion in accordance to the mechanical deformation of the NW.

Recently, we have applied the AC generator to harvest mechanical energy from body movement under in vitro conditions.^[8] However, the applications of the nanogenerators under in vivo and in vitro environments are distinct. Some crucial problems need to be addressed before using these devices in the human body, such as biocompatibility and toxicity. To directly interface nanowires with cells, our studies have indicated that ZnO nanowires can be safely used for in vivo applications and they are biodegradable.^[9] In this Communication, in vivo biomechanical-energy harvesting using an AC nanogenerator

has been achieved for the first time. We demonstrate the implanting of the nanogenerator in a live rat to harvest energy generated by its breath and heartbeat. This study shows the potential of applying nanogenerators for the scavenging of low-frequency dynamic muscle energy created by very small-scale physical motion for the possible driving of in vivo nanodevices.

The fabrication process of a SWG was presented in detail in our previous publication.^[7] The piezoelectric ZnO NW was grown using a physical-vapor deposition process and had a diameter of 100–800 nm and a length of 100–500 μm. The two ends of the NW were tightly fixed to the surface of a flexible polyimide substrate by applying silver paste and two lead wires, isolated from the environment, were connected to the ends. Because of the presence of bio-fluids under the in vivo working condition, the entire device was covered with a flexible polymer to isolate it from the surrounding medium and to improve its robustness. The short-circuit current (I_{sc}) and open-circuit voltage (V_{oc}) were measured to examine the performance of the SWG. All of the measurements were performed in a well-grounded and screened environment and the noise level was carefully minimized.

The output V_{oc} and I_{sc} of the SWG are typically less than 50 mV and 500 pA, respectively, in most cases. Therefore, careful experiments have to be conducted to rule out possible artifacts introduced by factors such as the measurement system, change in capacitance of the nanowire and the electric circuit, and/or the coupling of the SWG with the measurement system.^[7] A series of testing criteria has been established before to identify the true signal generated by the SWG.^[10] An effective SWG must exhibit Schottky behavior at one end before and after measurement (Fig. 1c). The output voltage and current of a SWG should meet the switching polarity test. For easy notation and reference, we define the side of a SWG with Schottky contact as the positive side. When the positive and negative probes of the measurement system are connected to the positive and negative sides of the SWG, respectively, the configuration is described as being a forward connection. The configuration with the two probes switched over is defined as a reverse connection. Both configurations were tested. The magnitude of the signal from different connecting configurations may differ because of the influence of a small bias current in the measurement system. So the magnitude of the true signal is an average of those under forward and reverse connections.

The first group of experiments was based on the conversion of the mechanical deformation related to the periodic expansion and contraction of the diaphragm of a rat into electricity (Fig. 1a). Adult rats (Hsd: Sprague Dawley SD, male, 200–224g) were used for the experiment. Our procedure in handling the animals followed National Institutes of Health (NIH) policies and guidelines, university policies, and Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)

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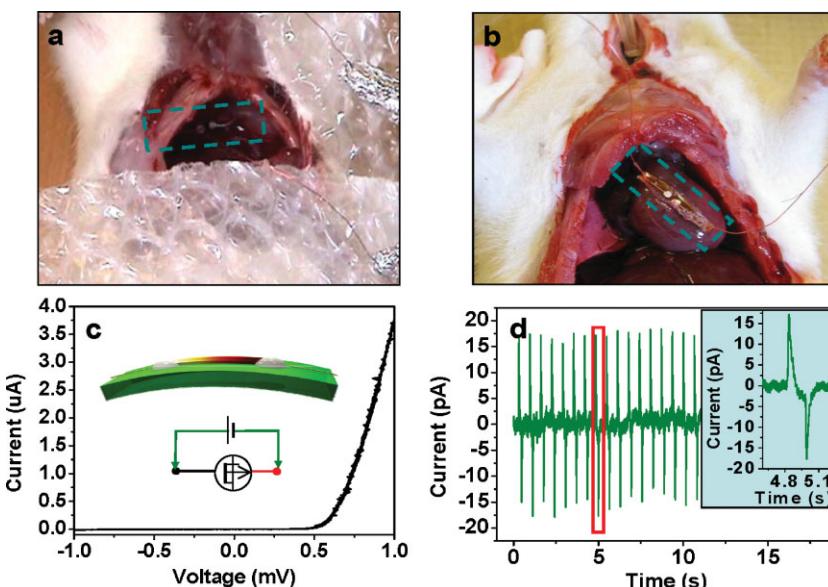


Figure 1. Energy harvesting from the breath and heart beat of a live rat using a SWG. a,b) A SWG attached to a live rat's diaphragm (a) and its heart (b), which drives the SWG to periodically bend and produce an AC power output. c) I - V characteristics of the SWG. The inset illustrates the schematic of the SWG and its connection configuration in reference to the measurement system. d) Typical current output recorded from a SWG under in vivo conditions [from the set-up in (a)].

accreditation standards. We followed the protocol approved by the Institutional Animal Care and Use Committee (IACUC) of the Georgia Institute of Technology. The anesthesia procedure of the rat started with the intake of isoflurane gas (1–3% in pure medical grade oxygen), followed by the injection of a ketamine cocktail (intraperitoneal, ketamine 50–90 mg kg⁻¹, xylazine 5 mg kg⁻¹) and buprenorphine (intraperitoneal, 0.03 mg kg⁻¹) for anesthesia induction and maintenance, respectively. A tracheotomy was first performed; and a tracheal intubation was connected to a respirator, which provided artificial respiration and sustained the life of the rat throughout the entire experiment. Then the rat's abdominal cavity was opened to make the ventral-side of the diaphragm reachable for implanting a SWG (Fig. 1a). Part of the liver was cut off after proper ligation for easy observation and operation.

Before a SWG was placed inside the body of the rat, the I - V characteristics were measured to ensure the presence of at least one Schottky contact, as shown in Figure 1c. The SWG was then attached to the diaphragm surface by applying a synthetic absorbable tissue adhesive (tissuemend II SC, methoxypropyl cyanoacrylate composition, Veterinary Products Laboratories), as shown in Figure 1a. The inhalation and exhalation of the rat resulted in the alternative expansion and contraction of the diaphragm, which in turn produced periodical stretching and releasing of the SWG, respectively. The piezoelectric potential

created in the piezoelectric wire drove the electrons to flow back and forth through an external circuit in response to the physical expansion and contraction of the diaphragm (Video 1 in Supporting Information). A typical current output is presented in Figure 1d.

Figure 2 shows the short-circuit current and open-circuit voltage output from the SWG when the breathing of the rat was driven and controlled by the respirator at a constant rate of about 110 times per minute. When the measurement equipment was forwardly connected to the SWG, a positive voltage/current pulse was produced during inhalation, immediately followed by a negative voltage/current pulse during exhalation (Fig. 2a). When the measurement instrument was reversely connected to the SWG, the sign of the voltage/current pulse flipped over and corresponding processes were obtained (Fig. 2b), thus satisfying the switching-polarity test proposed for SWGs.^[8] It should be noted that there are about 110 “paired peaks” in one minute, which is consistent with the breathing rate controlled by the respirator. Detailed inspection of the insets in Figure 2 reveals that the second peak (ca. 0.05 s) is slightly wider than

the first one (<0.05 s). This difference indicates that the exhalation took longer than the inhalation, which is consistent with the physiological breathing of the rat. On average, the magnitude of the voltage and current signals were about 1 mV and 1 pA, respectively, which is appreciably lower than the outputs of the SWG driven by a mechanical simulation

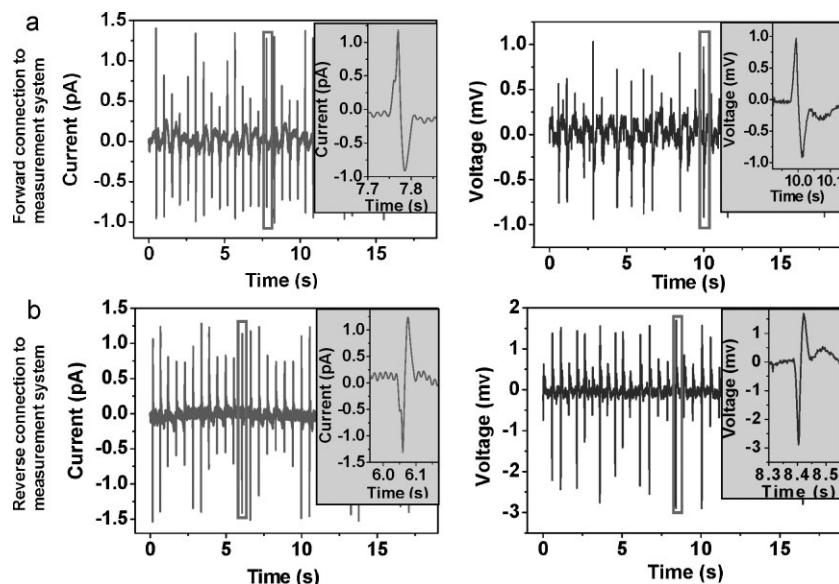


Figure 2. Energy harvesting with a SWG from the breath of a live rat whose breathing is sustained by a respirator. a) Electric power output (short-circuit current and open-circuit voltage) when the SWG is forwardly connected to the measurement system. b) Electric power output (short-circuit current and open-circuit voltage) when the SWG is reversely connected to the measurement system. The insets illustrate the enlarged views of the electric signals from the boxed areas.

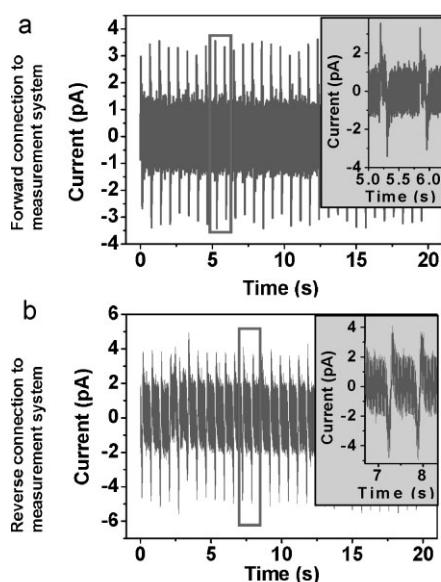
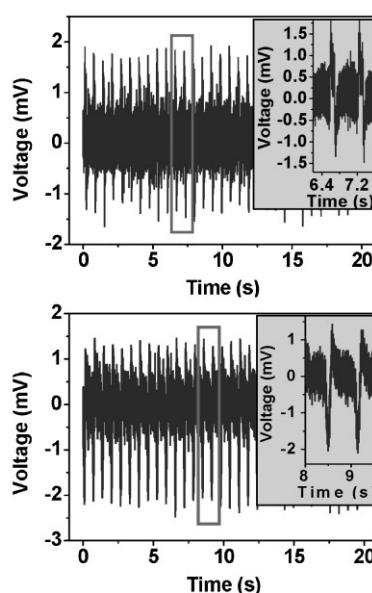


Figure 3. Energy harvesting with a SWG from the autonomous breathing of a rat. a) Electric power output (short-circuit current and open-circuit voltage) when the SWG is forwardly connected to the measurement system. b) Electric power output (short-circuit current and open-circuit voltage) when the SWG is reversely connected to the measurement system. The insets illustrate the enlarged views of the electric signals from the boxed areas.

machine,^[7] which has a higher straining rate and a larger degree of mechanical deformation.

In order to rule out possible artifacts induced by the respirator, although it was carefully screened to be isolated from the SWG and the measurement system, a control experiment was conducted, in which the rat breathed in an autonomous manner without the help of the respirator. All the other experimental conditions remained the same. Under a forward connection configuration, both the positive and negative signals were recorded for inhalation and exhalation, respectively (Fig. 3a). Reverse connection produced an electric output of the opposite sign (Fig. 3b). It can be seen that there are approximately 90 paired peaks for every minute, indicating the respiration rate to be about 90 times per minute. Compared to the respirator-driven breathing, the autonomous breathing was deeper and longer with a larger amount of air intake for every breath. This means that the diaphragm could expand to a larger extent but at a slower rate. Such movement affected the corresponding electric signal. Larger deformation of the SWG resulted in a higher magnitude of the output signals, namely about 4 pA and 2 mV for the current and voltage, respectively. The slower and longer movements of the diaphragm during autonomous breathing contributed to wider electric signal peaks (> 0.2 s), as shown in the insets in Figure 3.



physiological reasons and neural feedback regulation. The actual amount of oxygen needed by the rat depends on many factors, mostly its physiological condition. The respirator might not provide the exact amount of oxygen needed by the rat. If the provided amount of oxygen was insufficient and saturation of the blood oxygen was low, the neural feedback regulation of the rat

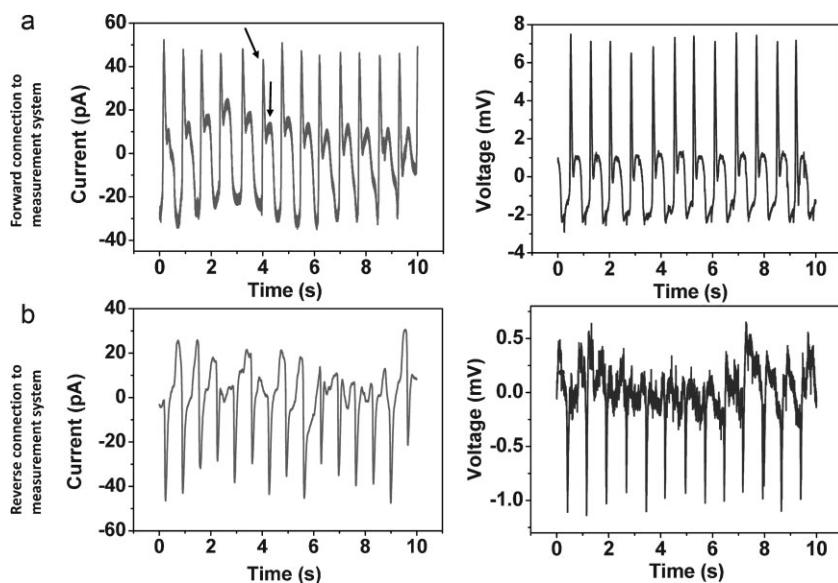


Figure 4. Energy harvesting from the heartbeat of a live rat by using a SWG. a) Electric power output (short-circuit current and open-circuit voltage) when the SWG is forwardly connected to the measurement system. b) Electric power output (short-circuit current and open-circuit voltage) when the SWG is reversely connected to the measurement system.

Physiologically, the difference between inhalation time and exhalation time is expected to be larger for autonomous breathing than for respirator-driven breathing. Such trend was clearly confirmed and can be seen in the four insets in Figure 3, in which the second peak (ca. 0.3 s) of each pair of peaks is appreciably wider than the first one (ca. 0.2 s). However, the noise level for the electric output was appreciably higher than that in Figure 2. This is possibly related to the fact that, in the absence of the respirator, the unstable breathing of the rat under anesthesia might give rise to irregular vibrations of the diaphragm.

It should also be noticed that in most cases there was a modulation in the magnitude of the electric output, as shown in Figure 2. This is likely related to the interference between respirator-sustained breathing and autonomous breathing, which occur at different frequencies. The natural breath frequency was 90 times per minute (Fig. 3) and the respirator-driven breathing occurred at 110 times per minute (Fig. 2). In such a case, an interference pattern at a frequency of 20 times per minute is possible, which is consistent with the observations shown in Figure 2. The observed phenomenon can also be due to

might autonomously deepen for a few breaths to ensure a higher intake of oxygen after several shallow breaths driven by the respirator. Such a process could periodically occur, which correspondingly would produce an electric power output of different magnitude. Alternatively, when excessive oxygen was provided by the respirator and saturation of the blood oxygen was too high, the neural regulation feedback might suppress the depth of the breath so as to decrease the amount of oxygen in a periodical manner, which might also result in a periodical change in the magnitude of the electric signal.

The second group of experiments was geared to applying a SWG to harvest mechanical energy from the heart beat of a live rat (Fig. 1b). The expansion and contraction of the heart can also stretch and release the SWG, respectively, producing an AC output. The anesthesia and tracheotomy were performed in the same way as before. The chest cavity of the rat was opened and the chest bone was removed to expose the heart. A respirator was also used to serve as a life-sustaining device throughout the whole experiment to ensure a heart beat. Then a SWG was tightly fixed to the surface of the heart with the help of the tissue adhesive (Fig. 1b). Figure 4 shows the open-circuit voltage and short-circuit current output. The non-asymmetric output of the SWG before and after switching of the polarity was likely caused by a bias current in the measurement system, which was added to the current generated by the SWG in the forward configuration, and subtracted from the generated current in the reverse configuration. On average, the voltage and current outputs were around 3 mV and 30 pA, respectively. It should be noted that a heart beat is not a simple stretching-releasing movement. It consists of ventricle beating and auricle beating, which may be responsible for generating the larger peaks and the smaller ones, respectively, as pointed out by arrows in Figure 4a.

In summary, we have demonstrated the *in vivo* application of a SWG for harvesting biomechanical energy inside a live animal. The SWG has successfully converted the mechanical vibration energy from normal breathing and a heartbeat into electricity.

Our research shows a feasible approach to scavenge the biomechanical energy inside the body, such as heart beat, blood flow, muscle stretching, or even irregular vibration. This work presents a crucial step towards implantable self-powered nanosystems.

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