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Wireless and batteryless biomedical microsystem for neural recording and epilepsy suppression based on brain focal cooling

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Abstract: This work presents a biomedical microsystem with a wireless radiofrequency (RF)-powered electronics and versatile sensors/actuators for use in nanomedicinal diagnosis and therapy. The cooling of brain tissue has the potential to reduce the frequency and severity of epilepsy. Miniaturised spiral coils as a wireless power module with low-dropout linear regulator circuit convert RF signals into a DC voltage, can be implanted without a battery in monitoring free behaviour. A thermoelectric (TE) cooler is an actuator that is employed to cool down brain tissue to suppress epilepsy. Electroencephalogram (EEG) electrodes and TE coolers are integrated to form module that is placed inside the head of a rat and fastened with a bio-compatible material. EEG signals are used to identify waveforms associated with epilepsy and are measured using readout circuits. The wireless part of the presented design achieves a low quiescent current and line/load regulation and high antenna/current efficiency with thermal protection to avoid damage to the implanted tissue. Epilepsy is suppressed by reducing the temperature to reduce the duration of this epileptic episode. Related characterisations demonstrate that the proposed design can be adopted in an effective nanomedicine microsystem.

1 Introduction

Physical signal measurement and stimulation in vivo real time are frequently adopted to obtain biomedical information. Nanomedicine and biological research depends on microsystems to identify and develop treatments for brain disorders. Most biophysical signals are detected using wire connections and the transmission of signal is sometimes terminated using wound wires or deformed connectors between an amplifier and electrodes. Disease rats may shake or turn around continuously and these behaviours must be observed experimentally. The use of wireless transmission in animal experiments can eliminate factors that terminate experiments. To suppress epilepsy, several strategies have recently been employed to reduce the frequency and severity of neocortical seizures. These include resection and stimulation in an electric field. Some brain slice studies have established that the direct application of a constant or DC electrical field can diminish neuronal excitability and experimental seizure discharges [1]. Although DC fields have not yet been applied clinically, some researchers now have some experience of numerous versions that is use of intermittent electrical stimulation to treat human epilepsy. Studies have identified subsets of patients who responded favourably to intermittent hippocampus or thalamic stimulation [2–4].

A miniaturised long-term and reliable wireless/batteryless nanomedicine implantation with versatile bio-sensors/actuators for nanomedicinal applications is required to monitor in real time the free behaviour of implanted animals. Most current commercial implants include a heavy battery to supply power to the system. Systems with integrated circuits, bio-potential sensors [5] and a miniaturised power supply, developed with a coil inductor to receive radiofrequency (RF)-power receiving from an external host are highly desirable.

An attractive alternative strategy for terminating and preventing focal seizures is the application of focal cooling and the use of wireless transmission is used in this microsystem to measure biophysical signals in a free space. The literature on the effectiveness of cooling in reducing synaptic transmission in the mammalian brain is extensive and new engineering technology should to be able to be sued to deliver highly focused cooling [6–9]. Such a therapeutic microsystem is designed to suppress epilepsy and transmit wirelessly. The system is implemented and its effectiveness is verified.

2 System overview

Fig. 1 displays the electrical architecture of the presented wireless and batteryless microsystem, which provides microsystem parts for bio-potential, chemical, temperature measurement and driving ability of thermoelectric (TE) cooler actuators. The proposed microsystem with versatile biomedical sensing/actuating properties therefore meets the

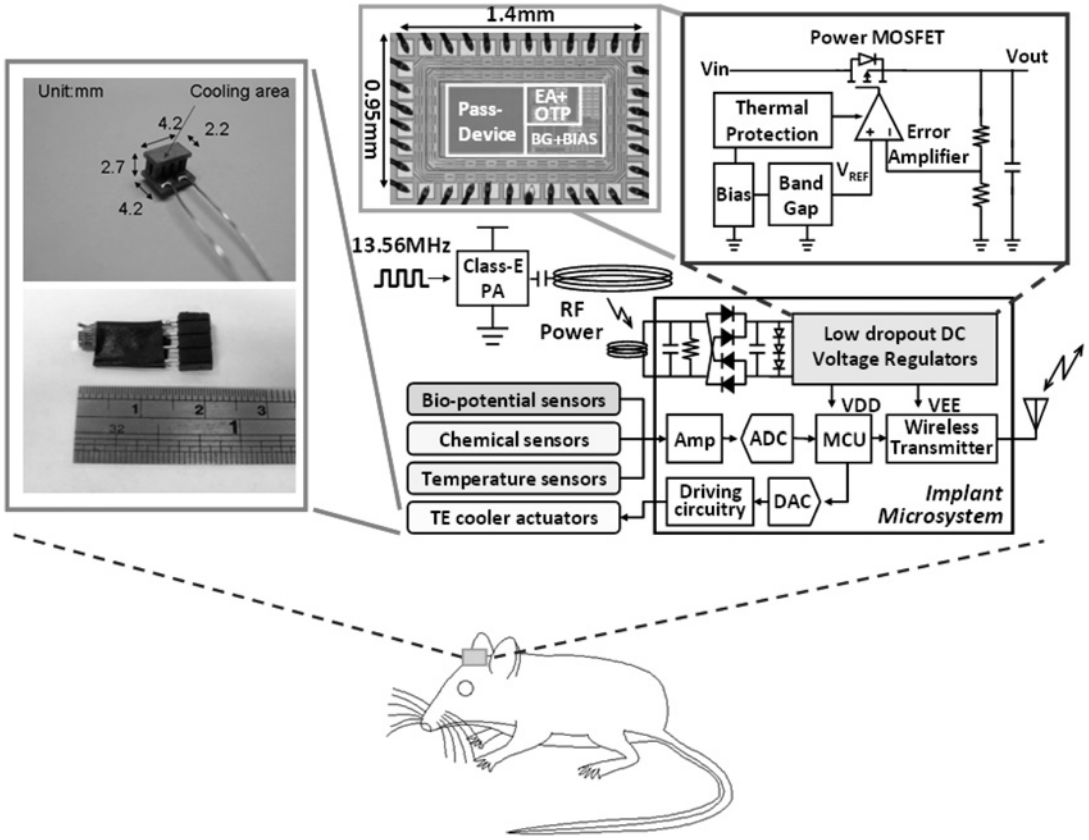

Fig. 1 *System structure of the presented wireless powering device in an implant microsystem*
Photographs of a Chip, a LDO RF-DC regulators and a TE module are also displayed

requirements for nanomedicinal diagnosis and therapy applications. As shown in Fig. 1, the batteryless function, realised by RF-powering, consists of spiral coils, full-wave rectifiers and low-dropout (LDO) voltage regulators for RF transmission/reception, AC–DC transformation and stable supply output. A 13.56 MHz RF-power supply is chosen to minimise absorption by tissue to prevent damage [10]. External RF power is supplied by a Class-E amplifier, which is coupled into the microsystem via a tuned LC network followed by a full-wave rectifier and LDO regulators to produce stable 1.8 and 0.7 V as system and reference supplies. The LDO regulator also achieves low quiescent current at 45 μA and a high loading current of 0–200 mA capability. Additionally, developed linear regulator has thermal protection (<40°C) to prevent it from damaging the target when used in an implanted device [11].

Bluetooth is commonly used in many wireless biomedical systems [12] because of its convenient usage and easy communication with laptop. Bluetooth approach also shows its low power and EM safety in many human–machine interface applications. The Bluetooth module used in the proposed microsystem is BTM-182 (Rayson Technology Co., Ltd., Taiwan) with Bluetooth v2.0 chip BC-417 (CSR Bluetooth, USA) and printed printed circuit board (PCB) antenna. Its RF output power is 0 (min) to 4(max) dBm, implies 1–2.51 mW RF power appears near antenna. The power is much smaller than the IEEE standard [13] even if all the output RF power is absorbed by the tissue. Also, system noise that induced by the wireless communication can be ignored because the pass band of the recording system is below several tens of hertz, which is much lower than the RF frequency.

The wireless transceiver in the microsystem transmits biopotential/chemical/physical data to and receives commands from an external host. Raw electrical signals that are acquired by the bio-sensors are firstly conditioned, filtered and amplified by the analogue front-end amplifiers. Then, digitised biopotential data provided by the ADC are packaged and transmitted to the Bluetooth transmitter by the Micro-Controller Unit. The property of the sensor channels and maximal resolution of the transmitted data highly depend on the maximal transmission rate of the wireless module. The wireless module also receives commands from an external host. Commands may include system turn-on/off, reset and setting of the signal conditioning/digitising parameters and powering-on the driving circuitry of the TE cooler to terminate epileptic episode. A brain disease can be identified and classified, as epilepsy for example, in an external host such as a laptop, and then, the appropriate command is wirelessly transmitted to the implant microsystem. Fig. 1 presents a microphotograph of the proposed TE cooler that is used to suppress epilepsy with dimensions. The full microsystem has a head-stage design with bio-sensors and a TE cooler in the tissue with the inductive coil and antenna exposed outside of the skull to improve transceiver efficiency. The RF-powered design makes the presented microsystem small in volume, light in weight and operable without a battery module.

The evolution of TE devices and the necessary supporting technology has provided an opportunity for reevaluating cooling as a viable therapy for some forms of epilepsy. Local cooling therapy requires a cooling actuator. A commercial TE cooler is fabricated and packaged using bio-compatible materials. In this study, the cooling side of a TE cooler is put into direct contact cortex and platinum is used as an appropriate bio-material to cover the surface of the TE cooler.

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Fig. 2 *Placement of an EEG electrodes and cooler modules in a head of rat*

Platinum is deposited on a silicon substrate by DC sputtering. After deposition of platinum material and cutting, the covered substrate was bonded onto the cold side of a TE cooler using a high thermal conductivity adhesive. Cooling by a TE cooler via a silicon substrate and platinum film can reduce the temperature of the brain tissue. Polydimethylsiloxane (PDMS) is utilised to cover the other part of a TE module, which may also be in contact with brain tissue. PDMS is a kind of bio-material adhesive and can easily be formed at an elevated temperature. PDMS is electrically isolated, and hence prevents electric current from damaging brain tissue that. A TE cooler has a cooling area of 4.2 mm × 2.2 mm. This area is large because the cooler includes several pairs of cooling units. The range of temperatures that can be obtained using a commercial TE cooler can be as large as 70°C with evaluated current control but the temperatures achieved are too low to harm a mammalian. A suitable control signal for use in the experiment will be calculated. A TE cooler and connectors are integrated in a single module that can be embedded inside the head of a rat and connected to an amplifier. Fig. 1 shows such an integrated module.

Fig. 2 shows the surgical operation of embedding sensors and actuators inside the head of a rat. A rat was fastened to mark and remove part of the skull and dura. The area removed was approximately 4 mm × 4 mm. Then, electroencephalogram (EEG) and Electromyography (EMG) sensors were placed in the middle line of the head to detect EEG and EMG waveforms. Two cooling modules were located on both sides of the head. The components that were placed on the side of brain were covered with an appropriate material to protect the head from them and to protect them from unpredictable impact. EEG sensors were used to detect a brain signal associated with epilepsy and cooling modules were utilised to suppress it. A Sprague–Dawley rat was experimented upon.

3 Prediction temperature of heat exchange in a mammalian

To prevent damage by over cooling, the temperature of brain tissue must be kept stable and the variance from body temperature must not exceed ±2°C. Accordingly, a hot plate and water were adopted to establish an isothermal environment whose temperature is close to that inside a rat's head. Isothermal animals have a constant body

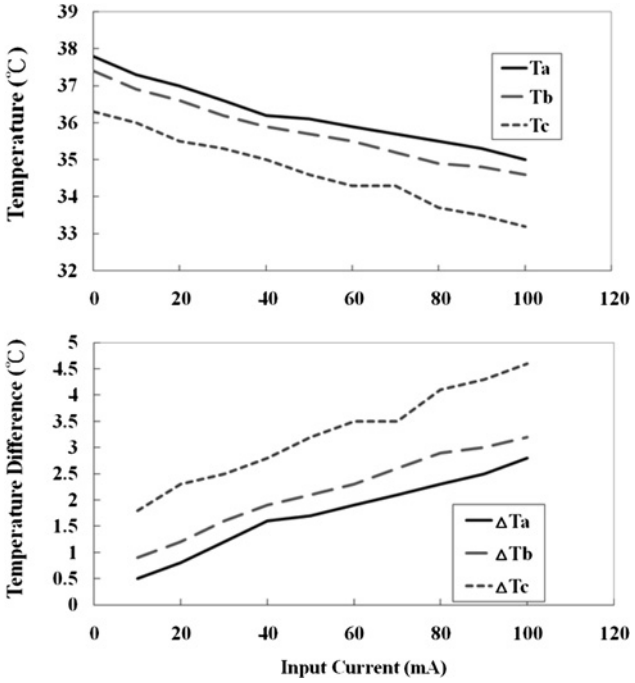

Fig. 3 *Prediction of cooling effect of mammalian animals*

temperature. A cooling module was placed in a tank, which was filled with water, and the module and the tank were then placed on the hot plate.

At the beginning of experiment, water was heated using a hot plate to 37°C to simulate a thermal environment similar to that in a mammalian. Then, the cooling module was employed to reduce the temperature of the water. The purpose was used to determine the interaction between the cooling effect of the cooling module and the heating effect of the isothermal animal. Fig. 3 plots measurements of temperature during cooling. The operational current range of a TE cooler is from 10 to 100 mA for various initial temperatures. Fig. 3*a* reveals that temperature is inversely proportional to the input current and different initial temperatures yield similar slopes. Increasing the input current reduces the temperature because the optimal current exceeds 100 mA. Various initial temperatures are utilised to evaluate the effectiveness of the cooler because the body temperature may change the temperatures of the cooling module. Fig. 3*b* indicates that the cooling effect at a lower initial temperature is greater than at a higher initial temperature because cooling more easily affects a lower initial temperature. To prevent damage to the brain by cooling, the temperature variance cannot exceed ±1.5°C [14]. Consequently, the input current of the cooling module is set to 35 mA and the temperature is reduced to 35.7°C as determined by interpolation.

4 Experimental set-up and results

Fig. 4 presents the experimental set-up that was adopted to suppress epilepsy. EEG and EMG signals were detected and transmitted to a DAQ card and then converted to a waveform that was displayed in Labview on a computer. Cooling modules were controlled by varying a DC current, temperature is inversely proportional to the DC current. However, the input cooler current to cooling modules must be precisely set, because current ripple can cause brain

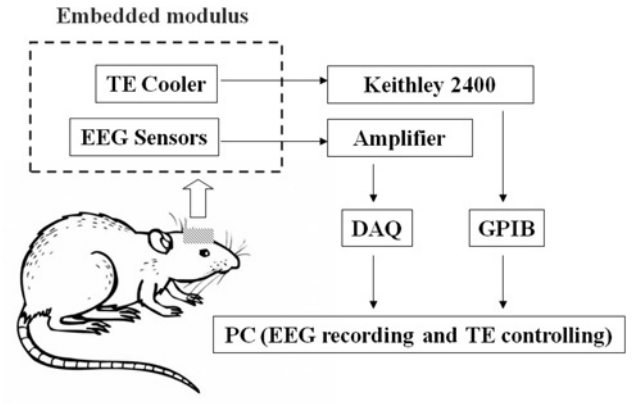

Fig. 4 *Experimental set-up*

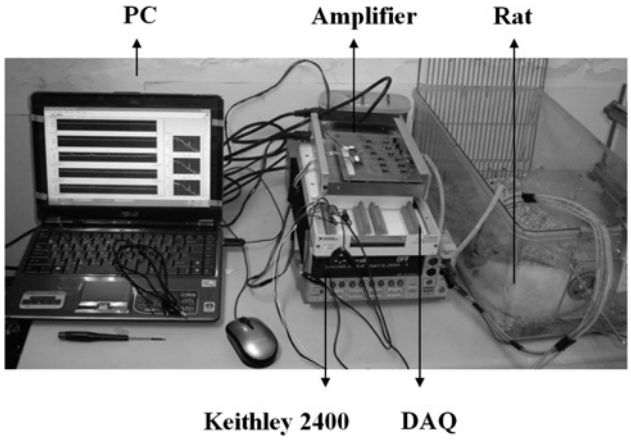

Fig. 5 *Measurement equipments*

damage. The Keithley 2400 outputs a precise current and controlled using Labview via general purpose interface bus (GPIB). Fig. 5 displays the experimental apparatus.

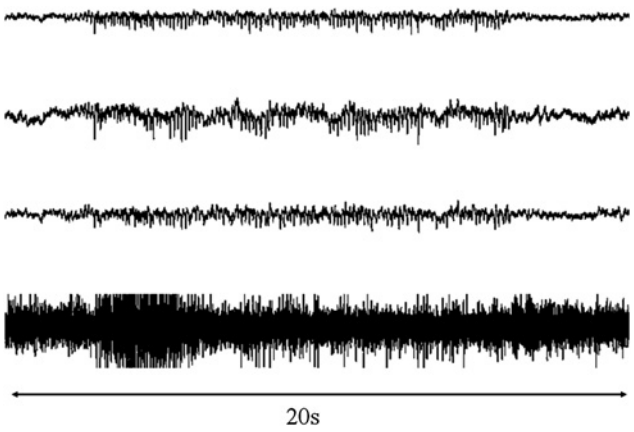

Fig. 6 *Epilepsy EEG and EMG waveforms*

Fig. 6 plots the classic waveform associated of epilepsy and it is composed of three EEG signals and one EMG signals. It is induced by injecting pentylenetrazol (PTZ) into a rat. These induced EEG waveforms from a rat have characteristic peaks that are displayed under the base line and are commonly over −0.5 V. Most periods of epileptic waveforms are approximately 5–15 s long. The last signal is the EMG waveform. It indicates that the rat does not sleep or walk because epilepsy causes it to stay statically and shake its

Table 1 Epilepsy suppressed by cooling

Suppression	Duration of epilepsy, s				
	1	2	3	4	5
without cooling	1038.8	622.5	936.2	1299.7	778.2
with cooling	712.1	663.2	505.5	432.7	970.6

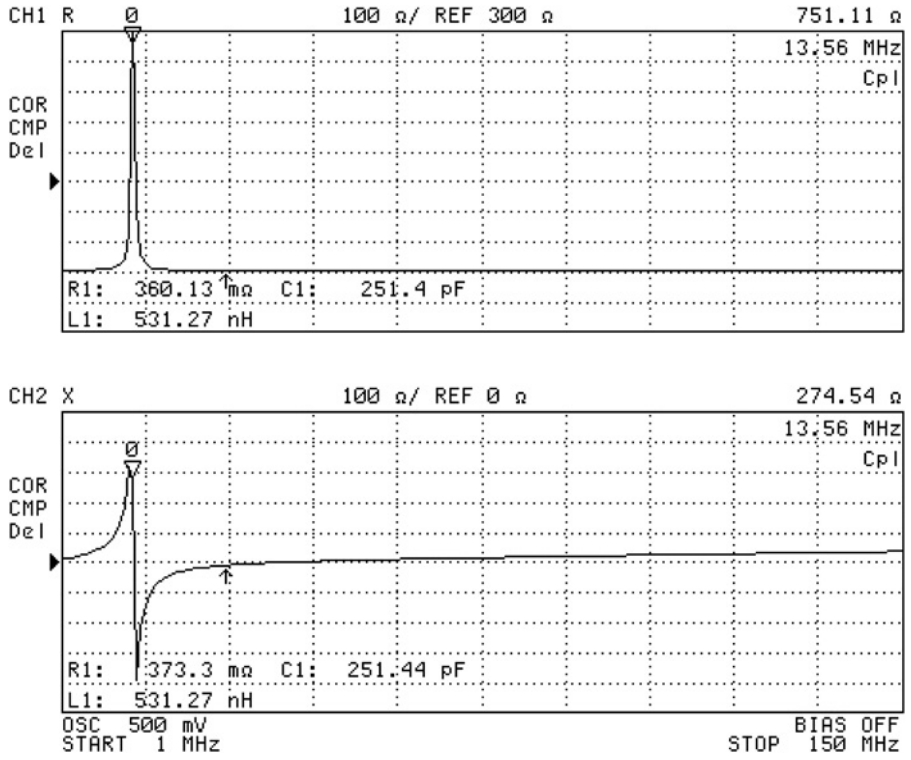

Fig. 7 *Frequency of wireless transmission*

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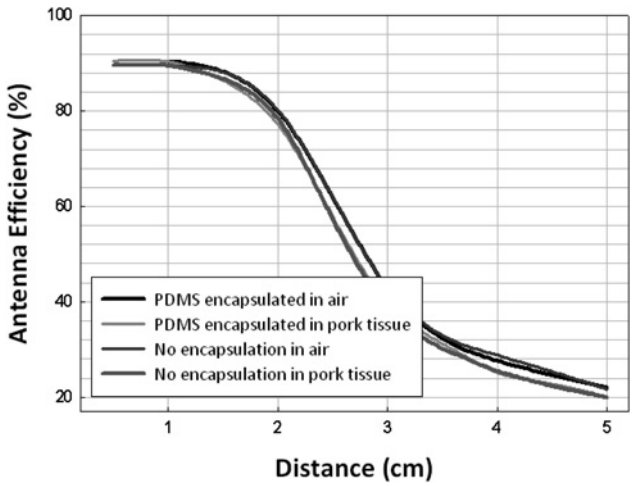

Fig. 8 *Antenna efficiency with different packages*

whiskers. Therefore these waveforms demonstrate that the EEG signal is caused by the induced epilepsy.

Table 1 presents measurements concerning the suppressions of epilepsy. PTZ was injected into rats to induce the epileptic EEG waveform. The dose of PTZ depended on the weight of the rats. The ratio of induced time with/without cooling suppression is utilised to represent the severity of the epilepsy and the performance of improvement. Each experiment lasted for 90 min after PTZ was injected.

Measurements were made repeatedly for ten times. Five sets of measurements were obtained using cooling therapy and the five were obtained without cooling. According to these results, cooling can suppress epilepsy. All the data are used to identify the performance of suppression. The durations of epilepsy without and with suppression are 20.78 and 14.60% for cooling therapy, respectively. This improvement provided by cooling is thus verified.

The receiving and external power-supply coils, made by 24/16 AWG copper wire, had diameters of 1.5 and 4 cm, respectively. The coils were designed to pass a frequency of 13.56 MHz, as measured using an impedance analyser that is presented in Fig. 7. The high antenna efficiency is characteristic of the PDMS coating as bio-protection in implanted tissue. Fig. 8 plots measurements made in air/tissue (pork) and with/without PDMS encapsulation. The results indicate no obvious effect of packaging. Miniaturised modules are therefore suitable for batteryless requirements in the microsystem design.

5 Conclusion

A bio-application microsystem with versatile biomedical sensing/actuating properties is presented. It meets the requirements for nanomedicinal diagnosis and therapeutic applications. Spiral coils, full-wave rectifiers and LDO voltage regulators are also designed for wireless transmission. They are used to measure physical signals and drive the actuators. Cooling therapy for epilepsy using a TE cooler reduces the temperature of brain tissue. A TE cooler with a dielectric thin film can prevent the driving current from damaging brain tissue and PDMS can be used to cover a TE cooler to make it bio-compatible. To contact cortex directly to ensure effective cooling, the dura is removed. Wireless transmission with spiral coils is used to measure free behaviour and cooling therapy for epilepsy is demonstrated. The system can be further miniaturised using a system-level integrated mixed-signal circuit design, which is currently being developed.

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