# Epileptic Burst Measurement Using Microelectrodes Equipped on A Cryogenic Microprobe for Minimally Invasive Brain Surgery of Intractable Epilepsy Treatment

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**Abstract:**

*A microprobing system, which has the functions of measuring the intracranial EEG(IC-EEG) and freezing brain tissue, is proposed for the minimally invasive brain cryogenic surgery of intractable epilepsy treatment. Two ϕ76 μm platinum electrodes were equipped on a ϕ0.8 mm cryogenic probe. Epileptic burst, which was evoked on a brain sample of a rat, was measured by the electrodes. The freezing function was confirmed with the experiments with sliced hippocampus samples of a rat.*

***Keywords:*** *epilepsy, cryogenic surgery, minimally invasive, microelectrodes, CMOS IC.*

## 1. Introduction

About 50 million people worldwide have epilepsy at any one time. The lifetime prevalence of epilepsy (i.e. the number of people presently in the world who have epilepsy now or have had it in the past, or will experience it in the future) is approximately 100 million people. The mean prevalence of active epilepsy, which causes continuing seizures and needs treatments, is 0.82 % of the general population around the world [1]. In 70% of cases of the epilepsy patients' seizures can be controlled with medications, even though it cannot be cured. However, up to 30% of the patients do not respond to the medications even with the best (strongest) available medicines. In that case, surgeries are applied to remove the brain tissue (neocortex or hippocampus, usually) of the epileptogenic focus. The removing area of the brain tissue is determined by the detected epileptogenic focus. However, the detection accuracy is up to several centimeters. Thus the risk of the side and after effects cannot be avoided.

In this paper, a cryogenic microprobe, microelectrodes, and intracranial EEG(IC-EEG) sensing CMOS interfaces are proposed to be compatible with the minimally invasive cryogenic surgery of intractable epilepsy treatment.

The proposed microprobe system has the functions of measuring the IC-EEG and freezing the brain tissue around the microprobe's tip for few millimeters.

## 2. Cryogenic Microprobe System

Figure 1 shows the block diagram of the proposed minimally invasive cryogenic microprobe system. This system mainly consists of 4 blocks: the cryogenic microprobe, the EEG instrumentation amplifier, the brain stimulation current source, and the thermocouple amplifier.

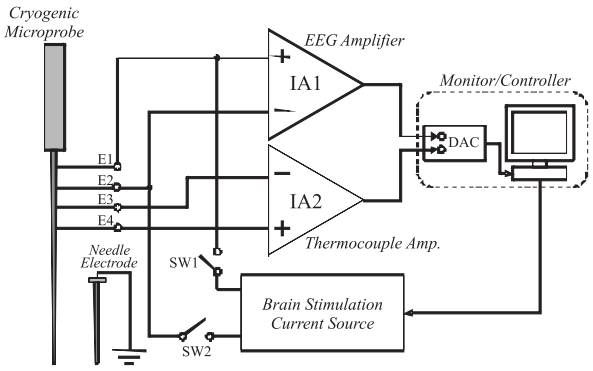


*Fig. 1. Proposed cryogenic microprobe system.*

The system operation is briefly explained below.

1) The cryogenic microprobe is inserted to the predetected epileptogenic focus, which is the breakout area of the epileptic burst.
2) In order to confirm that the probe is inserted to the correct location, IC-EEG is measured by the EEG amplifier with SW1 and SW2 opened. If the epileptic burst is observed, the probe-inserted position is determined to be an epileptogenic focus.
3) The refrigerant gas flows into the probe through the inner pipe, then the temperature of the probe's tip falls. Hence the brain tissue around the tip is frozen.
4) The brain stimulation current is applied in order to confirm that the brain tissue of the epileptogenic focus is adequately neutralized. When the epileptic burst does not occur after the stimulation, the epileptogenic focus no longer exists.

The details of the EEG amplifier and the cryogenic microprobe are explained in the following subsections.

### 2.1. Cryogenic Microprobe

The multifunctional microprobe and its cross sectional view is shown in Fig. 2. The needle pipe consists of the microelectrodes and coaxial pipes. The microelectrodes are made of platinum and acts as stimulating/measuring electrodes (ELECTRODE 1, ELECTRODE 2). The outer pipe is made of stainless steel SUS304 and acts as a negative thermocouple electrode (ELECTRODE 3). The inner pipe is made of Kovar (Fe54%-Ni29%-Co17%) and acts as a positive thermocouple electrode (ELECTRODE 4) and a refrigerant guide to evaporate it. Thus the tip of the needle pipe acts as rapid cooling/freezing probe and also acts as temperature measuring probe. The diameter of the tip is 0.8 mm. The refrigerant cylinder is filled with the

refrigerant gas, and is connected to the inner pipe of the needle pipe. Here, HFC(hidrofluoro-carbon)-152a is used as the refrigerant gas, since it has relatively high boiling point (-24 °C). The freezing ability of the microprobe has already been confirmed in the experiments with saline solidified by gelatin [2].

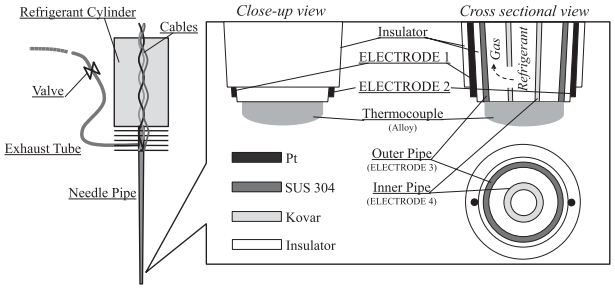


*Fig. 2. The proposed cryogenic microprobe and its cross sectional view.*

### 2.2. EEG Amplifier

Two instrumentation amplifiers (IA1 and IA2) are used in the proposed system: the EEG amplifier and the thermocouple amplifier. The same circuit design is adopted for both instrumentation amplifiers except the value of the gain-controlling resister RG. Figure 3 shows the circuit diagram of the instrumentation amplifier.

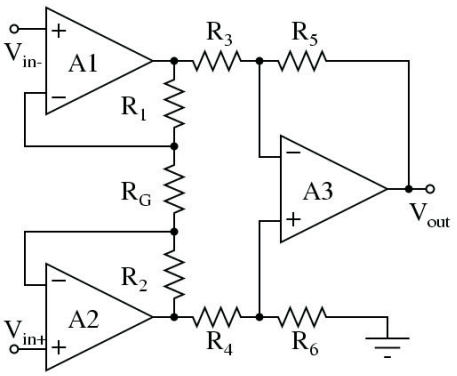


*Fig. 3. The circuit diagram of the instrumentation amplifier.*

The instrumentation amplifier adopts the 3-Op-amp architecture, which is commonly used for the high CMR (Common Mode Rejection) amplifiers [3]. The output voltage $V_{out}$ in Fig. 3 is given by the following equation (1) when $R_1=R_2$, $R_3=R_4$, and $R_5=R_6$ are satisfied.

$$V_{out} = (V_{in+} - V_{in-})\left(1+\frac{2R_1}{R_G}\right)\frac{R_5}{R_3} \quad (1)$$

In the depth EEG measurement, 100~300μV of the epileptic burst can be measured by depth electrodes (the electrodes are equipped on a 1mm-diameter catheter, electrodes distance: 5 mm ~10 mm) [4]. The gain is set to 60~80dB in the proposed EEG amplifier. The thermocouple amplifier is designed to have a gain of 80dB, since the Seebeck coefficient of the thermocouple, which appears at the probe's tip, was 47μV/K. For the proposed instrumentation amplifiers, a bipolar supply voltage is necessary. The element values used in the circuits are shown in Sect. 3.

## 3. Results

### 3.1. Epileptic Burst Measurement Using the Microelectrodes

Typical market-available microelectrodes are not suitable for this application because of the sharp tip shape. On the other hand, even though several types of microelectrode array mounted on a flexible film have been developed (e.g. [5]), they are not suited to attach 0.8 mm-diameter rounded surface of the cryogenic probe. The proposed microelectrodes were equipped on the surface of the cryogenic probe by using Teflon-coated platinum wires, which have the diameter of 76 μm. Heat-shrinkable tubes and a biocompatible bond were used to fix the electrodes on the surface of the cryogenic microprobe. The tip of the electrodes was polished with sanding papers (#600, 1000, 2000) and with a diamond polisher of #8000, in order to strictly flatten the contacting surface. The microscopic photograph of the probe's tip is shown in Fig. 4.

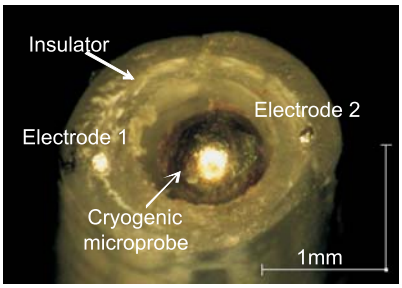


*Fig. 4. Microscopic photograph of the probe's tip.*

For the measurement of epileptic bursts, epilepsy was formed on the CA3 area of a male Wister rat's sliced hippocampus sample by intermittent pulse current stimulation through Electrode 1. The epileptic discharge was observed by using the electrodes, as shown in Fig. 6.

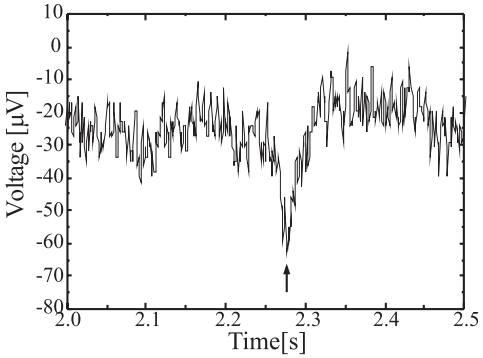


*Fig. 5. Epileptic burst measured by the microelectrodes.*

### 3.2. Cooling and Freezing of the Epileptogenic Focus

Focal brain tissue cooling and freezing were performed by the cryogenic probe. The probe's tip was vertically attached to the epileptogenic focus evoked on CA3 area. Figure 7, Fig. 8, and Fig. 9 show the epileptic spikes measured before cooling, after cooling of 30 seconds, and after cooling of 150 seconds, respectively.

When after cooling of 4 minutes, the epileptic spikes disappeared. These results suggest that the proposed multifunctional microprobe might be useful for surgical treatment of epilepsy.

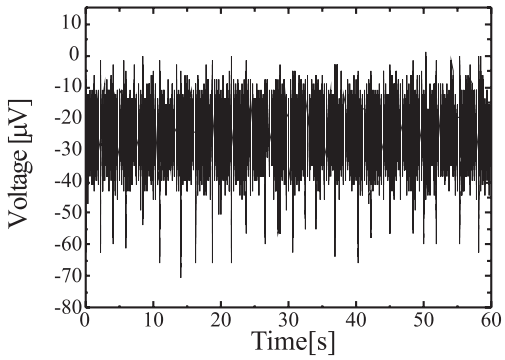


*Fig. 6. Epileptic spikes measured before cooling.*

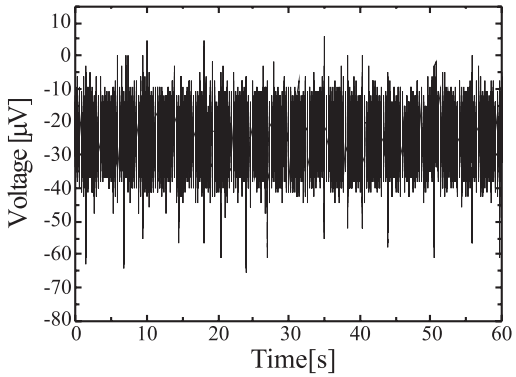


*Fig. 7. Epileptic spikes measured after cooling of 50 seconds.*

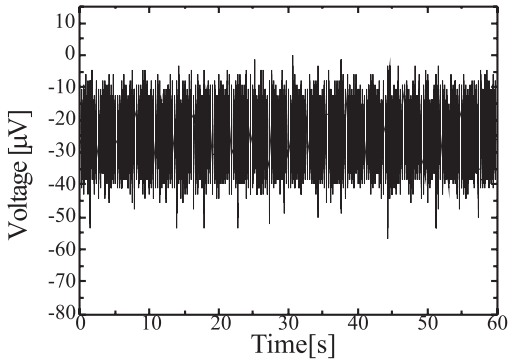


*Fig. 8. Epileptic spikes measured after cooling of 150 secondes.*

### 3.3. HSPICE CMOS Circuit Simulation Results of the EEG amplifier

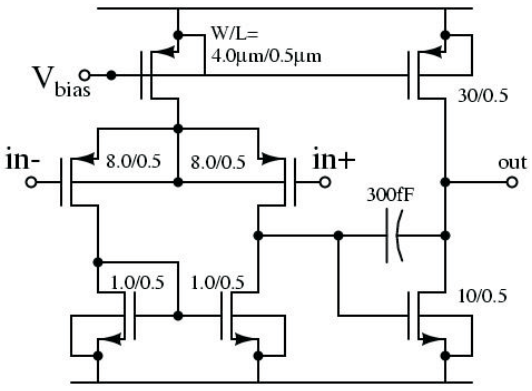


*Fig. 9. Op amp used in the simulation.*

HSPICE simulations were performed to confirm the operation of the proposed circuits. Level 52 HSPICE device parameters of a 0.18 μm 2-poly 4-metal CMOS process were used in the simulation. The bipolar supply voltage of ±1.5 V is applied. The circuit in Fig. 10 is used as the Op amp (A1, A2, and A3) in the circuit in Fig. 3. The bias voltage $V_{bias}$ of the Op amp is set to 0.5 V. The epileptic burst measured by the proposed microelectrodes (the upper part of Fig. 11) was used as a differential input of the circuit in Fig. 3. The epileptic burst was successfully amplified with the gain of 72dB (x4000), as shown in the lower part of Fig. 11.

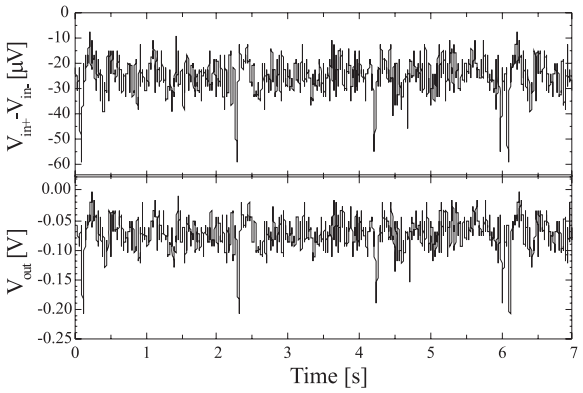


*Fig. 10. The differential input (upper) and the simulated output signal amplified by the circuit in Fig. 3 (lower).*

## 4. Conclusion

A system for intracranial EEG measurement and for minimally invasive cryosurgery of intractable epilepsy treatment was proposed in this paper. The epileptic burst was measured by the proposed microelectrodes in the experiments using hippocampus samples of a rat. Experimental results showed that the epileptic spikes were suppressed by cooling performed by the microprobe. The operation of the EEG amplifier was confirmed by the HSPICE simulations.

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