Development of a High-T<sub>c</sub> SQUID-Based System for Neurophysiology Studies In-Vitro

Per Magnelind<sup>1</sup>, Ed Tart<sup>2</sup>, Dag Winkler<sup>1</sup>, and Eric Hans<sup>3</sup>

<sup>1</sup>MC2, Chalmers University of Technology, SE-412 96 Göteborg, Sweden
<sup>2</sup>Electronic, Electrical & Computer Eng., Univ. of Birmingham, Birmingham, B15 2TT, UK
<sup>3</sup>Dept. of Physiology, Göteborg University, SE-405 30 Göteborg, Sweden

E-mail: per.magnelind@mc2.chalmers.se

Abstract. In this paper we report on the development of a system based on a high-T<sub>c</sub> SQUID (HTS) sensor for measurements of the neuromagnetic field generated by neurons inside tissue slices. SQUIDs have successfully been measured inside the system. The system white noise level is lower than 7 pT/Hz<sup>1/2</sup>, which is only slightly higher than previously reported 4.5 pT/Hz<sup>1/2</sup> for the same kind of SQUID measured inside a superconducting shield.

1. Introduction

Signal transport inside neurons is mediated by ion currents which generate both electrical and magnetic fields around the neurons. To study the physiology of the neurons either of these fields can be measured in-vivo or in-vitro. The common electrophysiological method usually employs insertion of a glass micropipette into a brain tissue slice preparation to record the field potential due to the activity of the neurons. Another, less common, method is to measure the generated magnetic field outside a tissue slice, which is the aim of this work.

Previously, only low-T<sub>c</sub> (LTS) SQUID-based systems have been employed to perform neurophysiology studies of tissue slices [1, 2] (see ref. [3] for a short review of previous LTS work).

We have previously reported on design aspects of our high-T<sub>c</sub> (HTS) SQUID system for in-vitro neurophysiology studies of hippocampal tissue slices [3, 4]. Moreover, we have reported in ref. [4] that a high-T<sub>c</sub> SQUID-based system would perform better than the previously used LTS systems, due to smaller sensor-to-source separation.

In this paper we report on the development of the system and results on SQUID measurements inside the system. Moreover, we report on the procedure for the initiated slice measurements.

2. Experimental set-up

The measurement set-up is described in ref. [3]. Since then a magnetic shield consisting of four layers of µ-metal shielding [5] and a hoist have been built inside a single-layer shielded room (see Fig. 1). The hoist system has a sand-filled counter-weight and steering fins to provide a smooth lowering of the magnetic shields. The system now rests on partially inflated rubber inner tubes and the table is supported by rubber mounts.

The SQUIDs that have been measured inside the system are of the same layout as described in ref. [3]. An YBa<sub>2</sub>Cu<sub>3</sub>O<sub>y-δ</sub> (YBCO) film of 200 nm was deposited by pulsed laser deposition.
on a SrTiO$_3$ bicrystal substrate with a symmetric 12$^\circ$–12$^\circ$ misorientation. The YBCO film was capped in-situ by a laser ablated Au layer. Au contact pads were fabricated by a lift-off technique. The SQUID patterns were obtained by standard lithography and subsequent Ar-ion milling through a resist mask. The in-situ Au was subsequently removed by a ion milling for a short time. After initial characterization the junctions were decreased in width from 4 µm to 2 µm by ion milling through a resist mask to decrease the critical current of the SQUIDs.

The ongoing experiments are performed on 400 µm thick transverse hippocampal slices from rats. The slices are prepared at the department of Physiology and in accordance with the guidelines of the local ethical committee for animal research. After approximately 30 minutes of room-temperature storage a single slice is transferred to the recording chamber where it was submerged in a constant flow (\(\sim\)2 ml/min) of artificial cerebrospinal fluid (aCSF) at room-temperature. The slice is positioned on top of the sapphire window and held down by nylon fibres stretched on a Pt grid.

The CA1 neurons are stimulated by 0.2 ms long negative constant current pulses (\(\sim\)20 µA) through a tungsten wire electrode. The stimulation frequency is 0.1 Hz.

A glass micropipette (filled with 1 M NaCl) is inserted in the stratum radiatum to record the electrical evoked signals from the neurons. The potential is amplified in a head-stage amplifier and subsequently in an A-M Systems 3000 amplifier [6] with low-pass and notch filters.

A SQUID sensor is brought close to the window and positioned under the slice. After closing the shields the SQUID is heated to remove any trapped flux.

For data acquisition a NI DAQ card was used and data was read into a custom-made Igor Pro software at a sampling frequency of 10 kHz.

We are in the process of characterizing the system and the slice measurements will be reported later.

3. Results and discussion

As part of characterizing the system, measurements of SQUIDs inside the system have been carried out. The critical current, $I_c$, of the SQUID has been adjusted by pumping on the nitrogen bath (see Fig. 2). The measurements shown in Fig. 2 (except the dashed line) were performed after an initial pressure increase to release any trapped flux. This is why the measurement without prior pressure increase shows a larger $I_c$ than the first measurement after the flux release. The $I_c$ increases \(\sim\)4 times by pumping on the nitrogen bath, which also increases the voltage modulation two times to the needed level (see Fig. 3). The SQUID electronics requires a voltage modulation of around 10 µV in order for the amplifier noise of 0.4 nV/Hz$^{1/2}$ [7] not to exceed the SQUID noise. The maximum voltage modulation, $\Delta V = 7.4$ µV, was obtained at

Figure 1. A picture of the measurement set-up showing: (a) top and bottom shields, (b) cryostat, (c) slice chamber ontop of the SQUID chamber and stimulation and recording electrodes with manipulators, (d) SQUID electronics, (e) amplifier for electrophysiology recordings, (f) counter weight for the hoist system, and (g) steering fins for the shields.
the lowest temperature with a bias current, \( I_{\text{bias}} = 213 \, \mu\text{A} \) (see Fig. 3).

An external Helmholtz coil was employed to determine the effective area, \( A_{\text{eff}} = 5.2 \cdot 10^{-3} \, \text{mm}^2 \), of the SQUID (which is used in Fig. 3).

The SQUID was biased at \( I_{\text{bias}} = 213 \, \mu\text{A} \) with an external magnetic flux \( \Phi_{\text{ext}} = \Phi_0/4 \) and then locked in a flux-locked loop. The spectrum of the SQUID’s magnetic flux noise is shown in Fig. 4. The limited bandwidth (\( f_{3dB} = 20 \, \text{kHz} \) — see fitted line) is due to poor coupling between the SQUID and the coil. At high frequencies the spread in the signal is large due to the small voltage modulation, which makes the amplifier noise of the same level as the SQUID noise. The high \( 1/f \) noise (here \( 1/f^{0.5} \)) is due to unexpected inability to use bias-reversal. This makes the white noise level hard to determine. However, one can estimate the white noise level of the system to be \(<7 \, \text{pT/Hz}^{1/2} \), which is comparable to the previously reported 4.5 pT/Hz\(^{1/2} \) [3] magnetic field noise of a SQUID with the same layout measured inside superconducting shields. Hence, the system seem not to add much magnetic field noise to this SQUID design. However, for the measurements on the neurons a SQUID sensor with a larger effective area is needed. A directly coupled magnetometer is beeing fabricated and the system noise using this sensor has to be investigated.

4. Conclusion

SQUID sensors have successfully been measured inside the system. The temperature of the sensor has been adjusted by pumping on the nitrogen bath, resulting in a four time increase in \( I_c \) and a two time increase in \( \Delta V \). The white noise level of the system magnetic field noise
was less than 7 pT/Hz$^{1/2}$. The increase of the magnetic field noise compared to measurements inside superconducting shields is small for the presently used SQUID layout.

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