Magnetoencephalography System Based on Quantum Magnetic Sensors for Clinical Applications

Carmine Granata, Antonio Vettoliere, Oliviero Talamo, Paolo Silvestrini, Rosaria Rucco, Pier Paolo Sorrentino, Francesca Jacini, Fabio Baselice, Marianna Liparoti, Anna Lardone and Giuseppe Sorrentino

Abstract In this paper, we present the magnetoencephalography system developed by the Institute of Applied Sciences and Intelligent Systems of the National Research Council and recently installed in a clinical environment. The system employ ultra high sensitive magnetic sensors based on superconducting quantum interference devices (SQUIDs). SQUID sensors have been realized using a standard trilayer technology that ensures good performances over time and a good signal-to-noise ratio, even at low frequencies. They exhibit a spectral density of magnetic field noise as low as 2 $\mathrm{fT/Hz^{1/2}}$. Our system consists of 163 fully-integrated SQUID magnetometers, 154 channels and 9 references, and all of the operations are performed inside a magnetically-shielded room having a shielding factor of 56 dB at 1 Hz. Preliminary measurement have demonstrated the effectiveness of the MEG system to perform useful measurements for clinical and neuroscience investigations. Such a magnetoencephalography is the first system working in a clinical environment in Italy.

Keywords SQUID · Magnetometer · Magnetoencephalography

C. Granata (✉) · A. Vettoliere · O. Talamo · G. Sorrentino
Institute of Applied Science and Intelligent Systems "E. Caianiello" of National Research Council, 80078 Pozzuoli (Naples), Italy
e-mail: carmine.granata@cnr.it

P. Silvestrini
Mathematics and Physics Department, University of Campania "L. Vanvitelli", Caserta, Italy

R. Rucco · F. Jacini · M. Liparoti · A. Lardone · G. Sorrentino
Department of Motor Sciences and Wellness, University of Naples Parthenope, Naples, Italy

P. P. Sorrentino · F. Baselice
Department of Engineering, University of Naples Parthenope, Naples, Italy

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1 Introduction

Magnetometers based on the superconducting quantum interference device (SQUID) are very sensitive low-frequency magnetic field sensors, reaching a spectral density noise of a few fT/Hz$^{1/2}$ [1, 2].

Due to their ultra-high sensitivity, SQUID devices are widely used in several applications [1, 2], such as from biomedicine, non-destructive tests, geophysics, magnetic microscopy and fundamental science. One of the most important application is the biomedical imaging. In particular, the interest is mainly focused on multichannel system for magnetoencephalography (MEG), which provide useful information on brain functionality [2, 3]. MEG systems measure magnetic fields produced by neuronal activity. Reflecting the intracellular electric current flowing in the brain, the MEG measurements provide direct information about the dynamics of evoked and spontaneous neural activity. The magnetic fields generated by brain activity are minimally distorted by the layers surround the brain, allowing for a temporally and spatially accurate reconstruction of the neural signals within the brain (source space). Furthermore, the phase of such signals can be exploited in order to evaluate the amount of information exchanged between brain areas. Among the available brain functional imaging methods, MEG uniquely features both a good spatial and an excellent temporal resolution, allowing useful investigation in neuroscience and neurophysiology. In fact, by using suitable algorithms [4] it is possible to estimates synchronization [5] between areas, thereby providing complementary information to the fMRI.m. Some of the properties of the interactions among brain areas can be analyze through graph theory [6]. In fact, the human brain can be modelled as a network, where the brain areas are the nodes and their interaction are the edges. However, such metrics are influenced by network size or thresholding, making difficult to give a topological interpretation of the results, especially when they come to brain signals [7]. In this paper we will present a multichannel system for Magnetoencephalography operating in a clinical environment.

2 Magnetic Sensors

A SQUID is magnetic flux to voltage transducer. It consist in a superconducting loop interrupted by two Josephson junction [1, 2]. At least the magnetic field sensitivity is proportional to the loop area. However, it is not possible to increase the area of loop to increase the magnetic field sensitivity, because the flux noise increases with the ring inductance. An efficient way to increase the field sensitivity consists of using a proper superconducting detection circuit (flux transformer) consisting of a series of pickup coil having a flux capture area much higher than the SQUID one, and an input coil inductively coupled to the SQUID loop [1]. Typically, the

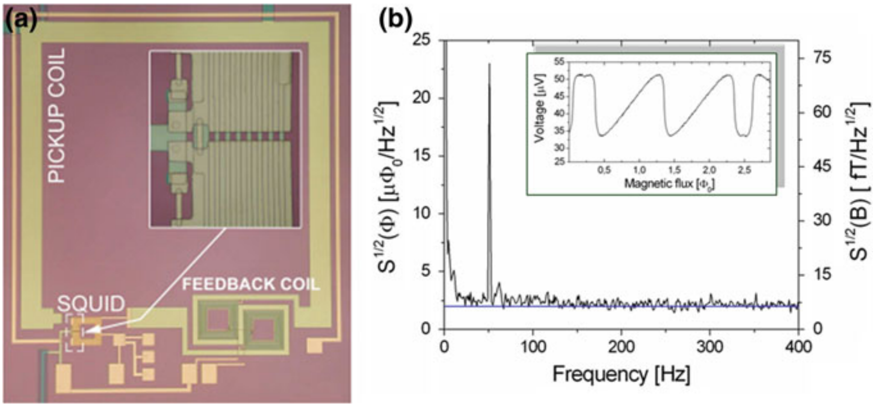

Fig. 1 **a** Fully integrated miniaturized dc SQUID magnetometer. **b** Magnetic flux anf firld spectral density measured at T = 4.2 K in flux locked loop configuration. Theoretical prediction for the white noise is indicated by the straight blue line. The inset report the voltage-magnetic flux characteristic

pickup coil consists of a single square shaped coil including, in one of its sides, a planar multiturn input coil which is located upper to the SQUID loop acting as a secondary coil of flux transformer. A suitable SQUID loop design consists of a single coil having a square "washer" shape. In such a configuration, the SQUID inductance does not depend on external dimension of the washer but only on the hole dimension. The coupling between the washer and the input coil is very good and the input coil inductance is proportional to turn numbers and hole inductance. Hence, the input coil inductance can be adjusted to match a particular load by varying the outer dimension of the washer to accommodate the required number of turns in the input coil. In the Fig. 1a, a fully integrated SQUID magnetometer employed in the MEG system is reported. The above design has been optimized to keep a suitable sensitivity [8]. It has an area less than 10 mm^2 and includes a superconducting flux transformer, an additional positive feedback (APF) circuit and a bipolar feedback coil for low crosstalk operations [9]. The sensing pickup circuit consisting of a superconducting square coil is connected in series with a 8-turn input coil, which is coupled to SQUID loop in a washer configuration. Apart from a better spatial resolution, a small pickup coil minimizes its antenna gain, reducing the effects of radio frequency interference. The spectral density of both flux and magnetic field noise of the miniaturized SQUID magnetometer is reported in Fig. 1b. The sensor exhibits a magnetic flux noise level of 2.2 $\mu\Phi$ $0/\sqrt{\text{Hz}}$ in the white region corresponding to 5.8 $\text{fT}/\sqrt{\text{Hz}}$ [8]. In the inset of Fig. 1b, the magnetic flux-voltage characteristic is reported. It is evident that there are that there are not resonances ensuring a good stability during operation.

3 Magnetoencephalography System

The MEG system shown in Fig. 3, consists of 163 fully integrated dc SQUID magnetometers, featuring adequate field sensitivity and bandwidth for brain imaging. Since these sensors are placed close each to other, the integrated feedback coil for Flux-Locked-Loop (FLL) operation have been properly designed in a bipolar multiturn shape, in order to reduce the crosstalk effect between neighbor sensors. The SQUID magnetometer are arranged on a multisensorial array designed and realized in a helmet shape. The measurement plane consists of 154 SQUID-channels suitably distributed over a fiberglass surface to cover the whole scalp and to record effectively the MEG signals (Fig. 2b) [10]. Further 9 channels, installed on three bakelite towers, are arranged in three triplet each having three orthogonal SQUID sensors and are used as references in order to detect background residual magnetic field far from the scalp (about 9 cm) and to subtract its contribution, via software properly implemented to this aim, from the brain signal detected on the measurement plane.

The sensor array, as shown by Fig. 3a, is located in a fiberglass Dewar with a helmet shaped bottom, at a distance of 18 mm from the outside, where the head of patient is housed. The SQUID sensors are connected to the room temperature

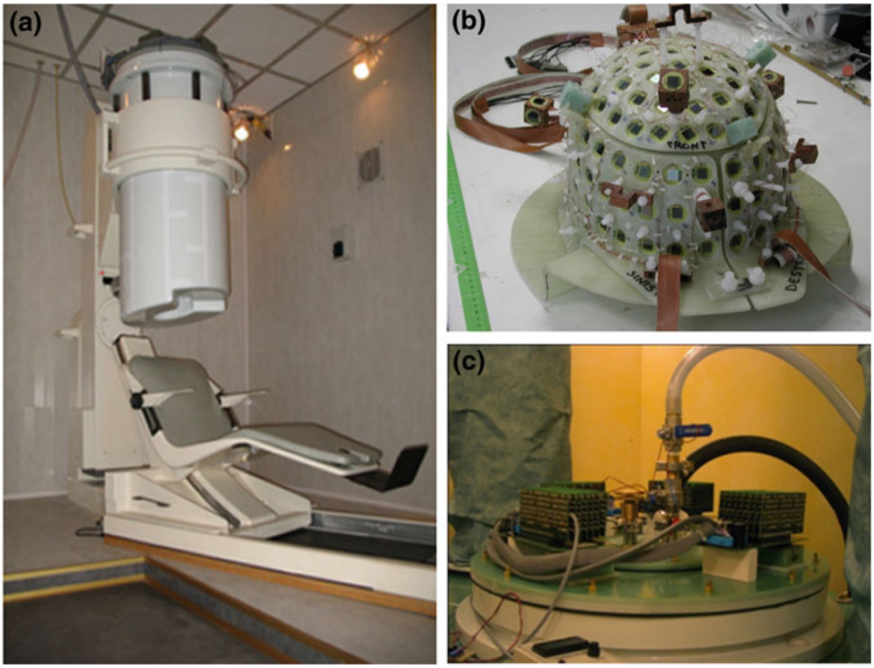

Fig. 2 **a** General view of the Magnetoencephalographic (MEG) system in the shielded room; **b** helmet-shaped array consisting of 163 fully-integrated SQUID magnetometers; **c** top view of MEG system showing the read-out electronics

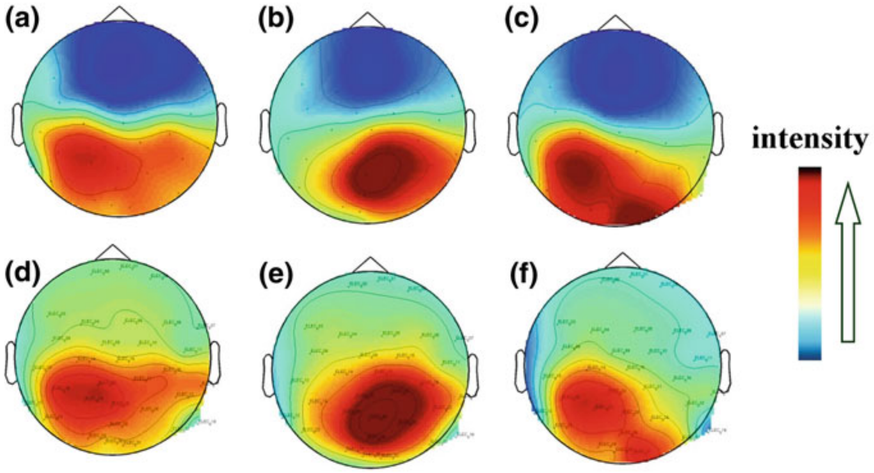

Fig. 3 Preliminary measurement performed by the MEG system. The imaging refers to the activated brain areas detected by the MEG (top row) and EEG (bottom row) during a spontaneous activity (alpha rhythm) (**a**, **d**) and evoked activity (tapping of the left (**b**, **e**) forefinger and the right (**c**, **f**) forefinger

read-out electronics by means of more than 800 copper wires having a diameter of 0.08 mm and twisted in pairs to avoid a parasitic area. The SQUID readout is a direct coupled electronics and is integrated in low-power, miniaturized boards (Fig. 3c). A single card drives six channels and is plugged in a shared motherboard located on the top of the dewar. In turn, the motherboard containing also the control logic unit and the filtering stage before the A/D conversion up to 10 kHz. A remote console allows to manage the electronics parameters setting digital filtering, amplification, undersampling, on-line average, and on-line software gradiometer composition based on selectable configuration files.

The system is equipped also with a 32 channels system for EEG allowing to record simultaneous both magnetic and electrical signals. To eliminate any ambient disturbance the system operates in a suitable magnetic shielding room (MSR). The MSR consists of an external aluminum layer 12 mm thick and two inner layers of soft magnetic material having a thickness of 1.57 mm. designed on the basis of the environmental magnetic field measured on site before the installation. The resulting shielding factor is about 35 dB at 0.01 Hz, that increases up to 107 dB at 20 Hz.

4 MEG Acquisition and Test Measurements

Before to acuire MEG data, it is necessary to perform the following procedure. Using a suitable tool (Polhemus FASTRAK®) is detected the position of four coils, placed on the forehead and behind the ears of the participants, and of four reference points on the head (nasion, right and left preauricular points, vertex). Hence, electrical currents passing through the four coils are recorded by the MEG sensors. Participants to a study are seated inside a magnetically shielded room to reduce background noise Electrocardiographic (ECG) and Electrooculographic (EOG) signals are co-recorded, for subsequent artefacts removal. Spontaneous brain activity is recorded for almost 5 min, in resting-state condition, with closed eyes. The system has a sampling frequency of 1024 Hz. Data are then band-pass filtered at 0.5–49 Hz. Environmental noise, recorded by the 9 references, is subtracted from the signals through Principal Component Analysis (PCA). Noisy channels are removed manually through visual inspection of the whole dataset by an experienced rater [11]. Independent component analysis (ICA) [12] is performed to eliminate the ECG and the EOG component from the MEG signals.

The data is reconstructed in ninety areas of interest, applying a linearly constrained minimum variance beamformer [13] based on a template atlas or on the native MRI [14] and a modified spherical conductor model [14, 15]. This procedure yield epochs made of 90 time series, one per area of interest (just the cortical regions and the basal ganglia).

In the Fig. 3, preliminary measurements are reported. The first one (Fig. 3a) concerns a spontaneous activity. The so-called alpha rhythm, which appears in a human's brain awake but with eyes closed, has been recorded. The frequency range involved is 9–11 Hz. The second one (Fig. 3b, c), concerns an evoked activity: the brain imaging during the forefinger tapping of a volunteer, has been recorded. Figure 3b refers to the left finger tapping and, as expected, the activate motor cortex area is in the right hemisphere. In the Fig. 3c, instead, the imaging related to the movement of right forefinger is reported; as in the previous case, the contralateral area is involved. In this case the frequency signal are located around 7–9 Hz. The good agreement between EEG and MEG imaging indicates that the system operates properly.

5 Conclusions

A muitichannel system based on high sensitive quantum magnetic sensors for neurological applications has been described. The ultra-low noise of the magnetometers allow to measure the weak magnetic fields associated with the neurological activity. Preliminary test measurements have shows the effectiveness of the magnetoencephalographer. Very interesting measurements concerning Alzheimer disease (AD) and amyotrophic later sclerosis (ALS) on a large cohort of patients are in progress. The connectivity will be obtained by measuring synchronization between brain areas and a graph theoretical approach will be used to study disease staging in ALS. We will compare ALS patients and controls in order to verify that the topology of the brain networks brain show appreciable differences according to the disease stage.

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