NeuroImage 149 (2017) 404–414

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

A new generation of magnetoencephalography: Room temperature measurements using optically-pumped magnetometers

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ABSTRACT

Advances in the field of quantum sensing mean that magnetic field sensors, operating at room temperature, are now able to achieve sensitivity similar to that of cryogenically cooled devices (SQUIDs). This means that room temperature magnetoencephalography (MEG), with a greatly increased flexibility of sensor placement can now be considered. Further, these new sensors can be placed directly on the scalp surface giving, theoretically, a large increase in the magnitude of the measured signal. Here, we present recordings made using a single optically-pumped magnetometer (OPM) in combination with a 3D-printed head-cast designed to accurately locate and orient the sensor relative to brain anatomy. Since our OPM is configured as a magnetometer it is highly sensitive to environmental interference. However, we show that this problem can be ameliorated via the use of simultaneous reference sensor recordings. Using median nerve stimulation, we show that the OPM can detect both evoked (phase-locked) and induced (non-phase-locked oscillatory) changes when placed over sensory cortex, with signals ~4 times larger than equivalent SQUID measurements. Using source modelling, we show that our system allows localisation of the evoked response to somatosensory cortex. Further, source-space modelling shows that, with 13 sequential OPM measurements, source-space signal-to-noise ratio (SNR) is comparable to that from a 271-channel SQUID system. Our results highlight the opportunity presented by OPMs to generate uncooled, potentially low-cost, high SNR MEG systems.

Introduction

Magnetoencephalography (MEG) is a non-invasive technique for imaging electrophysiological brain activity (Cohen, 1972). Dendritic current flow, synchronised across neural assemblies, generates small changes in magnetic field outside the head. An array of highly sensitive magnetic field sensors is used to detect these small changes and 3-dimensional images depicting moment-to-moment changes in brain current are then reconstructed using mathematical modelling. In the past decade, MEG has become an important tool for neuroscience providing a bridge between the spatially detailed (but slow and indirect) haemodynamic imaging measures in humans, and the temporally rich (but sparsely spatially sampled) information provided by invasive electrophysiological metrics in animals (Hall et al., 2005; Zumer et al., 2010). MEG is capable of tracking the formation and dissolution of electrophysiological networks in real time and with high spatial precision (O'Neill et al., 2015; Troebinger et al., 2014). Because of this, MEG is now having impact on our understanding of the healthy brain, and on a wide range of clinical research areas ranging from neurodevelopment (Ciesielski and Stephen, 2014) to severe psychoses (Robson et al., 2016; Uhlhaas and Singer, 2010). The further development of MEG technology is therefore an important and evolving focus.

Despite its potential, MEG is limited by low signal-to-noise ratio (SNR). This is because the magnetic fields generated by the brain are much smaller than environmental and biological magnetic interference. This problem severely limits sensitivity (e.g. comparisons of

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http://dx.doi.org/10.1016/j.neuroimage.2017.01.034
Received 1 August 2016; Accepted 15 January 2017
Available online 25 January 2017

invasive local field potential metrics (Mukamel et al., 2005) and MEG (Zumer et al., 2010) suggest that the latter is relatively insensitive to networks oscillating at high frequency). Moreover, many studies have shown how improvements in SNR give direct benefits in terms of spatial resolution in MEG (Brookes et al., 2008; Brookes et al., 2010; Gross et al., 2003; Hillebrand and Barnes, 2002; Troebinger et al., 2014a; Vrba, 2002). In principle, SNR could be improved by moving detectors closer to the head; this is because the field from the brain follows an inverse square law meaning that halving the source-to-detector separation would quadruple the measured signal amplitude. However, current MEG systems are based around superconducting circuits housed in a liquid-helium-cooled dewar. This means that thermal insulation must be maintained between the scalp and detector, and so detectors are sited 3–6 cm from the adult brain surface. The requirement for cryogenic cooling also means that sensors are held in a fixed position within a 'one size fits all' helmet. The average brain-to-sensor distance is therefore even greater in subjects with smaller heads (e.g. infants). Further, the inflexibility in sensor placement means that some regions can have poor coverage (e.g. the cerebellum). It follows that the introduction of room-temperature detectors, with a similar performance to superconducting devices, but enhanced flexibility to enable positioning anywhere on the scalp surface, would bring about a step change in the capability of MEG. Indeed simulations (Boto et al., 2016) have shown that a MEG system with a similar geometry to current instruments, but with scalp-mounted detectors, would afford approximately a fivefold improvement in signal magnitude (depending on subject head size and location of interest in the brain), and a similar improvement in source-space SNR and spatial resolution.

Recent advances in the field of quantum technology have led to the development of small, optically-pumped magnetometers (OPMs). These devices measure the transmission of laser light through a vapour of spin-polarised rubidium atoms, which provides a highly sensitive measure of the local magnetic field. OPMs have theoretical sensitivity comparable to that of the superconducting quantum interference devices (SQUIDs) used in current MEG systems (Dang et al., 2010), but operate without cryogenic cooling (the vapour cell is heated, but the external surface remains close to room temperature). This means it is now possible to consider a MEG system with sensitive detector volumes just 6 mm from the scalp surface. Robust and easy to use OPM sensors have recently become available commercially; these sensors are fabricated such that they have a small footprint meaning that a large number of sensors can be placed flexibly around the head and whole-head coverage is feasible. The utility of OPMs for MEG has been shown previously: several papers have described the successful detection of phase-locked evoked responses generated by auditory (Johnson et al., 2010, 2013; Xia et al., 2006) or somatosensory (Johnson et al., 2010; Sander et al., 2012) stimulation. Other groups have shown how sensors positioned over the occipital lobe enabled detection of the induced changes in alpha (8–13 Hz) rhythm by opening and closing the eyes (Kamada et al., 2015; Sander et al., 2012). In addition, a recent study has demonstrated the detection of epileptiform activity in rodents (Alem et al., 2014). These empirical demonstrations, coupled with recent commercialisation, decreased sensor size (Shah and Wakai, 2013) and the introduction of multi-channel measurements (Colombo et al., 2016; Johnson et al., 2013; Kim et al., 2014) show the potential of OPMs to transform the utility of MEG, with the promise not only of high SNR, but also access to traditionally challenging subject groups such as infants.

Although OPMs have the potential to form the basis of a high SNR and flexible MEG instrument, the practical implementation of such a system requires significant work. The increased signal provided by moving the detectors closer to the scalp is easily achieved. However translating this into high precision images of electrical brain function is non-trivial. First, most OPMs are configured as magnetometers (as distinct from gradiometers which are used in many SQUID-based MEG systems) and as such are more sensitive to environmental interference. Effective methods must therefore be employed to reduce interference. In addition, spatial specificity and reconstruction accuracy depend not only on SNR, but also on accurate modelling of magnetic fields generated by the brain (i.e. accurate forward solutions). This problem is exacerbated in OPMs since, perhaps counterintuitively, increases in SNR mean that modelling accuracy must also increase; indeed simulations show that even small (5%) modelling errors could negate any advantages in SNR afforded by OPM systems (Boto et al., 2016). One significant cause of modelling errors in current MEG systems comes from inaccurate knowledge of the head location relative to the sensor array (Hillebrand and Barnes, 2003). It follows that to realise the benefits of an OPM system, detector locations and orientations relative to the brain anatomy must be known with high spatial accuracy. In this paper, we show that the use of a 3D-printed head-cast can accurately inform sensor position and orientation, thus facilitating accurate forward modelling and source imaging. We employ a single commercial OPM (QuSpin Inc., Louisville, CO, USA) to make measurements of evoked (phase locked) and induced (non-phase locked oscillatory) neural signals in sensory cortex during median nerve stimulation. We show that the use of interference cancellation via a reference array, i.e. similar to ideas behind synthetic gradiometers (Vrba, 2002; Vrba et al., 1991; Vrba and Robinson, 2002, 2001) improves significantly the SNR of OPM measurements. Finally, we show that OPMs generate the expected increases in signal magnitude over SQUID recordings.

Methods

Data acquisition

Optically-pumped magnetometer

The OPM used in this work has a theoretical noise level comparable to SQUIDs (10 fT/√Hz above 1 Hz), a bandwidth greater than 100 Hz, an operational dynamic range of ± 5 nT, a size of 14×21×80 mm^3, and can be placed such that the sensitive volume is 6.5 mm from the scalp head surface. The OPM sensor head is self-contained with all the necessary optical components, including a semiconductor laser for optical pumping, optics for laser beam conditioning, a 3×3×3 mm^3 ^{87}Rb vapour cell, and silicon photodiodes. The vapour cell is electrically heated to around 150 °C to achieve optimum ^{87}Rb vapour density. The sensor head connects to a small electronics controller via a 5 m cable. The electronics controller is placed outside the magnetically-shielded room (MSR) to minimize magnetic interference. The output from the electronics controller is an analogue voltage proportional to magnetic field, which is digitized using a 16-bit DAQ system. The effective resolution of this digitisation is increased via oversampling at 10 kHz. The scaling of output voltage to measured field is 2.8 V/nT.

The magnetometer relies on a zero-field level crossing resonance for detection of ambient magnetic field, described in detail by Kastler (1973) and Dupont-Roc et al. (1969). A 795 nm laser tuned to the D1 transition of ^{87}Rb is used to spin-polarize the rubidium atoms, and the intensity of laser light transmitted through the cell is detected using a photodiode. The sensor includes three electromagnetic coils which can be used to null any static field components in the cell; subsequent field changes (e.g. due to neural currents in the brain) can then be detected via the change in transmitted light intensity which they produce. The transmitted intensity manifests a zero-field resonance, which is a Lorentzian function of the magnetic field components transverse to the laser beam, with a full width at half maximum of 30 nT. A small, sinusoidally modulated magnetic field is applied at ~1 kHz perpendicular to the laser beam by the on-sensor coils. The modulation of the transmitted light, which is monitored using a lock-in process, is sensitive to the ambient field component along the modulation axis (Dupont-Roc et al., 1969; Shah et al., 2007). The amplitude of the two components of the magnetic field that are perpendicular to the beam can be simultaneously measured by applying oscillating currents to two coils in quadrature. A photograph of the sensor is shown in Fig. 1A.