Title: Biomedical field mapping using optically pumped magnetometer arrays

Abstract

Neurodegenerative and cardiac pathologies are disabling diseases. With the population ageing in Europe, advanced diagnostic imaging techniques are required for earlier and correct diagnosis and for monitoring treatments. Optically pumped magnetometers (OPMs) are a promising non-cryogenic and low-cost biomagnetic imaging technique able to detect biologically relevant magnetic fields. It is expected that OPMs will supersede other magnetometers in many applications as they can be tailored for various needs. However, for their use in medical applications, the design and performance of existing OPMs have to be technologically improved.

Keywords

Optically pumped magnetometers, neurodegenerative and cardiac diseases, magnetoencephalography, air-borne ultrasound exposure limits, magnetocardiography.

Background to the Metrological Challenges

Cardiac diseases are ubiquitous and a multitude of diagnostic methods exist, including Magnetic resonance imaging (MRI) and ultrasound. Measurements necessary for foetal and adult arrhythmia diagnostics are difficult to assess. Detecting the P- and T-wave of the foetal heart cycle is difficult with electro- or echocardiography, but foetal magnetocardiography (fMCG) can detect those waves in the later gestational weeks. This in turn allows arrhythmia detection and a targeted treatment of the foetus, but fMCG has a limited distribution in hospitals due to intrinsic limitations of superconducting quantum interference devices (SQUIDs). In adults, atrial fibrillation (AF), a poorly understood arrhythmia which affects 3 - 5 % of the population over 70, is currently the most significant challenge in cardiac treatment. Generating a heart conductivity map is an essential tool in the clinical treatment of AF but standard mapping involves an invasive and prolonged surgical procedure. A radio-frequency OPM could be used for non-invasive conductivity mapping of the heart muscle by magnetic induction tomography (MIT). The widespread use of OPM based devices in the diagnostic of cardiac diseases would reduce treatment costs and increase benefits to patients through fewer procedures and better outcomes.

Parkinson´s disease is one of the most common neurodegenerative diseases and its study in patients frequently involves the use of magnetoencephalography (MEG) systems. Existing MEG devices are used for studying the brain function of healthy subjects and patients with neurodegenerative and psychiatric diseases. In movement disorder patients, e.g. Parkinson´s disease, cortico-subcortical networks for movement execution are dysfunctional and MEG yields information about these networks.

The effect of ultrasound exposure has been measured using MEG devices, but the effects of exposure to air-borne ultrasound at working places and in public are not yet well understood. Because of the lack of understanding in the perception mechanisms no safety limits and assessment recommendation exist within the European Union.

Despite their widespread use, MEG devices involve an initially high investment cost and require a steady supply of ultracold liquid Helium (l-He) for SQUIDs that need cooling to 4 K and therefore have to be mounted inside a cooling vessel filled with l-He. The need for a cooling vessel affects the effectiveness of SQUIDs for monitoring the brain, as this prevents close proximity to the base of the head and therefore reduces signal strength from the cerebellum. In addition, the price for l-He has increased fivefold over the last ten years.

There is an ongoing search for magnetic field sensors with similar or better performance than SQUIDs, but easier to operate and manufacture and with lower initial costs. Likely candidates are sensors similar to compact atomic clocks based on transitions in alkali atoms. Using atomic transitions with a high sensitivity to magnetic fields (high gyro magnetic factor) enabled the development of OPM sensors that operate at room temperature and do not require l-He. Those bench top setups demonstrated the feasibility of OPMs for magnetic field measurement at sensitivities similar to SQUIDs, but they were still too bulky as standalone devices. The operation of individual miniaturised sensors has been demonstrated in man sized magnetically shielded rooms useful for biomagnetic applications but challenges have been identified that require further investigations. To improve existing OPM designs to a technological level required for medical applications it is necessary to assess them in well controlled magnetically shielded environments and to calibrate them using existing magnetic field sensors, namely SQUIDs. Furthermore an optimal OPM cell design needs to consider the different approaches implemented in high precision atomic clocks as found in metrology, because OPMs and atomic clocks are based on the same physical principles. In the design phase highly stabilised lasers as used for atomic clocks are needed to assess OPM cell quality.

Magnetic nanoparticles (MNPs) enable promising cancer therapy improvements due to their function as drug carriers in magnetic drug targeting and as focussed heat generators in magnetic hyperthermia, but the quantitative knowledge of the MNP distribution inside the body is essential for the success of these promising new therapy concepts. While magnetic particle imaging (MPI) enables the quantification of this information, it requires modification of MPI towards the audio frequency range where radio frequency coils have to be replaced by OPMs for the detection of the MPI signals.

Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on the traceable measurement and characterisation of human biomagnetic fields using novel optically pumped magnetometer (OPM) sensors suitable for medical applications.

The specific objectives are

1. To develop an experimental OPM sensor with a bandwidth from 0.1 Hz to 1 kHz and a noise level of sub-pT/Hz$^{1/2}$ for operation in a non-zero magnetic field environment (from 100 nT for the case of three layer magnetically shielded rooms to 1 µT for the case of basic compensation coils);
2. To design a multichannel OPM sensor array for a commercial MEG system. In addition, to adapt the OPM sensor array for magnetic nanoparticle based methods such as magnetorelaxometry or MPI for medicine;
3. To develop a greater understanding of specific medical conditions /physiology using OPM based approaches:
   - To identify abnormal cortical-cerebellar networks from OPM MEG recordings of movement disorder patients with tremor (Parkinson´s disease, dystonia);
   - To diagnose arrhythmia through fMCG (extraction of foetal heart rates) and magnetic induction tomography (MIT) (mapping of heart conductivity);
   - To determine the perception mechanisms of airborne ultrasound through auditory OPM MEG responses to support the development of safe ultrasound exposure limits;
4. To facilitate the take up of the technology and measurement infrastructure developed by the project by healthcare professionals (clinicians) and industry (instrumentation manufacturers).

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, medical (academic) hospitals and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this. In particular, proposers should outline the achievements of the EMRP project HLT01 (Ears) ‘Metrology for a universal ear simulator and the perception of non-audible sound’ and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the "end user" community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the "end user" community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the healthcare and industry sectors.

You should detail other impacts of your proposed JRP as specified in the document "Guide 4: Writing Joint Research Projects".

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.