Title: Quantum detection for increased sensitivity of chemical and biological measurement

Abstract

Demand for increased sensitivity of chemical and biological detection is burgeoning. Mass spectrometry is one of the most powerful methods for biological measurement with millions of measurements taken worldwide every day. Super-conducting Quantum Interference Devices (SQUIDs) show great promise in overcoming noise limits for this technique and could improve the signal-to-noise ratio tenfold. Electron microscopy coupled with X-ray spectrometry is routinely used to visualise the distribution of elements within materials and combining this with Transition-Edge Sensors (TES) and SQUIDs could improve sensitivity 100-fold. Such improvements in detection would not only greatly benefit many areas in the life-science sector but also revolutionise chemical analysis in many high-technology sectors, such as aerospace, electric vehicles, satellites and semiconductor industries.

Keywords

SQUID, nanoSQUID, Transition-Edge Sensor, Quantum metrology, Mass spectrometry, X-ray spectroscopy, TES, FTMS

Background to the Metrological Challenges

The life-science sector, including cancer biology, antimicrobial resistance, neurodegenerative diseases and the pharmaceutical sector is the biggest user of high-performance mass spectrometry for chemical and biological detection owing to the high-sensitivity and high-specificity of these instruments.

Superconducting quantum interference devices (SQUIDs) contain two superconductors (Josephson junctions) and electrons moving between these exist in a state of superposition allowing these devices to measure extremely weak changes in an electromagnetic energy field. Due to this SQUIDS have to potential to increase the sensitivity in a range of analytical devices.

Fourier Transform Mass Spectrometry (FTMS) instruments have the highest mass-resolving power and mass-accuracy but signal to noise limits prevent detection in demanding applications. Genetic sequencing technologies now permit single-cell studies of the genome and transcriptome but deep genomic sequencing of these cannot currently be achieved for the proteome. Major advances in sample preparation and processing are increasing the sensitivity of mass spectrometry but the ultimate sensitivity for high-resolution FTMS instruments is currently limited by noise which could be overcome utilising SQUIDs. Advances in detection sensitivity will directly increase their speed of analysis and depth of identifying the proteome and will make an important contribution to break-through technologies to achieve single-cell proteomics.

High-technology industries such as aerospace, electric vehicles, satellites and semiconductors rely on chemical analysis of materials. Electron microscopy coupled with X-ray spectrometry is one of the most widely used techniques in industry where it is routinely used to visualise the distribution of elements within materials. Current energy-resolving detectors for X-ray spectroscopy are based on silicon drift detectors and these are capable of single particle sensitivity and of resolving the X-ray fluorescence lines of most elements. Typical energy resolutions are of the order of 100 eV, which is insufficient to separate a number overlapping lines and to enable chemical state analysis the energy resolution must be improved by two orders of magnitude, from the current > 100 eV to approximately 1 eV. A Transition-Edge Sensor (TES) is an exquisitely sensitive bolometer capable of measuring the temperature change after a single particle impact and SQUIDs have demonstrated single particle detection capability, from photons through single ions and other charged particles to phonons. TES, with SQUID readout, are capable of overcoming current spectroscopy limitations having reported energy resolutions better than 1 eV within the relevant energy range between 100 eV and 10 keV. SQUIDS have previously been used in an ion trap mass spectrometer and demonstrated the ability to achieve

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single ions sensitivity. However, this design only operated for one frequency (one mass) and not for a spectrum of masses. New developments are needed to overcome impedance matching of a SQUID to match ion orbital frequencies from 100 kHz to 1 MHz.

Nano-sized SQUIDs, or nanoSQUIDs, are one of the most promising quantum detectors for nanoscale applications because these exhibit an ultra-high magnetic moment sensitivity, reaching few Bohr magnetons or spins per unit of bandwidth. The fabrication technology for nanoSQUIDs has been significantly improved in recent years. As these nanoSQUIDs are fabricated in a planar technology, implemented auxiliary components and design features for complex SQUID designs can be directly integrated. The understanding that SQUIDs are also quantum devices which themselves can be placed in a superposition of states or entangled with other SQUIDs has broadened the approach to use of SQUIDs for measurement at, or beyond, the standard quantum limit. Theoretical studies are needed to explore if quantum superposition as well as squeezed and entangled states can be exploited to achieve higher sensitivities in mass spectroscopy.

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 Super-conducting Quantum Interference Devices (SQUIDs) necessary to support the increased sensitivity of chemical and biological detection of elements within materials.

The specific objectives are

1. To conduct a theoretical study on the use of SQUIDs and super-conducting circuits to overcome noise limits in image charge detection in electrostatic FTMS and to increase the bandwidth of TES for X-ray spectroscopy.
2. To design and fabricate novel SQUID devices for electrostatic FTMS to detect the image charge with a 10-fold improvement in signal to noise compared to the performance of commercially available instrumentation to enable single ion sensitivity, while specifying the mass-to-charge ratios and charge states of the ions to be monitored.
3. To design and fabricate novel SQUID readout devices and TES for particle detection with 1 eV energy resolution over the energy range 100 eV to 10 keV and a bandwidth greater than 10 MHz. In addition, nanoSQUIDs will also be designed and fabricated for ion and x-ray detection with integrated auxiliary components and the noise floor and device performance quantified.
4. To investigate quantum metrology concepts using superposition and entanglement for measurement of physical parameters to achieve higher accuracies than classical methods such as used in mass spectrometry.
5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain (e.g. NMIs, DIs) and end users (FTMS manufacturers, pharmaceutical industries, life science and medicinal sectors).

Proposers shall give priority to work that aims at excellent science exploring new techniques or methods for metrology and novel primary measurement standards, and brings together the best scientists in Europe and beyond, whilst exploiting the unique capabilities of the National Metrology Institutes and Designated Institutes.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.5 M€, and has defined an upper limit of 1.8 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 40 % of the total EU Contribution across all selected projects in this TP.

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 mass spectrometry sector.

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

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.