Project:

Real-time multispectral flourescence spectroscopy using energy resolved single-photon detector arrays (**Real-MFM**)

Technological keywords:
biomedical tool, sub kelvin cooling technology, multispectral fluorescence microscopy, biomedical imaging, cell biology

Industrial sectors addressed: instruments for research

Total cost: 992.000 €

Partners' descriptions:

- Supracon AG, active in the field of superconducting sensors (SQUID) and electronic system based on these sensors, Germany, SME, coordinator and system integrator as well as seller and distributor of the entire system. Supracon participates in different research projects like THz-Videocam (BMBF), THz-TWO (BMBF), E-SQUID (EC FP7) as well as SEMAG (TAB) and OMEGA (ZIM, BMWI): www.supracon.com

- QMC Instruments Ltd. was founded in 1976 and its main activity is the development, design and manufacture of bespoke cryogenic Far-Infrared (THz) detection systems, including cryogen-free single pixel and passive imaging instruments. Products also include polarizing spectrometers, along with passive components such as filters and polarisers. QMC participates in TeraTOP and SpaceKIDs (both FP7). www.terahertz.co.uk

- Leibniz Institute of Photonic Technology, (IPHT), Germany, develops technological solutions for life sciences and medicine with focus on biophotonics, fibre optics and photonic detection. In Real-MFM, IPHT will design and fabricate superconducting single-photon detectors and pre-assemble and test the system components. Planning and execution of the demonstration experiment will also be done at IPHT. Related projects: THz-Videocam (BMBF), THz-TWO (BMBF), E-SQUID (EC FP7). www.leibniz-ipht.de

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- Entropy GmbH is a cryostat manufacturer specialized in closed-cycle technology for the Kelvin and milliKelvin temperature range. The company was founded in 2010 and is based in Munich, Germany. Entropy designs and manufactures several types of cryostats such as GM and pulse-tube cooler based cryostats for temperatures < 4K, closed-cycle Joule-Thomson cryostats for temperatures < 1K, Adiabatic Demagnetization Refrigerators (ADR) and Dilution refrigerators. http://www.entropy-cryogenics.com/

ENTROPY

- Chase Research Cryogenics Ltd, design build and sell custom sub-Kelvin cryo-coolers, mainly for research purposes in Astronomy, but also in nano-technology and other fields. Our main products are single stage (He-4, He-3) two-stage (He-7) and three-stage (He-10) evaporation coolers. Customers include ESTEC and SRON in Europe, NASA and NIST in the USA, as well as many university departments in both Europe and America. www.chasecryogenics.com

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Project abstract:

In modern medical analysis, fluorescence microscopy has become an indispensable tool for imaging of biological tissue at cellular level, thus permitting the study of life processes in situ. As an advanced option, multi-staining techniques are able to tag different organelles in a cell using specific fluorophores. Multispectral imaging makes it possible to observe multiple cell components at the same time, and to study interactions between them.

With current techniques, information at different wavelength needs to be multiplexed either in time (sequential) or in space (holographic). The sequential method exploits tuneable filters or pixel scanning with a spectrometer, whereas the holographic technique computes a complex image from, for example, a coded aperture. Both approaches have drawbacks and limitations.

The radical approach proposed here is to use a photon detector which discriminates single photons in terms of both time and energy. This technique demands performance in detection which closely approaches fundamental physical limits. Conventional single-photon detectors such as avalanche diodes have poor energy resolution because the band gap of such detectors is similar to that of the energy of the photon to be detected. By contrast, the very small energy gap of superconducting detectors (of order meV)

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enables a single photon from the visible spectrum to create up to one thousand electrons to be measured.

Developed originally for astrophysical research projects, such detectors have not thus far found their way into industrial applications. The RealMFM project, aims to demonstrate a scalable focal-plane array of superconducting single photon detectors with a moderate intrinsic spectral resolution of about 20 nm @ 500 nm wavelength. We will use a commercial fluorescence microscope in conjunction with a modest imaging instrument with 64 pixels. This unique combination will be used to image relevant biological samples. Such a detector array promises a number of unique features:

- acquisition of multispectral images without signal power loss due to time-division multiplex disadvantage or filter/aperture absorption.
- true real-time imaging of dynamic processes (e.g. calcium signaling transients), thus reducing problems such as sample photobleaching or image deterioration due to sample/camera movement.
- high detection quantum efficiency enabling operation at low excitation intensities, thus preventing sample damage and rapid photobleaching.

Expected results and exploitation plan:

- We plan to produce a prototype research tool specifically designed for use in clinical environments. The technique can be considered as high-end option for use with standard microscopes. This limits the potential market volume, but the high performance of such instruments constitutes a technology reference, paving the way for a new generation of diagnostic techniques and instruments.
- The planned R&D activities will have an impact on the advancement of partner's technologies and special expertise and on the competitiveness of the SMEs. Supracon will assemble the components of the planned instrument, including the cryogenic platform (Entropy & QMC, Chase), the sensor array module (IPHT) and the data handling (amplification and acquisition). It is expected that the results will advance the performance of other instruments. Moreover, the multiplexing electronics to be developed within the Real-MFM project can be exploited for focal-plane arrays for other applications e.g. in security.