MINERVA project newsletter #4

November 2014

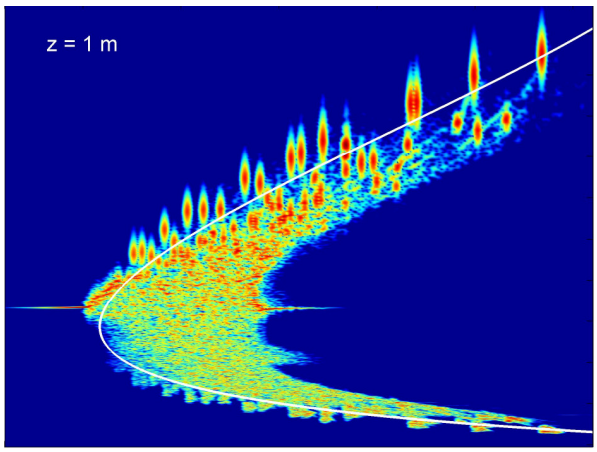
Welcome to the fourth MINERVA project newsletter!

This newsletter presents the first public reporting of the prototype "MINERVA Lite" high speed mid-IR imaging system, progress in infrared megapixel camera development, parallel advances in high resolution mid-IR imaging and the definition of standardised samples for mid-IR measurements.

There is much more information available from the project website (www.minerva-project.eu). For any other questions, further contact info is given below.

MINERVA mid-IR world record features in Nature Photonics

MINERVA has had several high profile publications in recent months. In August the original theoretical basis for the project was published in [Optics Express **22**, 19169 (2014)]. This showed that, in principle, extremely long wavelength mid-IR supercontinuum generation (SCG) is possible by exploiting some rather unusual novel fibre designs and pump conditions. This paper was selected as a Nature Photonics Research Highlight ["Supercontinuum: Reaching the mid-infrared", Nature Photonics **8**, 746 (2014)].



Spectrogram of SCG in a 1 m optical fibre.

Progress in the first two years of MINERVA has been dramatic. The DTU simulated predictions of dispersion and SCG in the Optics Express paper have been demonstrated experimentally using chalcogenide fibre made at the Univ. of Nottingham, pumped with DTU's tunable fs laser. SCG well beyond 13 µm was demonstrated: a huge leap into the mid-IR! This ground-breaking work was featured in Nature Photonics (Vol. **8**, p. 830) in Nov. 2014 (doi:10.1038/nphoton.2014.213) and highlighted in the News & Views section of the same issue. See:

http://minerva-project.eu/documents/publications

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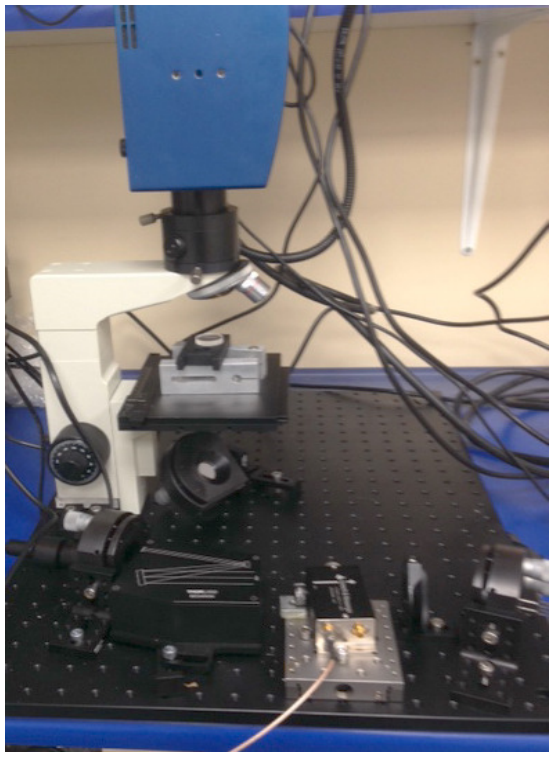
"MINERVA Lite" system demonstrates high speed mid-IR spectral imaging

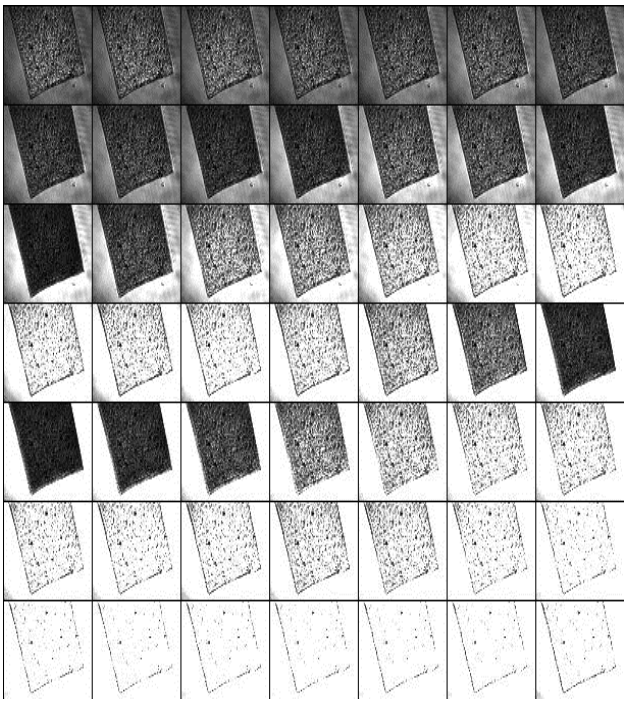
A prototype MINERVA system that operates in the 2-4.5 µm wavelength band has been assembled so that the individual parts being developed by partners in the project can be evaluated together. The final MINERVA system will operate at even longer wavelengths.

The key components in the integrated system are:

- NKT supercontinuum source
- G&H acousto-optic tunable filter
- Xenics IR camera
- Commercial microscope and IR optics
- Control electronics.

The breadboard system is shown on the right. This system can take 0.3 megapixel images with 20 µm spatial resolution at a rate of 85 frames per second. Each image is taken at a different wavelength so that a set of 49 spectral images can be built up in 0.6 s. These images can form an (*x, y, λ*) "image cube."

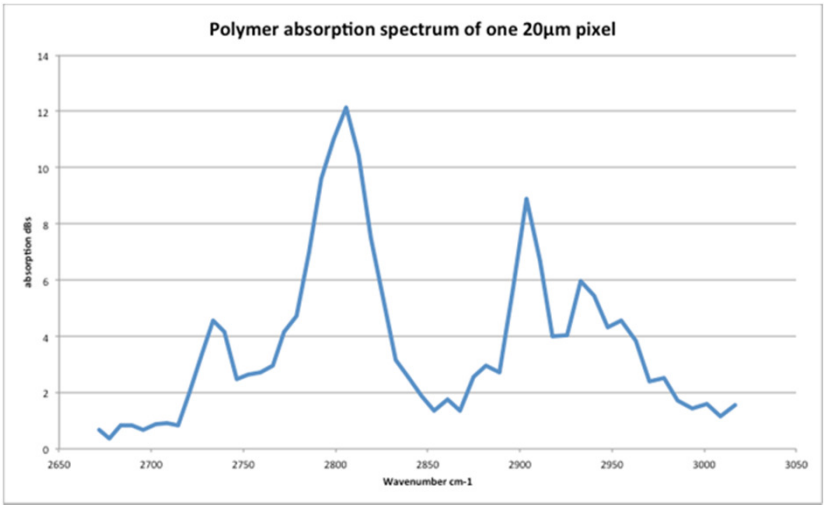




Above: Photo of part of the "MINERVA Lite" laboratory set-up.

Left: 0.3 Mpixel images at 49 wavelengths which can be used to form an (x, y, λ) image cube in 0.6 s.

Below: Spectrum from a single pixel: plotting a line along λ (i.e. fixed x and y) in the image cube.

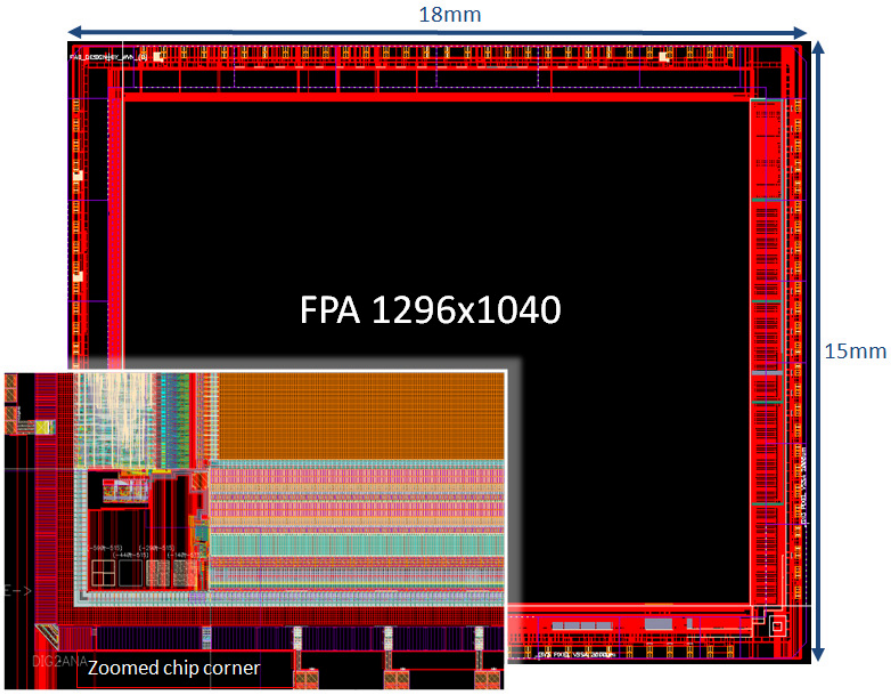


Each pixel records a spectrum and this has enabled MINERVA researchers to identify a polymer film in the sample image as shown above. This important preliminary result will be extended in MINERVA to identify spectra from cancerous cells in tissue samples and in real time on live patients.

For more info contact Dr. Mark Farries mfarries@goochandhousego.com

Infrared megapixel camera development

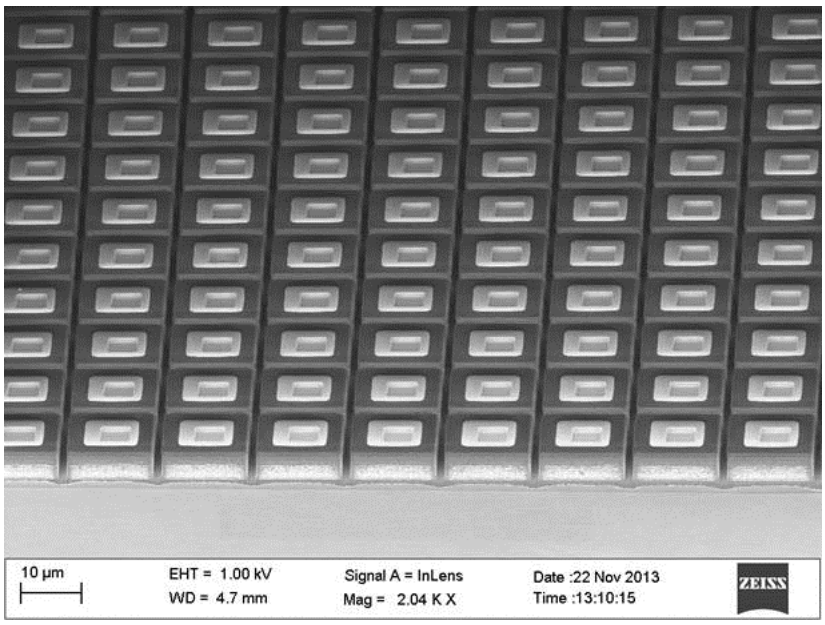
The sensing unit for MINERVA is being developed in a joint effort between IRnova and Xenics. From the start of the project Xenics has been working on the design of a Read-Out IC (ROIC), to be integrated through flip-chip technology with the T2SL (Type-2 Super Lattice) photodiode material, which is being developed by IRnova.



Global and zoomed view of the designed ROIC, currently in manufacturing.

To provide sufficient resolution for reliable data analysis, a 1280 × 1024 pixel array was chosen, on an aggressive pitch of 12 µm. Project requirements including frame rate, sensitivity and noise level were taken into account in the design process. After extensive simulations and test sample manufacturing, the final design was taped out to a manufacturing foundry. The use of advanced 0.18 µm CMOS technology is required to allow all necessary functionality within the available space of 144 µm^2 per pixel. The first wafers are currently available for post-processing to be followed by wafer-level verification of the electrical functionality.

In parallel, IRnova has been working on the optimisation of the design and processing of the T2SL material, towards cut-off wavelength matching and dark current minimisation. Once the ROIC chips become available later this year, they will be hybridized to the sensor chip, and IRnova will integrate the resulting hybrid in a Sterling-cooled Dewar. The so-called engine will in its turn be integrated into a full camera by Xenics, to be supplied to the other MINERVA project partners to be used for capturing spectroscopic images of prepared tissue samples and live cell phantoms.



Microscopic view of manufactured array of T2SL photo diodes.

For more info contact Koen van der Zanden
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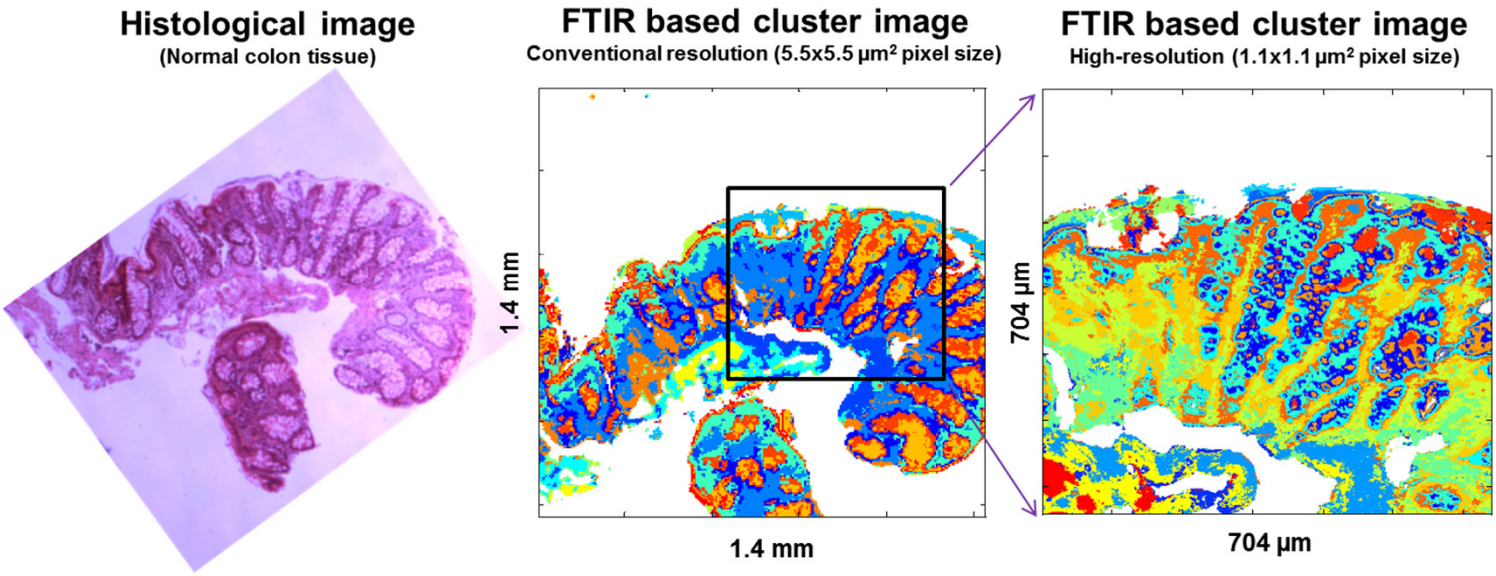
High resolution mid-IR imaging at University of Exeter

One of the main objectives of Prof. Nick Stone's group at the University of Exeter within the MINERVA project is large scale pathology screening using mid-infrared (mid-IR) spectroscopy. Currently FTIR spectral histopathology, which has the potential to develop as a cancer diagnostic tool, is carried out using a heated silicon carbide rod ("Globar") as the mid-IR light source and focal plane array (FPA) based detectors. This technology is limited by the low flux of the light source and the limited tissue area that can be measured in a given amount of time.

The novel technologies being developed in the MINERVA project; consisting of mid-IR super-continuum light source (instead of a "Globar") and new generation mega-pixel (FPA) detectors (instead of a 128 × 128 pixel FPA), will be tested on pathological samples at the University of Exeter.

Currently the base instrument, a commercially available Agilent FTIR imaging system, in addition to the conventional Globar source coupled to FPA based imaging, has been retro-fitted with a new high-resolution imaging capability. The FTIR images acquired using this set-up provided a five-fold improvement in image resolution from 5.5 μm^2 of the current technology to 1.1 μm^2 using the high magnification optics (see figure below).



FTIR based K-means cluster images obtained using conventional and high-resolution imaging compared with the histological image. Histological features based on the bio-molecular composition are partitioned in the cluster images. In the high-resolution imaging, tissue and cellular features are more apparent.

Future work in MINERVA will combine these novel technologies for large scale pathology screening, and also high-resolution imaging in tissue regions of interest, with the aim to develop faster and accurate cancer diagnostic tools. Initially this will integrate with a 4.5 μm NKT MINERVA source, and later in the project it will be extended to very long mid-IR wavelengths: possibly out beyond 10 μm.

For more info contact Prof. Nick Stone
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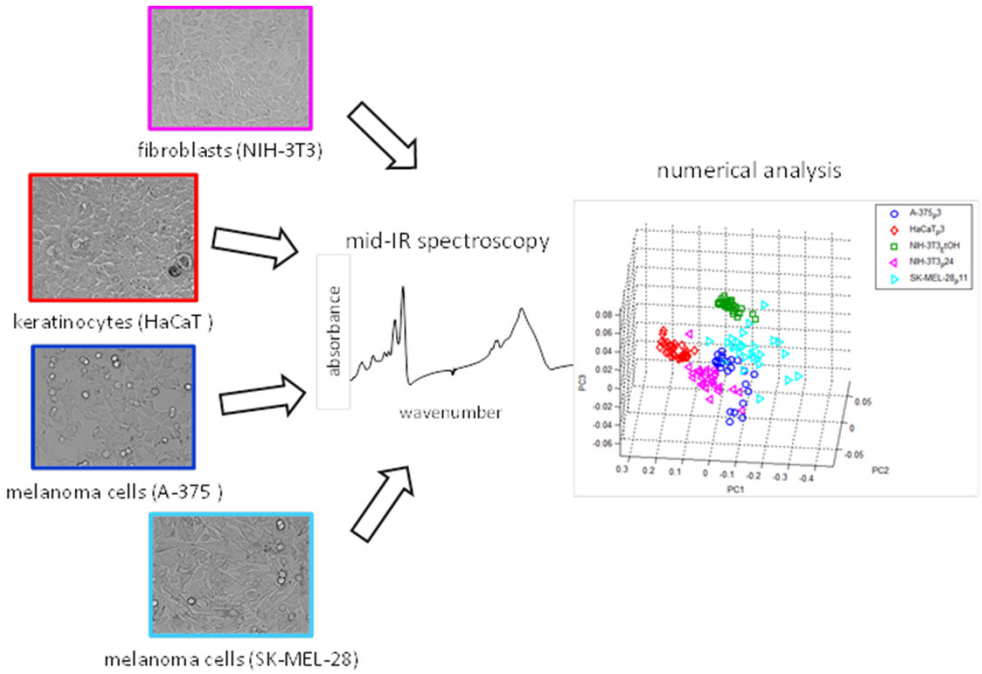
Development of standardised samples for mid-IR spectrometer instruments testing

A key task of Westfälische Wilhelms-Universität (WWU) in Münster is to transfer the MINERVA technologies to skin diagnostics and to use mid-IR spectroscopy for the fast screening of human body surfaces and identification of patho-physiologically altered cells and tissue lesions. This requires standardised cell and tissue sample standards with marker spectra for technology performance testing of the novel optical components and systems and for training of novel approaches for advanced data analysis.

The work of WWU in the first MINERVA project period thus focused on the establishment of standard samples with representative spectral information of human skin and skin cancer cells. WWU has established cell culture models which represent major cellular skin constituents and skin cancer cell types. Furthermore, sample preparation procedures on mid-IR compatible substrates have been developed that allow long-term storage of cell lines without significant losses in the quality of the spectral properties.

In order to identify suitable marker spectra of human skin, sample sets with different preparations and cell types were analysed with mid-IR spectroscopy in collaborative work with Gloucester Hospitals NHS Trust (GHNT) to retrieve reference data for technology performance testing and for the evaluation novel algorithms for sample analysis and classification developed by Universitat Politècnica de València (UPVLC). The principle component analysis (PCA) of mid-IR spectra from different cell types shows an excellent distinct grouping of skin components as fibroblasts and keratinocytes and cancer cells.



Principle component analysis (PCA) of mid-IR spectral data from fibroblasts (NIH-3T3), keratinocytes (HaCaT) and skin cancer cells (A-375, SK-MEL-28) illustrates the differentiation between different cell types.

For more info contact Dr. Juergen Schnekenburger schneke@uni-muenster.de

The figure above illustrates the analysis and differentiation of different cell types (cancer/non-cancer) that have been prepared at WWU for the example of results PCA of mid-IR spectral data from fibroblasts (NIH-3T3), keratinocytes (HaCaT), and skin cancer cells (A-375, SK-MEL-28). Based on these results, current and future activities at WWU in MINERVA focus on the development of novel mid-IR standards models for skin cancer detection that are based on 3D human skin equivalents in vitro.