MId- to **NE**a**R** infrared spectroscopy for impro**V**ed medical di**A**gnostics



MINERVA project newsletter #6

Nov 2015

Welcome to the sixth MINERVA project newsletter!

There have been a number of important developments in recent months, as the project enters its integration phase. This newsletter provides an update on several key topics:

- Image processing and data analysis at UPV (Universitat Politècnica de València)
- Record breaking calomel crystals for acousto-optics from BBT
- State-of-the-art T2SL detectors for long wavelengths from IRnova

And of course we are very excited by the strong MINERVA presence at Photonics West in February: see below for more info!

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

MINERVA at Photonics West 2016

SPIE. PHOTONICS

San Francisco, USA; 13-18 Feb-2016

It has now been officially announced that MINERVA will have two dedicated sessions at Photonics West 2016 as part of Conference 9703 Optical Biopsy XIV: Toward Real-Time Spectroscopic Imaging and Diagnosis

Sessions 1 & 2: Towards the Mid-Infrared Optical Biopsy: MINERVA-I & II Monday 15-Feb-2016: Session 1 (08:10 - 10:10) and Session 2 (10:40 -12:00).

Ten presentations will explore various aspects of the project work, with invited guest speakers. The agenda can be seen at: http://spie.org/PWB/conferencedetails/optical-biopsy

It will be an excellent opportunity to find out more about the project and meet some of the busy researchers! We hope to see you there!





<u>jward@goochandhousego.com</u> <u>bruce@vividcomponents.co.uk</u>





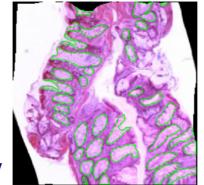
MINERVA image processing at UPV

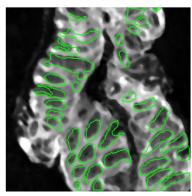


The team at UPV has developed a method to register the infrared spectroscopic and the H&E (hematoxylin and eosin; a standard stain used in medical samples) images. The first step of this process is to extract a representative gray image from the Fourier transform infrared spectroscopic (FTIR) hypercube that can be used as the input of the registration algorithm. This step is necessary because the H&E and FTIR images do not share the same spatial reference system because they have been acquired by completely different methods. Indeed the registration process is made even more challenging because each image corresponds to a different slice of the biopsy. The aim of this method is to be able to select, accurately and automatically, the outline of so-called crypt structures from the hyperspectral data. This process currently has to be done manually by an expert pathologist. Using this information, the GHNT

team will build models to discriminate between benign and cancerous biopsies.

- a) Left hand image shows the manual crypt segmentation made by an expert pathologist.
- b) Right hand image shows crypt information translated after registration to the representative image from an FTIR hypercube.



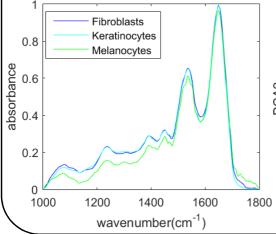


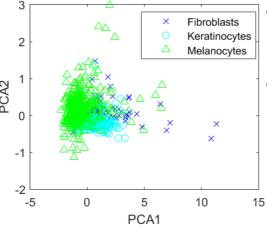
MINERVA data analysis at UPV

Another key task of the UPV team is to develop new algorithms for the diagnosis of skin cancer from FTIR images. To achieve this goal, the first step is to establish the procedure to discriminate spectra from different types of skin cells.

Multiple techniques of machine learning and pattern recognition are being exploited to complement traditional and novel methods applied to the data from spectroscopic analysis. The data to be analysed corresponds to the mid-IR spectra collected from primary cell cultures in collaboration with the MINERVA partners at WWU, GHNT and Exeter.

The preliminary qualitative results for the discrimination of three types of common skin cells (fibroblasts, keratinocytes and melanocytes) show that the differentiation between the populations is not obvious, as can be seen in the figures below. For this reason, more complex algorithms of feature extraction and classification must be developed. This will be the focus of UPV for the next period of MINERVA.





- Left-hand graph shows averaged spectra of different skin cells: fibroblasts, keratinocytes and melanocytes.
- Right-hand figure shows the principal components of spectroscopic data for different populations under study.

For more info contact Prof. Valery Naranjo vnaranjo@labhuman.com





Oriented and polished Hg₂Cl₂ substrate for processing





In the MINERVA project, an acousto-optic tuneable filter (AOTF) is the key to the wavelength selection of the broadband supercontinuum source. AOTFs for visible wavelengths generally use tellurium dioxide (TeO_2) as the interaction medium, which is transparent from the visible to c. 4.5 μ m. G&H (UK) is the world leader in these products. However, for longer IR wavelengths an alternative material is required. Very few materials with the appropriate properties exist.

One such material is mercurous chloride (also known as calomel), but until recently this has not been available in the appropriate size or quality for this application. BBT has developed world-leading growth and processing technology (cutting, lapping, polishing etc.) to provide a step change in the size of optical quality calomel crystals with characteristics for AOTFs.



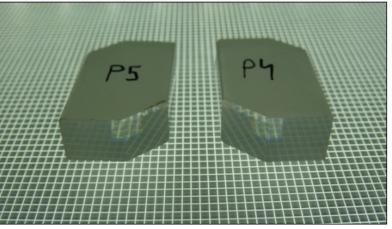
Two cultivation crystalliser units with calomel crystals

For more info contact Dr. Cestmir Barta: bartabbt@atlas.cz

Many challenges in processing techniques need to be overcome, and G&H together with BBT are working to overcome these issues.

These crystals can be applied to a device configuration which minimises the AO drive power (a key issue in the infra-red), by using a long interaction-length collinear AOTF to produce a narrowband filter. Novel apodised transducer technology (G&H US patent 7283290) may also be deployed to enhance the performance.

The combination of BBT's material expertise and G&H's design and manufacture expertise, allows mid-IR AO devices to be investigated. Using the data supplied by BBT, G&H has proposed a design of a prototype AOTF operating in the IR beyond 4 µm (the limit of TeO₂); the AO cell being manufactured by BBT for further processing and evaluation at G&H.



Calomel prisms for the spectrometer applications





Mid-IR camera development

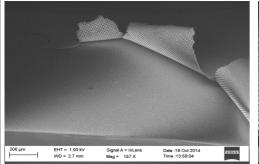


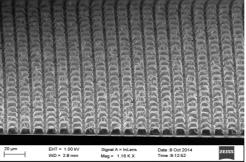


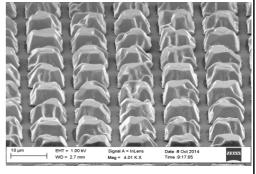
IRnova's task is to develop and manufacture an imaging detector, which will be part of the MINERVA demonstration instrument. This task is being carried out together with IRnova's partner, Xenics, whose first task was to provide IRnova with a read-out integrated circuit (ROIC) and in a later stage to complement the integrated Dewar-cooler assembly (IDCA) manufactured at IRnova with mechanical frame and case, optics and electronics to make it a camera.

The specification requirements were formulated ambitiously. IRnova was to develop a focal plane array (FPA) based on novel type two superlattice (T2SL) technology with high resolution, small pitch and wide bandwidth. T2SL technology has the potential to combine the performance of currently used HgCdTe technology with the stability, image quality, robustness and manufacturability of III-V technology. At the project start IRnova produced detectors based on T2SL technology with the resolution of 320×256 pixels at 30 μm pitch with the cut-off wavelength of 5 μm operating at 80-100 K. The MINERVA challenge was to push the technology to the edge and develop an FPA with the resolution of 1280×1024 at 12 μm pitch with the cut-off at 12 μm operating at 100 K. Such a detector is without doubt state-of-the-art for the current IR-technology.

In addition to developing the semiconductor structure with appropriate band-gap engineering, IRnova developed the semiconductor process for these large area/small pixel arrays, as well as the hybridisation process: in itself a huge challenge! The images below show a detector chip at the stage of deposition of indium (In) bumps for flip-chip bonding with a readout chip.



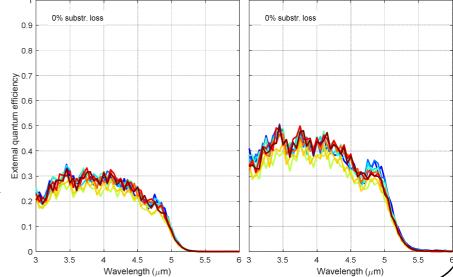




Micrographs of the lift-off processing step after deposition of In-bump (left), detector array with In-bumps prior to hybridisation step (centre and right), when a detector chip will be pixel-to-pixel bonded to a ROIC chip having similar bumps to create an electrical contact.

IRnova can now proudly report that most of the goals were successfully achieved. The first results of detectors with 12 μm pitch are available! Optical response is good and will be further improved by applying antireflective coating.

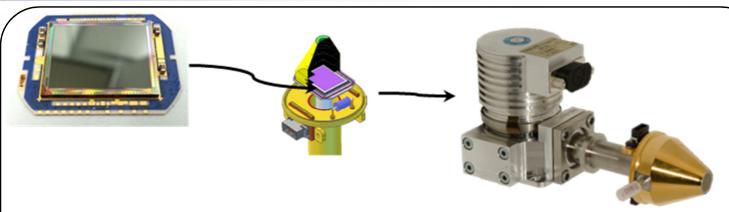
External conversion efficiency of the MWIR sample array (cut-off 5.3 µm) without antireflective coating at 80 K (left) and 120 K (right). The sample is part of a fully processed detector chip hybridized with a specially designed fan-out chip. No ROIC was involved in the measurements.





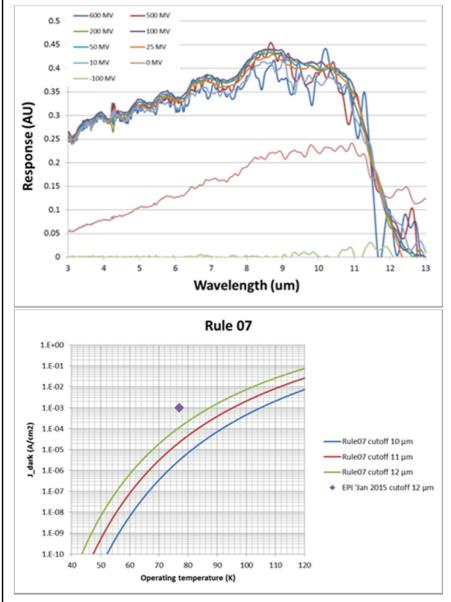
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A photo of newly hybridised FPA which shall be mounted in a Dewar (CAD schematics), which in turn will be integrated with a cooler to make an IDCA (photo).

Test FPAs were successfully hybridised, which is major landmark, and will be shipped to Xenics for the debugging and finalisiation of electronics, which will be later used for comprehensive characterisation of the FPA at operating temperature before integration into the Dewar.



a.) (Above) Optical response of the LWIR structure with cut-off wavelength 12 μm and b) (Below) Its performance in terms of dark current vs operating temperature according to Rule 07.

The target performance was achieved on the structure with the cutoff at 12 µm. Materials for longer wavelengths are more demanding to the passivation and more sensitive to the hybridisation process. However, the developed material showed good response and is very close to the state-of-the-art performance predicted by empirical Rule 07 for the HgCdTetechnology. [See Tennant et al., "MBE HgCdTe Technology: A Very General Solution to IR Detection, Described by Very Convenient 07", а Heuristic," J. of Elec. Mat. **37**. p. 1406-1410 (2008).]

There is still a lot of room for improvement in the band-gap engineering of the detector structure and the processing, but remarkable progress in the development commercially available wide bandwidth high-definition highperformance detectors with cut-off up to 12 µm has already been achieved, and the work continues!!!.

For more info contact
Dr. Sergiy Smuk:
Sergiy.Smuk@ir-nova.se

