Infrared Scanning Near-field Optical Microscopy in Material Science and Biology

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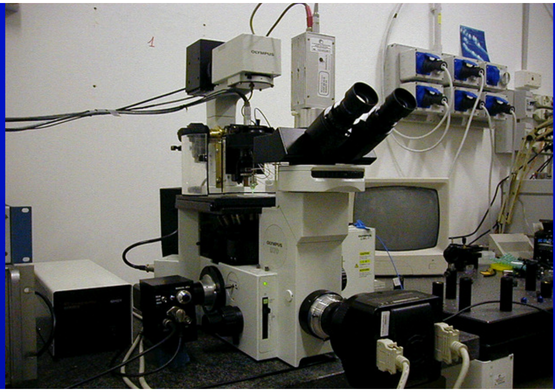
ISM, CNR-ITALY,

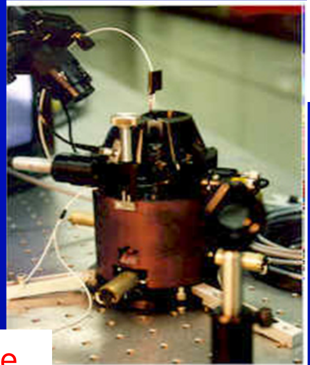
Introduction
Activity at Vanderbilt-IR FEL (1997-2008)
Acticity at Daresbury: early diagnosis of cancer (2011-)

NANOTECHNOLOGY

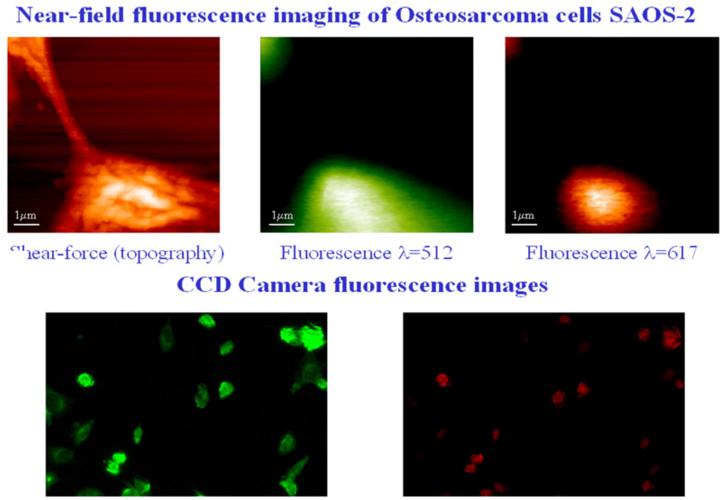
Design and implementation of new scanning probe microscopes (STM, AFM and SNOM). Study of metal-organic interfaces, clean surfaces of semiconductors and metal overlayer, low-dimensional systems and biological systems.

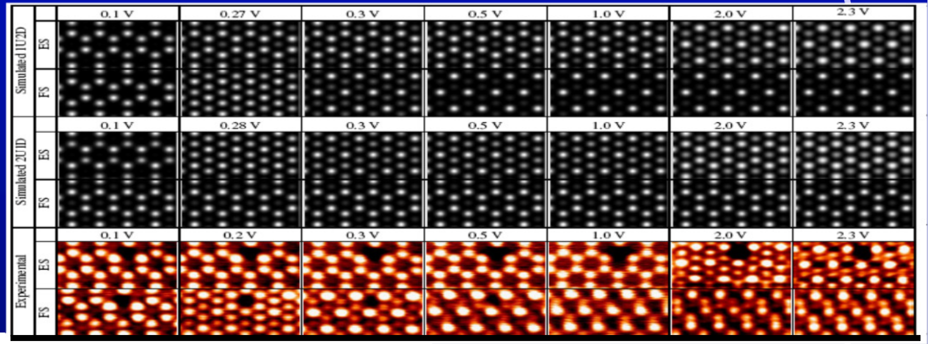


SNOM coupled with an inverted microscope

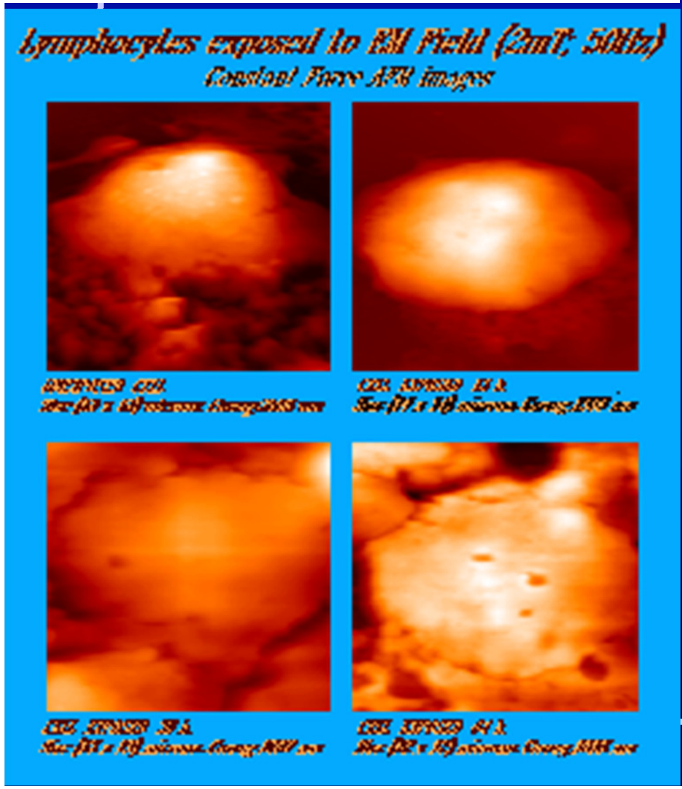


SNOM coupled with the FEL inNashville

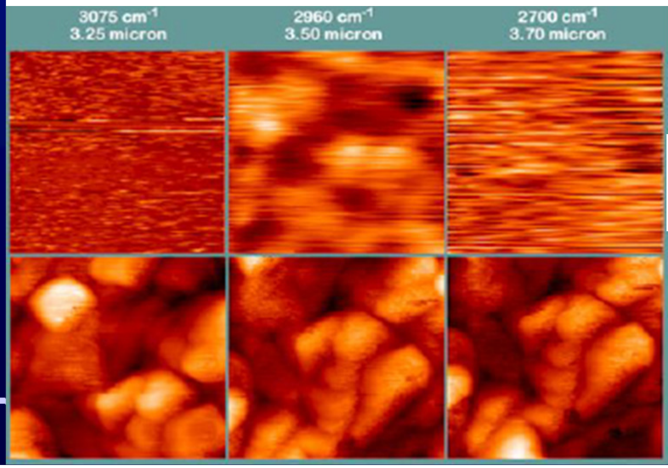




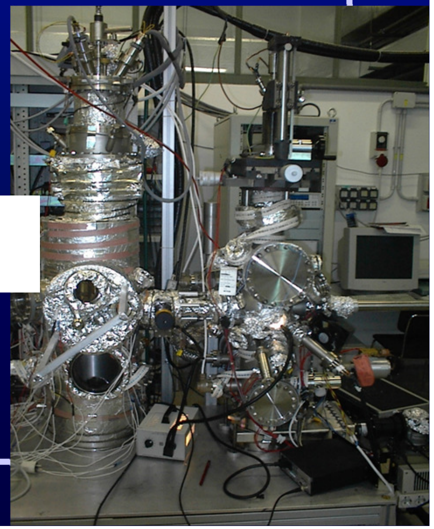
α-Sn/Ge(111) comparison STM images (70 K)- theory



Diamond grains observed with the SNOM coupled with the FEL in Nashville at 3,25 micron

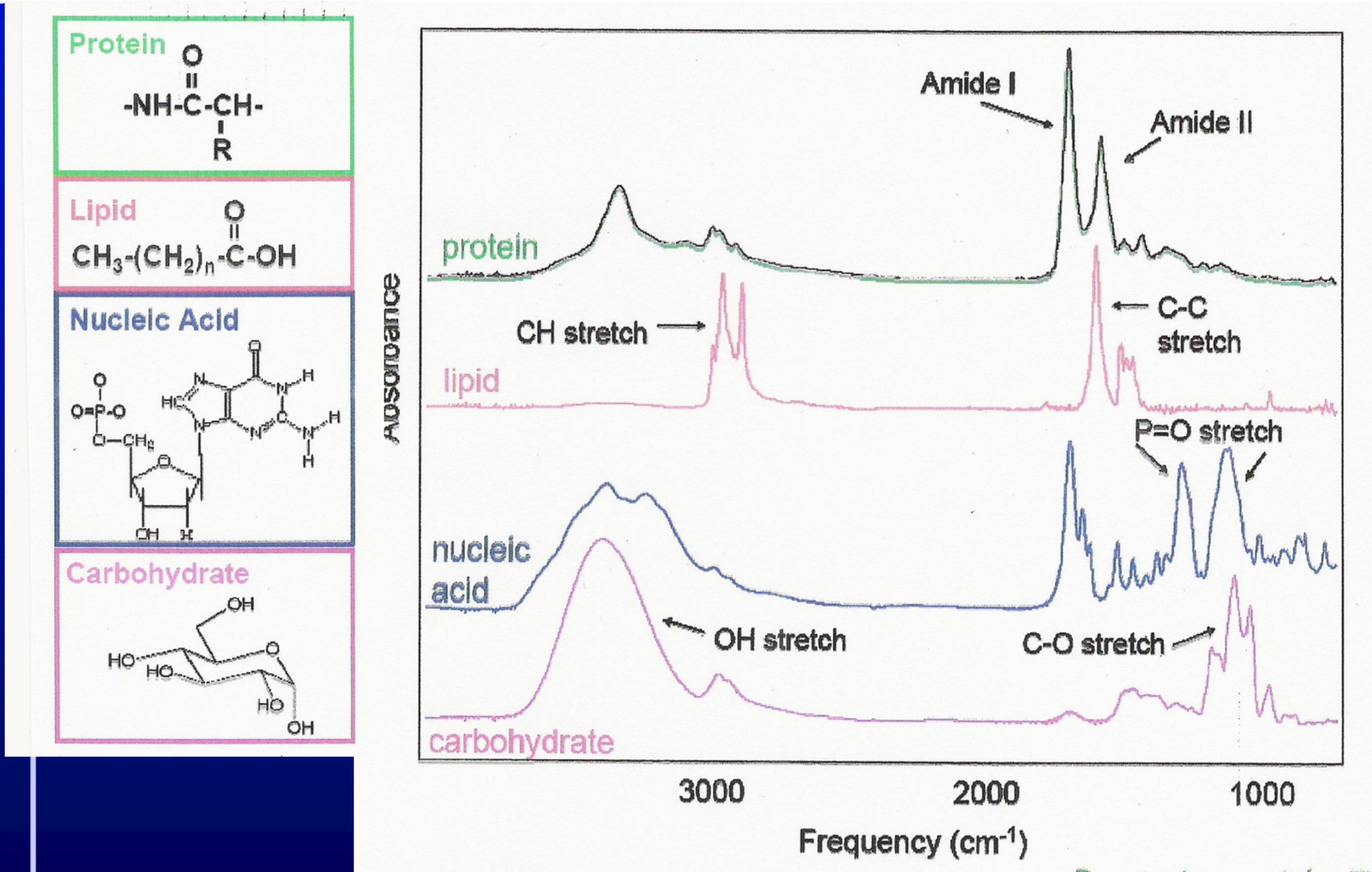


UHV STM



Spectroscopy and microscopy in the infrared

Strength: Spectral fingerprints of molecules

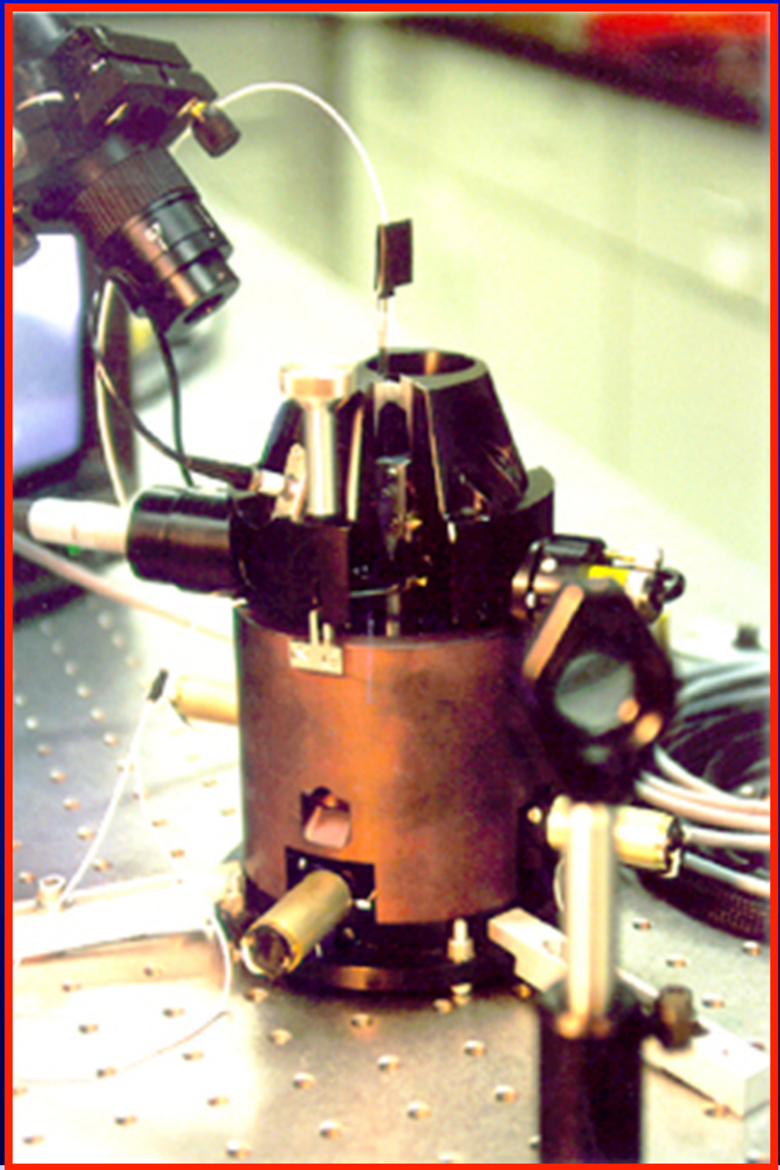


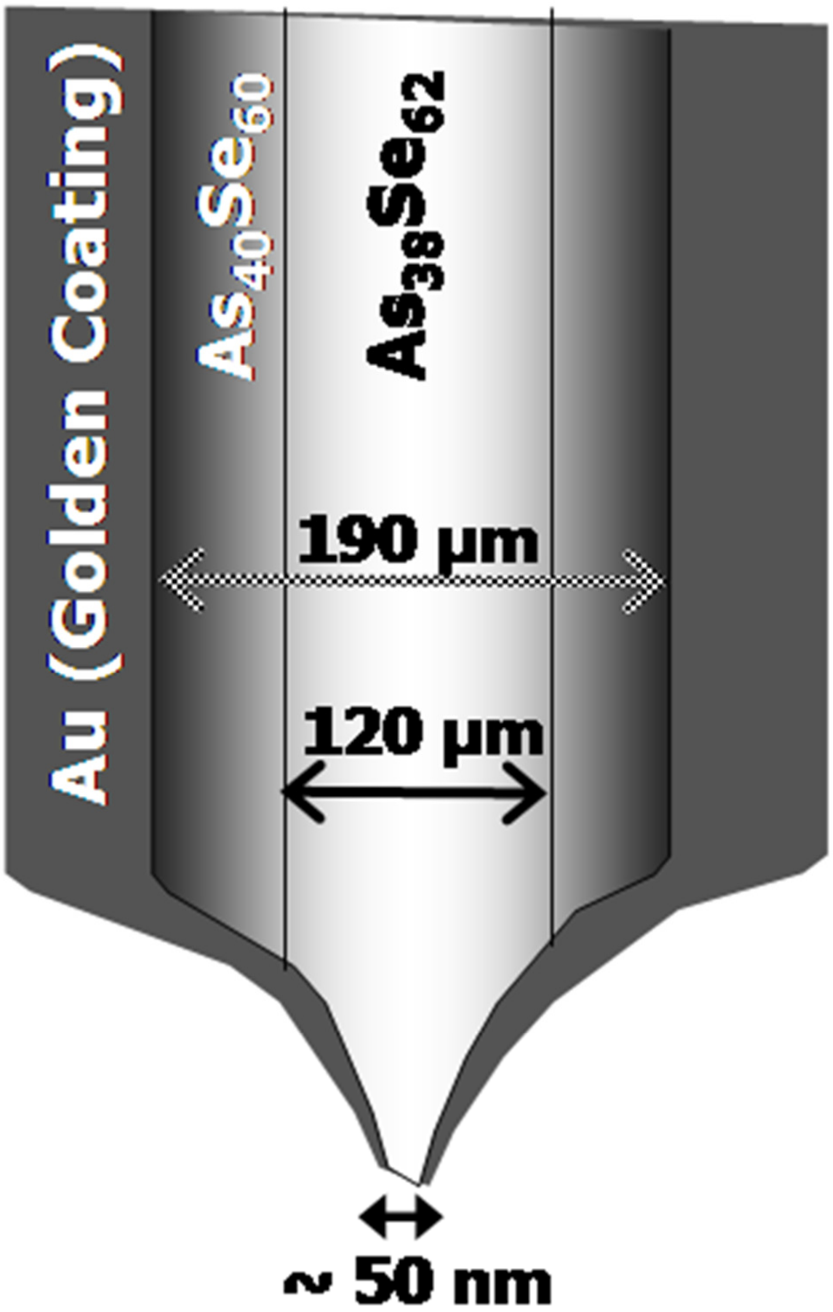
Weakness: Long wavelengths Spatial Resolution ~ λ/2

Solution: Near field optics ----> SNOM ---> needs high intensity

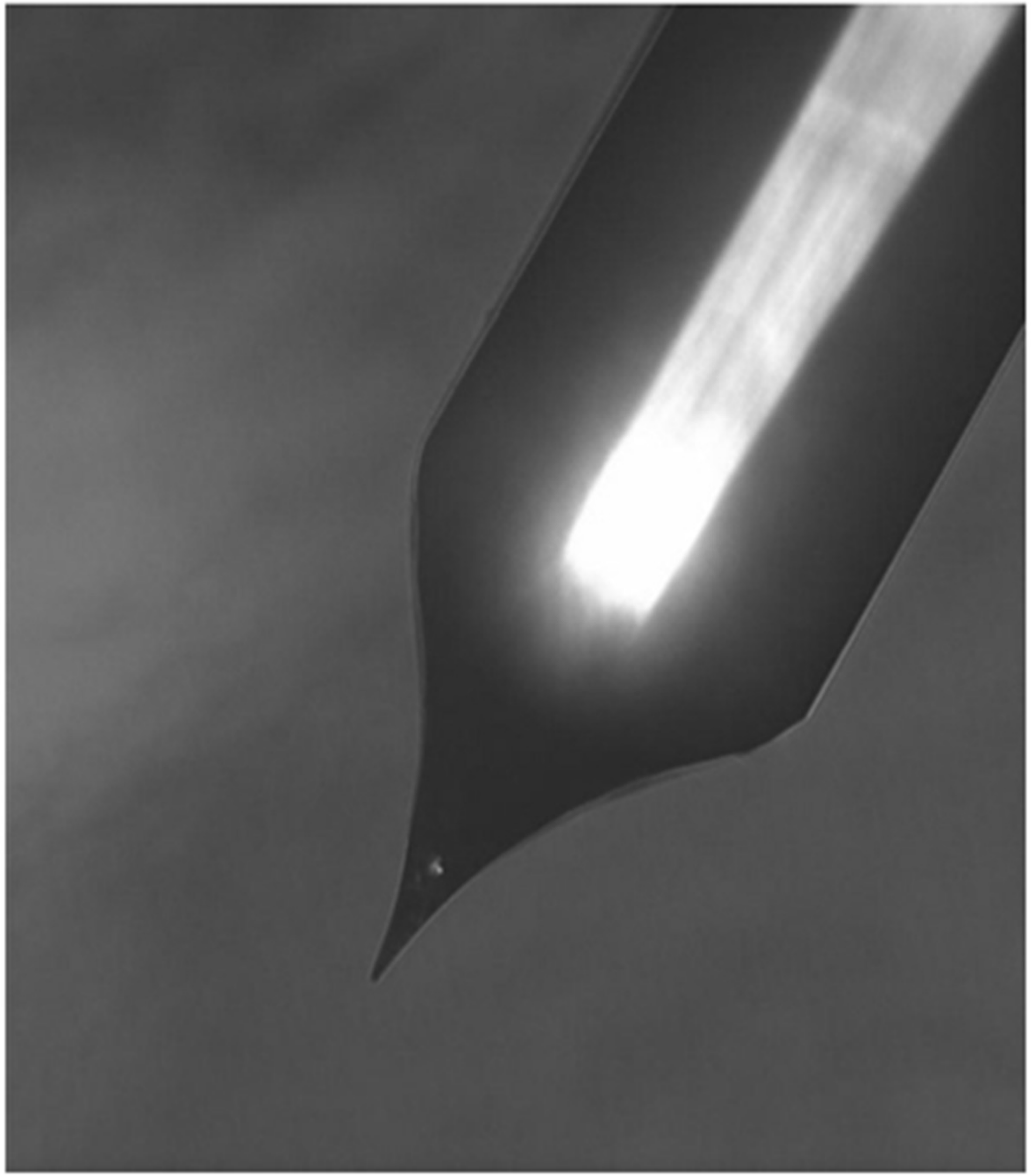
Combine Spectroscopy and SNOM ---> needs very high intensity ---> IR FEL

IR SNOM (range 2-10 Micron)





Au (Golden Coating)
$As_{40}Se_{60}$
$As_{38}Se_{62}$
190 μm
120 μm
~ 50 nm

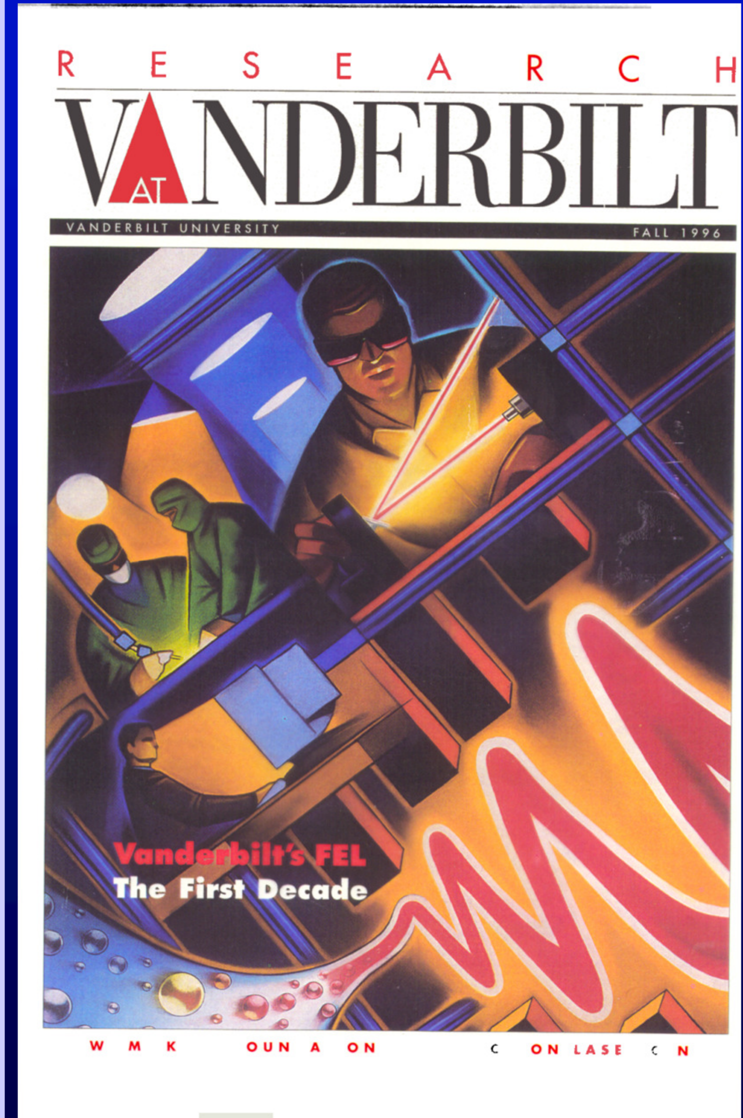


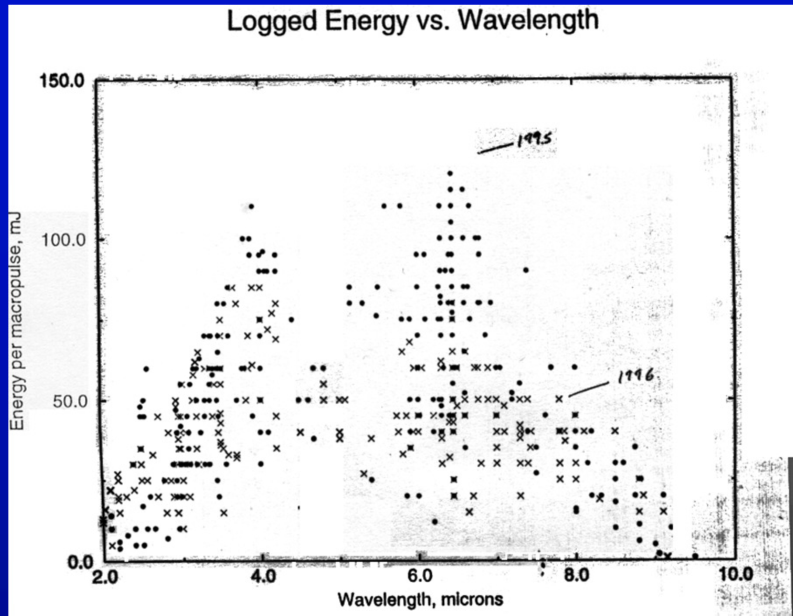
SNOM IN THE SPETTROSCOPIC MODE

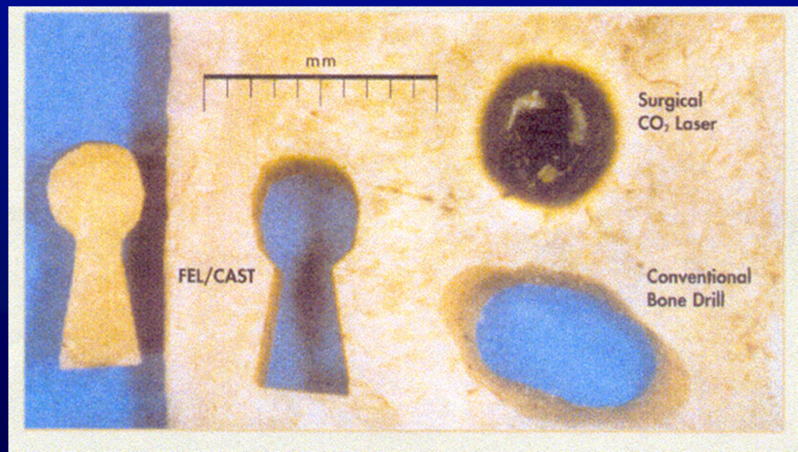
Take the image at λ values where the sample has a spectroscopic fingerprint

- absorption
- fluorescence
- ……

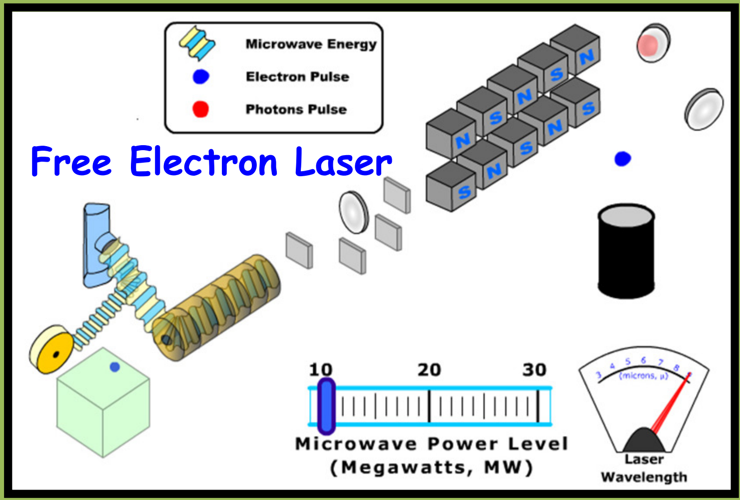
Need of a Tunable and intense IR source







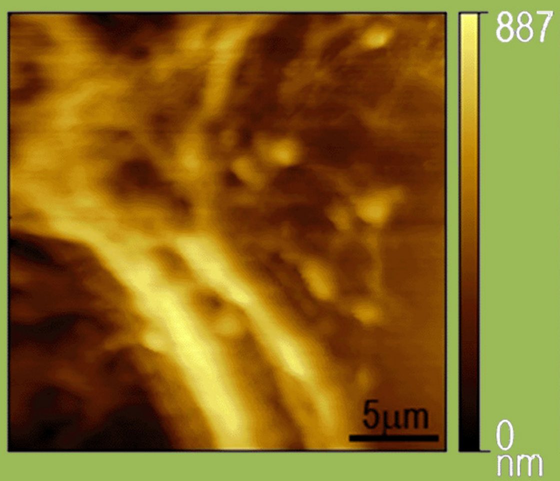
Free Electron Laser (FEL)



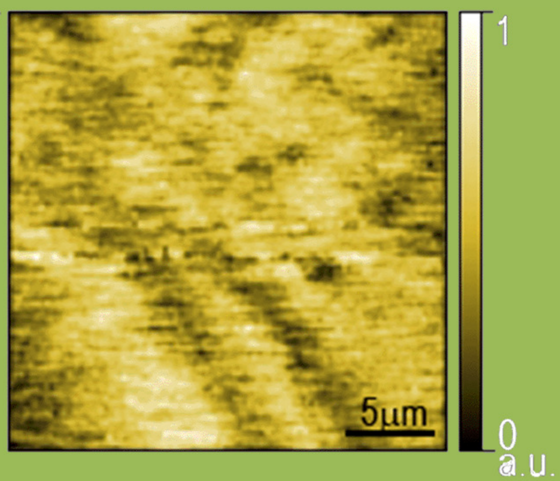
Chose wavelengths corresponding to vibrational modes of the interested chemical bonds

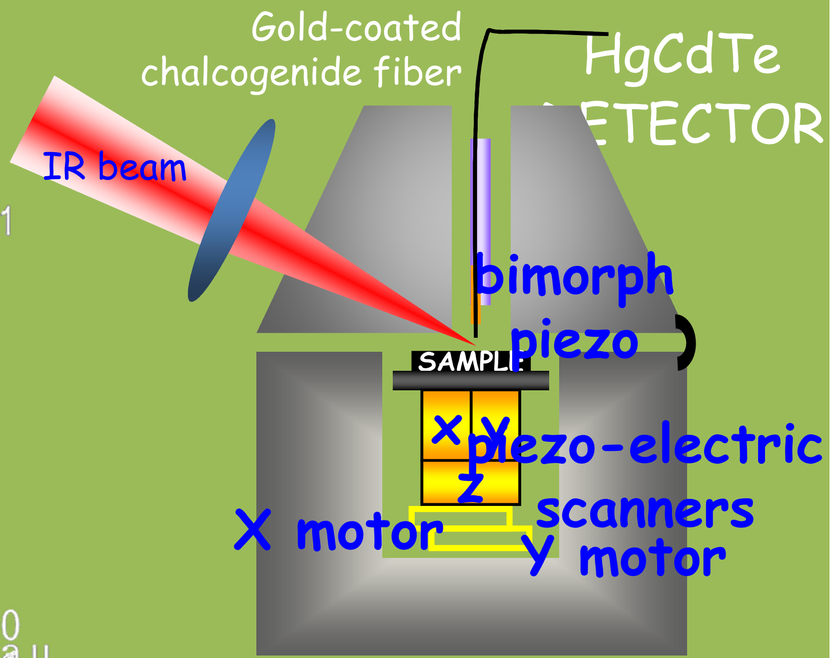
obtain a map of sample's chemical contents

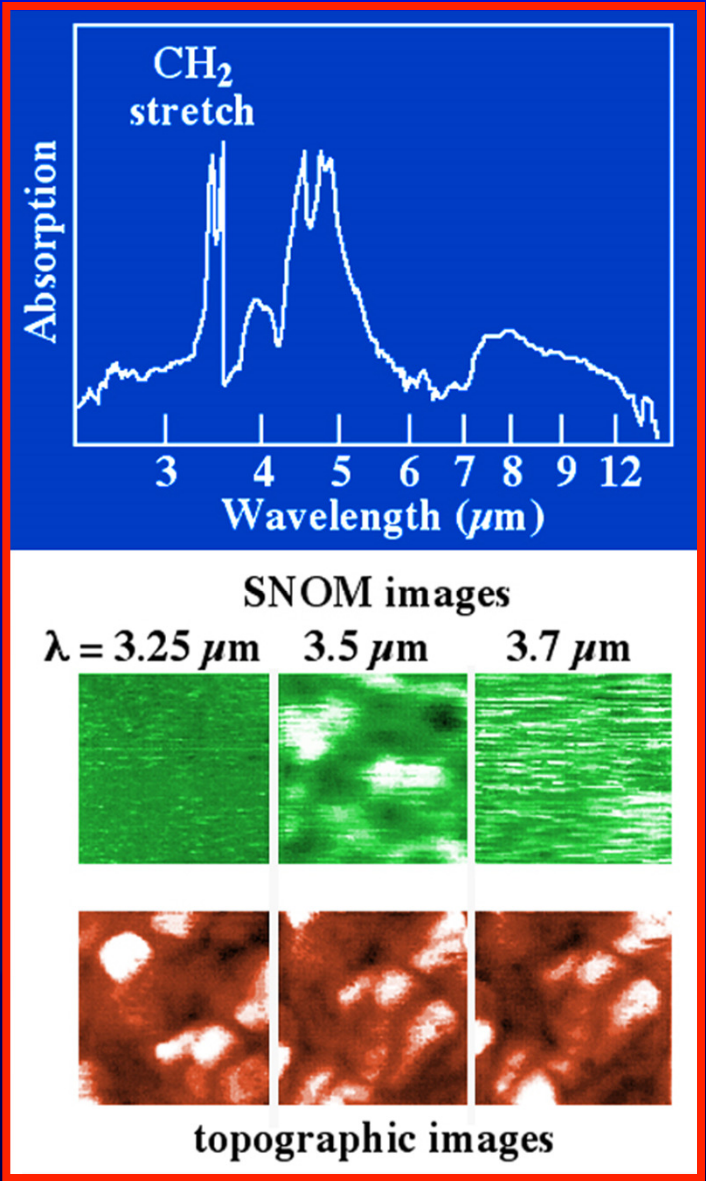
topography



optical signal







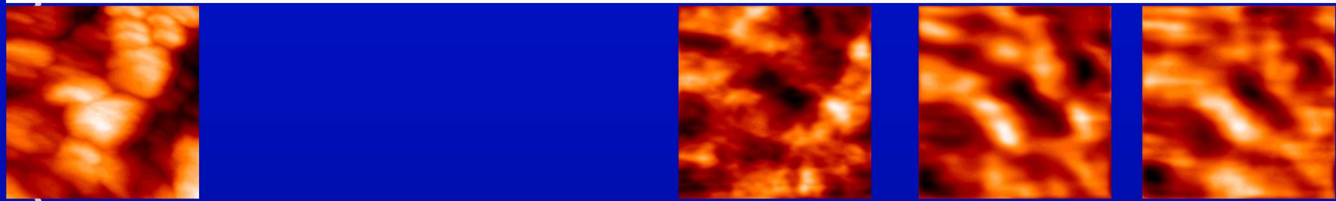
First example of IR Spectroscopic SNOM: diamond films

J. Microscopy 202, 446 (2001).

HaCaT cells exposed to 50 Hz 2 mT Magnetic Field

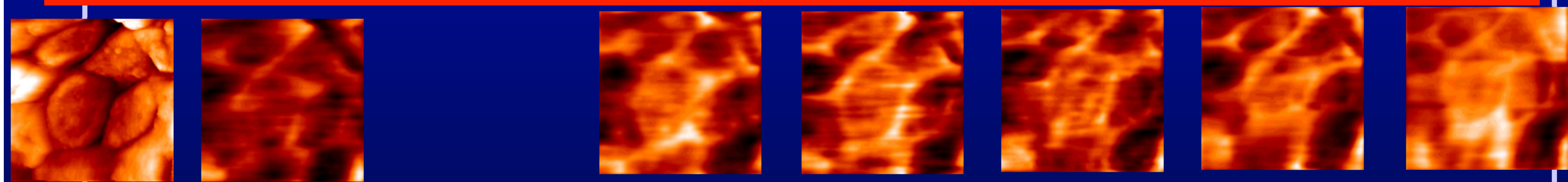
CTR

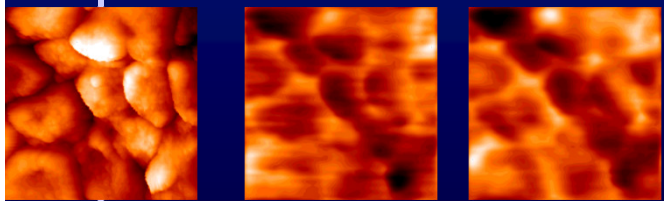
Topo λ 3.04 λ 3.4 λ 6.1 λ 6.45 λ 6.95 λ 7.6 λ 8.05



EXP

Topo λ 3.04 λ 3.4 λ 6.1 λ 6.45 λ 6.95 λ 7.6 λ 8.05





APL 2007

Diagnosis of cancer at Daresbury 2011-

Oesophageal Adenocarcinoma

Oesophageal cancer is the fastest rising incidence of cancer in the western world.

Most patients have distant metastases on diagnosis and are not suitable for surgery.

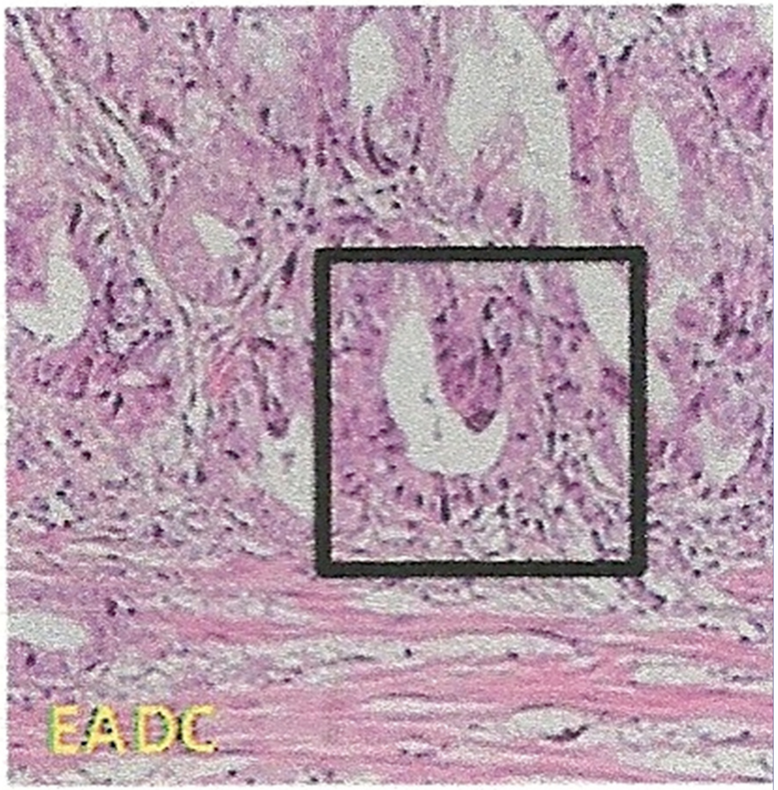
Surgery is the only potentially curative treatment so survival rates are very poor.

However, very low percentage (8%) in identify it

The challenge is to do early diagnosis on patients who can develop oesophageal cancer.

Detail: Stroma

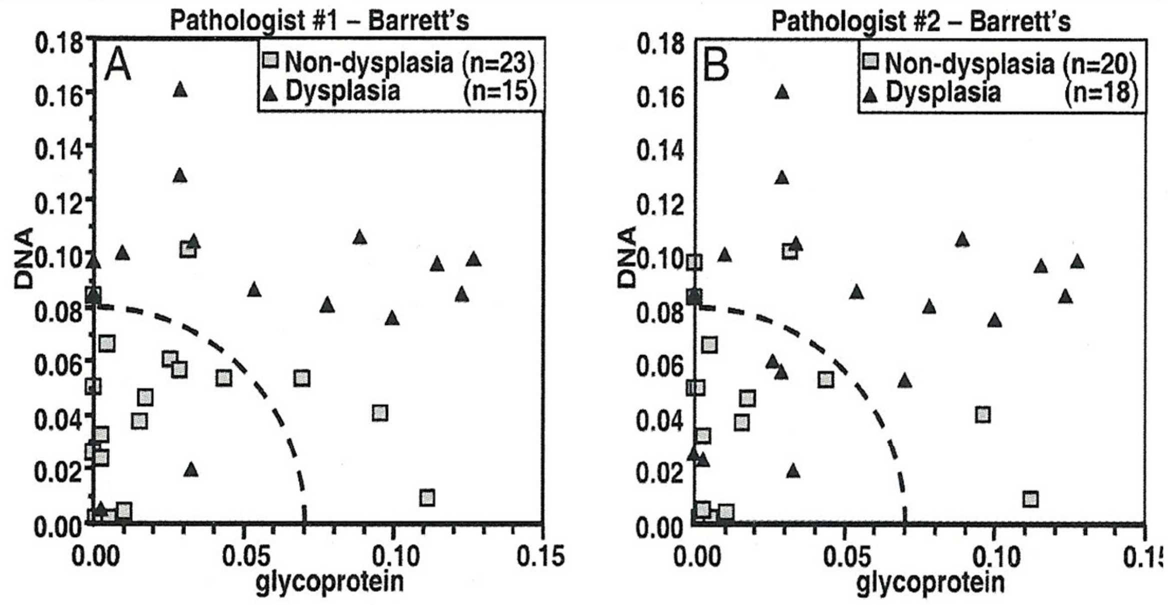
Oesophageal cancer consists of cancer cells surrounded by stroma made up of various (non-cancer)
cell types and extracellular matrix (ECM) proteins.



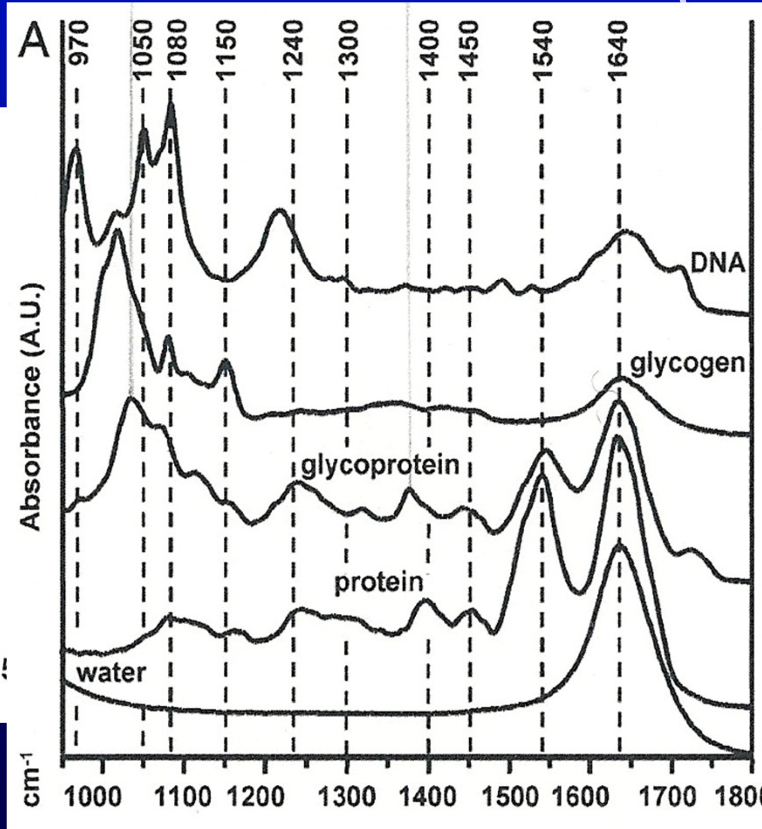
Visible light image of specimen of Barrett's oesophagus.

Previous work: FTIR on a Synchrotron

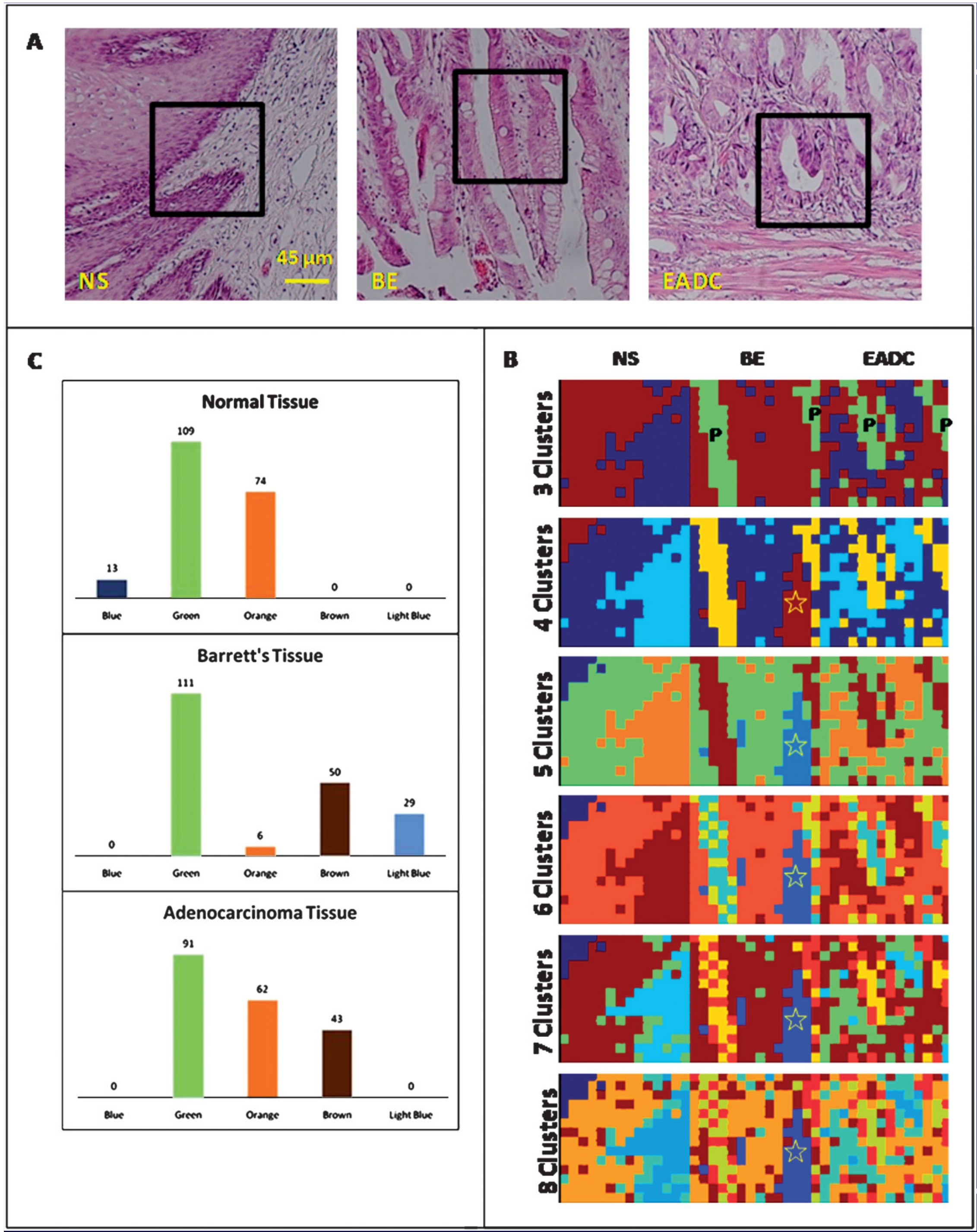
DNA to Glycoprotein ratio as determined by IR FTIR on Synchrotron



Infrared spectra



T.D. Wang et. al. PNAS 104 15864 (2007)



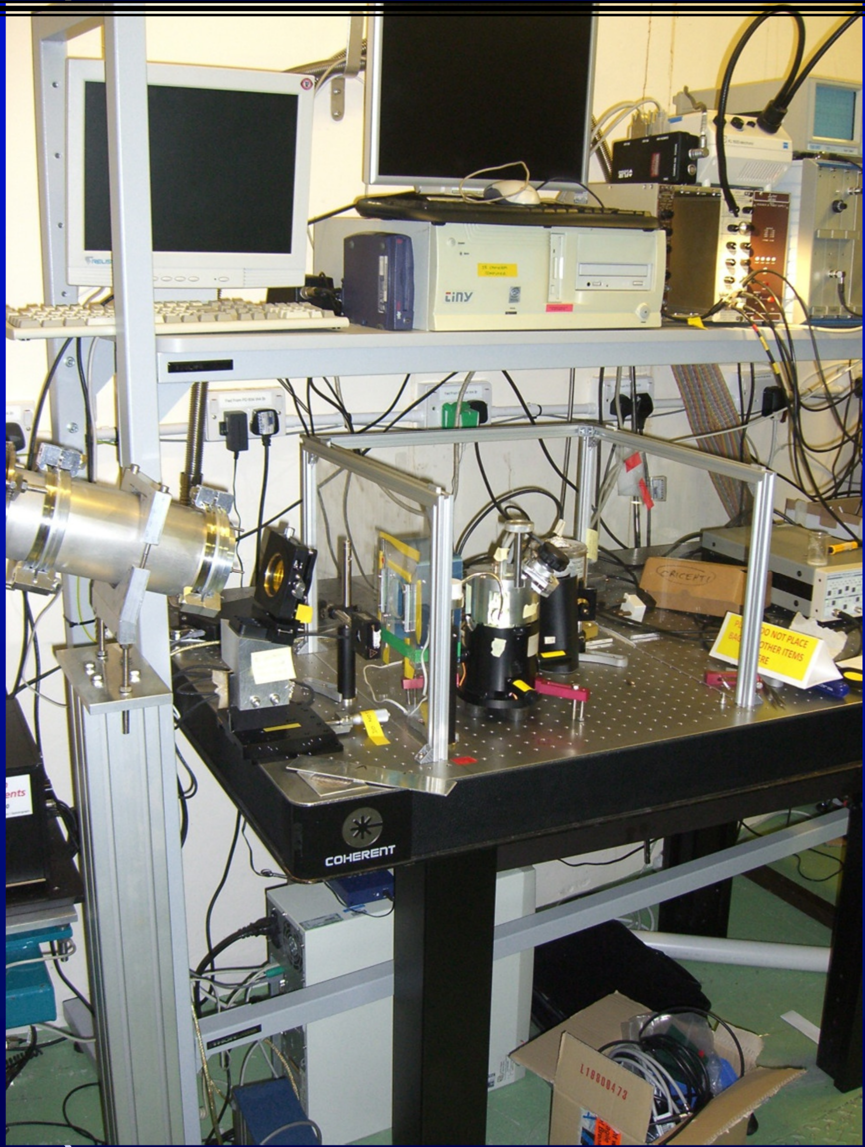
Quaroni et al. 2009
Esophagous cells
Synchrotron IR
15 micron step
900-1300 cm-1

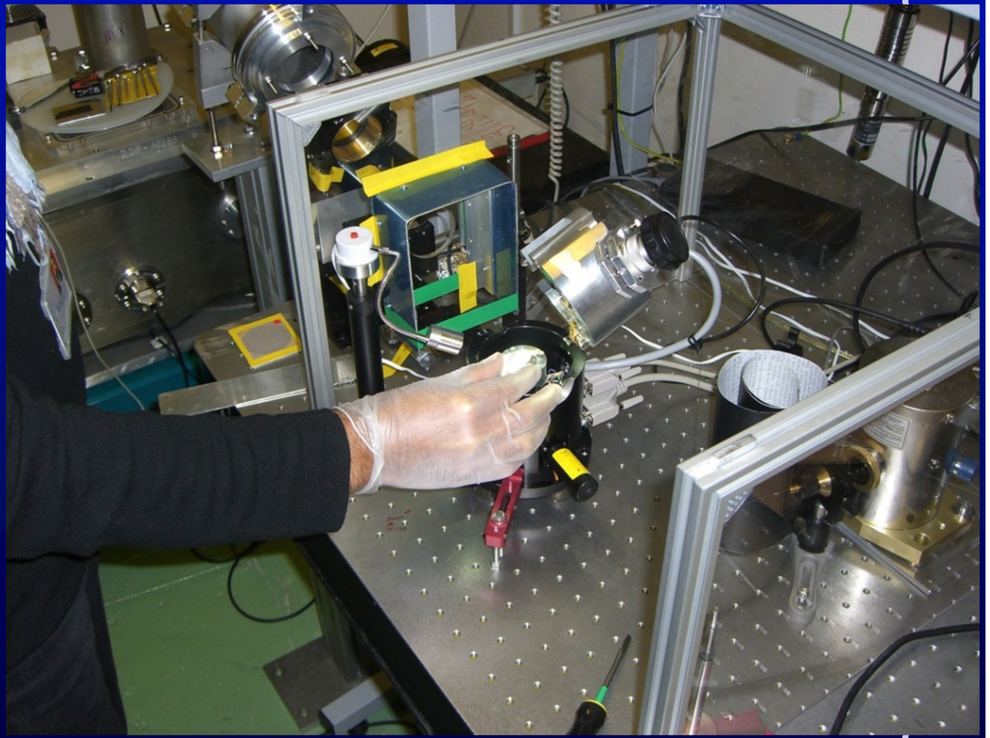
Blue bands of
glicogen

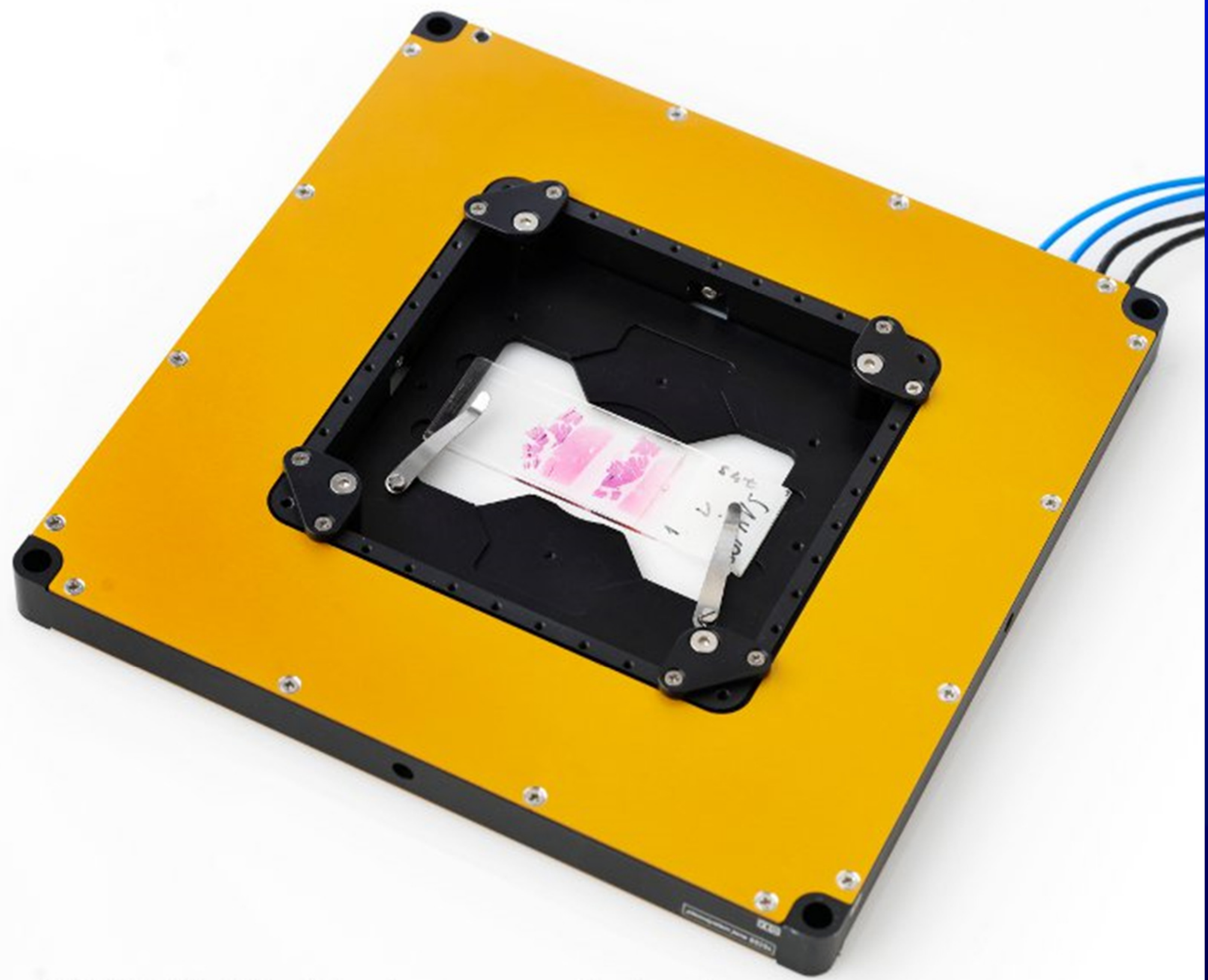
Number of pixels in a given region of normal, Barrett's and adenocarcinoma tissue in particular regions of the infrared spectrum

Problem of resolution with standard infrared microscopy

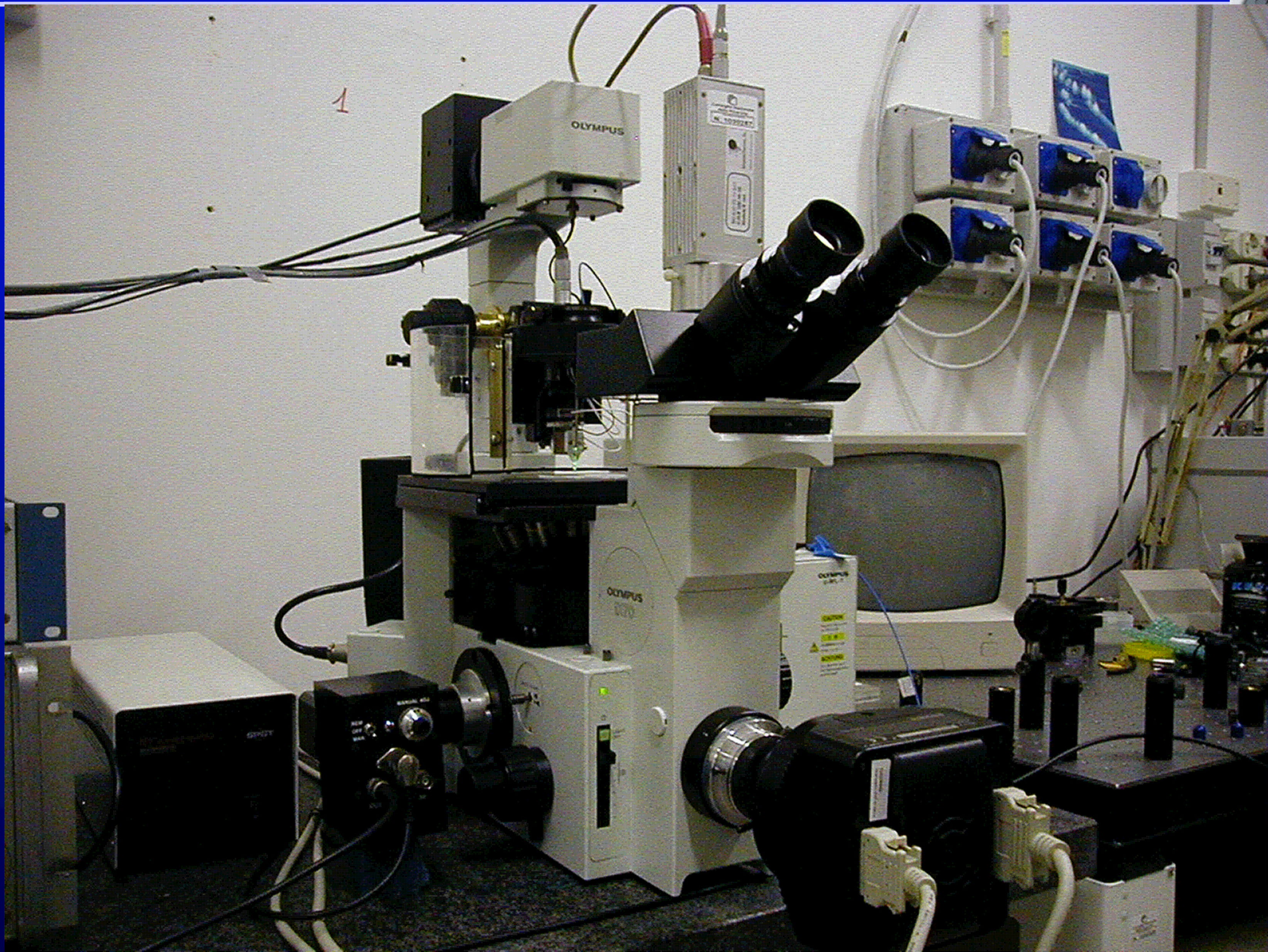
The tumor cells are localized in different and small areas (hundreds of nanometers), so if we want to prevent the desease we must look at single area: average techniques are not good enough


COHERENT





PXY 500 AP CAP with microscopy probe insert



Istituto Struttura della Materia

Technical Issues

Accelerator and IR FEL
Optimise performance of accelerator for IR FEL characteristics
Stability: intensity, frequency
Tuning: 4µm to 10µm
Macro bunch structure
ALICE 100 µs
Vanderbilt 25 µs

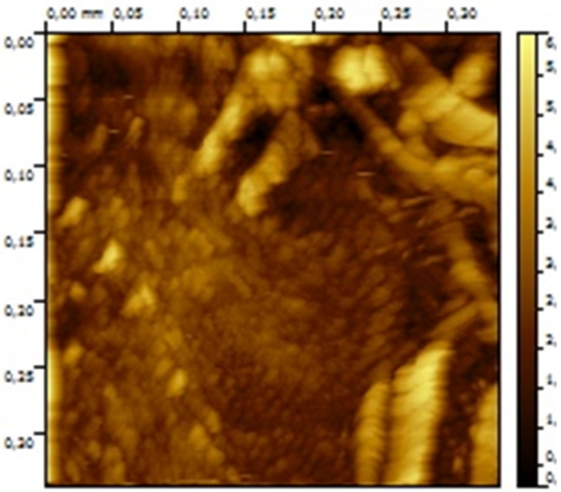
SNOM
Electronics matched to macro bunch
Control of scan
Optics: fabrication of tips
Performance
Images at different λ
10 µm x 10 µm at
0.1 µm spatial resolution
10000 points IR Intensity/stability is key

Beamline: Commissioned

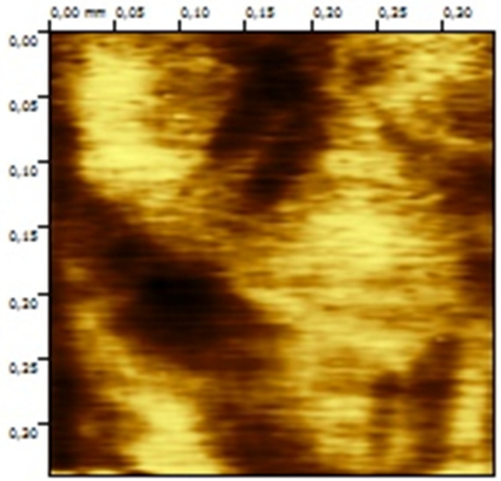
Tip
Diameter 300 µm
Aperture ~ 1 µm

Specimen
Scan 50 µm x 50 µm

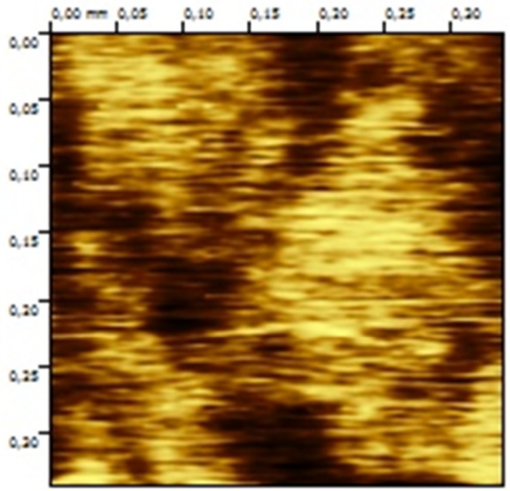
Benign cells



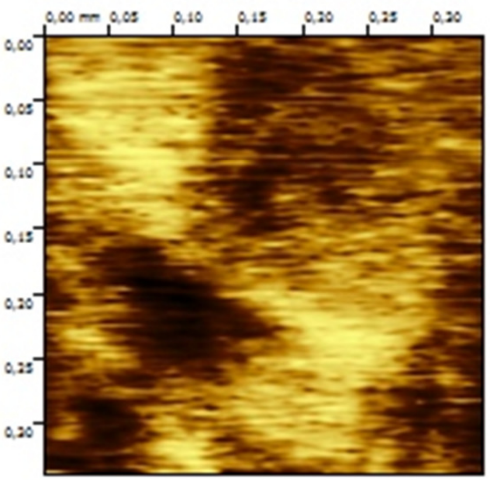
Topography



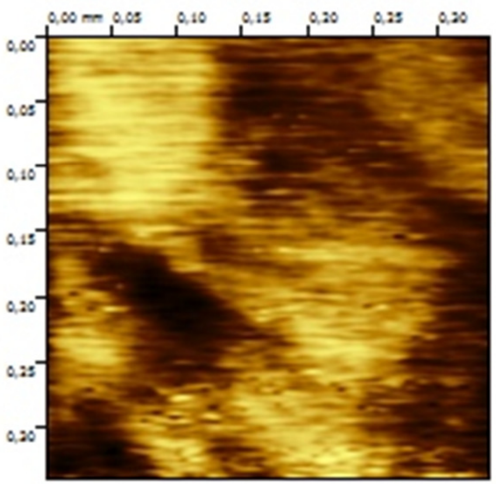
λ=8,60μ



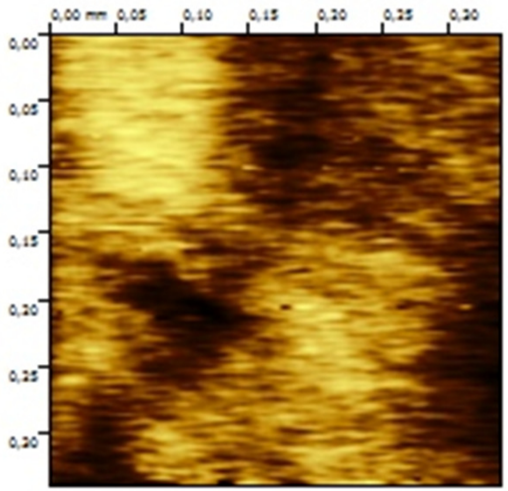
λ=8,05μ



λ=7,30μ

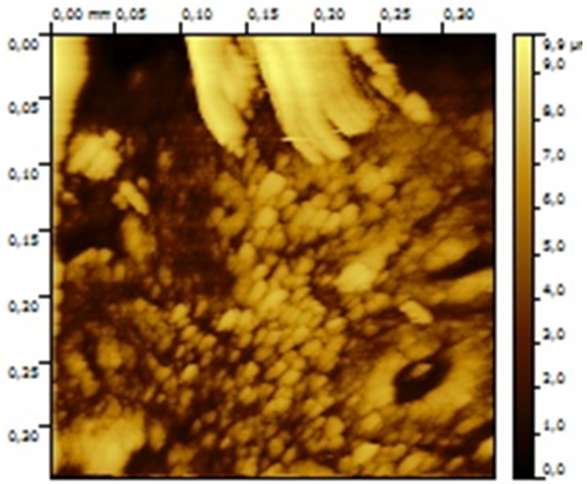


λ=7,00μ

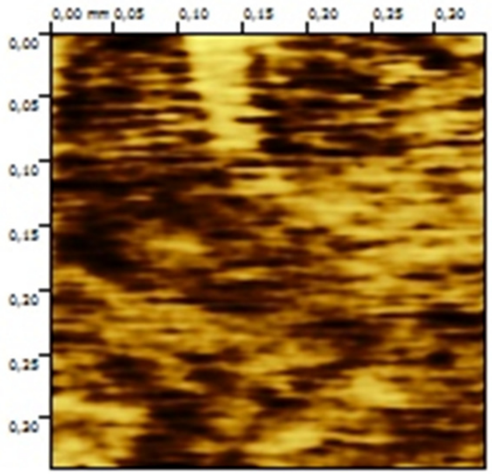


λ=6,50μ

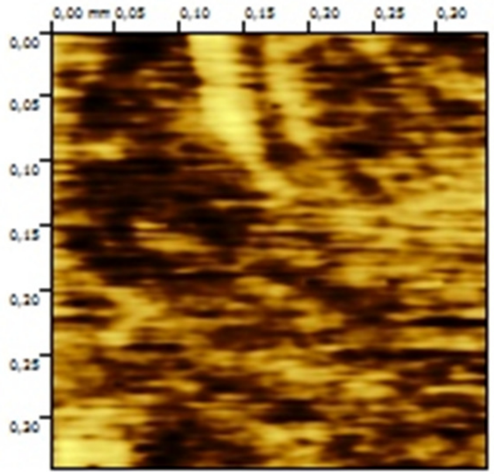
Cancer cells



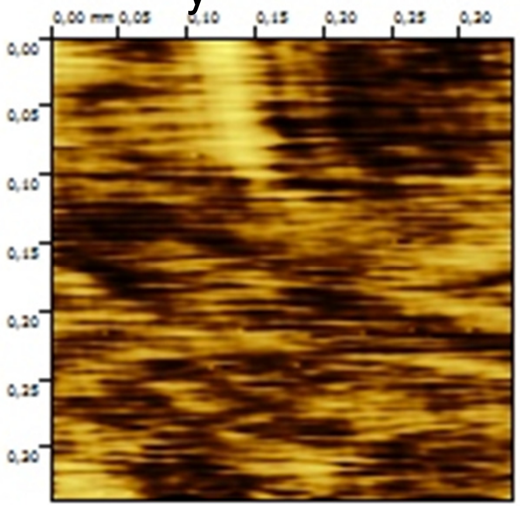
Topography



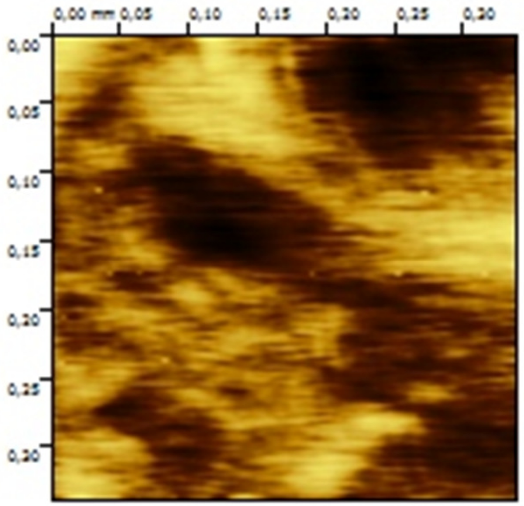
λ=8,60µ



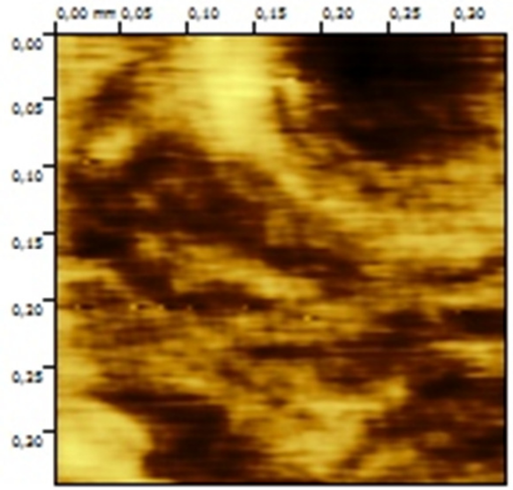
λ=8,05µ



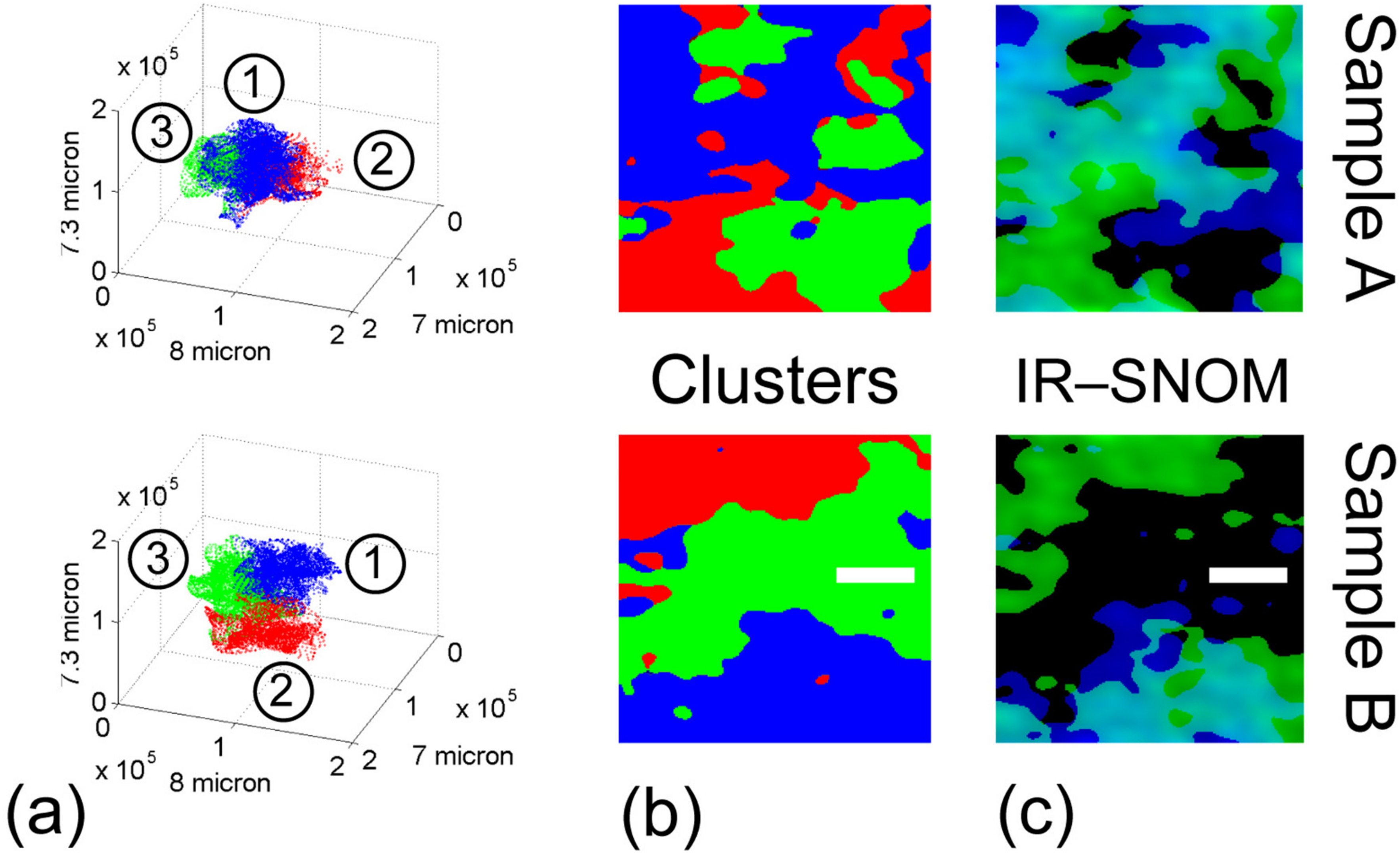
λ=7,30µ



λ=7,00µ



λ=6,50µ



x 10^5
2
1
0
7.3 micron
0
1
2
x 10^5
8 micron
0
1
2
x 10^5
7 micron
1
2
3
Clusters
IR–SNOM
Sample A
Sample B
(a)
(b)
(c)

Programme

Oesophageal Adenocarcinoma: A fast reliable diagnostic

The SNOM on the IR FEL on ALICE will provide an accurate diagnostic.

1) **Scan a wider area, 500 μm x 500 μm, at less spatial resolution**
2) **Improve signal to noise by normalisation for FEL intensity variation**
3) **Study a range of specimens from different patients: Patient variability.**
4) **Study tissue at all the stages in the progression to oesophageal cancer**

Extend research to other suitable cancers

Accelerator development

Design a low cost dedicated IR FEL (QCL) SNOM for hospitals.

Long term research programme: understand the disease - therapy

Use tissue culture facility to grow separate components of the Stroma.

SNOM studies of combinations of Stroma components to determine interactions.

ISM

M. Luce -

Cockcroft Institute

Michele Siggel-King, Gareth Holder, Andy Wolski, Swapan Chattopadhyay, Peter Weightman

ASTeC

David Dunning, Andy Smith, Mark Surman, Neil Thompson

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Andy Wolski, Swapan Chattopadhyay, Amy Schofield,

Rachel Williams (Eye and Vision Science, University of Liverpool)

Royal Liverpool and Broadgreen Hospital and University of Liverpool

Prof. Mark Pritchard, Head of Gastroenterology

Prof. Andrea Varro, Professor of Physiology

Thank you for your attention