Putting People Under the Microscope

From a world of atoms
to a world of living matter

Dr Steve Barrett FU3A 2 Nov 2022

Introduction

A World of Atoms	Imaging atoms and molecules
Perception vs Reality	Why can image analysis be such a challenge?
The Spin-Offs	Applications in earth sciences and medical sciences
A World of Living Matter	Imaging more complex systems
Investigating Cancer	Spectromicroscopy and infrared absorption

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Introduction

This talk is about images and how we look at images in a scientific context. Two concepts are important in what follows:

Image Processing > > > *Interpretation*

Image Analysis > > > *Quantification*

The talk will be illustrated with images from research projects old and new, from collaborators and from project students.

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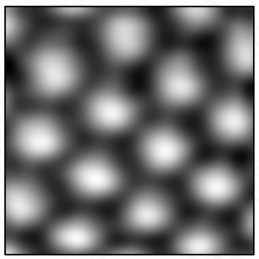
A World of Atoms



On this scale, a grain of sand would be about the size of the Moon.

" To see a world in
a grain of sand … "

William Blake

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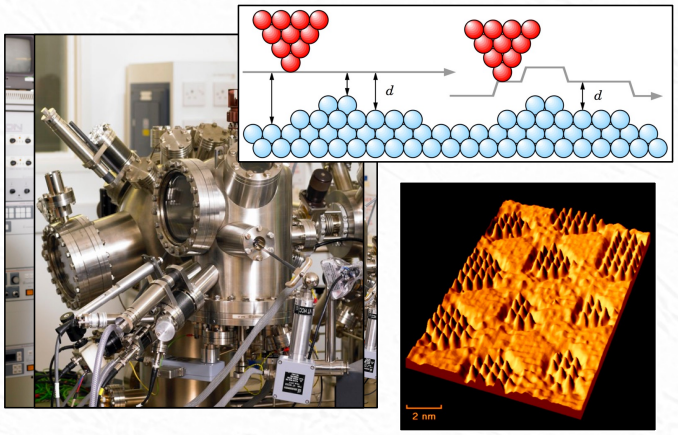
A World of Atoms



A World of Atoms

Working with STM images led to the development of image analysis software that supports various scanning microscopy systems:

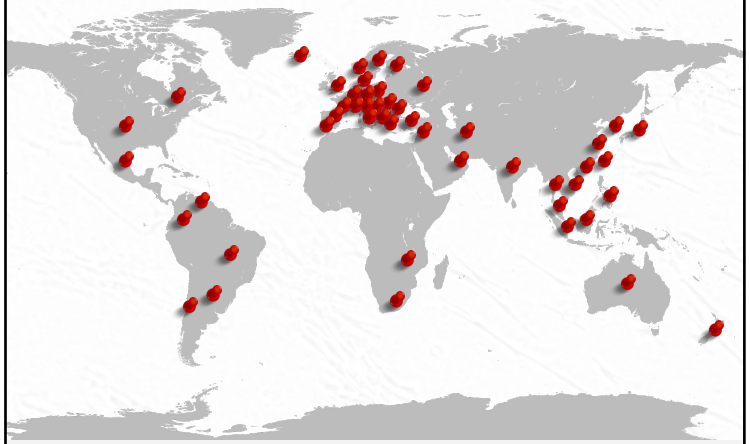
Scanning Tunnelling Microscope

Referring to any/all of these as SXM led to the unpronounceable:

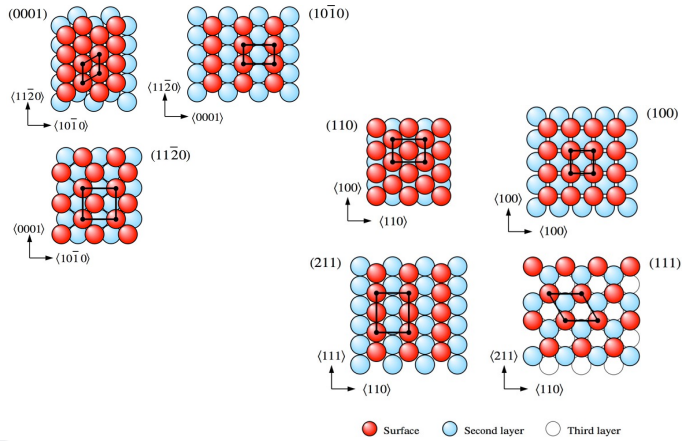
Image SXM
v 2.05
September 2022
Steve Barrett

> 50,000 downloads in the past 10 years by universities and research centres

Image SXM



A World of Atoms



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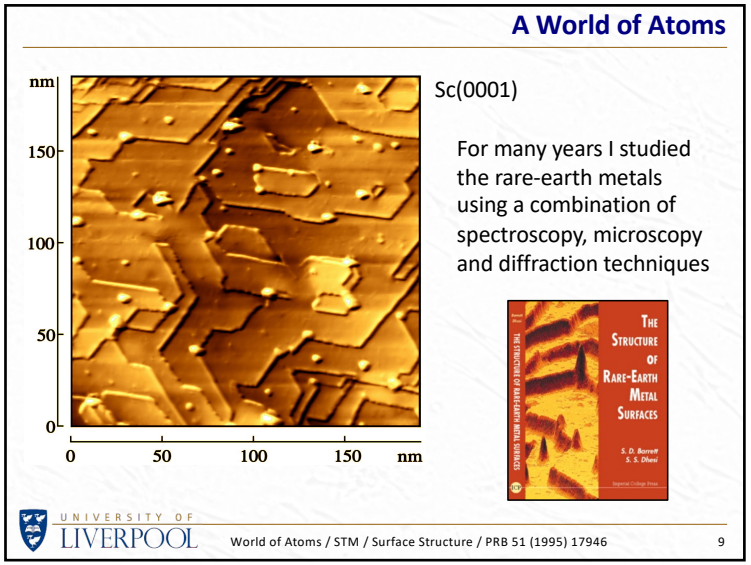
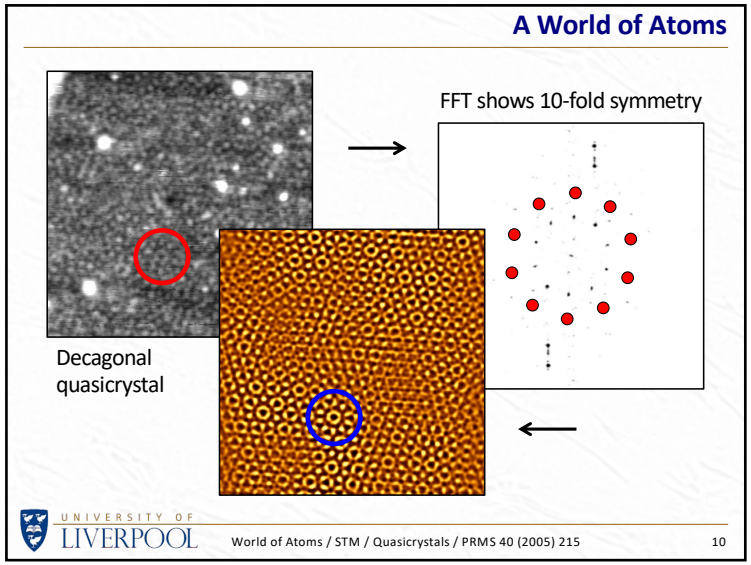
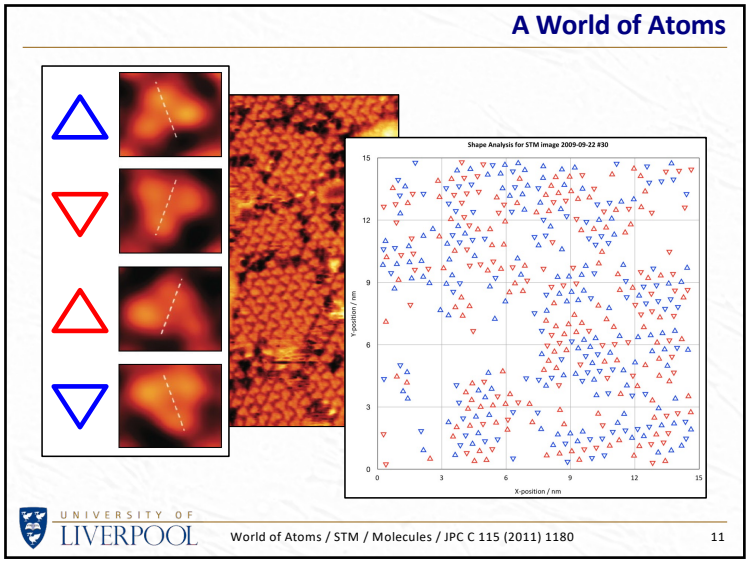
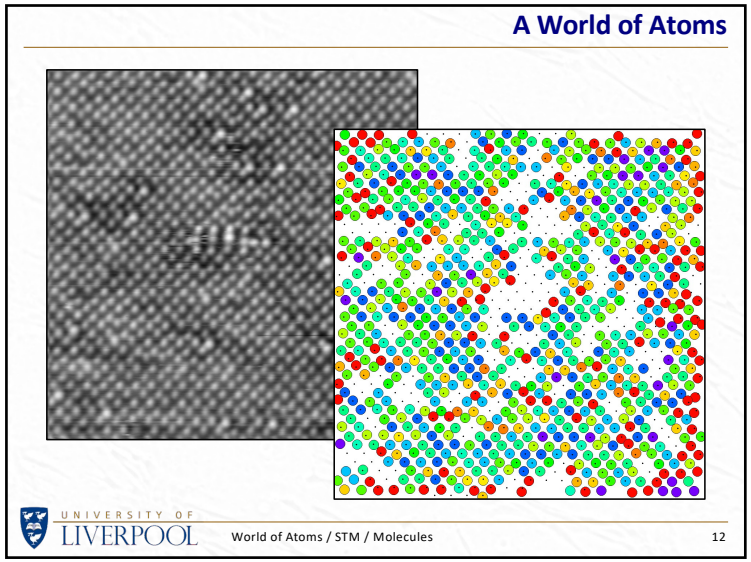








Astrophotography

The Milky Way from Kenya.
Due to the dark skies, very little image processing is required.

Astrophotography

NGC7000 North America Nebula

Single raw image

However, under the light-polluted skies of the UK, image processing can bring out hidden structures in a faint nebula.

Astrophotography

NGC7000 North America Nebula

Single raw image | 20 images stacked in *Image SXM* | Colours enhanced

A World of Atoms — Imaging atoms and molecules

Perception vs Reality — **Why can image analysis be such a challenge?**

The Spin-Offs — Applications in earth sciences and medical sciences

A World of Living Matter — Imaging more complex systems

Investigating Cancer — Spectromicroscopy and infrared absorption

Putting People Under the Microscope

Perception vs Reality

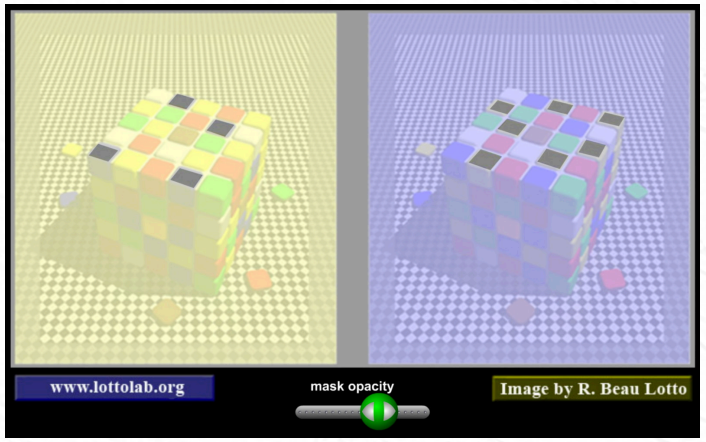
How we perceive images (what we ***see***) can be VERY different from the actual information content (what is ***there***). In most day-to-day situations we trust the former and don't worry about the latter.

Which is the better image processor?

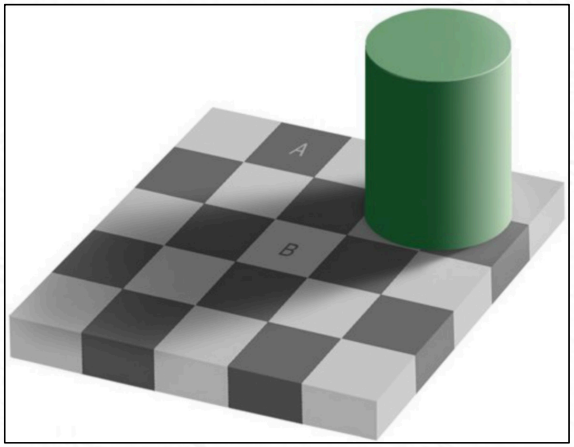
Brain vs ***Computer***

Carbon vs ***Silicon***

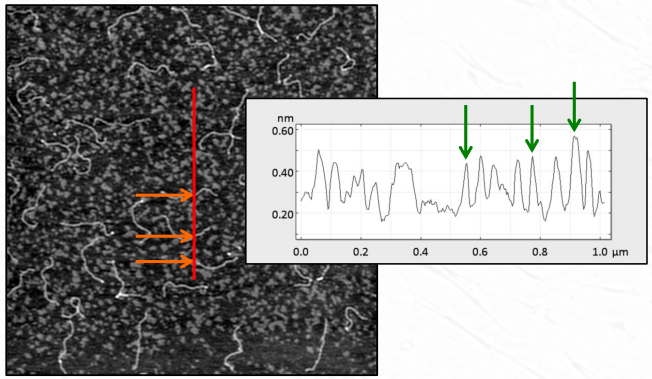
Perception vs Reality



Perception vs Reality



Perception vs Reality



DNA on glass

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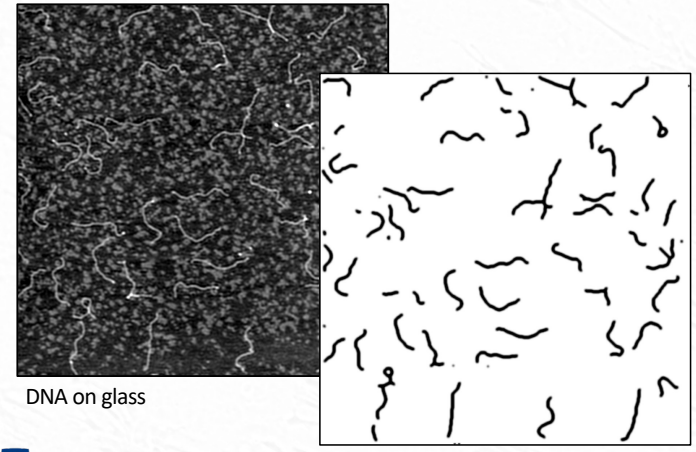
Perception vs Reality



DNA on glass

Spin-Offs

Applications to disciplines beyond physics and chemistry were a natural consequence of the interdisciplinary nature of image analysis. In particular …

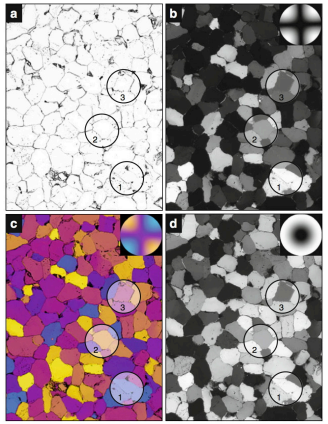
Earth Sciences — *PrinCIPia*

'Principles of Computer Integrated Polarisation Image Analysis'

Medical Sciences — MIASMA

'Microscopy Image Analysis Software for Medical Applications'

Earth Sciences



Imaging earth materials (to a physicist = 'rocks') using circularly and linearly polarised light produces colours and intensities that depend on the orientation of the crystallographic axes of the grains with respect to the optical axis of the microscope.

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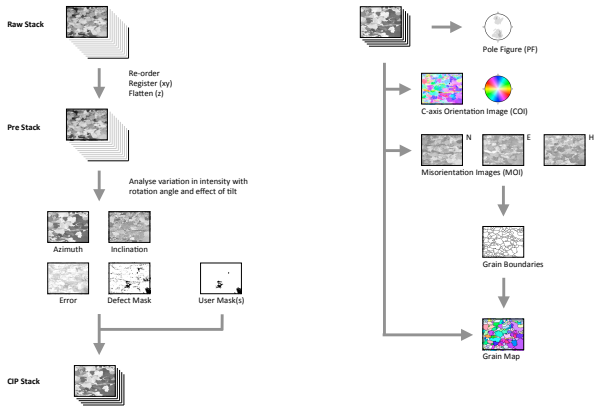
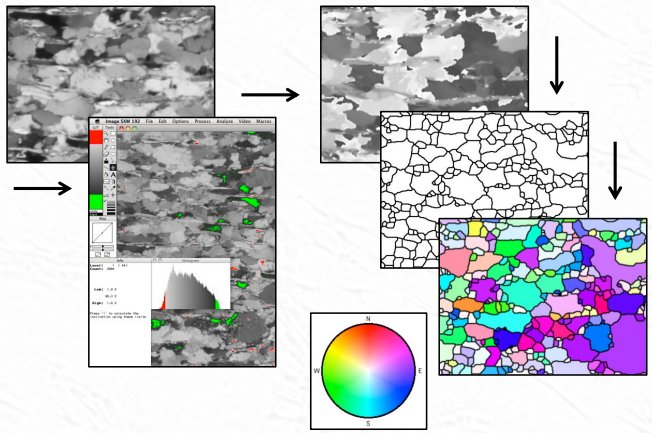
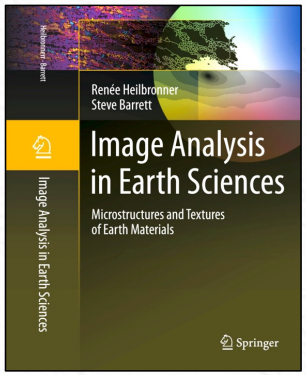
PrinCIPia



PrinCIPia



Earth Sciences

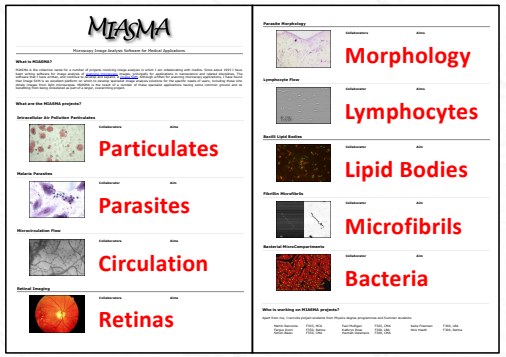


Ongoing collaboration with Professor Heilbronner at the University of Basel led to a book on Image Analysis …

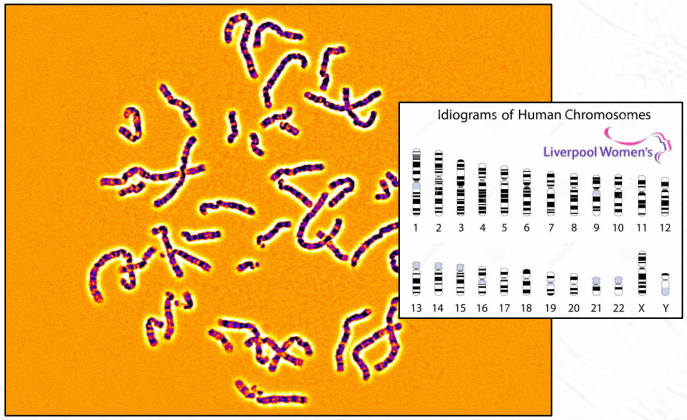
… available at a reasonable price from the author.

Medical Sciences

Medical spin-offs have expanded considerably in the past ten years:



Human Chromosomes



A World of Living Matter

Now very much in the world of living matter, we take a closer look at two research projects in which image analysis played a key role:

Microcirculation Analysis

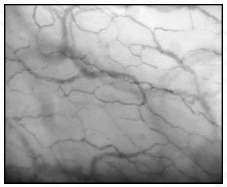
Investigation of Cancer

Microcirculation Analysis

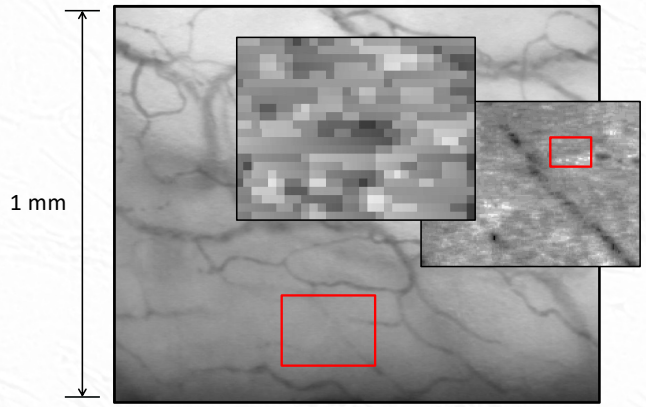
In collaboration with consultants at Alder Hey hospital, the first trials of *MIASMA* software were conducted on patients in the intensive care unit. Some of these patients suffered from meningitis, causing sepsis (aka blood poisoning).

The software quantified the flow of blood cells through a capillary network, the *microcirculation*, as imaged by a small portable microscope placed underneath the tongue of the patient.

Not so much
Putting People Under the Microscope
but rather
Putting the Microscope Under People.



Microcirculation Analysis



Microcirculation Analysis

Bear in mind that the blood vessels are invisible (as only the blood cells, containing haemoglobin, are imaged).

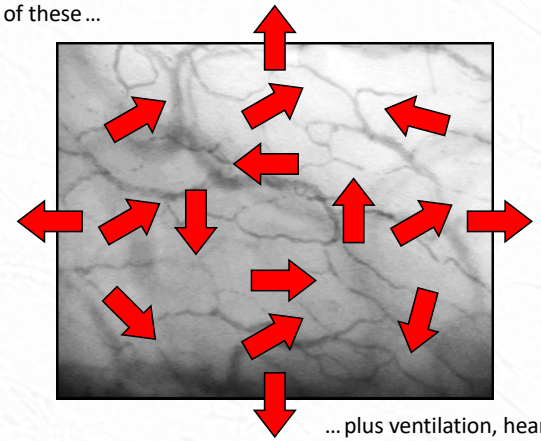
So the problem is to identify and quantify the motion of a blood cell relative to an invisible vessel in a sequence of video images that are not stable – ever tried to get a five-year old to sit still while you place a microscope under his tongue?

Any attempt at quantification will first have to deal with …

… Translation … Magnification … Rotation … Distortion …

Microcirculation Analysis

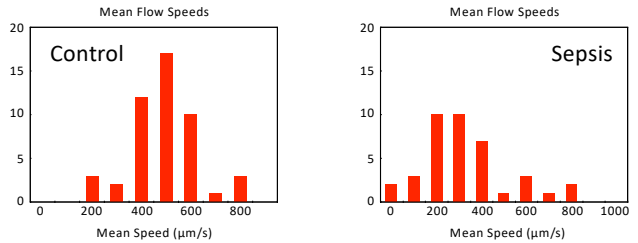
Or all of these …



… plus ventilation, heartbeat

Microcirculation Analysis

Through a combination of techniques, including cross-correlations (to stabilise the video images) and autocorrelations (to identify the motion of blood cells that are barely detectable) it is possible to quantify the blood flow speeds in vessels as small as 7 µm diameter.



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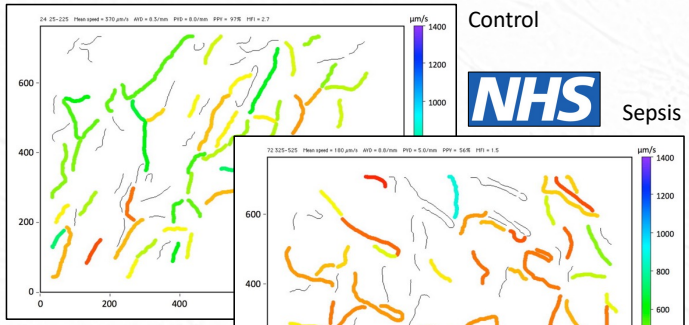
Microcirculation Analysis



Control

NHS

Sepsis

Colour-coded 'map'
of blood flow speeds

Investigating Cancer

This final section of the talk describes research funded through EPSRC and CRUK research grants:

"***Disease diagnosis through spectrochemical imaging of tissues***"

"***Early detection of oral cancer using infrared imaging***"

"***Development of a probe for the early diagnosis of cancer***"

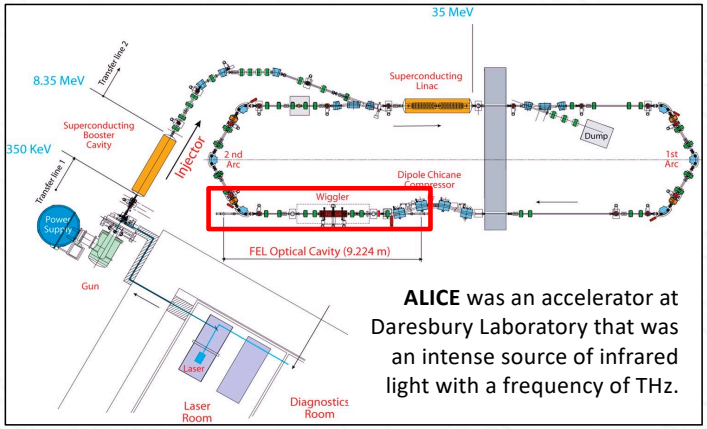
Roughly speaking, that translates to…

Can we identify an infrared absorption signature for tissue that is likely to become cancerous?

or…

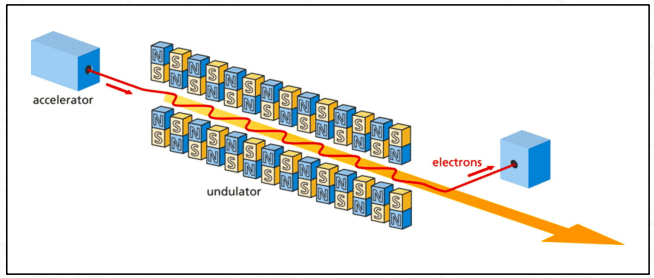
Can we detect cancer before it is cancer?

Free-Electron Laser



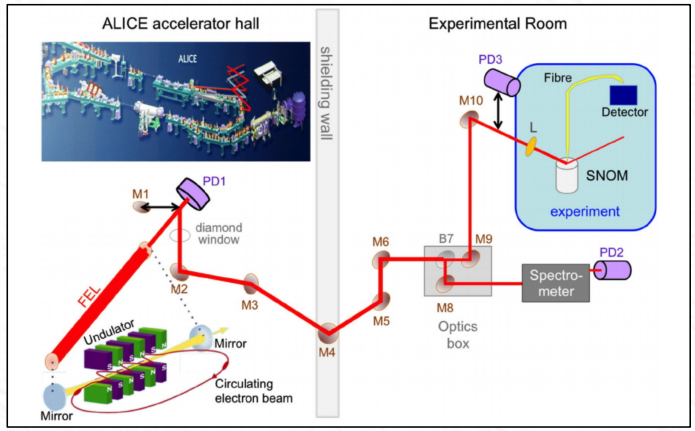
ALICE was an accelerator at Daresbury Laboratory that was an intense source of infrared light with a frequency of THz.

Free-Electron Laser

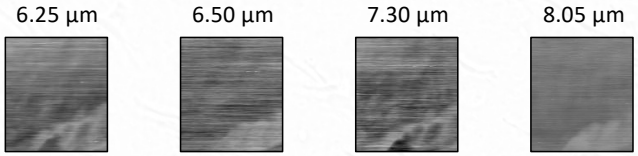


An array of magnets with alternating N-S orientation causes the electron beam to 'wiggle' and emit intense beams of synchrotron radiation. The strength and period of the magnet array determines the wavelength of the emitted radiation.

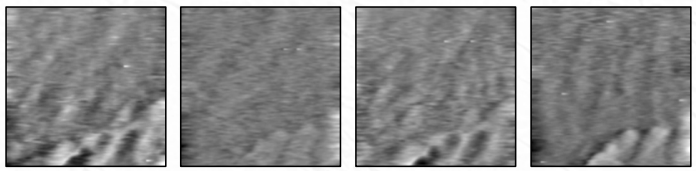
Free-Electron Laser



Scanning Near-field Optical Microscopy

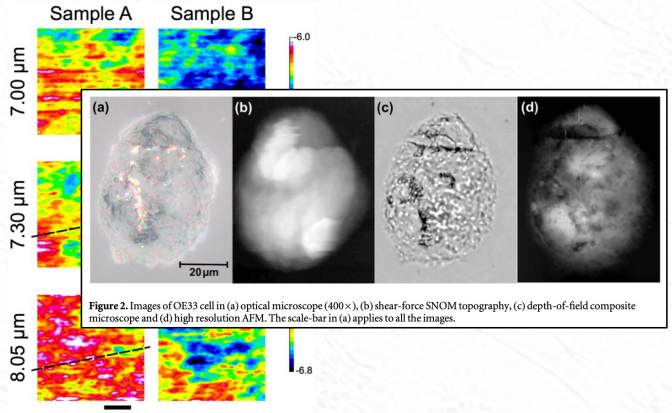


Raw images as acquired by the SNOM at different IR wavelengths

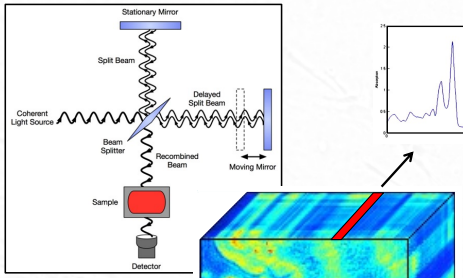


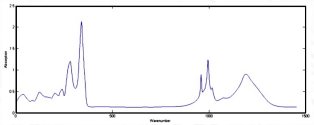
Processed to remove artefacts and make features easier to see

SNOM Imaging



Investigating Cancer





An infrared absorption spectrum at every pixel

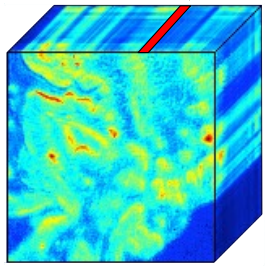


Image with spatial resolution ~5 µm

Question: Can we use the IR absorption at different wavelengths to identify the tissue type?

Image Fusion

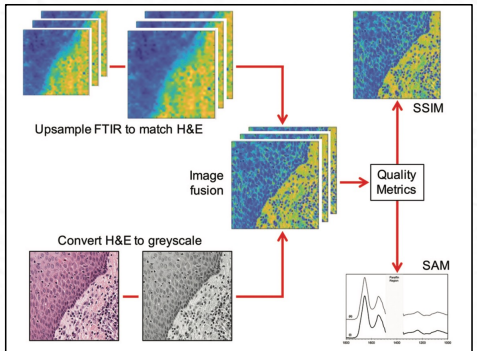
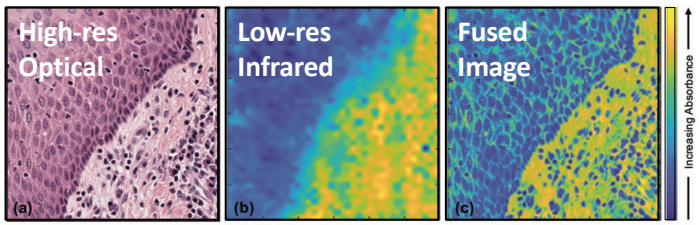


Fig. 1 Flow diagram of the fusion process. After fusion the quality metrics are calculated for the images (structural similarity index measure, SSIM) and the spectra (spectral angle mapper, SAM).

Image Fusion

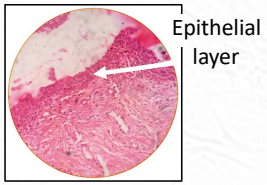


Tissue Types

What type of tissue are we studying?

Epithelium tissue covers all surfaces of the human body. This means not just your skin …

… but also the oesophagus and mouth.



After studying oesophageal cancer cells we are now focussing on oral epithelial dysplasia (OED) – changes in the cells that make up the lining of the mouth.

In particular, we want to improve the accuracy of prognosis so that we can say if a lesion found in the mouth will, or won't, progress to cancer.

LDIR Wand

SciaScan

Spectro Chemical Infrared Analysis Scan For Cancer

LDIR wand

Summary

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EPSRC Pioneering research and skills
NHS

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