

Imaging Atoms, Molecules and Cells

**Imaging Atoms,
Molecules and Cells**

**From a world of atoms
to a world of living matter**

Dr Steve Barrett **DU3A 15 Mar 2024**

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

UNIVERSITY OF LIVERPOOL

2

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**

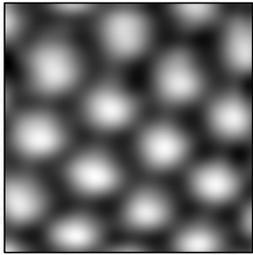
Image Analysis >>> **Quantification**

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

UNIVERSITY OF LIVERPOOL

3

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

UNIVERSITY OF LIVERPOOL

World of Atoms

4

Imaging Atoms, Molecules and Cells

A World of Atoms

UNIVERSITY OF LIVERPOOL
World of Atoms / Scanning Tunnelling Microscope

5

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
December 2023
Steve Barrett

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

UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Software

6

Image SXM

UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Software / Image SXM

7

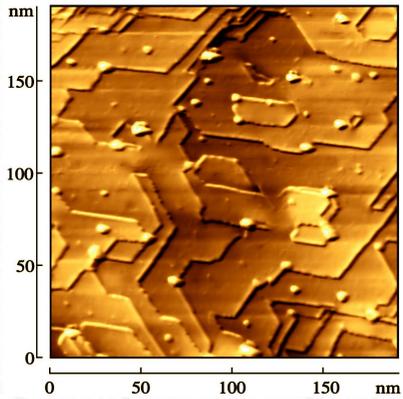
A World of Atoms

UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Surface Structure

8

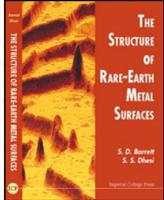
Imaging Atoms, Molecules and Cells

A World of Atoms



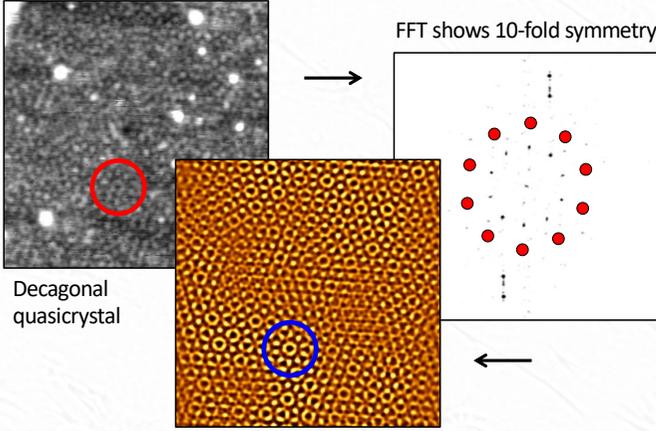
Sc(0001)

For many years I studied the rare-earth metals using a combination of spectroscopy, microscopy and diffraction techniques



UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Surface Structure / PRB 51 (1995) 17946 9

A World of Atoms

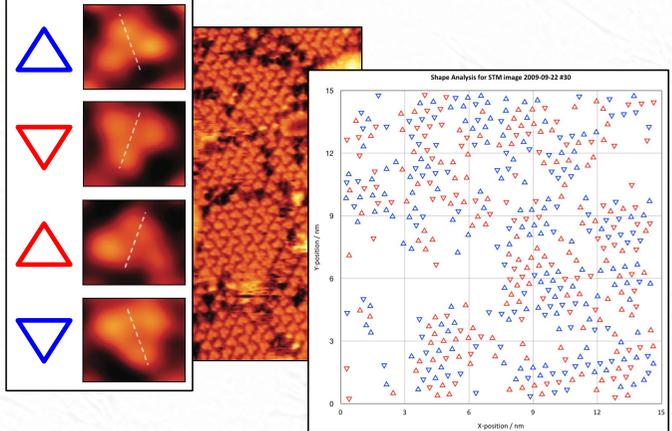


Decagonal quasicrystal

FFT shows 10-fold symmetry

UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Quasicrystals / PRMS 40 (2005) 215 10

A World of Atoms



Shape Analysis for STM image 2009-09-22 #30

UNIVERSITY OF LIVERPOOL
World of Atoms / STM / Molecules / JPC C 115 (2011) 1180 11

Astrophotography



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

UNIVERSITY OF LIVERPOOL
Beyond Microscopy / Astrophotography 12

Imaging Atoms, Molecules and Cells

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.

 UNIVERSITY OF LIVERPOOL
Beyond Microscopy / Astrophotography 13

Astrophotography

NGC7000 North America Nebula



Single raw image 20 images stacked in Image SXM Colours enhanced

 UNIVERSITY OF LIVERPOOL
Beyond Microscopy / Astrophotography 14

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

 UNIVERSITY OF LIVERPOOL
15

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?

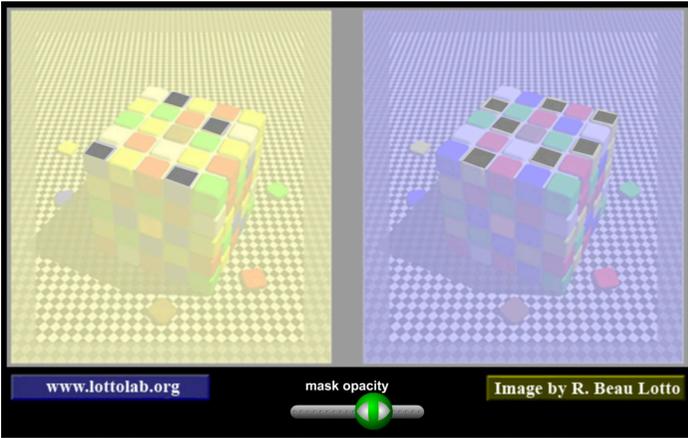
Brain vs **Computer**

Carbon vs **Silicon**

 UNIVERSITY OF LIVERPOOL
Perception vs Reality 16

Imaging Atoms, Molecules and Cells

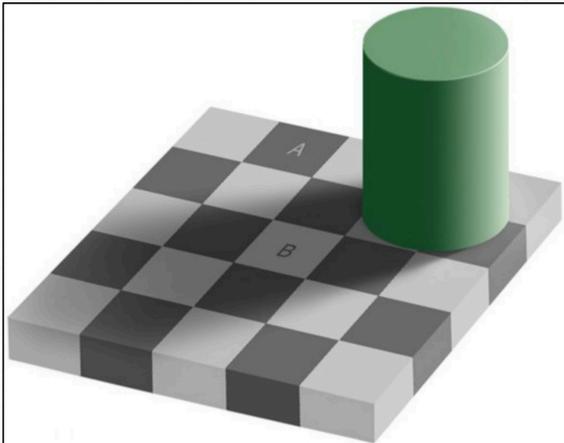
Perception vs Reality



www.loftolab.org mask opacity Image by R. Beau Lotto

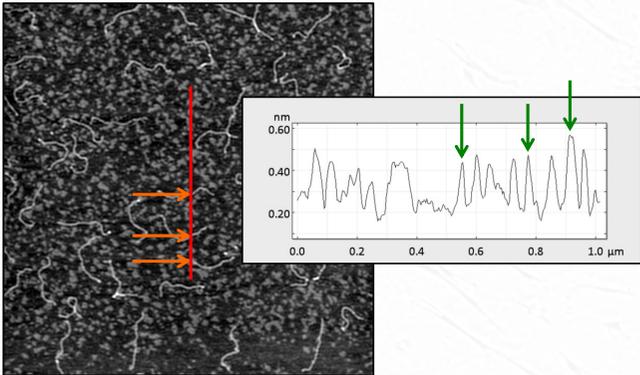
UNIVERSITY OF LIVERPOOL Perception vs Reality / Colour Perception 17

Perception vs Reality



UNIVERSITY OF LIVERPOOL Perception vs Reality / Grey Perception 18

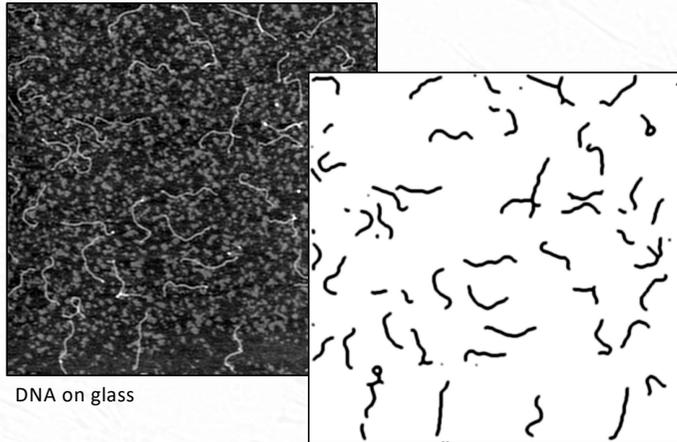
Perception vs Reality



DNA on glass

UNIVERSITY OF LIVERPOOL Perception vs Reality / Wood For the Trees 19

Perception vs Reality



DNA on glass

UNIVERSITY OF LIVERPOOL Perception vs Reality / Wood For the Trees 20

Imaging Atoms, Molecules and Cells

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**



21

Spin-Offs

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

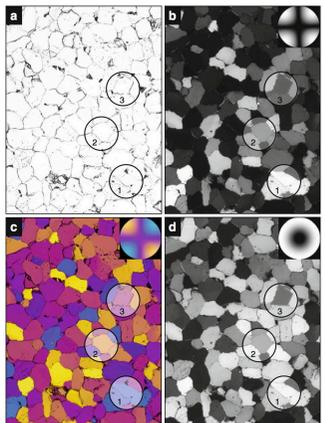
Earth Sciences *PrinCIPIa*
'Principles of Computer Integrated Polarisation Image Analysis'

Medical Sciences *MIASMA*
'Microscopy Image Analysis Software for Medical Applications'



Spin-Offs 22

Earth Sciences

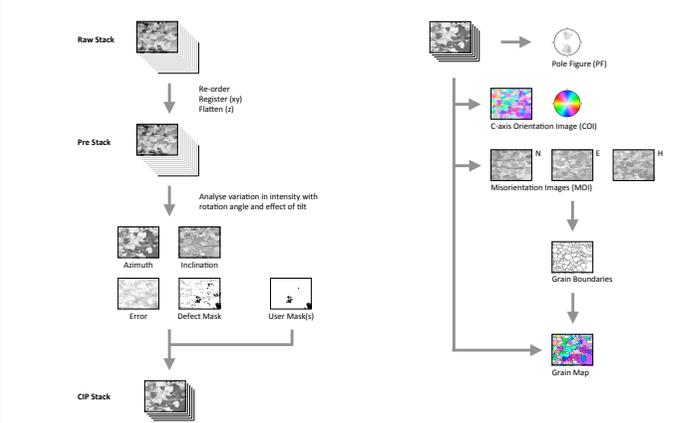


Imaging earth materials (to a physicist = 'rocks') using circularly and linearly polarised light produces colours and intensities that depend on the orientation of the crystallographic axes of the grains with respect to the optical axis of the microscope.



Spin-Offs / Earth Sciences 23

PrinCIPIa




Spin-Offs / Earth Sciences / PrinCIPIa 24

Imaging Atoms, Molecules and Cells

PrinCIpia

UNIVERSITY OF LIVERPOOL Spin-Offs / Earth Sciences / PrinCIpia 25

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.

UNIVERSITY OF LIVERPOOL Spin-Offs / Earth Sciences 26

Medical Sciences

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

<p>MIASMA Primary Image Analysis Software for Medical Applications</p> <p>What is MIASMA? MIASMA is a software package for image analysis of medical images. It is designed to be easy to use and to provide a wide range of analysis tools. It is available for Windows and Linux.</p> <p>What are the MIASMA projects? MIASMA is a software package for image analysis of medical images. It is designed to be easy to use and to provide a wide range of analysis tools. It is available for Windows and Linux.</p> <p>MIASMA projects:</p> <ul style="list-style-type: none"> Particulates Parasites Circulation Retinas 	<p>MIASMA projects:</p> <ul style="list-style-type: none"> Morphology Lymphocytes Lipid Bodies Microfibrils Bacteria <p>MIASMA projects:</p> <ul style="list-style-type: none"> MIASMA projects MIASMA projects MIASMA projects MIASMA projects MIASMA projects
---	---

UNIVERSITY OF LIVERPOOL Spin-Offs / Medical Sciences / MIASMA / Acta Bio. 10 (2014) 4843 27

Human Chromosomes

UNIVERSITY OF LIVERPOOL Spin-Offs / Medical Sciences / Chromosomes 28

Imaging Atoms, Molecules and Cells

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**

UNIVERSITY OF LIVERPOOL 29

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

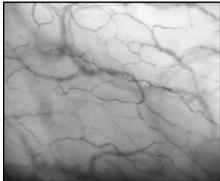
UNIVERSITY OF LIVERPOOL World of Living Matter 30

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).

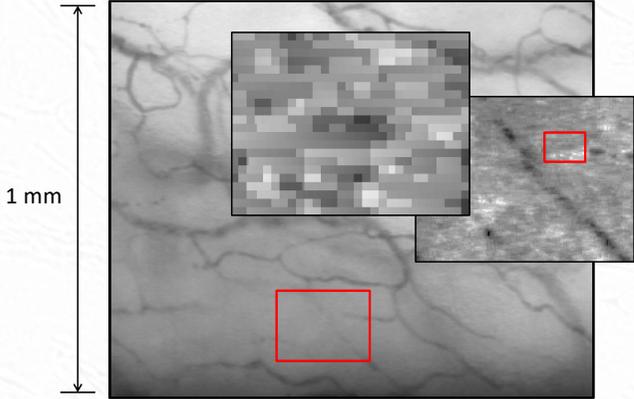
The software quantified the flow of blood cells through a capillary network, the *microcirculation*, as imaged by a small portable microscope placed underneath the tongue of the patient.

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



UNIVERSITY OF LIVERPOOL World of Living Matter / Microcirculation Analysis 31

Microcirculation Analysis



UNIVERSITY OF LIVERPOOL World of Living Matter / Microcirculation Analysis 32

Imaging Atoms, Molecules and Cells

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?

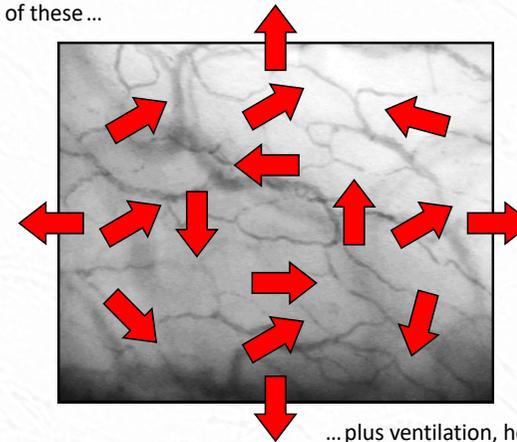
Any attempt at quantification will first have to deal with ...

... Translation ... Magnification ... Rotation ... Distortion ...



Microcirculation Analysis

Or all of these ...

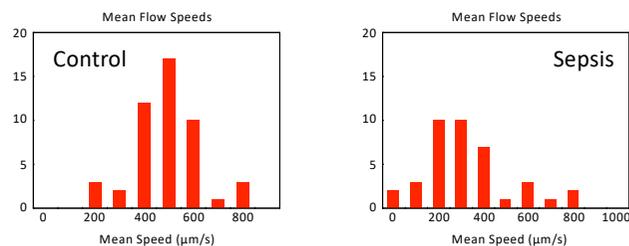


... plus ventilation, heartbeat

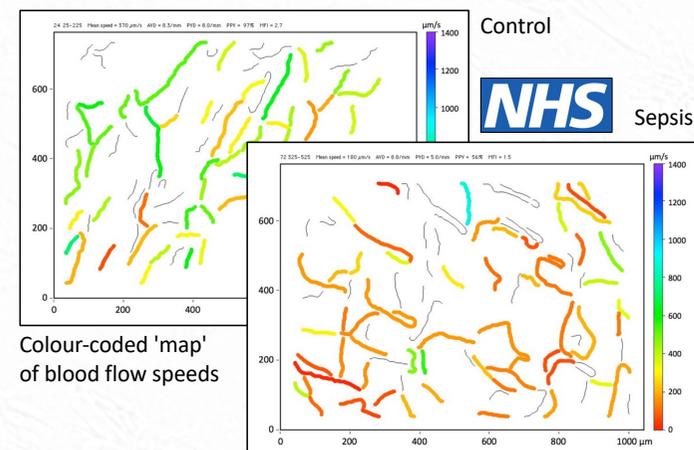


Microcirculation Analysis

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.



Microcirculation Analysis



Imaging Atoms, Molecules and Cells

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**



37

Investigating Cancer

This final section of the talk describes research funded through EPSRC, CRUK and NIHR research grants.

The main aim is to answer the question ...

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

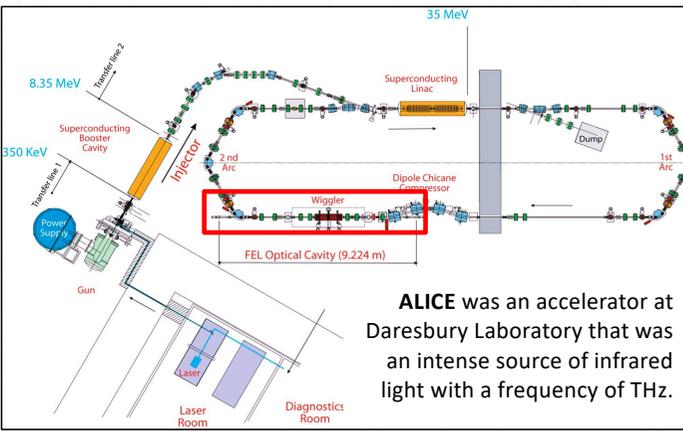
Or ...

Can we detect cancer before it is cancer?



World of Living Matter / Investigating Cancer 38

Free-Electron Laser

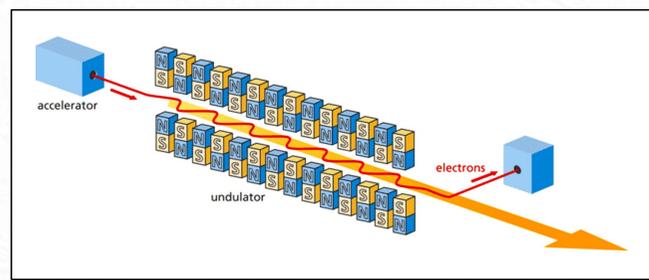


ALICE was an accelerator at Daresbury Laboratory that was an intense source of infrared light with a frequency of THz.



World of Living Matter / Investigating Cancer / SNOM / ALICE FEL 39

Free-Electron Laser

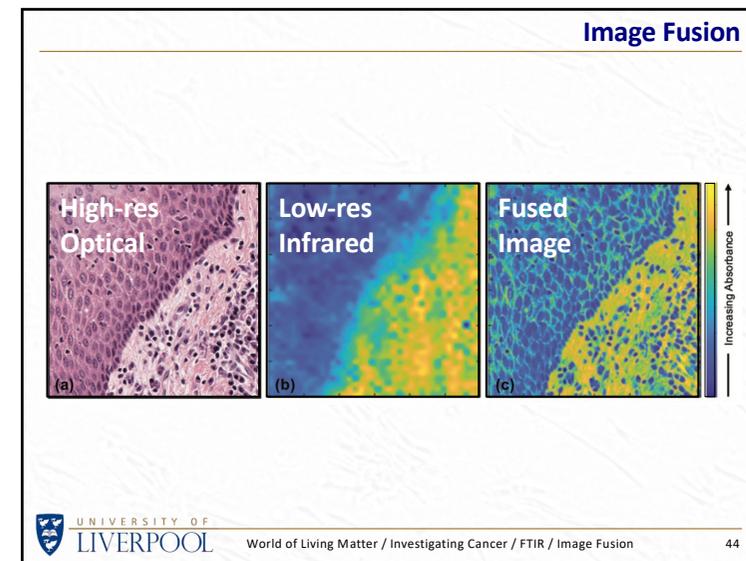
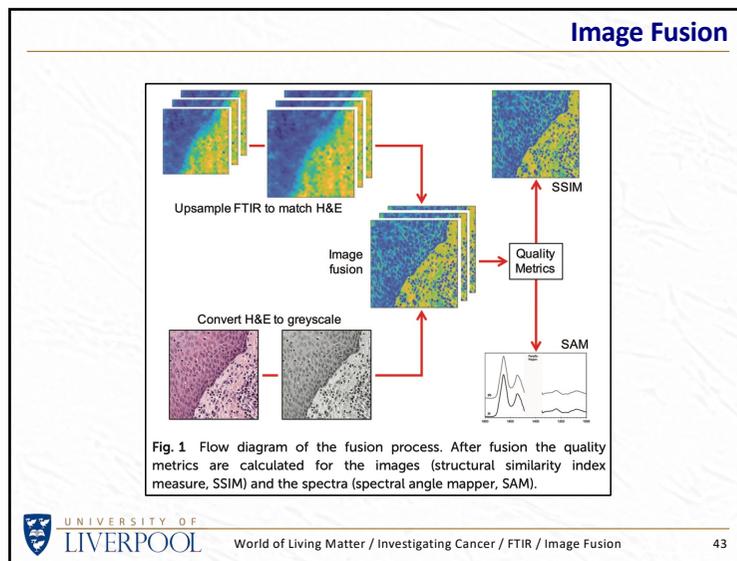
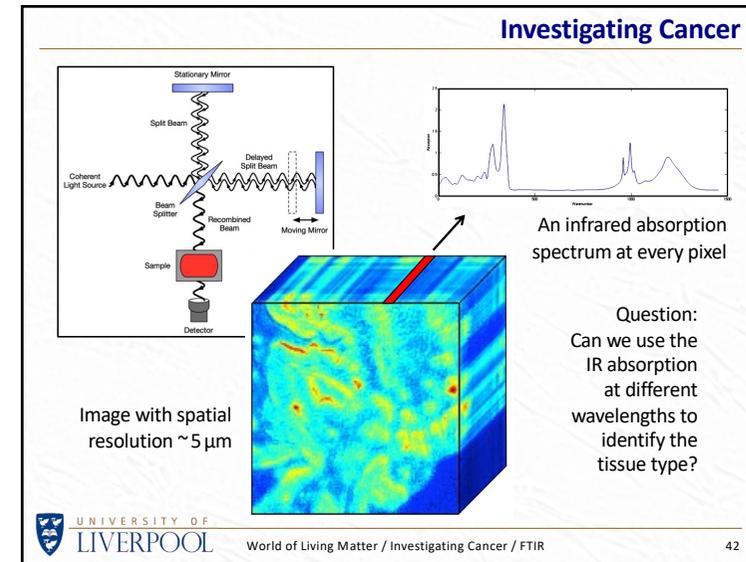
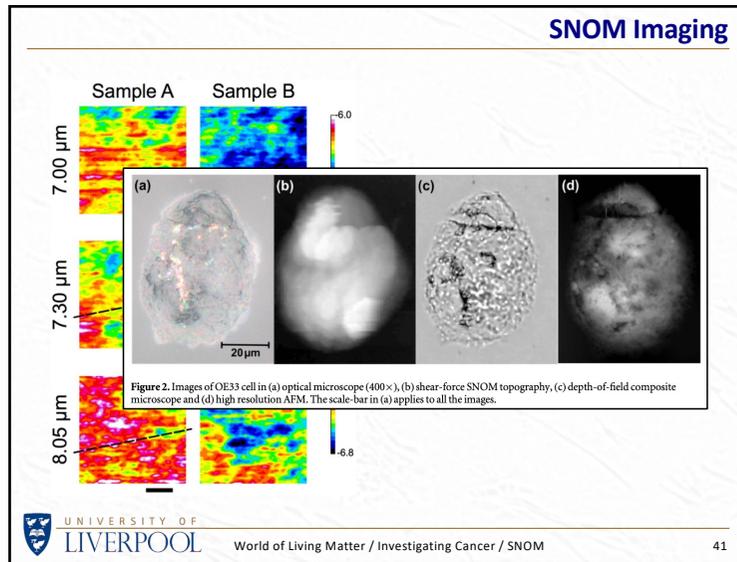


An array of magnets with alternating N-S orientation causes the electron beam to 'wobble' and emit intense beams of synchrotron radiation. The strength and period of the magnet array determines the wavelength of the emitted radiation.



World of Living Matter / Investigating Cancer / SNOM / ALICE FEL 40

Imaging Atoms, Molecules and Cells



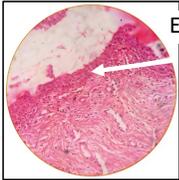
Imaging Atoms, Molecules and Cells

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.



Epithelial layer

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.

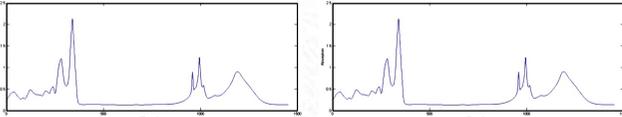
UNIVERSITY OF LIVERPOOL
World of Living Matter / Investigating Cancer / Tissue Types 45

Transforming or Non-Transforming?

Two oral lesions ... one will transform to cancer, the other won't.



But which is which?



UNIVERSITY OF LIVERPOOL
World of Living Matter / Investigating Cancer / Transformation 46

Artificial Intelligence

Training AI

Horse Octopus Dog



UNIVERSITY OF LIVERPOOL
World of Living Matter / Investigating Cancer / AI 47

Artificial Intelligence

Validating AI



Octopus Horse Octopus



UNIVERSITY OF LIVERPOOL
World of Living Matter / Investigating Cancer / AI 48

Imaging Atoms, Molecules and Cells

LDIR Wand



SciaScan
Spectro Chemical Infrared Analysis Scan For Cancer





UNIVERSITY OF LIVERPOOL World of Living Matter / Investigating Cancer / LDIR Wand 49

Summary

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

UNIVERSITY OF LIVERPOOL 50

Acknowledgements

<p>UoL staff David Martin, Andy Wolski</p> <p>UoL students Safaa Al Jedani, Thiazzi Anakrazia, Tim Craig, Barney Ellis, James Ingham, Marion Leibl, Sean Littlewood, Graham Smith, Conor Whitley</p> <p>SCANCan Collaboration Michele Siggel-King (UoL), Antonio Cricenti, Marco Luce (Rome)</p> <p>SciaScan Collaboration Paul Harrison, James Ingham, Caroline McCarthy, Janet Risk, Richard Shaw, Caroline Smith, Asterios Triantafyllou, Paul Unsworth, Peter Weightman</p> <p>ASTeC staff Mark Surman Neil Thompson</p>	<p>MIASMA Riaz Akhtar, Laura Burgess, Enitan Carroll, Rebecca Clements, Liz Laird, Luning Liu, Naga Puppala, Richard Sarginson, Richard Wilkes, Yalin Zheng</p> <p>PrinCIPIa Renée Heilbronner, Rüdiger Kilian</p> <div style="text-align: center;"></div> <div style="display: flex; justify-content: space-around;"><div style="text-align: center;"></div><div style="text-align: center;"></div></div> <div style="display: flex; justify-content: space-around;"><div style="text-align: center;"></div><div style="text-align: center;"></div><div style="text-align: center;"></div></div>
---	---

UNIVERSITY OF LIVERPOOL 51

Imaging Atoms, Molecules and Cells

www.liverpool.ac.uk/~sdb/Talks

Dr Steve Barrett **DU3A 15 Mar 2024**