

Recording You are viewing Mioara Larion's screen View Options

ONLINE WORKSHOP | FEBRUARY 26, 2021

SINGLE CELL METABOLOMICS WORKSHOP

ORGANIZED BY:
 Rima Kaddurah-Daouk, *Duke University*
 Jennifer Kirwan, *Berlin Institute of Health*
 Andrew N. Lane, *University of Kentucky*
 Mioara Larion, *National Cancer Institute*

PROGRAM

10:00 Welcome and Introduction Rima Kaddurah-Daouk, *Duke University*

Session I Chair: Mioara Larion, *National Cancer Institute*

10:05 "Single cell metabolomics for biomedical and drug research"
 Thomas Hankemeier & Ahmed Ali, *University of Leiden*

10:35 "High throughput metabolomics of individual cells in the brain"
 Jonathan Sweedler, *University of Illinois Urbana-Champaign*

11:05 "Optical methodologies to characterize the metabolic underpinnings of breast cancer"
 Nimmi Ramanujam, *Duke University*

11:35 Break


Session II Chair: Jennifer Kirwan, *Berlin Institute of Health*


11:55 "Towards super-resolution metabolic imaging using mass spectrometry imaging"
 Ian Gilmore, *National Physical Laboratory, London*


12:25 "Integrative approaches to study cancer and immune cell metabolism"
 Shawn Davidson, *Princeton University*

General Discussion Chair: Jonathan Sweedler, *University of Illinois Urbana-Champaign*

12:55 Discussants: S. Davidson, I. Gilmore, T. Hankemeier, I. Lanekoff, L-I. McCall, N. Ramanujam, J. Sweedler

Sponsored by:


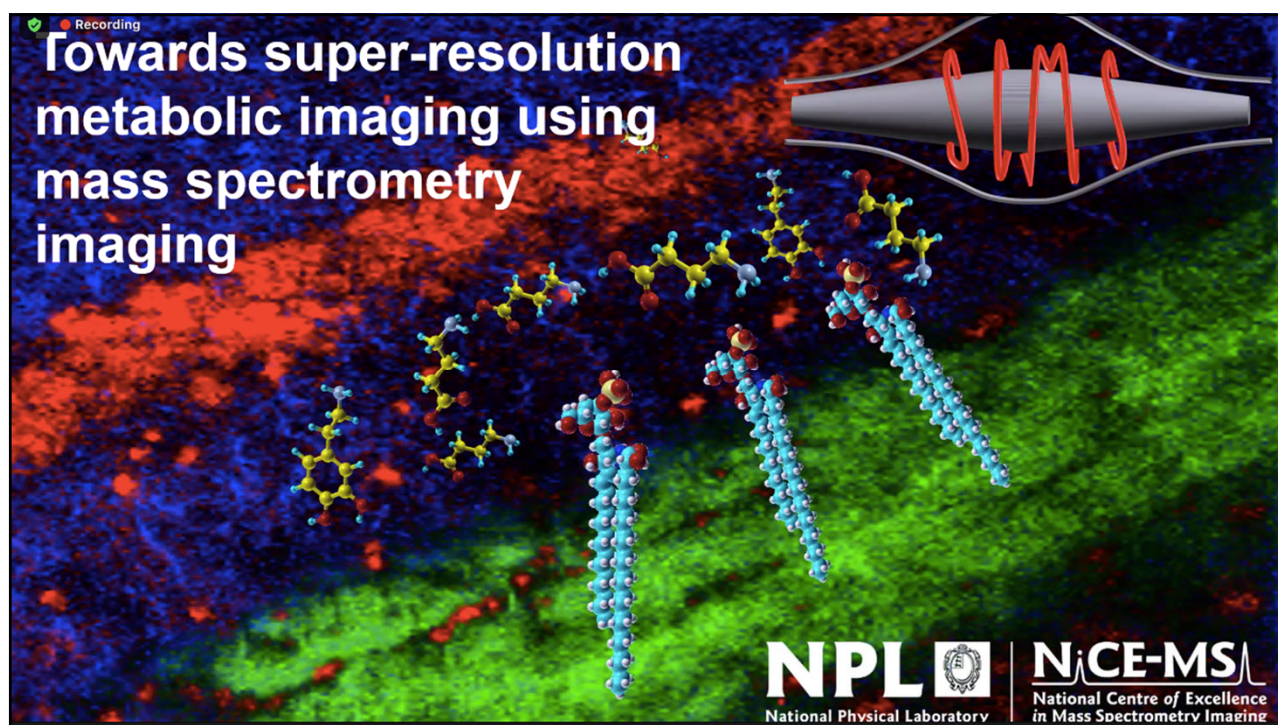
Metabolomics Association of North America




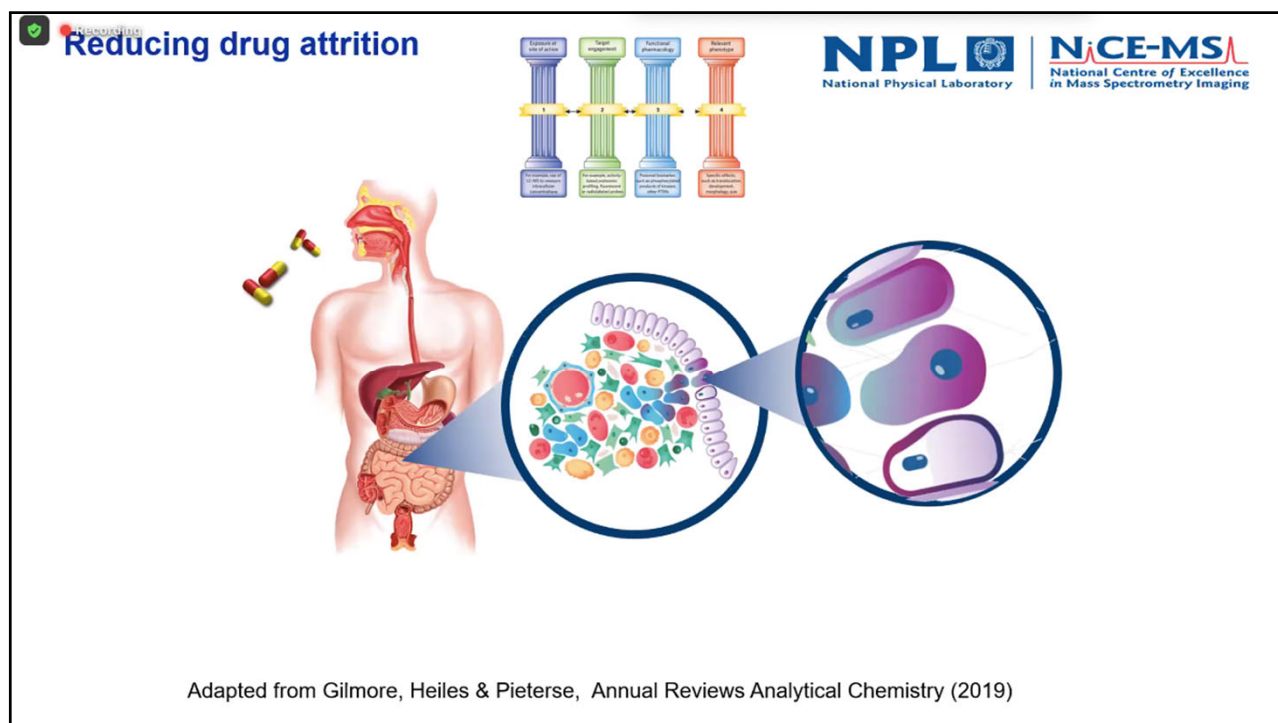
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Ian Gilmore
National Physical Laboratory, UK

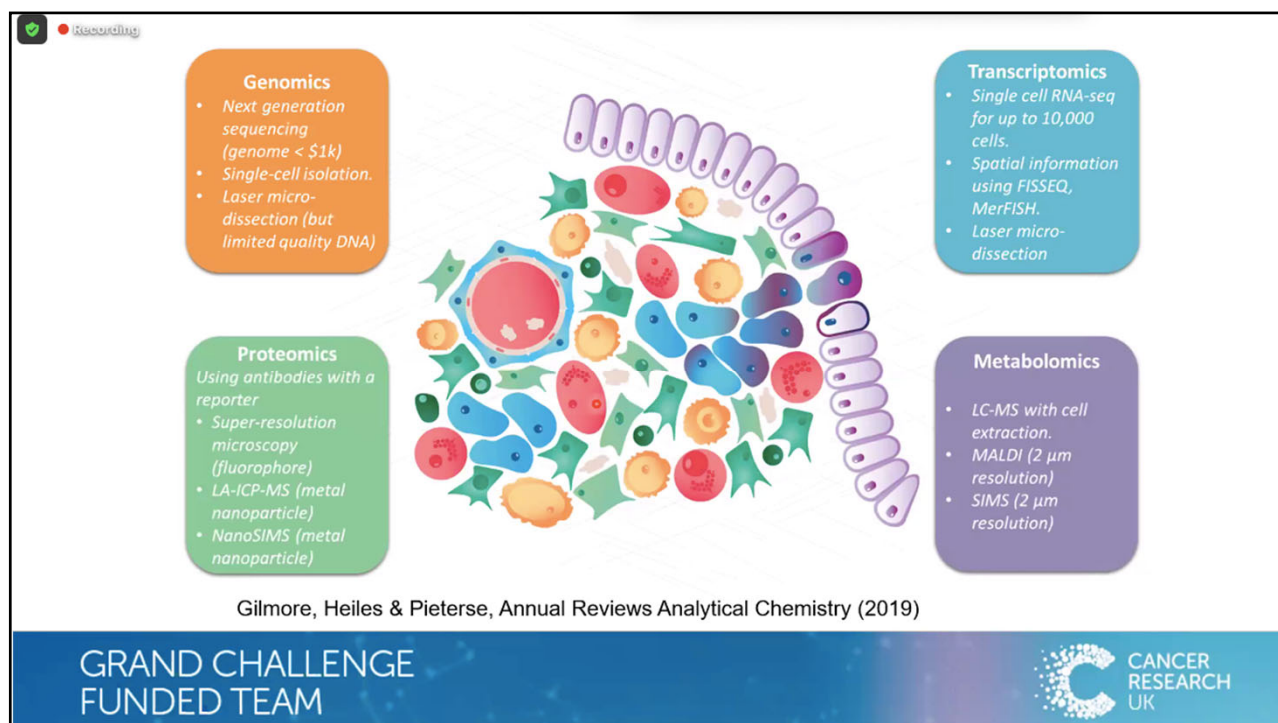
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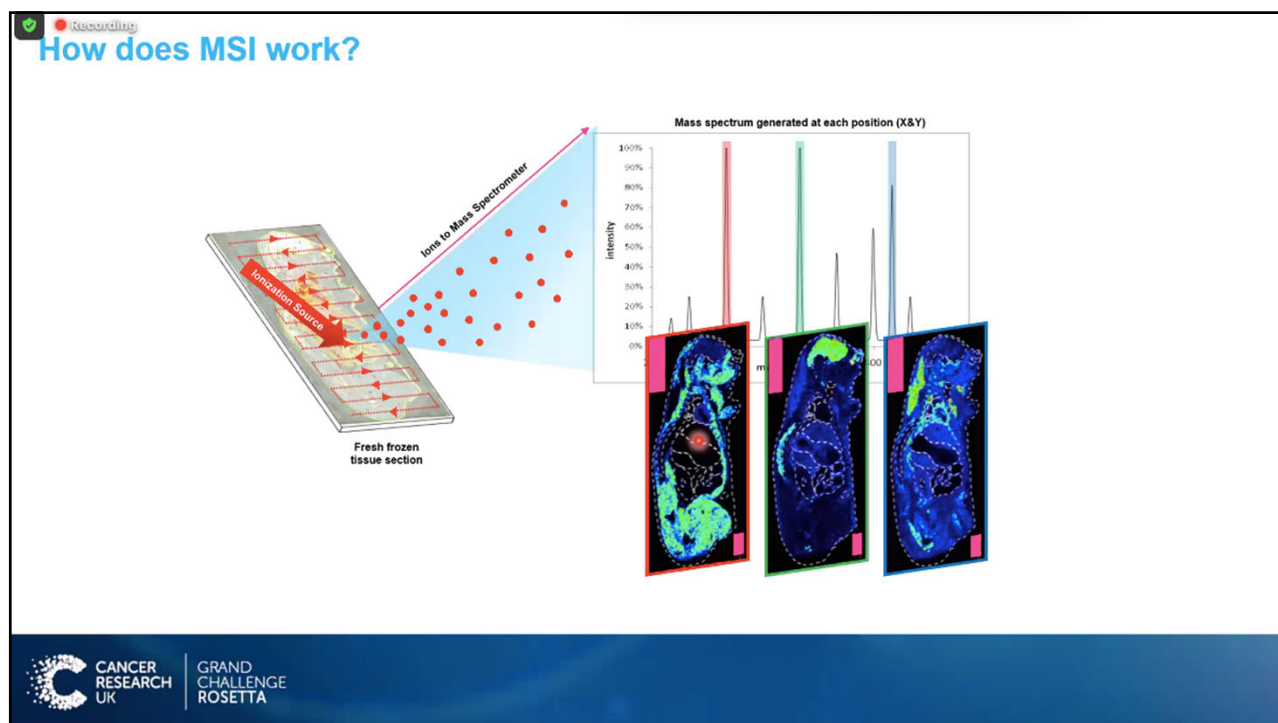
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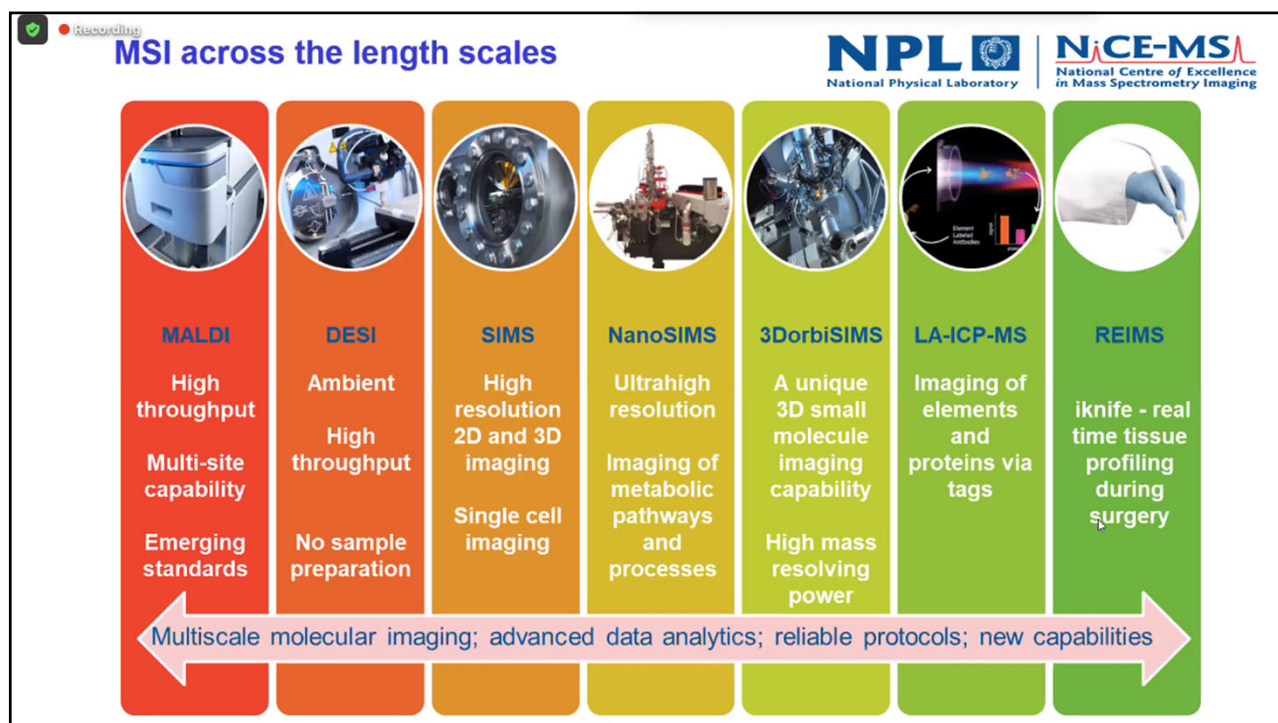
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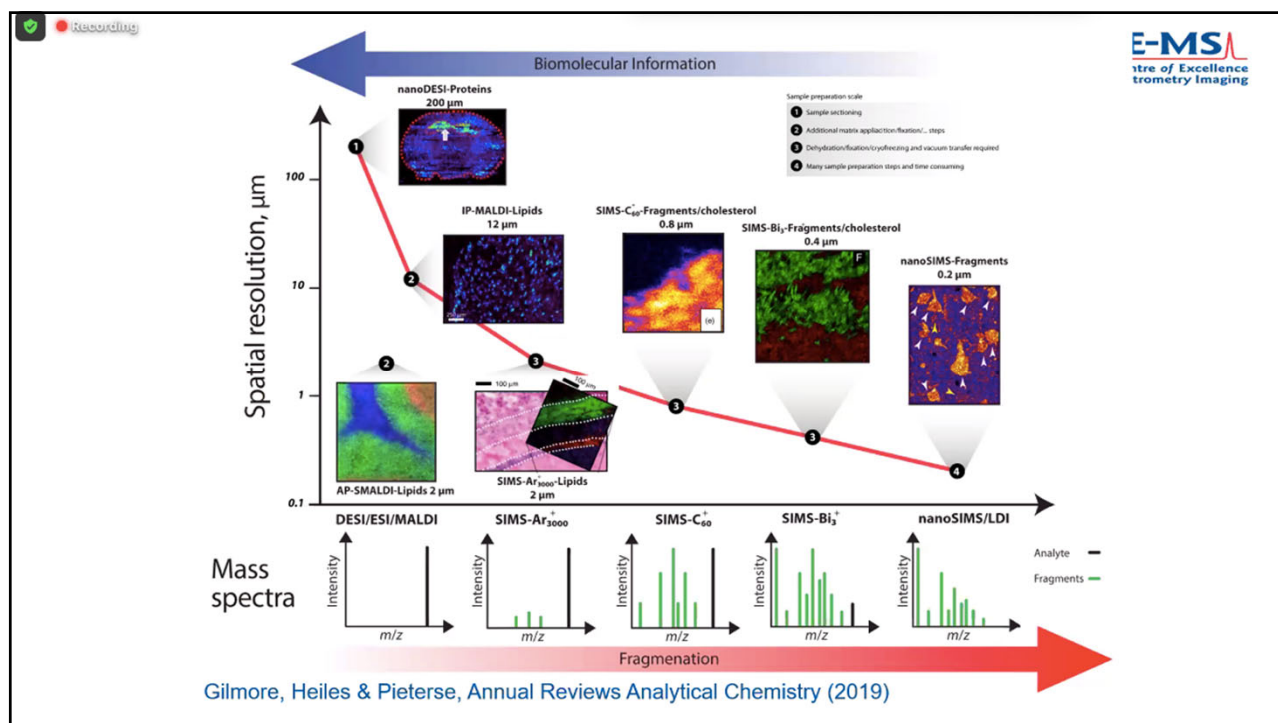
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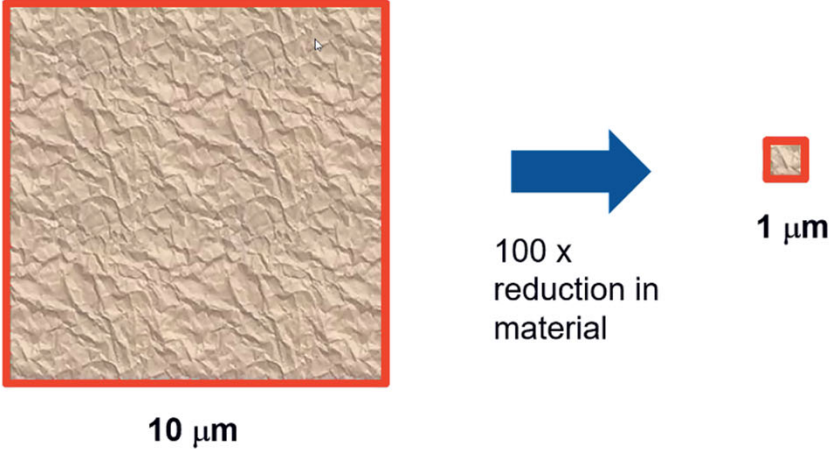


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Recording

Going small needs sensitivity!

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10 μm

100 x reduction in material

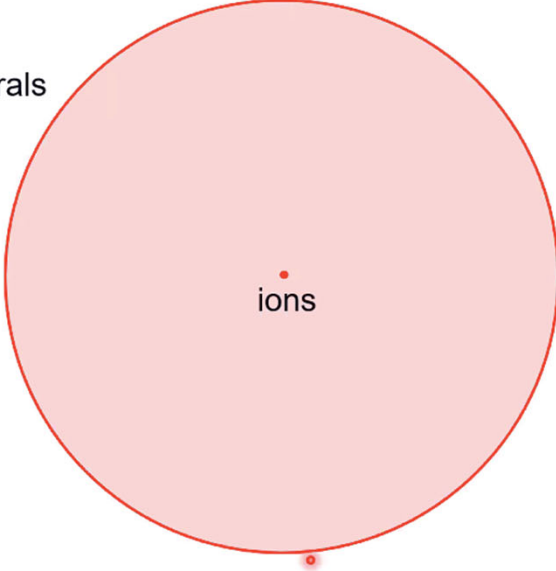
1 μm

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Recording

We need ions not neutrals!

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Neutrals

ions

Low ion yield:

- reduces sensitivity
- competitive ionisation limits quantification

Solutions:

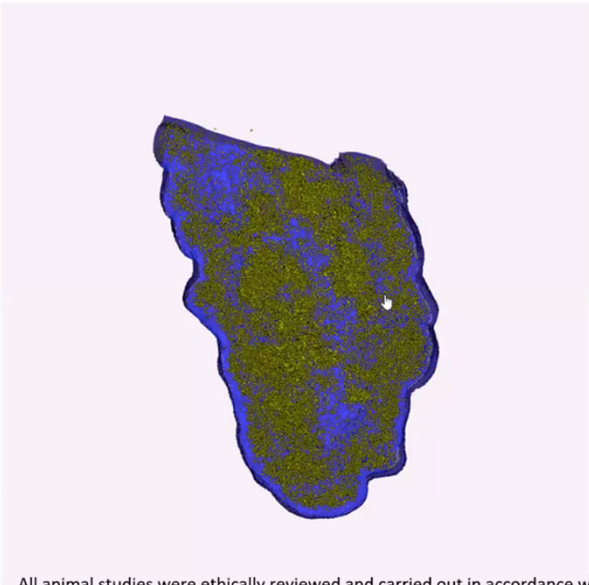
- photoionisation
- Chemical ionisation with matrix (e.g. MALDI) or ice


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Recording

Rat villus (~circa 2015)

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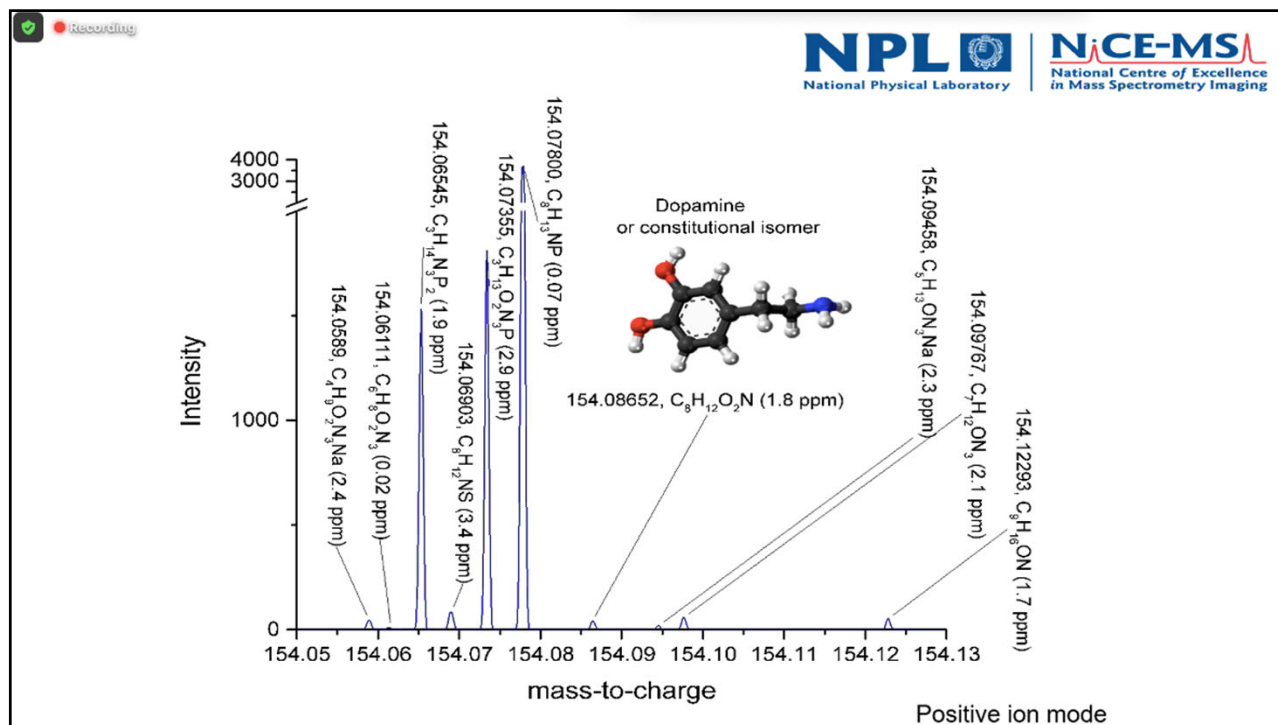




gsk GlaxoSmithKline

All animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Animals.

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Recording

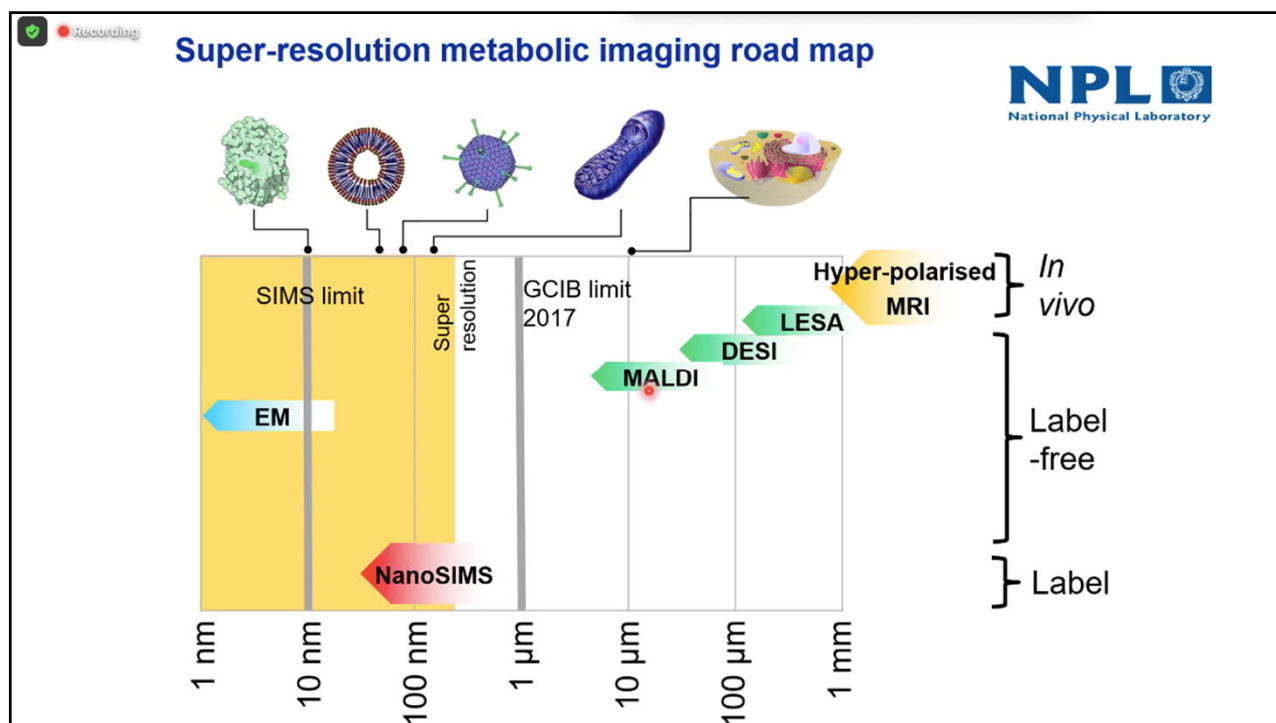
ToF-SIMS Challenges

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1. Sensitivity too low
2. Too much fragmentation
3. Mass resolution and mass accuracy too poor for identification

*If lucky enough to detect a signal, have **no clue what it is**, and it is probably a **fragment** of something else anyway.....*

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Recording 3D OrbiSIMS launched Nov 16

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gsk

IONTOF

Thermo SCIENTIFIC



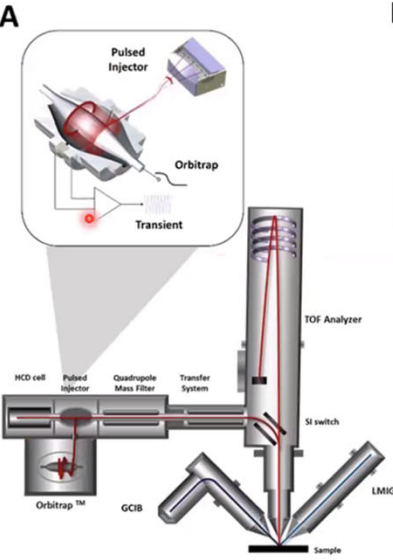
The University of Nottingham
UNITED KINGDOM • CHINA • MALAYSIA

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Recording 3D OrbiSIMS

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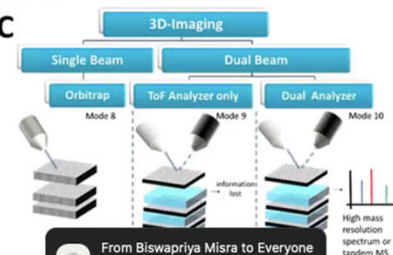
A



B

Method	Beam Modality	Mass Analyser	Mode
Surface spectra (1D)	Single beam (Bi or Ar)	ToF	1
		Orbitrap	2
Depth profiling	Single beam (Ar)	Orbitrap	3
	Dual beam (Ar and Bi)	ToF Orbitrap	4 5
Imaging (2D)	Single beam (Bi or Ar)	ToF Orbitrap	6 7
	3D Imaging	Single beam (Ar)	Orbitrap
Dual beam (Ar and Bi)		ToF Dual Analyser	9 10

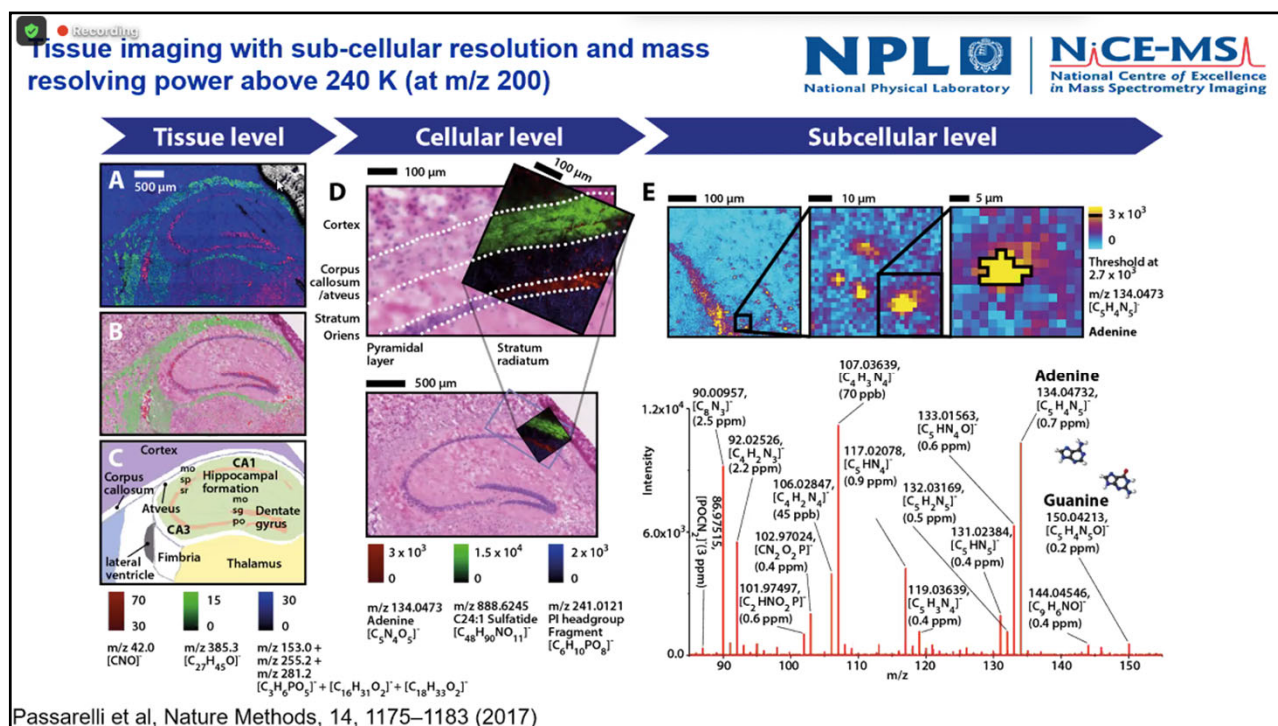
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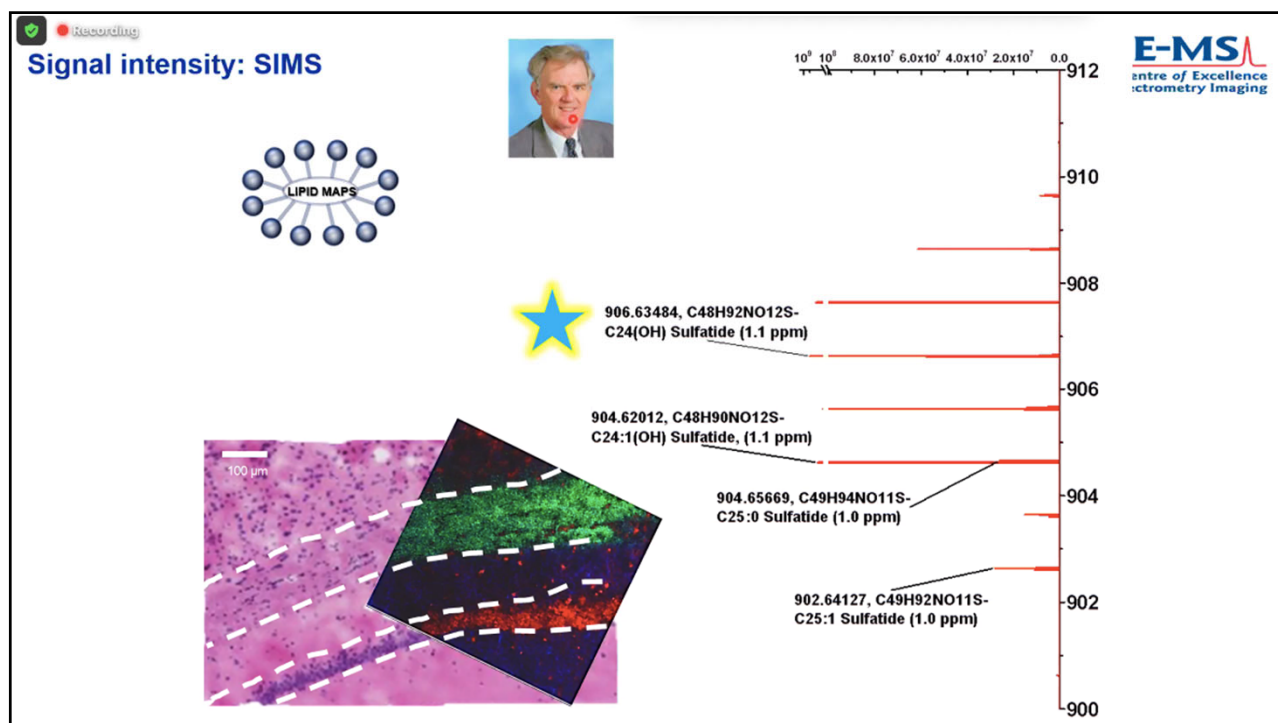
From Biswapriya Misra to Everyone
Lovely "super-resolution metabolic..."

Passarelli et al, Nature Methods, 14, 1175–1183 (2015)

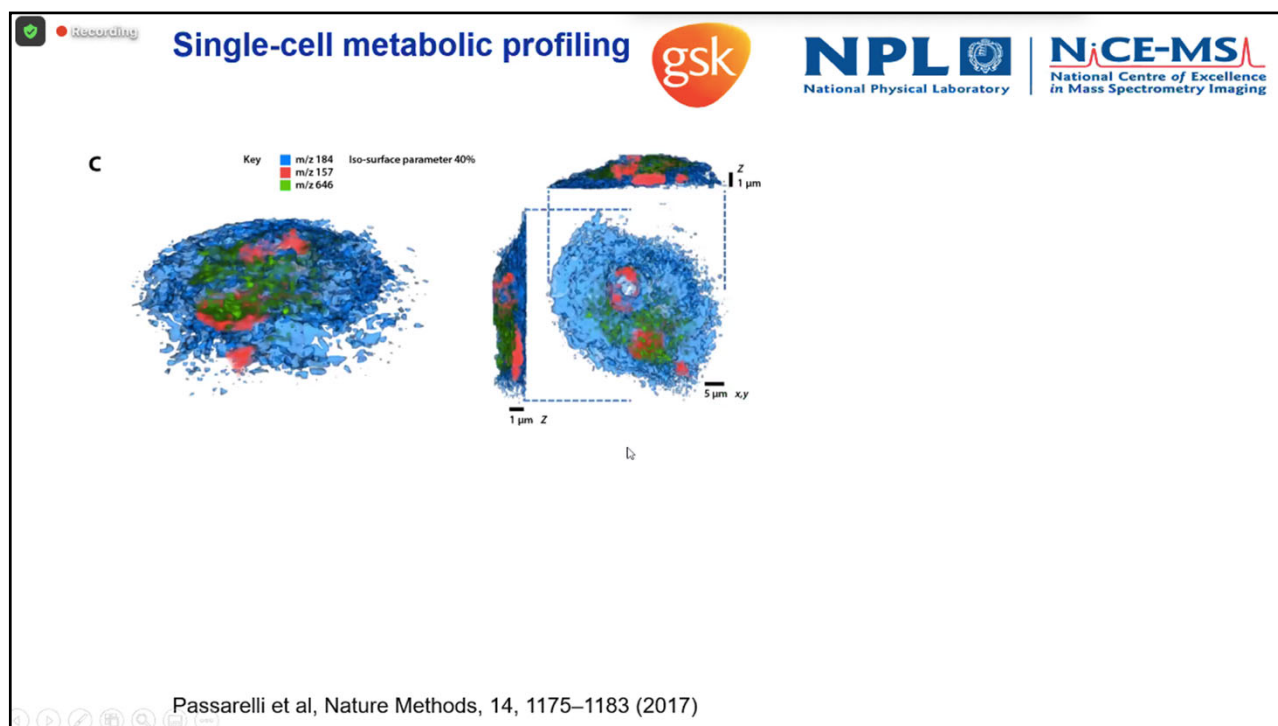
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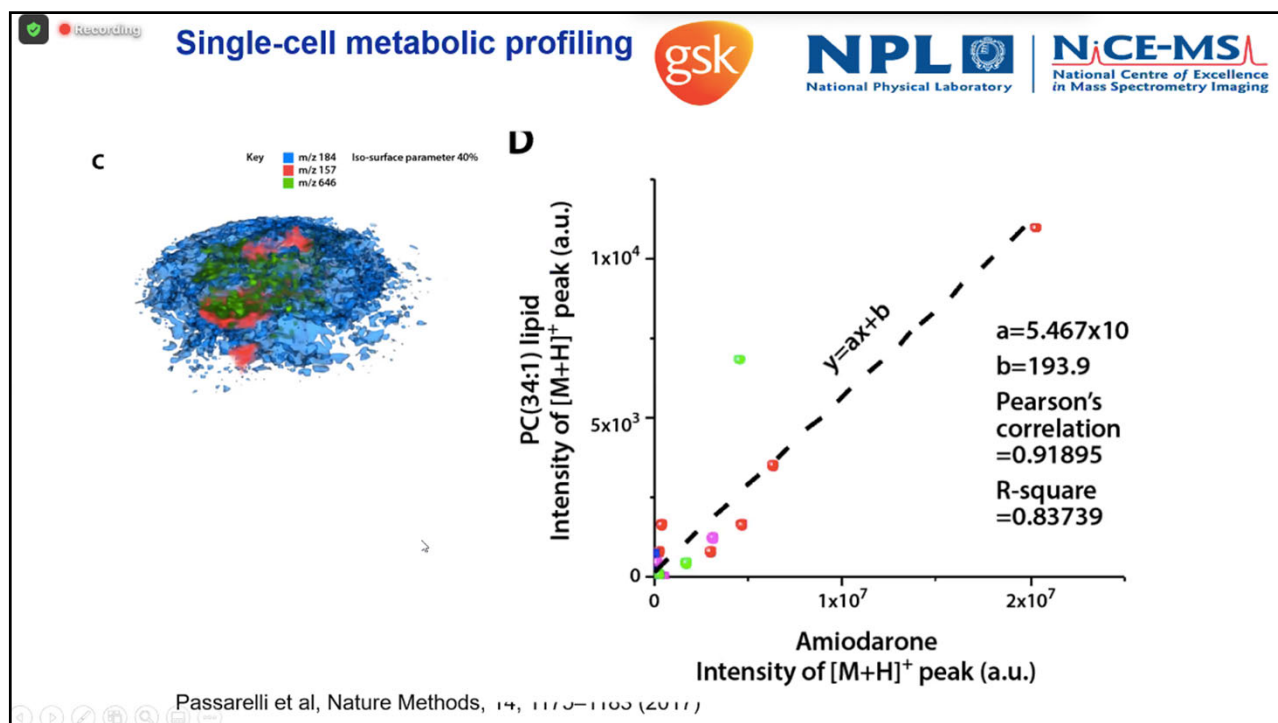
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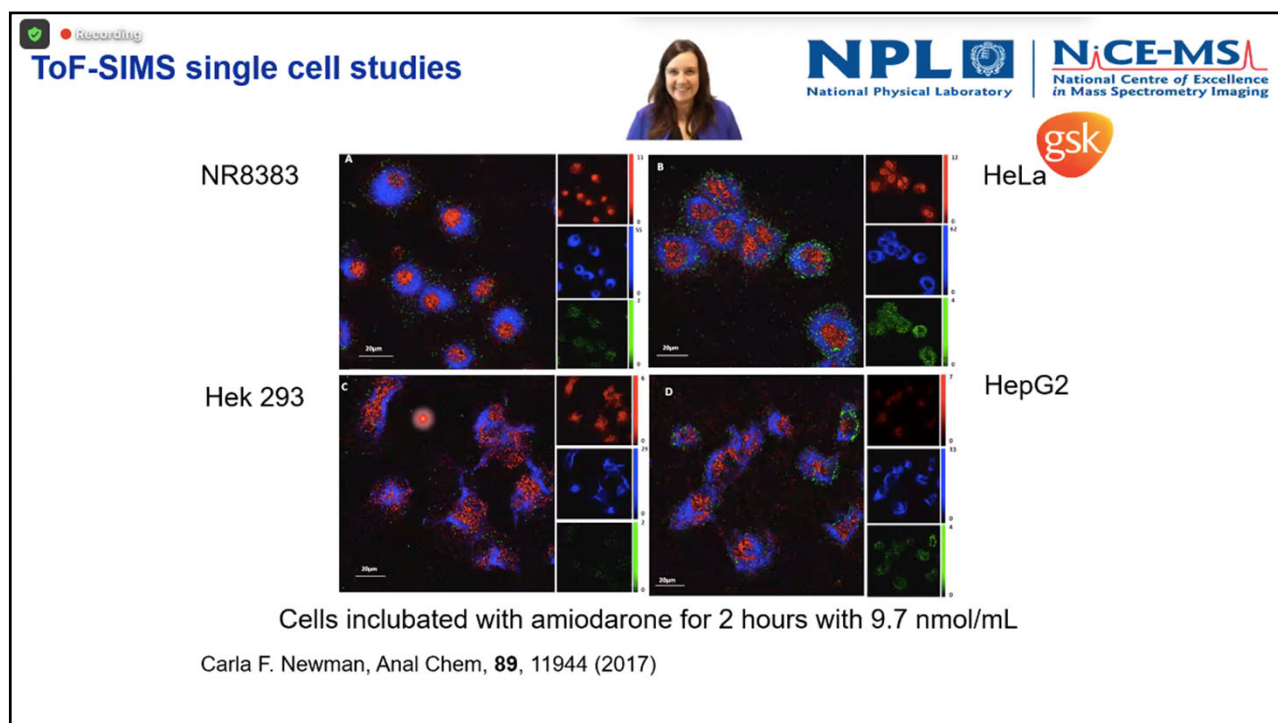
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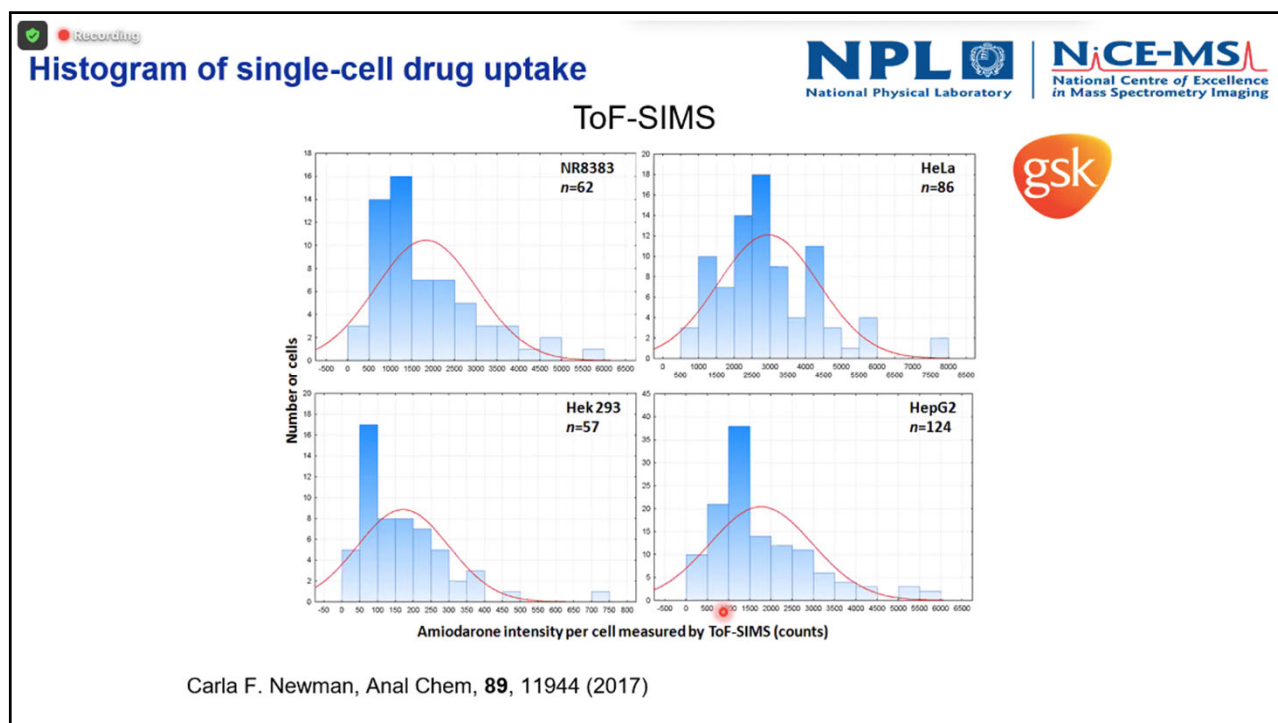
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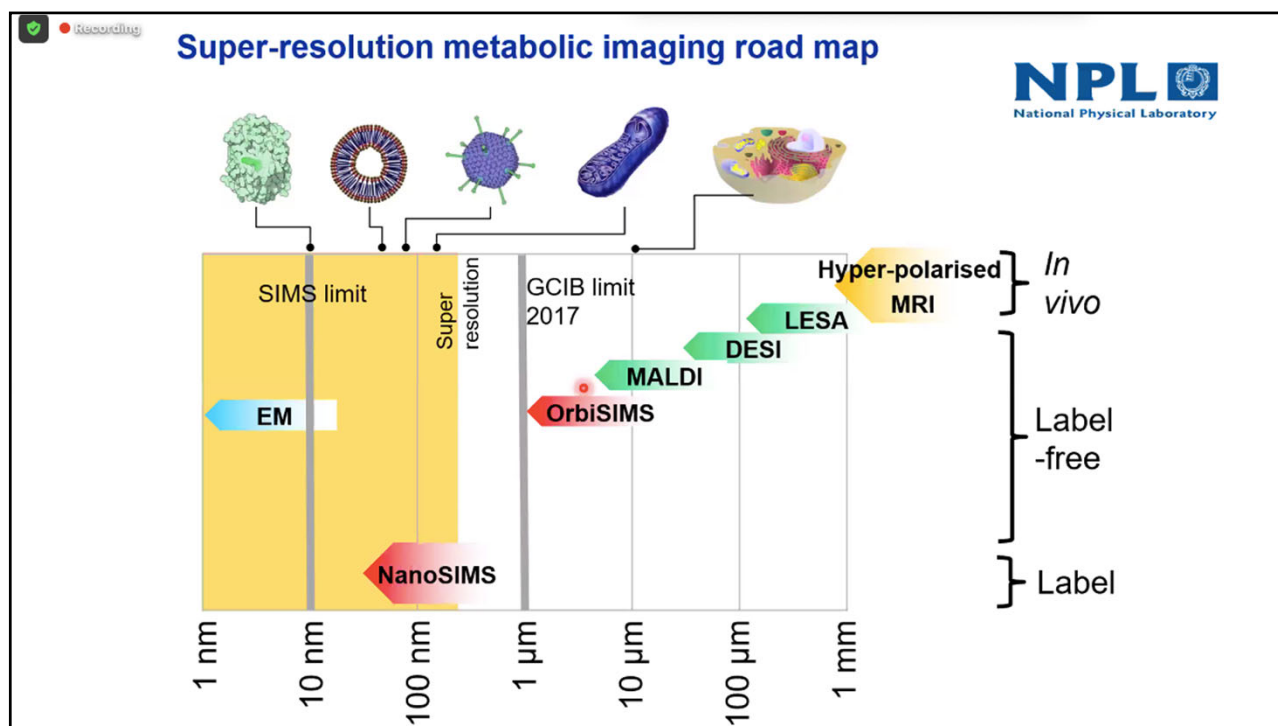
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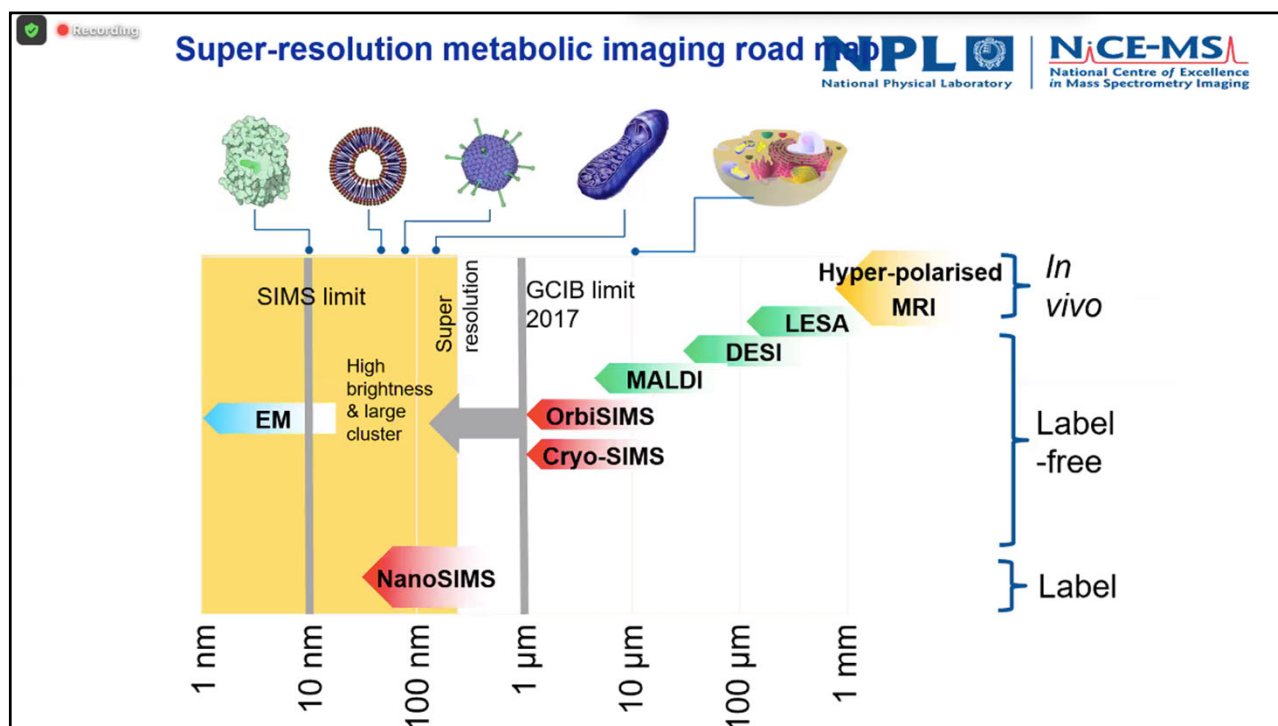
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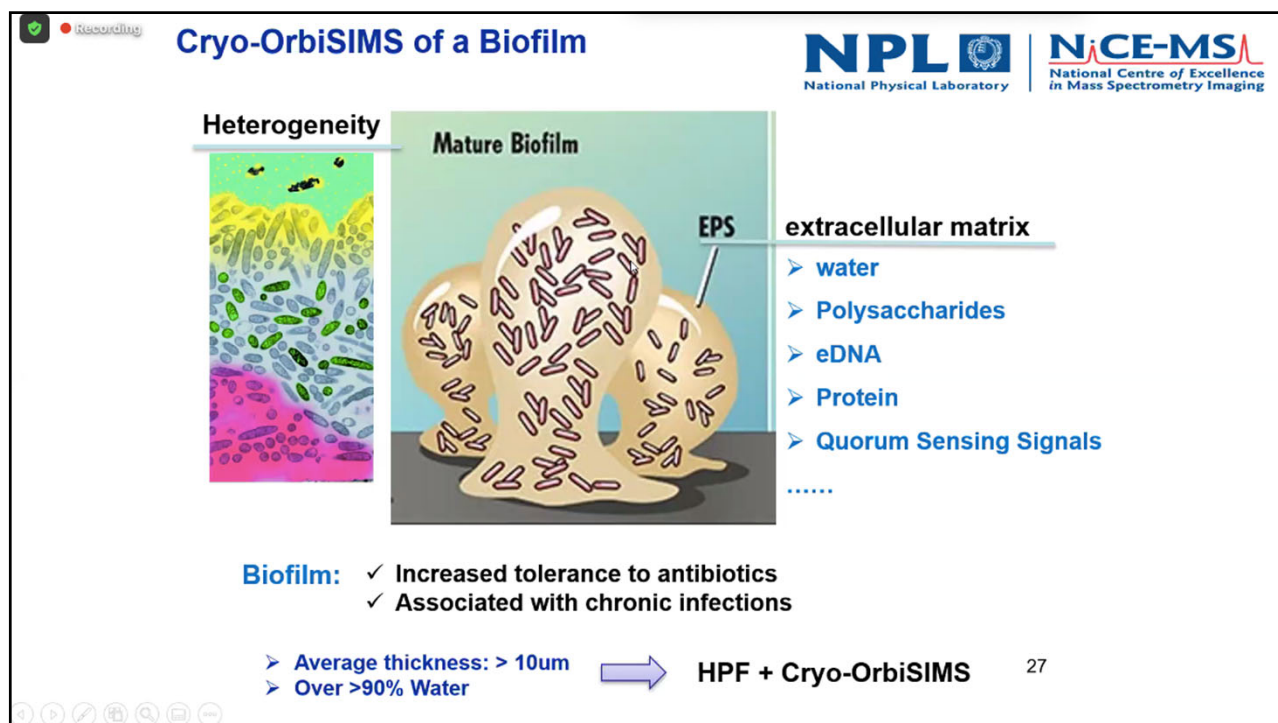
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Cryo-OrbiSIMS

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Sample mounting

a b c

Leica EM VCM

Sample transferring

a b

Leica EM VCT-500

Sample loading

a b

Cryo-OrbiSIMS

Zhang et al, Anal. Chem. 92, 9008 (2020)

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Cryo-OrbiSIMS of frozen-hydrated biofilm
-----LMIG-ToF Reconstructed 3D Images

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z-axis cropping

K⁺

30 keV Bi₃⁺ ToF MS 3D images
Field of View: 300 × 300 μm

Adenine/2-Aminoacetophenone

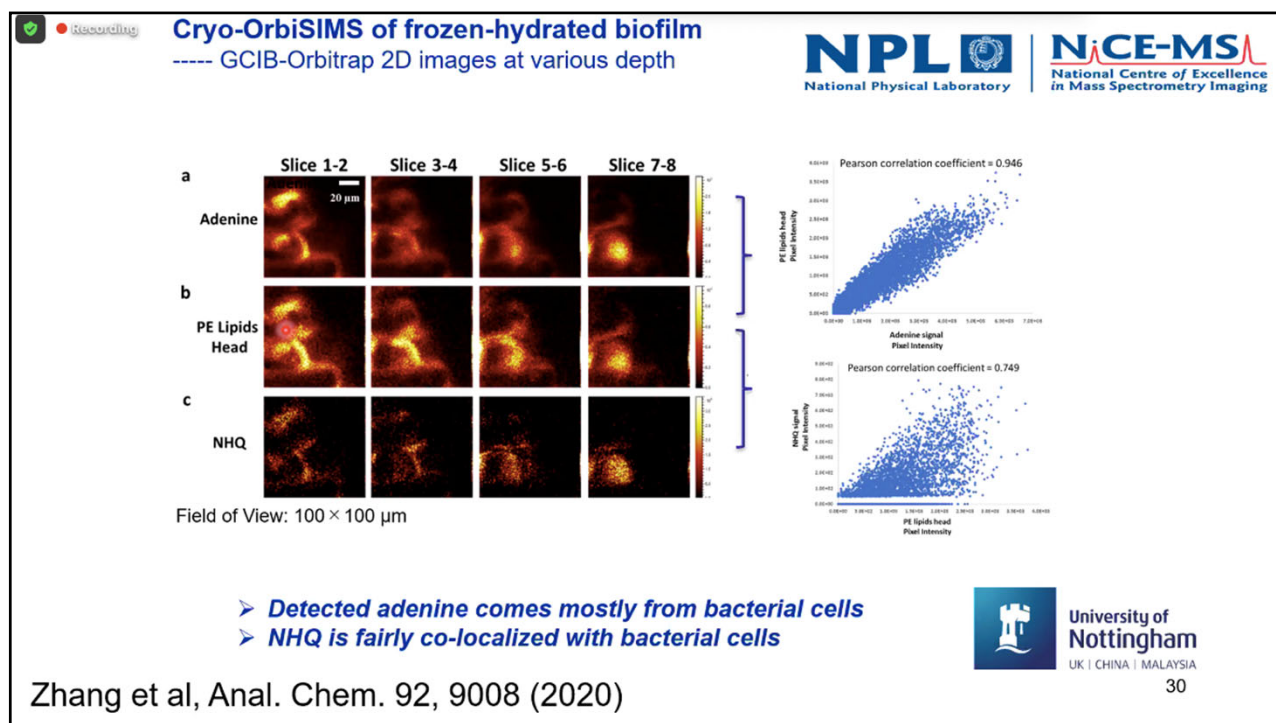
ToF MS

Orbitrap MS

University of Nottingham
UK | CHINA | MALAYSIA

Zhang et al, Anal. Chem. 92, 9008 (2020)

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Fundamental studies of nutrition and longevity in *Drosophila* - direct analysis of autotoxin lipids

Collaboration with: Alex Gould

Clare Newell

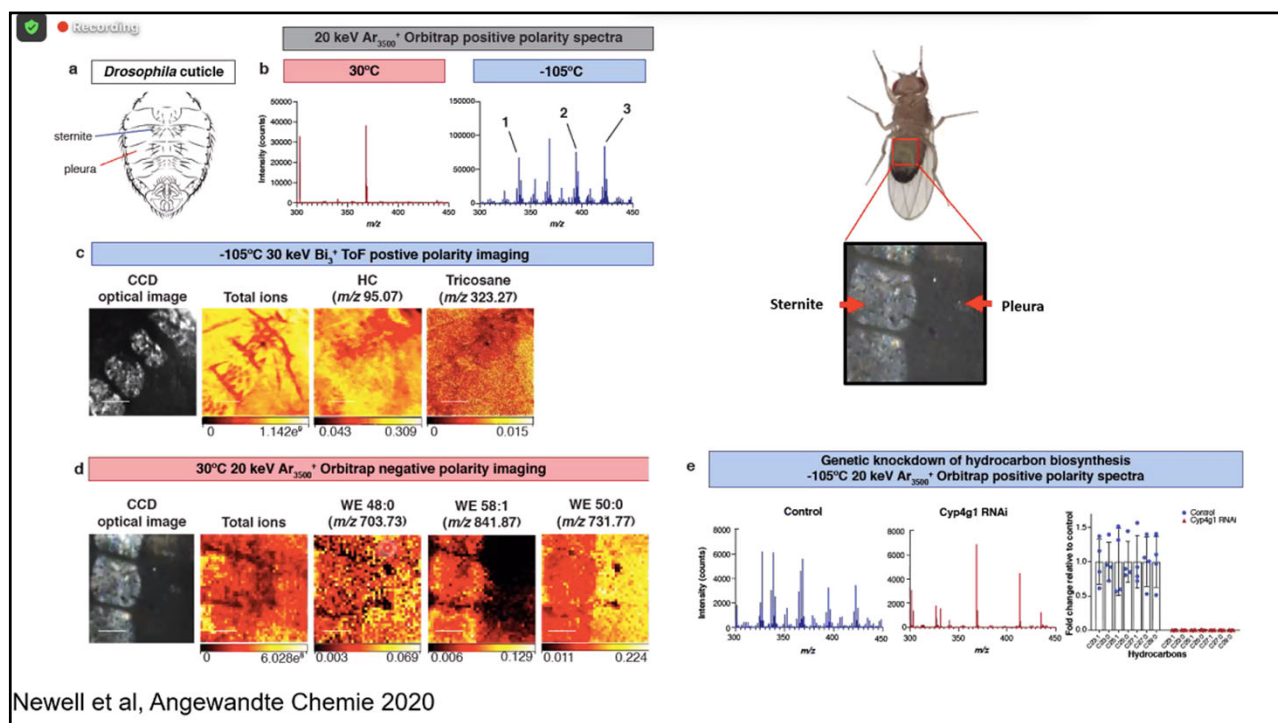
THE FRANCIS CRICK INSTITUTE

Why use fruit flies?

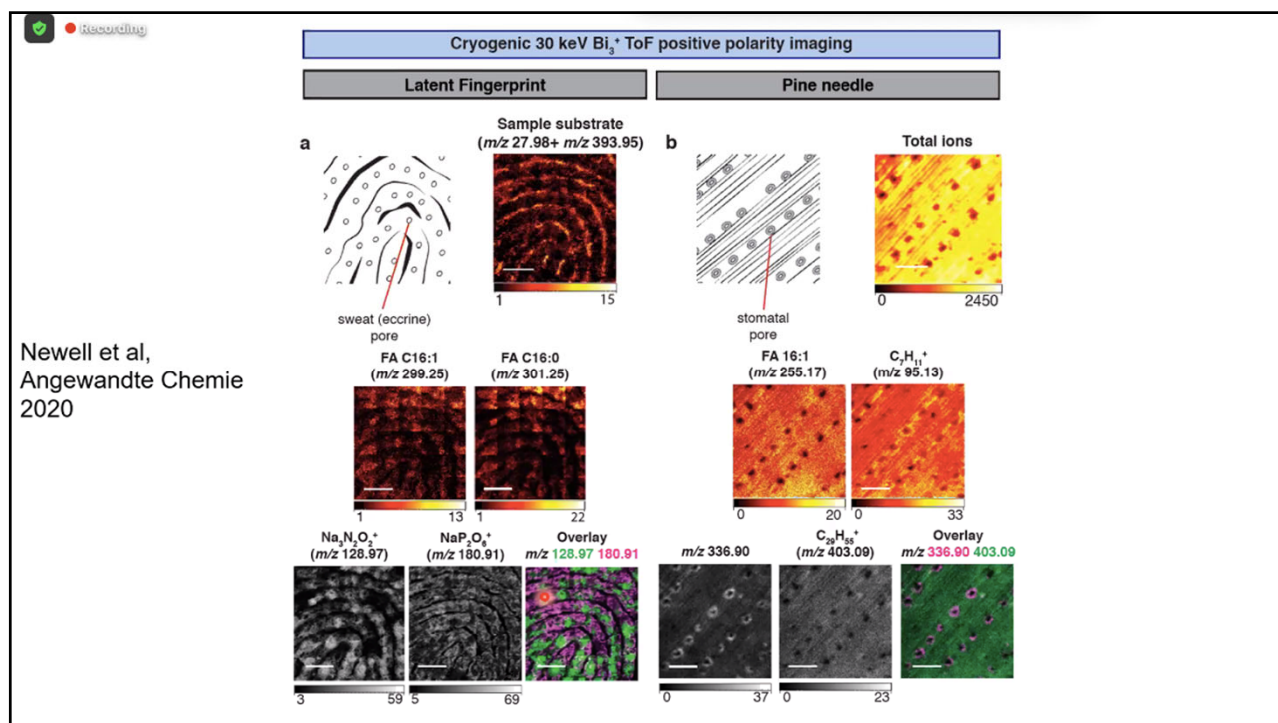
- Short generation time (10 days) and lifespan (2 months) beneficial for longitudinal studies.
- Sophisticated genetic tools are available – it is possible to increase or decrease expression of nearly every gene.
- 75% of genes causing disease in humans are also found in the fly.

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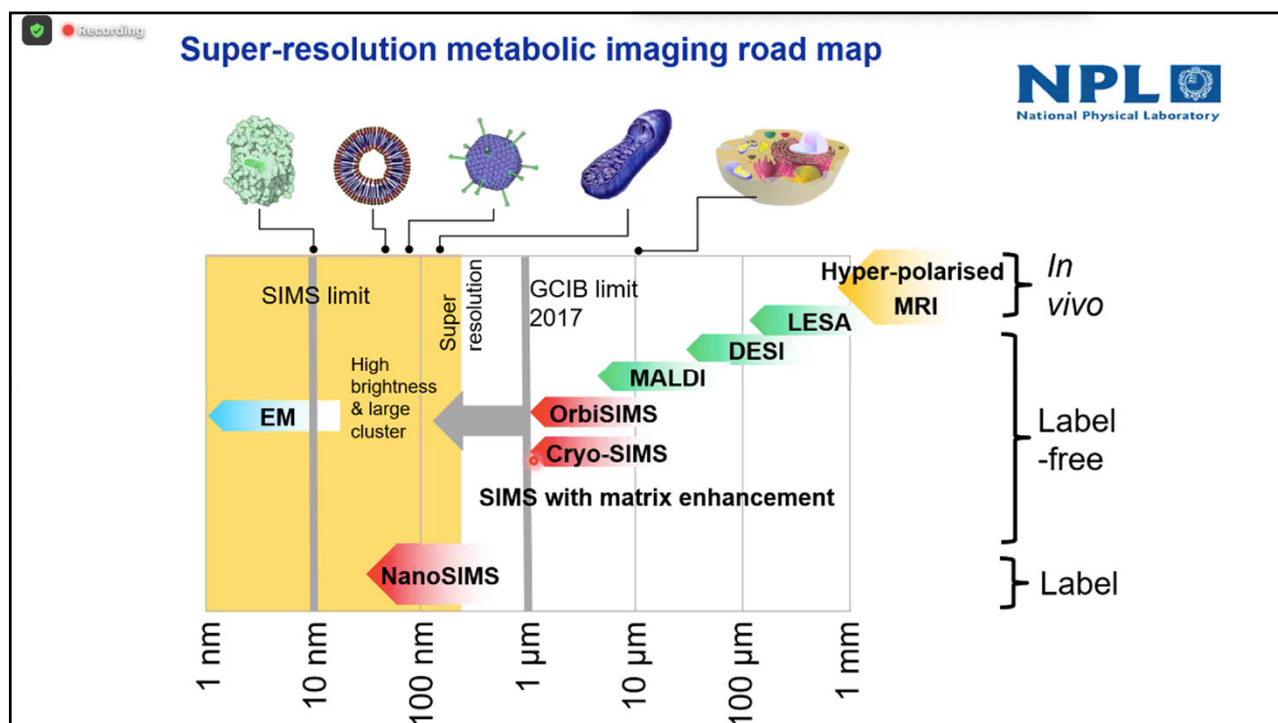
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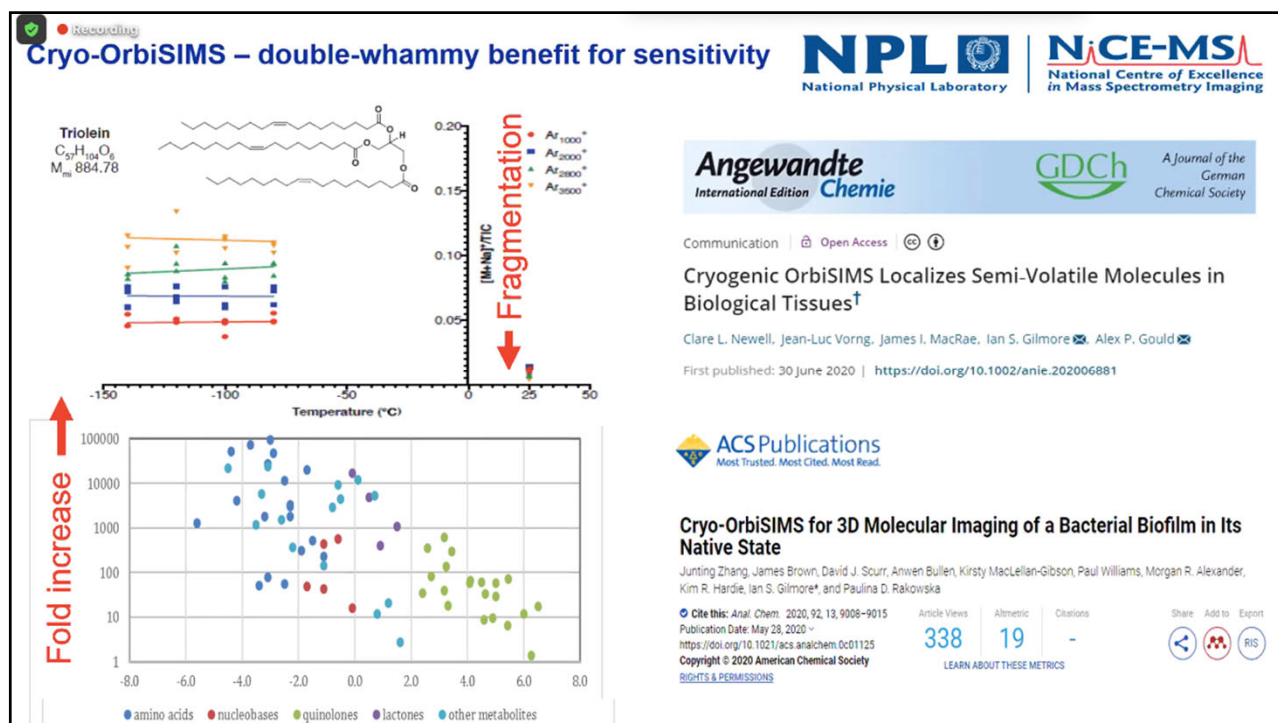
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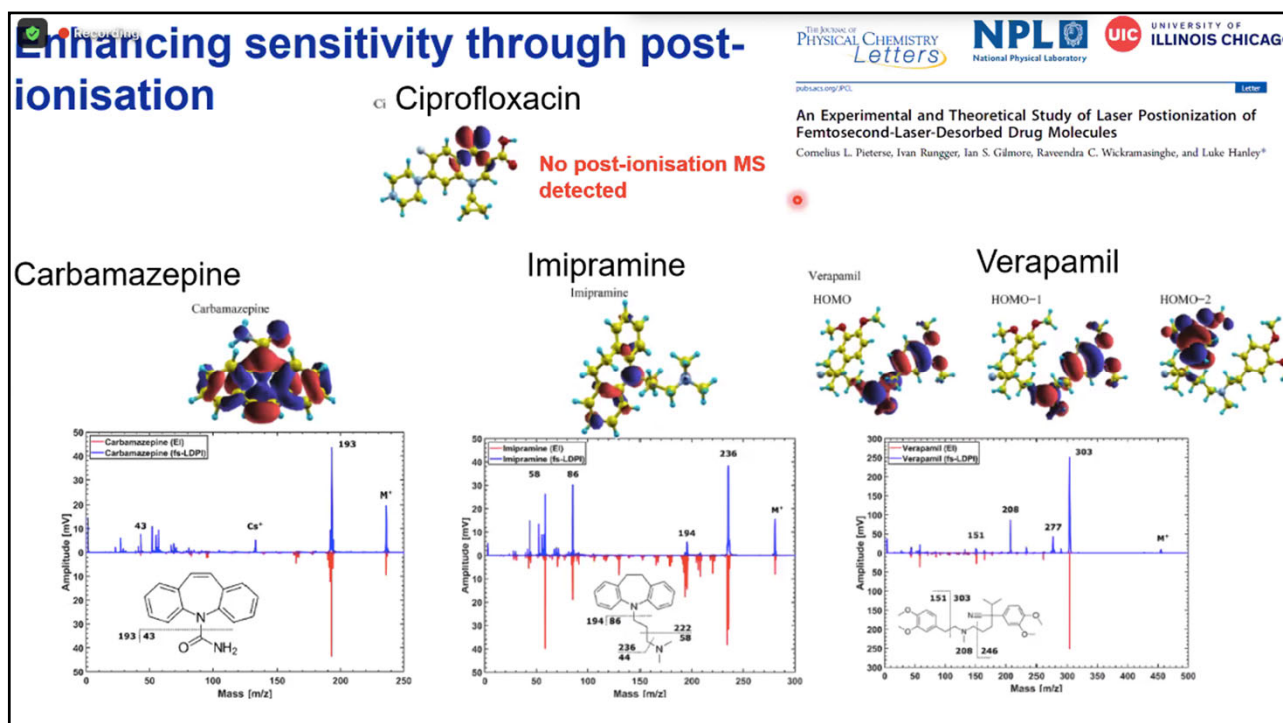
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Recording

Quantum detection

The diagram illustrates a quantum detection setup. An ion packet is trapped in a C-trap. The ion packet is then moved into an Orbitrap analyzer. The Orbitrap analyzer is connected to a Voltage ramp, which is connected to an Amplifier. The Amplifier outputs a Detected signal.

GRAND CHALLENGE FUNDED TEAM

CANCER RESEARCH UK

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Recording

Target to Patient

Creating tomorrow's drug discovery toolbox

Spring 2022
Wellcome Genome Centre,
Hinxton, Cambridge

Dr Tony Wood SVP, Medicinal Science & Technologies, GSK, UK	Prof Josephine Bunch NPL NCE Mass Spectrometry Imaging, Teddington, UK
Dr Astrid Ruefli-Brasse Head of Biology, 23 and Me, CA, US	Dr Mene Pangalos Exec VP, BioPharmaceuticals R&D, AZ, Cambridge, UK
Prof David Goldstein Dir. Inst for Genomic Medicine, Columbia, US	Dr Paul Clemons Director Comp & Chem Biology, Broad Inst, US
Dr John Skidmore CSO Alzheimer's Research UK, Cambridge, UK	Dr Anne Heatherington SVP, Head of Data Sciences Inst., Takeda, Boston, US
Dr Ruth McKernan FMedSci, CBE Venture Partner, Dementia Discovery Fund	Dr Ewan Birney Director of EMBL-EBI, Hinxton, UK
Dr Gitte Neubauer VP, GSK Cellzome, Heidelberg, Germany	Prof Michael Johnson Neuro & Genomic Medicine, Imperial College, UK
Dr Sarah Skerratt Head of Chemistry, MSD, London, UK	Prof Anne Barton Centre for Genetics & Genomics, Manchester UK
Dr Steve Rees VP Discovery Biology, AZ, Cambridge, UK	Dr Sandeep Menon SVP, Head Early Clinical Development, Pfizer, USA
Dr Paul Vulto CEO Mimetas, Leiden, The Netherlands	Dr Anja Schiel NoMA and Chair Science Advice Working Party, EMA

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gsk
GlaxoSmithKline

AstraZeneca

Pfizer

EMBL-EBI

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