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Tutorial SC2

Introduction to Biological Sample Analysis with SIMS

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Secondary Ion Mass Spectrometry (SIMS) originally emerged from materials science as a powerful tool for analysing the surfaces of inorganic solid samples. Over the last two decades, significant advances have transformed SIMS into a technique with immense potential in the life sciences.

This tutorial will review key developments, highlighting cluster ion beams for analysis and sputtering, as well as the introduction of orbitrap[1] and MS/MS analysers[2], which are particularly adept at handling organic and biological samples. Cluster ion beams have led to a reduction in fragmentation and an increase in the ionisation probability and ion yield of molecules in the higher mass range. The introduction of the Orbitrap brings a new level of precision through its high mass resolution and mass accuracy, which is particularly important for the correct assignment of biomolecules and biomarkers.[3]

Emphasis will be placed on the exceptional imaging capabilities of SIMS, which offers superior lateral resolution compared to alternative Mass Spectrometry Imaging (MSI) techniques. Coupled with the Orbitrap analyser, SIMS achieves unparalleled mass resolution, a critical aspect for biomedical applications such as subcellular metabolomic identification.

The lecture will cover a variety of real life science applications, including cell and tissue analysis, as well as insights from the field of botany. It will also address the fundamental issue of sample preparation. Biological samples present unique challenges when preparing them for high vacuum conditions, requiring delicate preservation of their chemical composition and prevention of compound delocalisation. We will discuss practical strategies to overcome these challenges and ensure successful analysis in biomedical research.

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2. G.L. Fisher, A.L. Bruinen, N. Ogrinc Potočnik, J.S. Hammond, S.R. Bryan, P.E. Larson and R.M.A. Heeren: A New Method and Mass Spectrometer Design for TOF-SIMS Parallel Imaging MS/MS. *Anal Chem* **88**, 6433 (2016).
3. A.M. Kotowska, G.F. Trindade, P.M. Mendes, P.M. Williams, J.W. Aylott, A.G. Shard, M.R. Alexander and D.J. Scurr: Protein identification by 3D OrbiSIMS to facilitate in situ imaging and depth profiling. *Nature communications* **11**, 5832 (2020).