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ToF-SIMS: Methods & Applications

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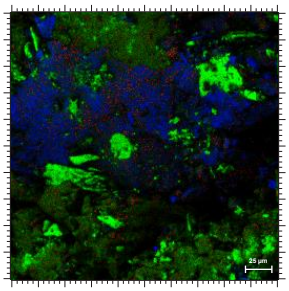
Introduction

- Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) is a powerful tool for investigating the elemental and molecular variation across surfaces and through sub-surface layers.
- Samples are bombarded with a high-energy primary ion beam that causes secondary ions to be released from the surface, generating a mass spectrum. By rastering the ion beam across an area of the surface, an ion distribution map of the surface can be created.
- Surface layers can also be removed using a sputter beam to expose a new area for analysis, creating a 3D image of the sample.
- ToF-SIMS applications include: impurity detection in crystals, API distribution in tablets, drug effects on cells, bulk material characterisation, monitoring surface uniformity in paints and coatings, trace metal detection, inorganic multilayer characterisation and many others.

Pharmaceutical

This includes monitoring for any structural changes as a result of changing crystallisation parameters or processes, such as using spherical agglomeration.

This can be seen in the total ion images of crystals before (above) and after spherical agglomeration (right), which are shown to have drastically changed in size and shape.

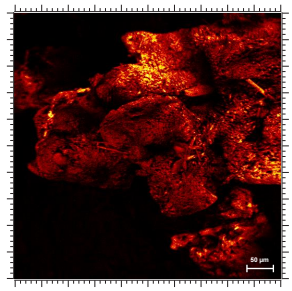


Large area mapping can be carried out using automated acquisition, moving step-wise across a sample and stitching together multiple smaller scans to create a larger image, as shown on the right.

This highlights the potential impact ToF-SIMS capabilities can have on the study of drug product performance, stability, manufacturability and digital design.

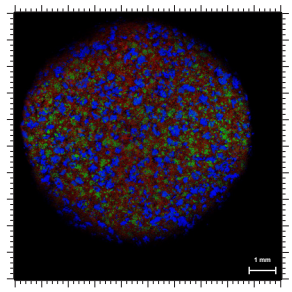
CMAC researchers have been investigating different crystallisation procedures in order to improve downstream processes such as blending and tabletting.

ToF-SIMS is being used at various points along the pharmaceutical manufacturing pipeline in order to improve and inform process development for medicines production.

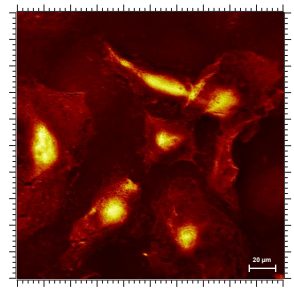


ToF-SIMS is also being used to investigate the distribution of APIs and excipients in tablets, including how the distribution changes after applying different processes or blending parameters.

Data is typically acquired over a field-of-view of ≤ 500 μm^2. The image on the left shows the overlaid distributions of three compounds across a 250 μm^2 area of a tablet surface.

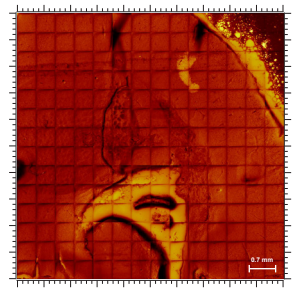


Biochemistry



Areas of high ion intensity are shown in the cell nuclei in the total ion image (above).

Individual ions or groups of ions can be coloured and overlaid (right) to highlight areas of similarity across the sample, such the effects of drug treatment and drug localisation within the cells

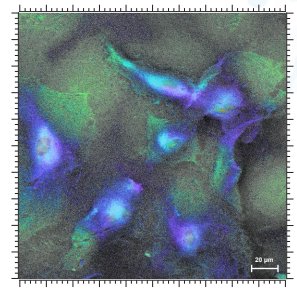


Multivariate statistical analysis methods such as PCA or MCR can be used on the spectra, images or profiles generated by ToF-SIMS in order to discover trends within the data.

These methods can pull out unexpected patterns and areas of commonality, as shown by comparing the total ion image of the tissue sample (above) with the image generated by MCR analysis (right).

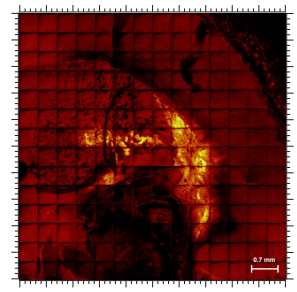
ToF-SIMS can detect the chemical, biological and structural changes occurring under different experimental conditions, such as temperature, environmental conditions, time and drug interaction.

In collaboration with colleagues in SIPBS, ToF-SIMS has been used to analyse cells, bacterial cultures and tissue samples.



Biological samples often require additional sample preparation in order to make them suitable for ToF-SIMS analyses. This could include freeze-drying, chemical fixation, cryosectioning and/or solvent washing.

Cryosectioned tissue samples need to be mounted onto a solid substrate such as a glass microscope slide for ToF-SIMS analysis.



Through the CMAC National Facility, ToF-SIMS is being used to support academic and industrial projects, providing surface characterisation and 3D imaging for a range of sample types. The data shown above has been acquired on a TOF.SIMS 5 (IONTOF GmbH) instrument, equipped with a bismuth liquid metal ion gun and an argon gas cluster ion beam.

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Contact cmac-national-facility@strath.ac.uk for more information about ToF-SIMS.