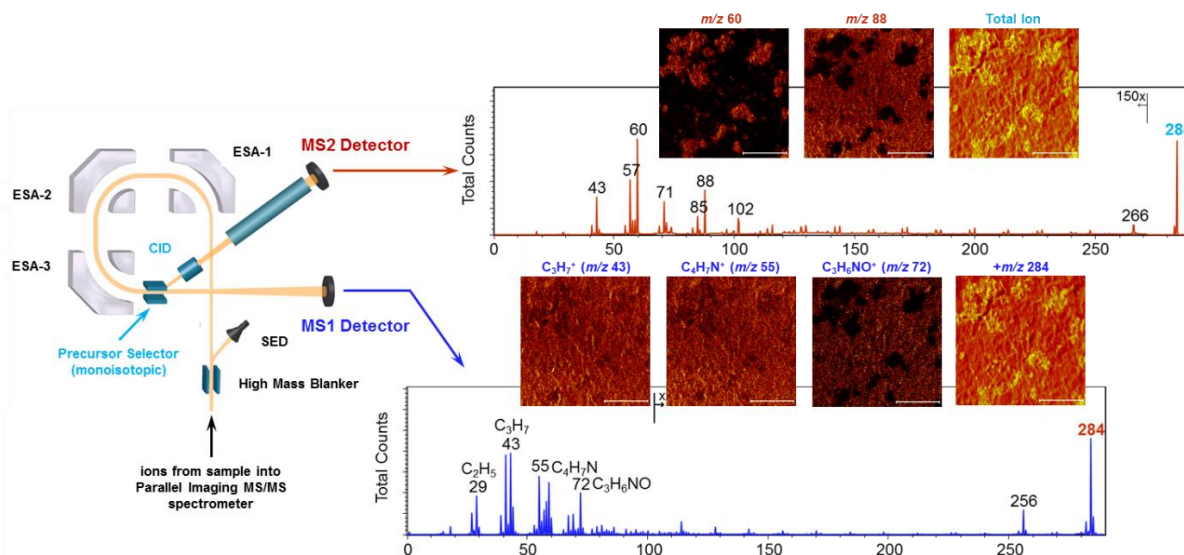


## The Spatially-Resolved Illumination of Chemical Processes by Means of Mass Spectrometry Imaging: from Click-Chemistry to Biogenesis

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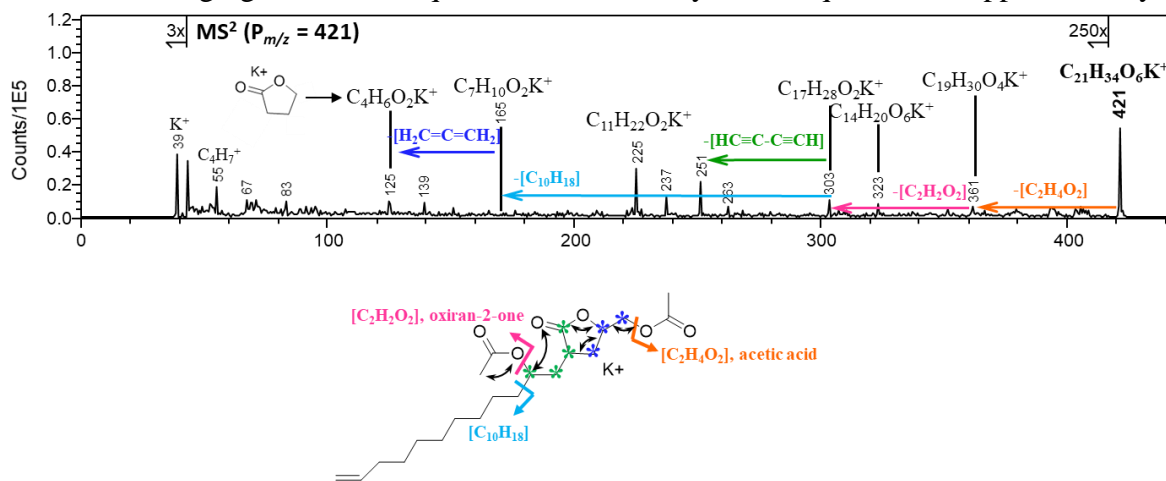
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The fundamental limitation of rapid, high lateral resolution mass spectrometry (MS) imaging, e.g. TOF-SIMS, has been a lack of capacity for confident identification of surface chemistry. A unique TOF-TOF imaging mass spectrometer allows TOF-SIMS ( $MS^1$ ) imaging and tandem MS ( $MS^2$ ) imaging to be achieved simultaneously and in parallel as illustrated by the data shown in Figure 1. Secondary ions for  $MS^1$  and  $MS^2$  analysis are produced from the same area of the surface by a pulsed and digitally raster-scanned primary ion nanoprobe. Unique and one-of-a-kind samples may be characterized without undesired erosion or degradation; even sub-monolayer 2D films are readily characterized. Monoisotopic precursor ion selection combined with kilo-electron volt (keV) collision-induced dissociation (CID) enables the identification and structural elucidation of surface-bound moieties as exemplified in Figure 2. This relatively new analytical capability has been brought to bear for straightforward molecular identification as well as multifaceted studies involving surface modification, polymers, composites, catalysis, forensic / failure analysis, biology and pharmaceuticals. Practical lateral resolution ( $\Delta\ell$ ) in both  $MS^1$  and  $MS^2$  images is always  $\leq 0.5 \mu\text{m}$ , and can be  $< 100 \text{ nm}$  when desired. Here, we will explore the utility of the TOF-SIMS tandem MS imaging method to unravel the click-chemistry of sub-monolayer films, and to shed new light and unlock the mystery of molecular biogenesis.



**Figure 1.** (LEFT) A schematic illustration of the TOF-TOF Parallel Imaging MS/MS spectrometer [1,2]. The major components are identified. (BOTTOM-RIGHT) TOF-SIMS ( $MS^1$ ) precursor ion spectrum of an unspecified sample. Several images (inset) are generated from the corresponding  $MS^1$  precursor ion peaks. The peak of greatest apparent mass-to-charge ratio ( $m/z$ ), centered at 284.31, is likely to be a molecular or quasi-molecular ion. (TOP-RIGHT) Tandem MS ( $MS^2$ ) product ion spectrum of the  $m/z$  284.31 precursor. Two images (inset), indicating two molecular components, are generated from the

corresponding MS<sup>2</sup> product ion peaks and are shown together with the total ion image. The TOF-SIMS tandem MS imaging data were acquired simultaneously in an acquisition of approximately 10 minutes.



**Figure 2.** TOF-SIMS tandem MS imaging keV-CID product ion spectrum of the  $m/z$  421 precursor ion that has been identified as the  $[M+K]^+$  adduct of a metabolic precursor in the botanical biogenesis of antifungal and pesticidal compounds [3,4]. The illustrated molecular structure, below the product ion spectrum, provides insight to the bond dissociations and rearrangements that produce the observed product ions.

#### References:

- [1] G.L. Fisher et al, *Anal. Chem.* **88** (2016), p. 6433.
- [2] G.L. Fisher et al, *Microscop. Microanal.* **23** (2017), p. 843.
- [3] T. Fu, et al *Anal. Chem.* **90** (2018), p. 7535.
- [4] T. Fu, et al *Nat. Sci. Rep.* **9** (2018), p. 1928.