The implementation of the time-stamping, multi-hit PImMS sensor in combination with a commercially available time-of-flight mass spectrometer

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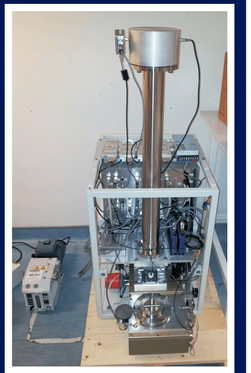
1) Motivation: Modifications to a conventional mass spectrometer

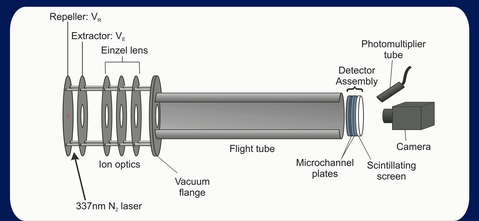
• The LaserToF LT2 Plus is a conventional, linear, MALDI, time-of-flight (ToF) mass spectrometer (MS) produced by SAI Ltd

• With minor modifications it can record imaging mass spectrometry (MSI) data in microscope mode [1,2]

• Microscope mode MSI allows for a much higher throughput for many analytical experiments that utilise mass spectrometry

• Mass-resolved images of tissue samples can be recorded without the need to raster across the sample, and arrays of ToF-MS samples can be analysed in parallel [3]

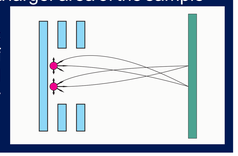




• In order to obtain images in microscope mode the detector, and laser of the mass spectrometer must be exchanged [4]

• The linear ToF electron multiplier detector is swapped for position sensitive microchannel plates (MCPs), and a fast camera; at the same time the laser has to be modified to illuminate a larger area of the sample

• By manipulating the accelerating electric field, it is possible to control the trajectories of the ionised analyte such that their final position at the detector depends on their initial position on the sample plate



2) The PImMS Sensor / Camera

• The PImMS camera utilises a novel, event-triggered CMOS imaging sensor [5]

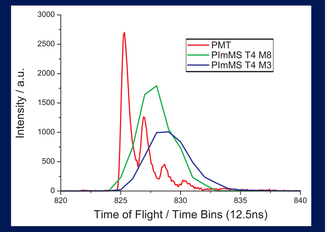
• Each pixel can record up to four ion arrival events independently of its neighbours

• The camera reads out the position and time-of-flight for each detected ion

• All this information can be accessed at a later point to increase the accuracy of any post processing algorithms

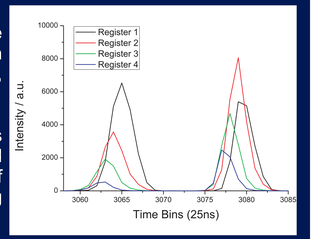
• Ion events recorded by the PImMS camera have a distinctive distribution spreading across multiple pixels and multiple time bins

• The data shown to the right compares two different levels of centroiding with the ToF recorded by a PMT



• Knowing the size of an ion event, and which register the ion event was recorded in allows for more accurate time information to be drawn from a given data set

• This data was taken with the prototype PImMS1 camera which has a pixel resolution of 72x72, and a timing precision of 12.5ns



• The next generation of PImMS is currently being characterised and has a much improved resolution of 324x324, and will have a timing precision of 6.25ns

• To learn more about the technical details of the camera see:

Thursday Posters, Imaging MS: Instrumentation ThP 068, The Pixel Imaging Mass Spectrometry (PImMS) Sensor - A Versatile High-Speed Position-Sensitive Detector for Imaging Mass Spectrometry

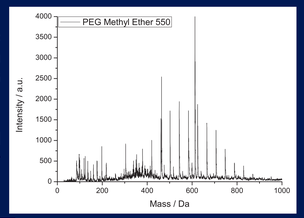
3) Results

• A number of simulations have been run in order to test, and characterise the instrument

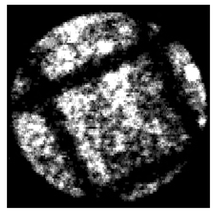
• Simulations were run using SIMION 8.0 software along with in-house analysis scripts

• The simulated data can then be compared to data collected using the instrument

• Experimentally the characterisation can be performed using a polymer such as PEG (polyethylene glycol)



• This gives a detailed mass spectrum over wide range of masses



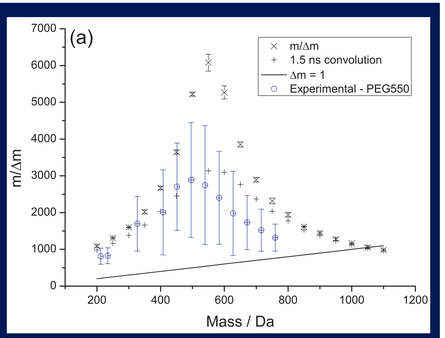
• Images have been collected of grid patterns; the grid has a wire diameter of 33.5μm, and an aperture size of 284.0μm

• The calculated resolution (rising edge width from 20% to 80% of the maximum) is found to be 24μm

• Graph (a) shows the variation in mass resolution as a function of the mass of the analyte

• It can be seen that there is a good agreement between experiment and simulation

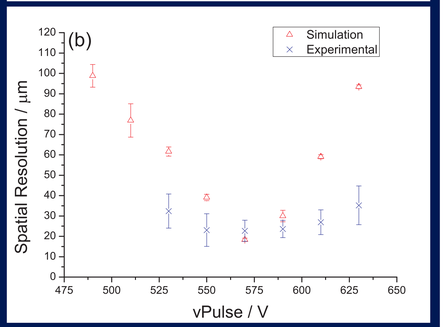
• It is necessary to convolute a contribution from the detector assembly to the simulated data in order to match the magnitude of the experimental data



• Graph (b) shows the variation in spatial resolution as a function of the voltage applied to the ion optics

• It can be seen that there is an good agreement in the absolute resolution achieved

• The response to changing voltage is much reduced in the experiment compared to that expected from simulation

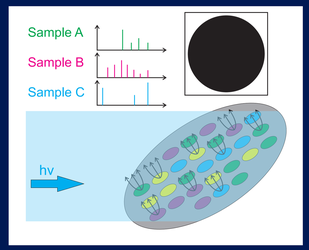


4) Conclusions

• The work presented here is a first step to creating a fully functional imaging mass spectrometer by simple modifications to a conventional ToF-MS instrument

• By adding a fast camera, such as the PImMS camera, it should be possible to analyse tissue samples, or arrays of samples with a very high throughput

• In this mode a small cluster of pixels on the PImMS camera would act as a single MS independently of the next cluster of pixels



• Images of tissue samples have been obtained before with the PImMS camera and a modified molecular dynamics instrument

• With this new apparatus it should be possible to identify pharmacologically important species and so to greatly increase the practical output of many analytical experiments [6]