Microscope Mode Imaging Mass Spectrometry – An Approach for Improved Imaging over Multiple Mass Ranges with Fast Detection Systems

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This work is subject to a patent application by ISIS Innovations ltd. the development company for the University of Oxford. Patent numbers: US20100294924A1, WO 2013007981 A1, Fast scintillator - patent applied

1) PEDA Technique

1. A large area of the sample is desorbed and ionised using a defocussed laser beam. Ions are extracted immediately with a static electric field formed between the repeller and the extractor electrode.

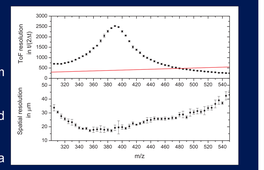
2. Once the ions of interest are situated between the extractor electrode and the last grounded plate, the extractor is pulsed to a higher acceleration potential.

3. The ions are time/spatially focussed as they traverse the field free region

4. When the time focus plane is coincident with the detector plane, microscope mode imaging with high ToF resolution becomes possible. The inital ion velocity spread can be corrected.

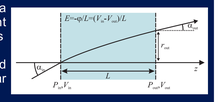
2) Ion Trajectory Simulation - Optic Design

- Developement of a PEDA based ion optic to image large samples with up to 4-5 mm diameter field of view
- The simulation result, shown on the right, indicate a spatial resolution of down to 20 μm, a ToF resolution of maximum 2500 m/Δm and a magnification of 10x for a small mass range between 350 to 450 Da..
- The figure shows that the PEDA method is limited to a relatively small mass range, since only the ions situated between the extractor and the Einzel lens upon field switching are time and spatially focussed.
- With a static extraction potential it is not possible to tune the optimised focussing properties of the spectrometer to a different mass range.



3) Velocity-Corrected Ion Extraction

- ToF and spatial resolution, are a result of the mass dependent focussing properties of the ion optics
- The output position *r* for a charged particle passing through a linear acceleration field is defined by:



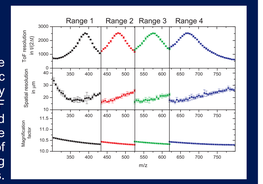
$$r_{out} = r_{in} + \sin(\alpha_{in})\frac{v_{in}^2 L}{eV_{red}} \times \left[\sqrt{\cos^2(\alpha_{in}) + \frac{2eV_{red}}{v_{in}^2}} - \cos(\alpha_{in})\right] \quad \text{with } V_{red} = (V_{in} - V_{out})/m$$

and depends on the particle mass, scaled by the reduced parameter, V_{red}.

- For two different particle masses, it is possible to maintain the mapping position by adjusting both applied potentials according to:

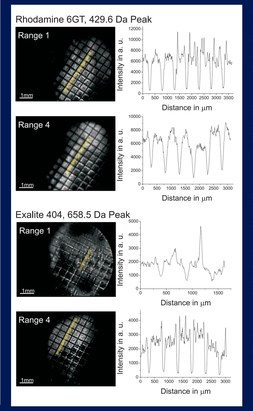
$$\frac{(V_{in} - V_{out})_1}{(V_{in} - V_{out})_2} = \frac{m_1}{m_2} = S$$

- By applying this principle to a complete electrostatic lens, the particle velocity component along the ToF axis is kept the same, and the spectrometer can be retuned to any mass of interest while maintaining the focussing specifications. Simulated data for four different optic settings are shown on the right.



4) Experimental results

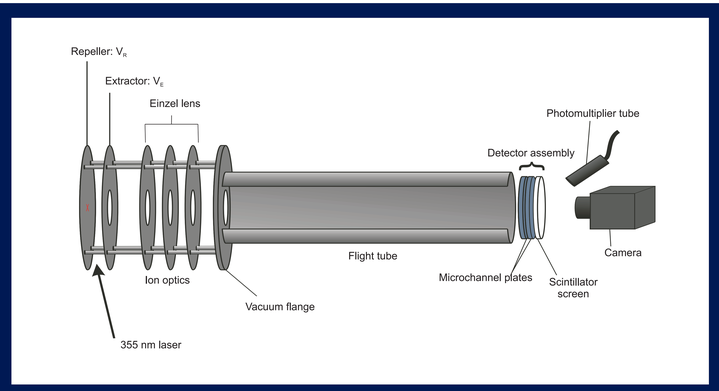
- To demonstrate the tunability of the spectrometer, spatial images of grid structures comprising different analytes were collected for all four mass ranges.
- Depending on the ion mass and the voltage/range settings employed, the images should exhibit different focussing properties.

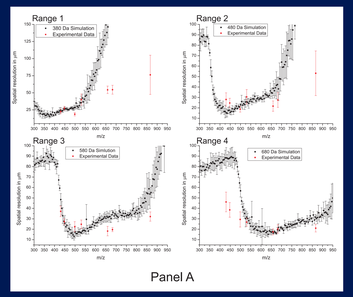


- Rhodamine 6G (429.6 Da) showed the best resolution in the first range, while Exalite 404 (658.5 Da) showed the best resolution in the fourth mass range.
- A comparison between the simulations and the experimental velocity corrected spatial resolutions is presented in the four graphs in panel A
- The best spatial resolution determined in these experiments are in agreement width SIMION simulations for all four mass ranges.
- The four graphs in panel B compares the experimentally determined ToF resolution with corresponding SIMION simulations. Again, a good agreement was found.
- By employing velocity-corrected ion extraction, the PEDA method can be **tuned to any mass of interest**.

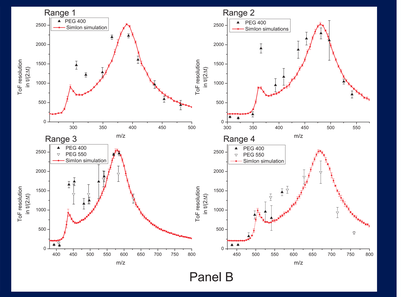
Aims

- **To build a linear microscope mode imaging mass spectrometer setup with improved spatial and time-of-flight resolution [1,2]**
- **To apply and improve the Post Extraction Differential Acceleration (PEDA) technique to achieve a high ToF resolution over a large mass range [3]**
- **To develope a sensitive and fast imaging detector assembly to perform high resolution IMS**





Panel A



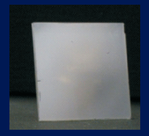
Panel B

1) Fast detection system

- Conventional imaging detectors consists of a chevron MCP set and a P47 phosphor screen.
- The long decay time of P47 (100 ns down to 10%) limits its application to multi-mass imaging mass spectrometry .
- The poor efficiency of available fast scintillators render them incompatible with ion imaging instruments.
- We have developed a novel organic scintillator which improves the time response in comparison to P47 by more than an order of magnitude; and with improved efficiency.

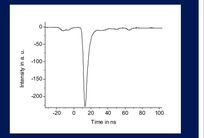
2) The novel Scintillator

- Based on an organic molecule
- Prepared by a vacuum sublimation process
- High layer homogeneity
- Low cost



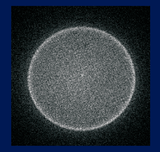
3) Time response

- Laser induced photoionisation experiments
- Electron ToF measurements
- Time response limited by experiment, not by the scintillator
- Decay time (10%): ≤7.3 ns

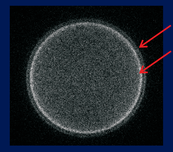


4) Spatial resolution

- Comparison between velocity-map images of CO fragments formed in the UV photolysis of OCS recorded with a commercial P47 phosphor and with the new organic scintillator



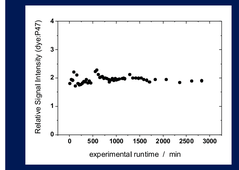
P47
V_{MCP} = 1.5 kV;
V_{scl} = 3.5 kV

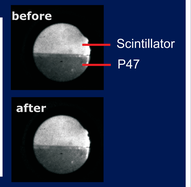


New Scintillator
V_{MCP} = 1.27 kV;
V_{scl} = 3.0 kV

5) Sensitivity and Stability

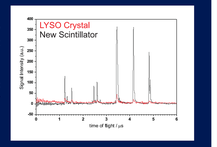
- Direct comparison of new scintillator with a P47 screen in a single experiment
- Sections of both scintillators mounted symmetrically behind MCP stack
- The new scintillator showed **1.8 x more light output than P47**
- No signal degradation was observed over a 4 day period





6) Single ion detection using MPPC

- New scintillator optically coupled to a Multi Pixel Photon Counter (MPPC)
- Single photon counting and direct ion detection with sub ns resolution
- No need for MCPs
- ToF mass spectra compared for new organic scintillator and inorganic (LYSO) crystal scintillator
- New scintillator transfers kinetic energy of an impacting ion into light far more efficiently.
  - **Improved Efficiency 3x**
  - **Lower detection threshold**



[1] R.M. Caprioli, T.B. Farmer, and J. Gile, Anal. Chem 69, 4751 (1997).
[2] S.L. Luxembourg, T.H. Mize, L.A. McDonnell, and R.M.A. Heeren, Anal. Chem. 76, 5339 (2004).
[3] J. Aoki, H. Hazama, M. Toyoda J. Mass Spectrom. Soc. Jpn. 59, 57 (2011).