Implementation of Ion Optical System for Miniaturized Time-of-Flight Mass Spectrometer

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Overview

Spatial and temporal ion-mapping with a miniaturized time-of-flight (ToF) mass spectrometer.

An optical system for microprobe mode IMS (Imaging mass spectrometry) to enlarge laser beam size was developed.

Introduction

Mass-spectrometric imaging (MSI) allows the simultaneous investigation of chemical and spatial information. MSI is performed with two different approaches, microprobe and **microscope** mode. Microprobe-mode imaging records mass spectra by raster-scanning across an image area; microscope mode irradiate the image area with enlarged laser beam. Additionally, most lasers possess a Gaussian beam profile, it is necessary to homogenize the laser beam.

Here, we characterize the potential to implement an optical system for microscope mode MSI to expand the laser spot diameter, and homogenize the laser beam profile.

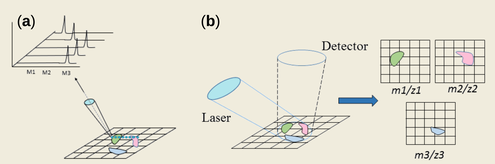

Figure 1. Schematic of the two approaches. (**a**) Microprobe mode area, (**b**) Microscope mode

The mass spectrometer used in the present study was modified based on a previously described home-build Time-of-flight (ToF) mass analyzer (11 in.× 5 in.× 8 in). Specifically, the "TinyToF"[1,2] is capable of mapping select ions of interests, while preserving the ability of performing traditional ToF measurements. The spatial distribution of ions with specific *m/z* can be obtained with detector 1, while full mass spectra can be reflected by detector 2.

In present study, laser spot size was enlarged by adjusting focal distance of the convex lens. And optical fiber or diffractive optical element were proposed to homogenize the laser beam profile.

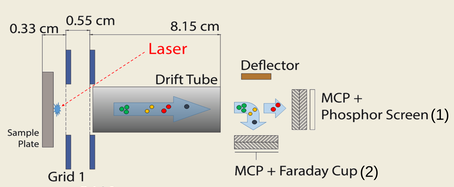

Figure 2. Schematic of TinyToF modified adaptation for selective image acquisition

Method

- **Time-domain mass-spectra acquisition:** The multi-channel plate (MCP) with a charge detector was connected to a digital oscilloscope to acquire time-domain information. The direct current (DC) coupling between the charge detector and the oscilloscope enabled semi-quantitative measurement of ion current. The sample rate on the oscilloscope was set to 500 MSa/s in order to obtain adequate time-domain data-density.
- **Ion spatial distribution:** The image sensor was synchronized with the laser pulse through a digital delay generator. Thus, the gate-timing of image capture was strictly controlled in a range of 1 to 10 µs. To minimize the ion loss during image capture, the exposure was set to 15 ms. The spatial resolution in this study was determined to be *ca.* 45 µm/pixel.
- **Image sensor:** A monochrome CCD image sensor with a resolution of 1288×964 pixel (1.3 MP) was used to acquire the image data. Meanwhile, the analog-to-digital converter of the CCD sensor was set to 16-bit for optimized resolution of optical intensity.
- **Image-data processing:** The acquired spatial distribution of ions were fitted with a Gaussian surface:

$$I(x,y) = A \cdot e^{\frac{-(x-\mu_x)^2}{\sigma_x}} \cdot e^{\frac{-(y-\mu_y)^2}{\sigma_y}}$$

The surface fitting was then globally optimized with Matlab v8.5.

ImageJ was also used to process part of image data.

- **Ion trajectory simulation:** the theoretical ion-trajectories were calculated with SIMION v8.0, where the experimental voltages were set based on the computation.
- **Sample preparation:** CsCl was dissolved in methanol (saturated solution). The MALDI sample were prepared by mixing P14R and matrix (α-cyano).
- **Laser:** A 400 µJ Nd:YAG laser of 355 nm was used as the desorption/ionization source. The laser was manually triggered for each analysis to synchronize with data acquisition instruments.

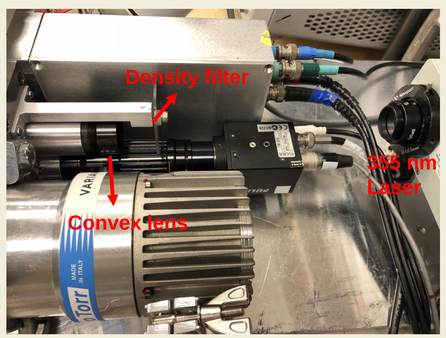

Figure 3. Schematic of TinyToF modified adaptation for selective image acquisition

- **Optics:** The laser beam diameter was adjusted by a beam expander. A convex with 15 mm focal length was used to focus laser beam. A density filter was adapted to control laser energy level.

Result

Direct Laser Ionization

- To test the system, the transient ion-signals and ion-maps of CsCl were recorded.
- The image detection in the simplest configuration mainly aimed at an experimental verification of generating an ion ensemble whole geometric shape that retains the original spatial distribution of sample.

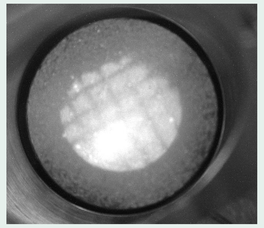

Figure 4. Results of a stigmatic imaging experiment obtained by the imaging detector. The CsCl deposits were patterned by fine grid meshes of 70 lines/in. Scale bars indicate image size.

- The patterns of detected ion ensembles reflected artificial geometries of the samples on the plate, although the uneven beam profile of laser affected the homogeneity of brightness.
- The alignment of laser beam still needs to be optimized. Moreover, the MALDI sample deposit is not homogeneous, other sample preparation methods need to be explored.

Adjust Laser Beam Size

- We further analyzed a standard biological analyte (P14R) with MALDI.

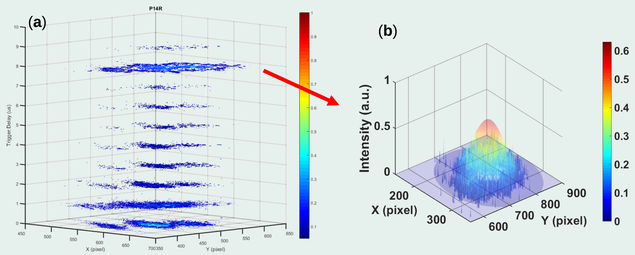

Figure 5. **(a)** Stacked P14R ion-image with respect to gate-time **(b)** Surface fitting of the P14R ion-map.

- The analyte ions was recorded at 8 µs. The fitted Guassian surface agreed with the recorded ion-map. This observation indicated that the spatial distribution of the ions is dictated by the ionization source and ion introduction, which was the pulsed laser in this study.

Result

- 300 and 600 µm laser beam sizes were tested. The diameter of the high ion-density area were *ca.* 2.4 mm and 4 mm. This result suggested by expanding laser beam size, larger image can be also obtained through single laser shot.

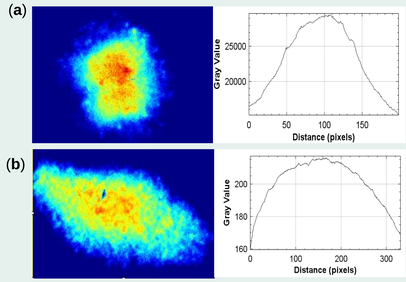

Figure 6. Ion-map and profile of P14R with (a) 300 nm and (b) 600 nm laser beam size.

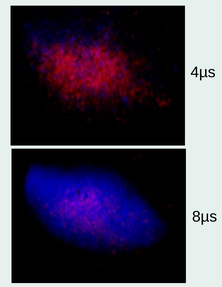

Figure 7. Ion-map of P14R (blue) and CsCl (red) mixture at 4 µs and 8 µs with 600 nm laser beam size.

- However, due to the use of refection mirror, the laser shape distorted when we increased the laser beam size (Figure 6).
- We further analyzed P14R and CsCl mixture (Figure 7). As previous stated, Cs^+ ion was found at 4 µs and P14R ion showed up at 8 µs. Therefore, The ion-map of mixture was record at 4 µs and 8 µs separately.

Conclusion

- Expanding laser beam could image larger area.
- Laser-based desorption/ionization produced Gaussian-like spatial profile of ions
- P14R and CsCl mixture ions were mapped with MCP-phosphor screen detector coupled to a high resolution digital image-sensor.

Future Works

- Diffractive optical element or square shape optical fiber for homogenizing the laser beam profile
- Implementation of continuous motion stage and simultaneously detection method

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References

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(3) Vallance, C.; Brouard, M.; Lauer, A.; Slater, C. S.; Halford, E.; Winter, B.; King, S. J.; Lee, J. W. L.; Pooley, D. E.; Sedgwick, I.; Turchetta, R.; Nomerotski, A.; John, J. J.; Hill, L. *Phys Chem Chem Phys* **2014**, *16* (2), 383–395.