MALDI-2 laser post-ionization on a trapped ion mobility orthogonal time of flight instrument

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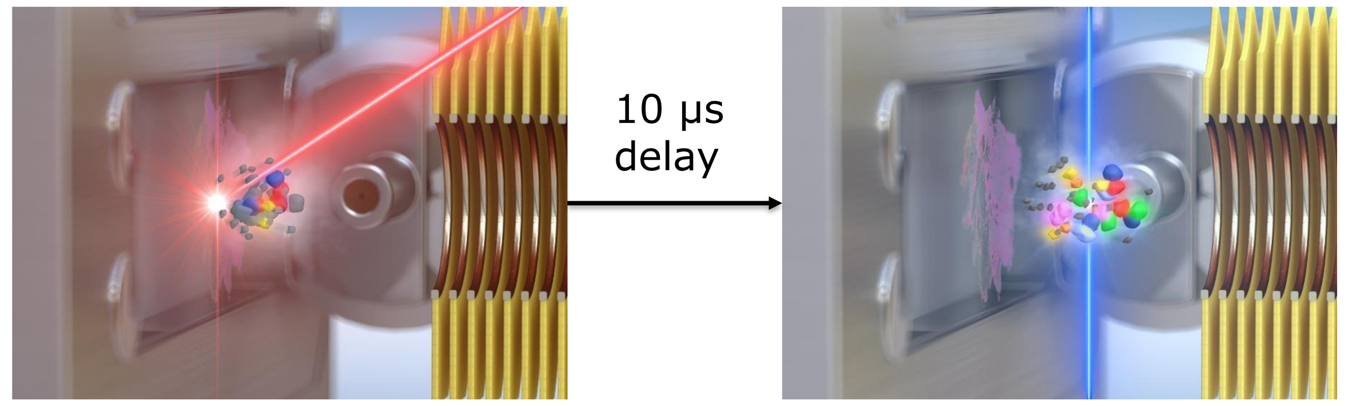
Introduction

Matrix-assisted laser desorption/ionization (MALDI) is known to have inherently low ion yields, a fact that was already acknowledged in the early days of MALDI. Since then, numerous attempts were made to improve ion yields, amongst others by use of a second laser. MALDI-2 was introduced by Soltwisch *et al.* in 2015[1] and was subsequently established in a couple of labs as an experimental setup. Here we show the first full integration of MALDI-2 functionality in a commercially available instrument (timsTOF flex) and employed it to investigate fundamental parameters of the MALDI-2 process, as well as applied experiments.

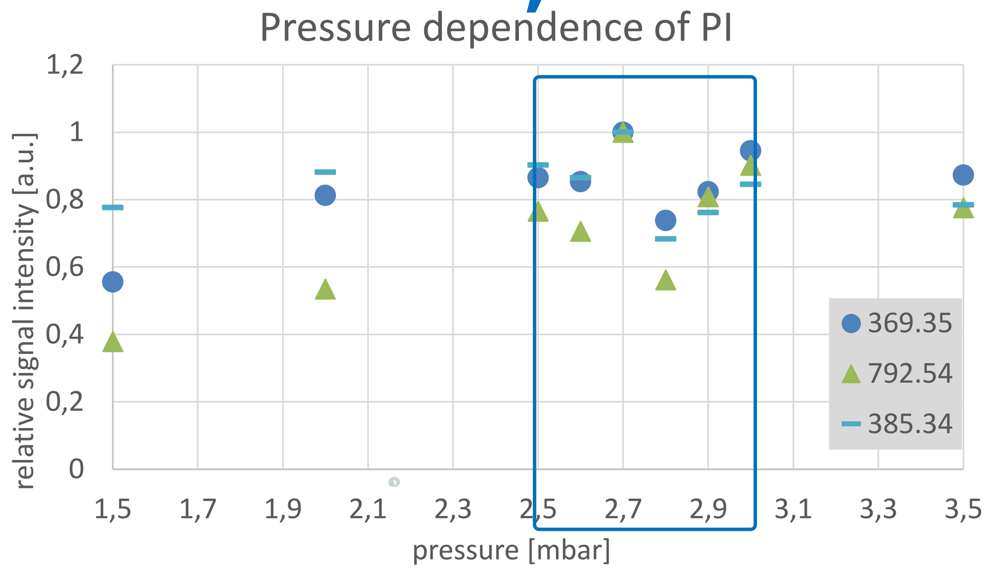


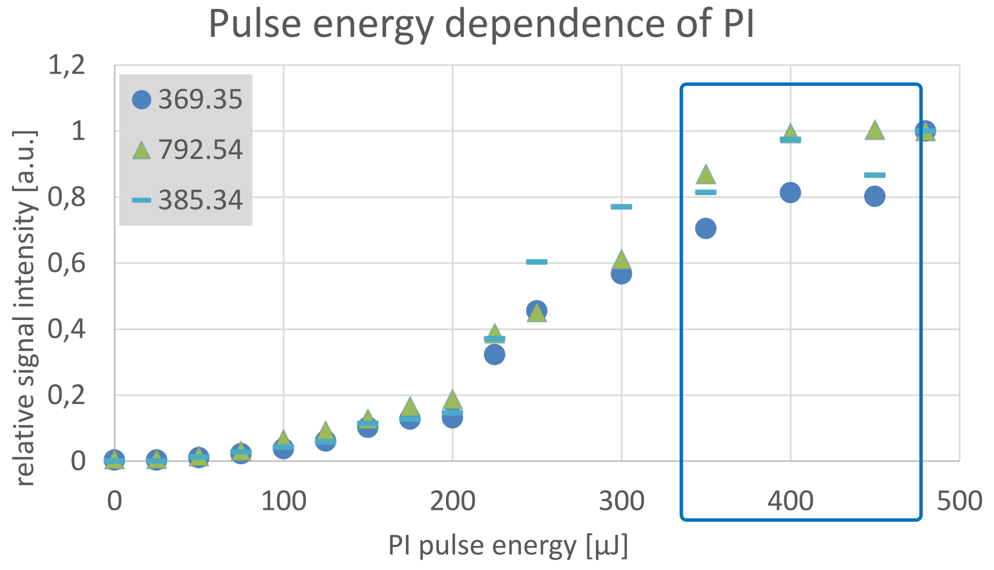
- First laser beam desorbs material as usual
- Ion yields typically in the range of 10^{-4}-10^{-7} → high abundance of desorbed analytes should be available for post-ionization
- Second laser beam intersects the evolving plume
- Resonant two-photon post-ionization of matrix
- Current working hypothesis: charge transfer from post-ionized matrix to analyte in temporary reaction vessel[1]

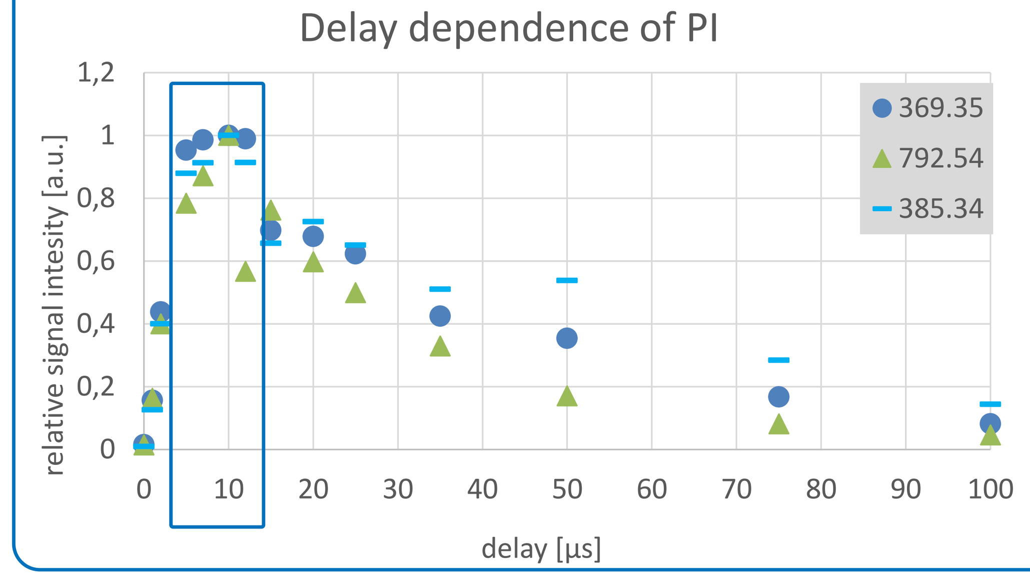
Methods

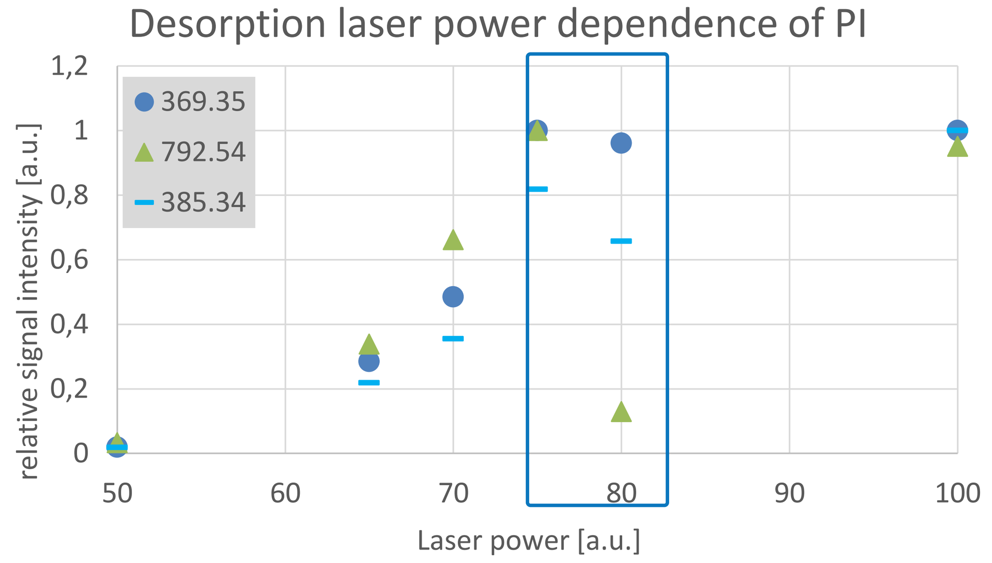
Rat brain tissue (RccHan: Wist) was covered with 15 mg/ml 2,5-DHAP (Bruker, Germany) in a mixture of AcN/H_2O/MeOH 8:1:1 *v/v/v*, as well as 2,5-DHB (Bruker, Germany) in can/H_2O 9:1 *v/v*. 100 px with a 5x5 µm² laser beam were irradiated with 30 shots. Conditions, unless each parameter was investigated: pressure 2.7 mbar, delay 10 µs, post-ionization (PI) pulse energy 350 µJ, distance sample to PI laser 500 µm, desorption laser power was ~1.7x above optima for normal MALDI.

Results – 2,5-DHAP

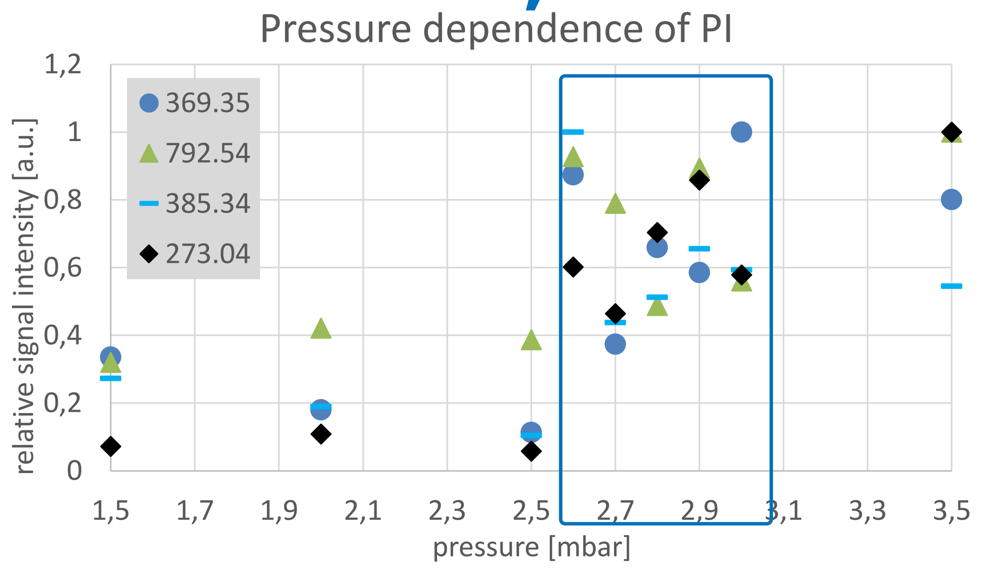


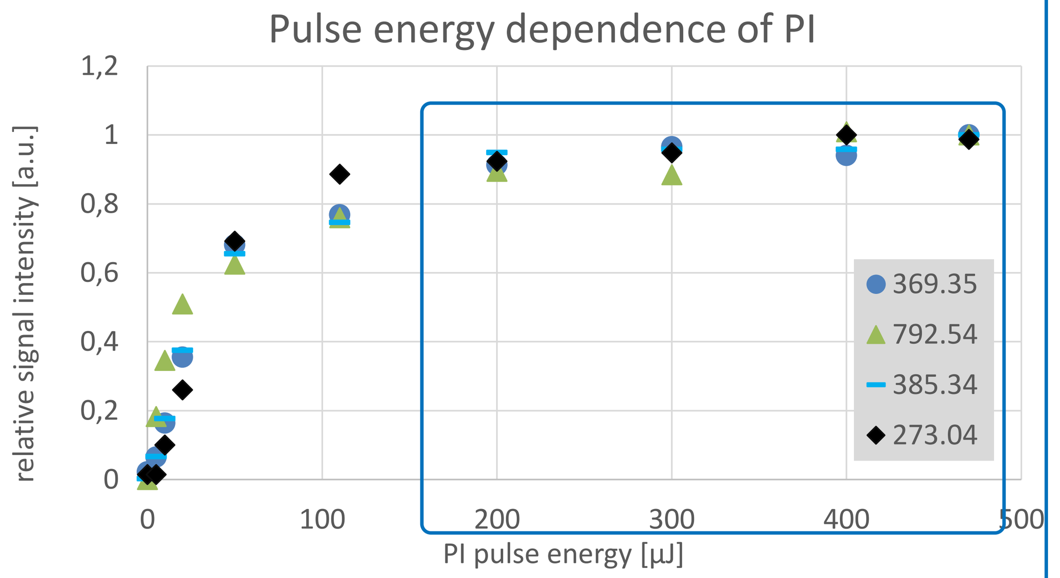


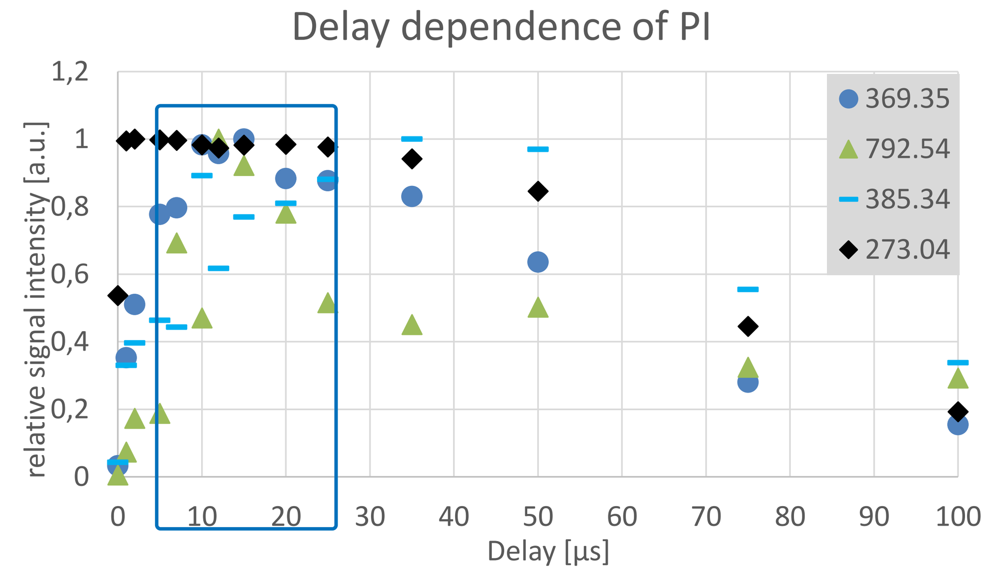


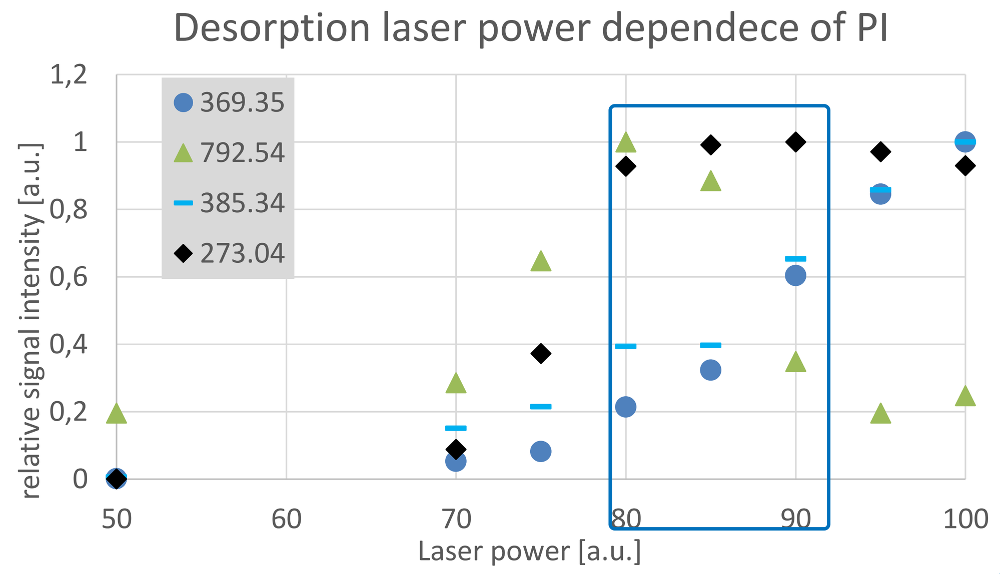


Results – 2,5-DHB









Results – MALDI-2

- MALDI-2 PI efficiency depends on source pressure, delay between desorption and PI laser, pulse energy of the desorption laser, pulse energy of the PI laser and distance between sample and PI laser.
- Pressure has least influence in range investigated, literature suggests PI efficiency decreases strongly below 1.5 mbar[1], best results are obtained for p>2.5 mbar.
- Delay range for lipids ideally 5-15 µs, broader range for 2,5-DHB than for 2,5-DHAP, suggesting a larger spread of particle velocities for 2,5-DHB.
- PI effect for 2,5-DHB reaches plateau at ~200 µJ/pulse, for 2,5-DHB at ~350 µJ/pulse. This conflicts with absorption spectra of the respective matrices (maximum for 2,5-DHAP[2], close to a local minimum for 2,5-DHB[1]) suggesting at least for 2,5-DHB the involvement of clusters in the absorption of the PI laser light. This assumption is also supported by the observation, that higher desorption laser power is required for optimal PI results for both matrices, than for normal MALDI.
- Signal increase for e.g. cholesterol, PE, GalCer, estradiol, prednisolone with 2,5-DHAP more than two orders of magnitude, comparable to previous results on other instruments[1,3].

Instrumental implementation

- PI laser is a Nd:YAG fourth harmonic at 266 nm, pulse width ~7 ns, 1 kHz rep. rate, max. energy output 600 µJ/pulse
- Delay can be adjusted in steps of 1 µs from 0-100 µs
- Pressure can be adjusted from ~1.5-4 mbar, tims functionality only ensured at ~2.7 mbar
- beam waist ~150 µm diameter at MALDI plume, can be adjusted by telescope

Conclusions

- MALDI-2 was successfully implemented on a timsTOF fleX
- MALDI-2 process depends strongly on pulse energies of the desorption laser and PI laser
- Post ionization works best with desorption fluences higher than for normal MALDI – likely through post-ionization of clusters
- Small molecules and lipids can be efficiently post-ionized with MALDI-2
- This instrumental setup allows the convenient investigation of MALDI-2 parameters

timsTOF fleX MALDI-2

Literature
1. Soltwisch *et al.*, Science 2015, 348, 211
2. Trimpin *et al.*, ChemPhysChem 2018, 19, 581
3. Ellis *et al.* Chem. Commun. 2017, 53, 7246