Design, Optimization, and Performance Evaluation of MALDI-TOF MS and MS-MS Instruments.

Poster Number ThP 624

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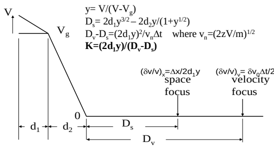
Introduction

In earlier work, theoretical techniques for optimizing the resolving power of MALDI TOF MS systems were presented, and validated for a single reflector instrument. In the work presented here, all of the known contributions to peak width are considered and ultimate limits with presently available technology are defined.

Objective

Establish the practical limits on performance of MALDI-TOF instruments and design and build instruments that test these limits.

Space and Velocity Focusing in MALDI-TOF Ion Source



$y = V/(V-V_g)$

$D_s = 2d_1y^{3/2} - 2d_2y/(1+y^{1/2})$

$D_v - D_s = (2d_1y)^2/v_n\Delta t$ where $v_n = (2zV/m)^{1/2}$

$\mathbf{K = (2d_1y)/(D_v - D_s)}$

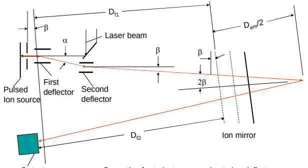
Contributions to Peak Width (dm/m):

$R_{s1} = 2K^{-1}(\delta x/D_e)$ $R_{v1} = [4d_1y/D_{eff}](\delta v_0/v_n)$

$R_m = R_{v1}[1-(m/m^*)^{1/2}]$ where m^* = focused mass

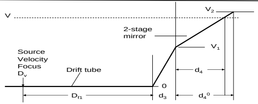
$R_{v2} = 2K^2(\delta v_0/v_n)^2$ $R_t = 2\delta t/t = 2\delta t v_n/D_e$

$R_{v3} = 2K^3(\delta v_0/v_n)^3$ δt is width of single ion pulse



Correction for trajectory error due to ion deflector

- Changes to correct mass independent errors
- Add voltage regulator at input to mirror HV supplies (removes low frequency noise)
- Correct trajectory error due to ion deflector
- Use faster detector (0.5 ns)
  - ETP DM167 in place of 5 µm dual channel plate
- Use faster digitizer
  - 0.5 ns bins>0.25 ns bins



Two-field mirror. The field-free distance D_f is the distance from the source velocity focus to the mirror D_{f1} plus the distance from the mirror to the detector D_{f2} (not shown).

Voltage ratio $w = V/(V-V_1)$ and $d_4 = d_4^0(V-V_1)/(V_2-V_1)$

At first and second order focus

$w = 3/[1-(4d_3/D_f)]$, $V_1/V = (w-1)/w$ and

$V_2/V = V_1/V + (1-V_1/V)(d_4^0/d_4)$

$d_4/d_3 = (D_f/4d_3)w^{-3/2} + (w+w^{1/2})^{-1} = [w^{1/2}(w-3)]^{-1} + (w+w^{1/2})^{-1}$

Effective length of the mirror

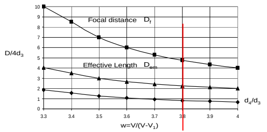
$D_{em}/4d_3 = (w-3)^{-1}+1$

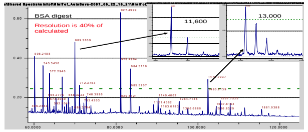
Total effective length of the analyzer

$D_e = D_{em} + D_f + D_v + D_{es}$ where $D_{es} = 2d_1y^{1/2}[1+(d_2/d_1)/(y^{1/2}+1)]$

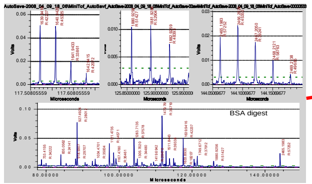
The principal benefit of the mirror is to increase D_e without increasing ion peak width.

Total effective length $D_e = D_f + D_{em}$





Before Correction



After Correction

Predicted Ultimate Resolving Power as Functions of Effective Length and Ion Velocity

Optimum values for ion velocity and focusing parameter K are given by:

$K = 6^{-1/14}[\Delta x/dv_0\delta t]^{3/7}[\delta x/D_e]^{1/7}$

$v_n = \Delta x/K\delta t = 0.0139(V/m)^{1/2}$

Typical values

$\Delta x = 0.01$ mm, $\delta v_0 = 400$ m/s $= 0.0004$ mm/ns, $\delta t = 0.5$ ns

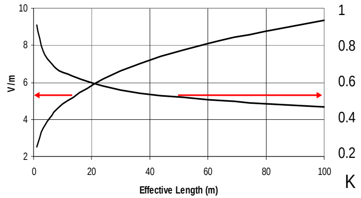
With these values for the parameters the optimum focusing parameter and ion energy are give by

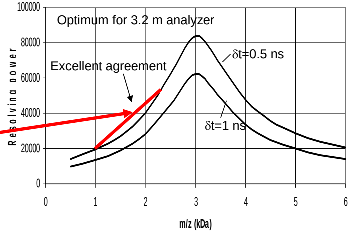
$K = 2.437D_e^{-1/7}$ and $V/m = 0.349D_e^{2/7}$

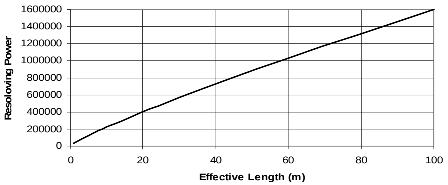
Other potential contributors to peak width include high voltage noise on The mirror or ion lenses and on the ion accelerating pulse, trajectory error, Jitter between the laser pulse and the accelerating pulse, and energy loss due to small angle scattering with residual gas in the analyzer. These Contributions to relative peak width are the following:

Contributor		limit
HV noise	$\Delta V/V$	$\beta(\Delta V/V) < R_{v3}/2$
Trajectory	δL	$\delta L < \Delta x/2$
Source jitter	δt_j	$K^{-2}(\delta t_j\delta v_0) < \Delta x/2$
Source voltage	ΔV_s	$(\Delta V_s/V)(D_v) < \Delta x/2$
scattering	δt_s	$p(torr) < 10^{-4}D_e(mm)$

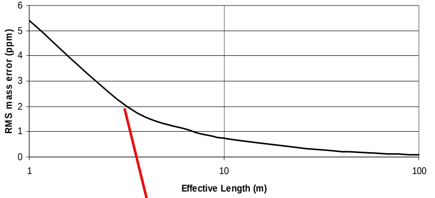
$\beta = D_m/D_e = 0.3$ (mirror) $=< 0.01$ (lens)

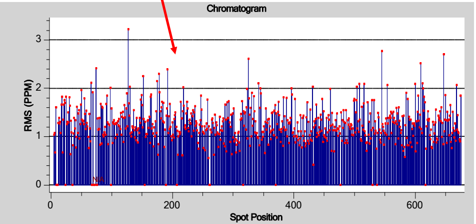






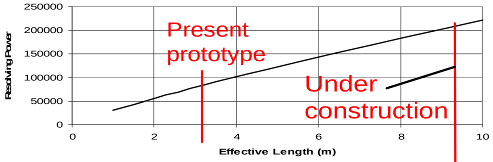
Optimum Resolving Power and Mass Accuracy as Function of Effective Length

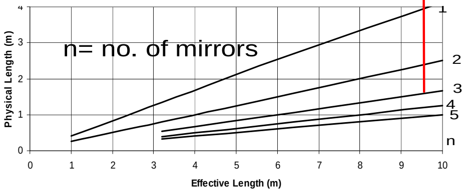




RMS error for 10 peaks in spectrum of tryptic digest of BSA for all 675 spots on a 102x108 mm sample plate with automatic 2-point internal Calibration for 3.2 m analyzer

Optimum Resolving Power and Mass Accuracy as Function of Effective Length





Physical length as function of effective length and number of mirrors.

Conclusions and future work

1. Experimental results on 3.2 m system in excellent agreement with theory
2. Trajectory error for single mirror analyzer <0.01 mm
3. Noise on mirror HV supplies <10 ppm in current analyzer
4. Noise on source HV pulser<500 ppm
5. Jitter of 10 ns between laser pulse and extraction pulse OK with reflector
6. Residual gas pressure<10^{-7} essential for high performance
7. Resolving power of 1,000,000 and mass accuracy of 0.1 ppm is feasible, but requires effective length of ca. 60 m.
8. Systems employing multiple reflections can provide practical configurations if trajectory error per mirror is sufficiently small.
9. Ultimate limits set by HV noise and residual gas pressure

Two analyzers with 10 m effective length are currently under construction to compare performance of single mirror vs. three mirrors.

Goal is >200,000 resolving power with RMS mass error <1 ppm

Reference: 1. M. L. Vestal, "Modern MALDI Time of Flight Mass Spectrometry" J. Mass Spectrom. 44, 303-317(2009).

Acknowledgements: This work was supported by the NIH, NCRR under grant RR 025705 and by the staff of Virgin Instruments.