A New Approach to TOF Mass Spectrometry for High Performance MS and MS-MS

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Elements of TOF Analyzer

- Ion production
  - MALDI
- Time focusing to reduce effect of initial position and initial velocity
  - Delayed extraction
  - Simultaneous space and velocity focusing (SimulTOF)
- Ion optics for efficient ion transmission of ions of interest and mass gate and filtering to remove ion noise
- Detector for efficient detection of broad range of masses with fast response

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  - MALDI 5 kHz operation
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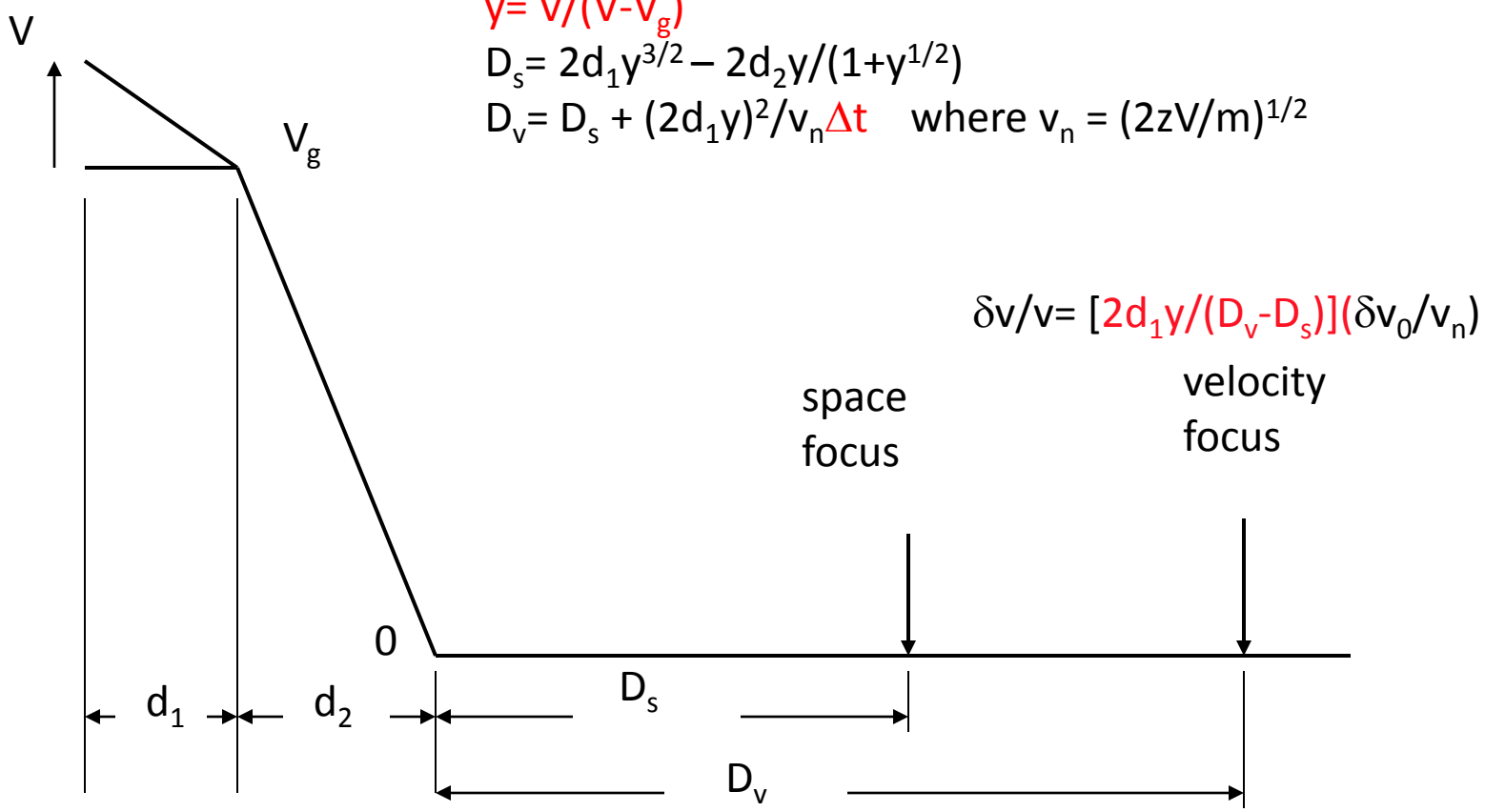
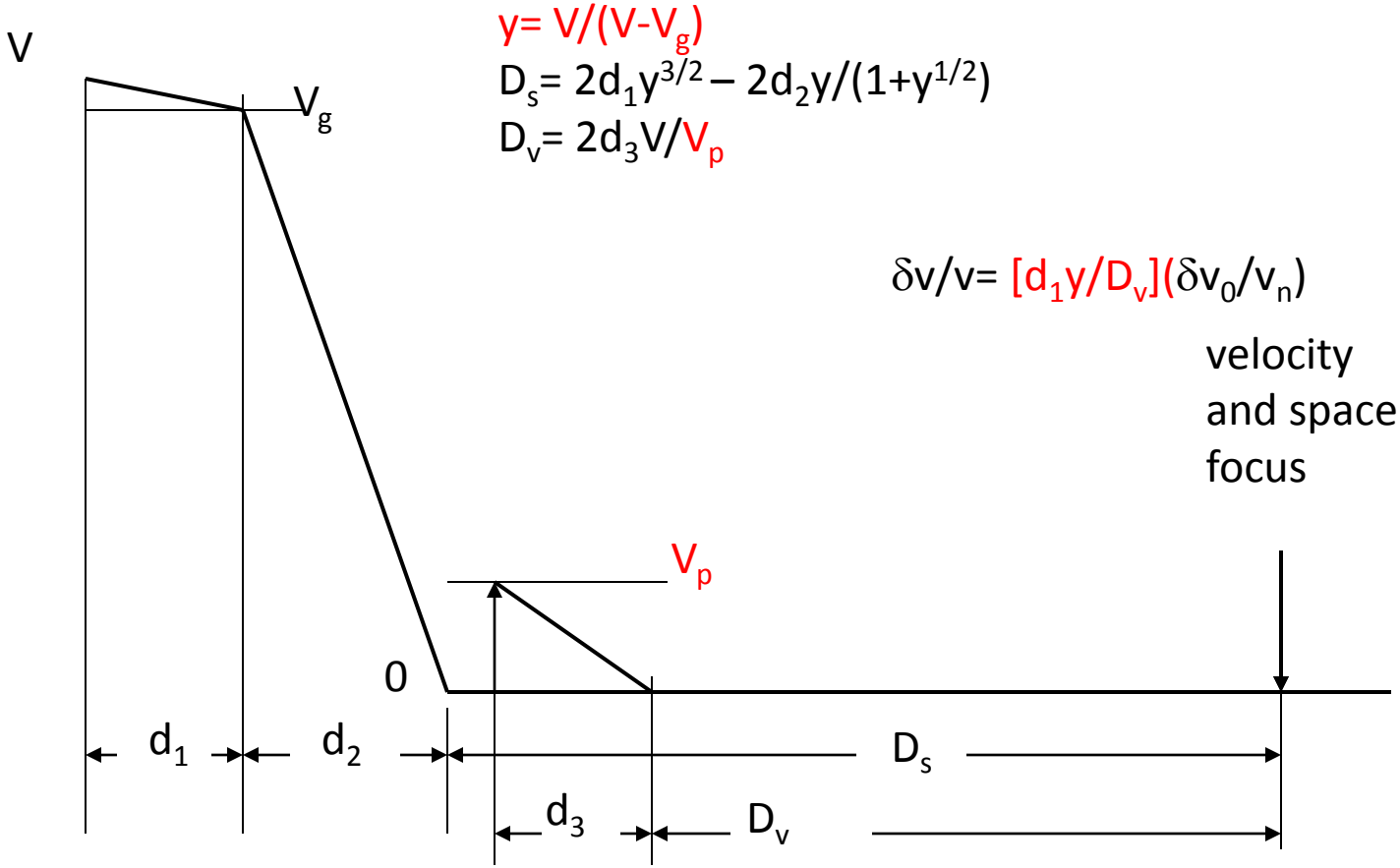
- Ion optics for efficient ion transmission of ions of interest and mass gate and filtering to remove ion noise
- Detector for efficient detection of broad range of masses with fast response
  - Destroy the myth that high mass singly charged ions cannot be detected by conventional detectors

Note: All data presented are "raw" directly from the digitizer.
No data processing, smoothing, or baseline correction has been employed.



Delayed extraction. The distance to the velocity focus D_v is always greater than the distance to the space focus D_s, and if the difference is small the velocity spread $\delta v/v$ is large. As a result it is not possible to obtain high mass resolution over a broad range with a linear analyzer, but refocusing with a two-field mirror can yield high resolution over a broad range.



$y = V/(V-V_g)$

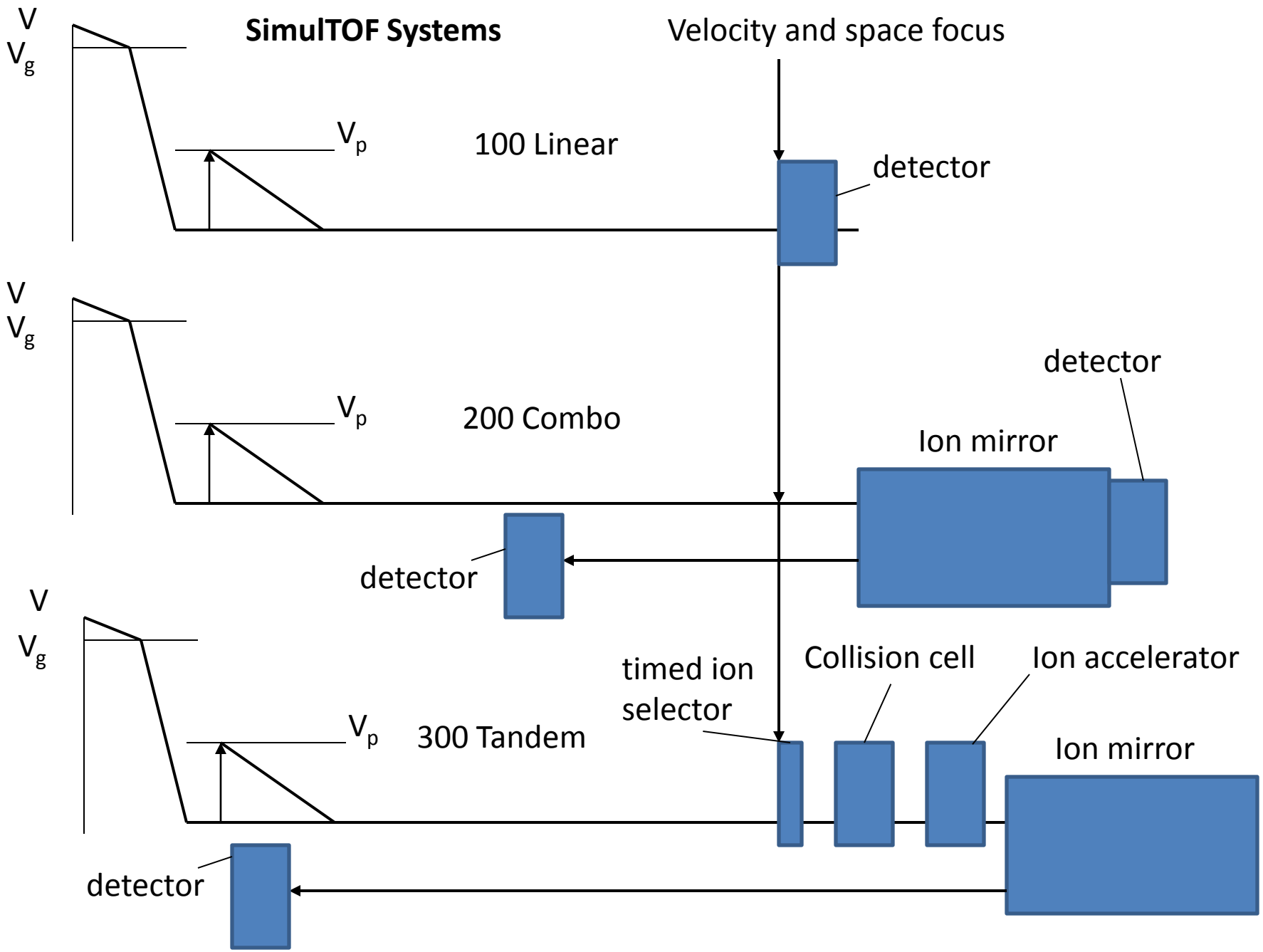
$D_s = 2d_1y^{3/2} - 2d_2y/(1+y^{1/2})$

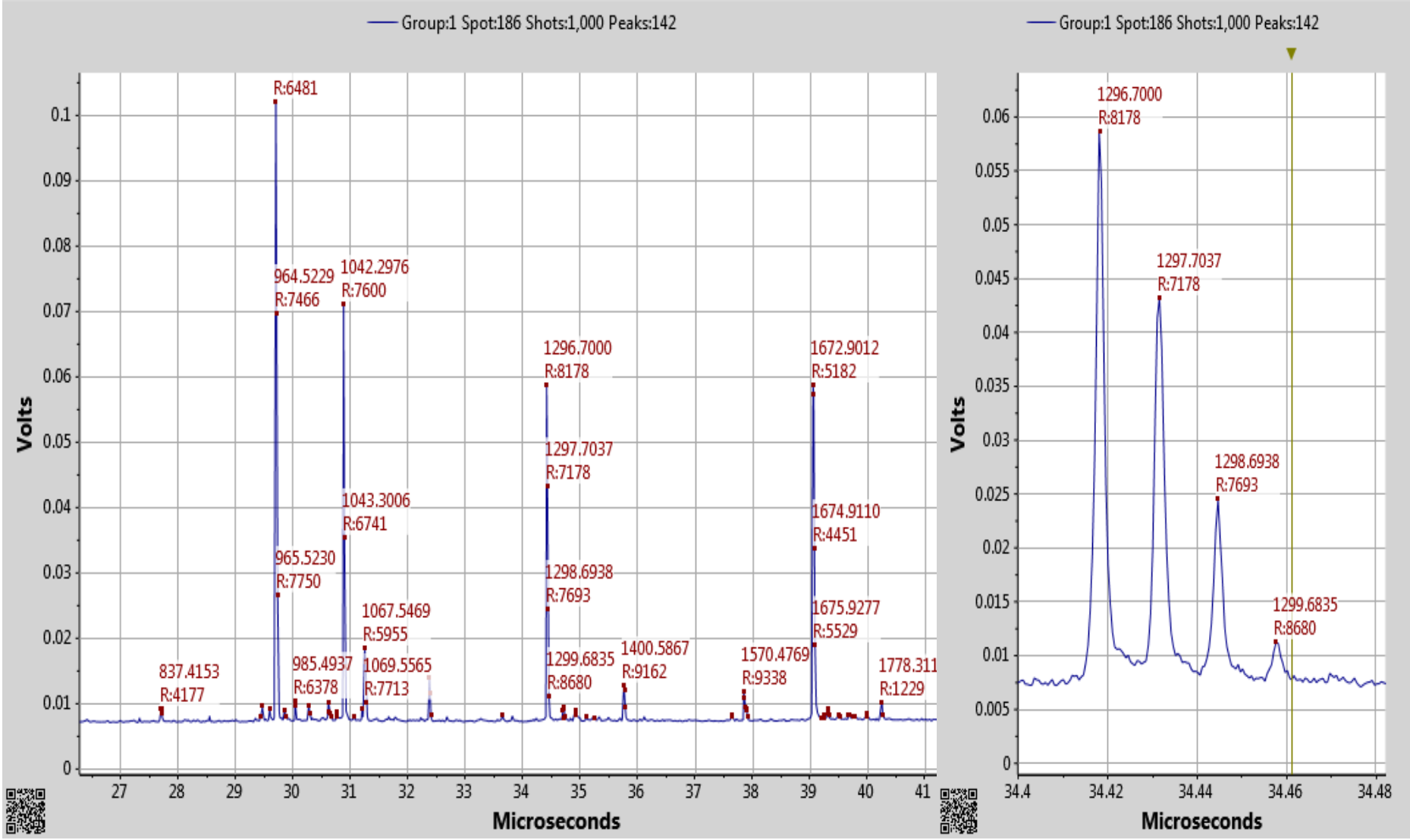
$D_v = 2d_3V/V_p$

$\delta v/v = [d_1y/D_v](\delta v_0/v_n)$

velocity and space focus

SimulTOF focusing: The velocity focus D_v is adjusted by varying the amplitude of the accelerating pulse V_p and the space focus D_s by adjusting the voltage ratio y, allowing simultaneous space and velocity focusing to be achieved. Moreover, if D_v is greater than d_1y then the velocity spread is reduced. Thus high resolution over a broad range is possible for a linear analyzer and it provides a preferred first stage for a reflecting analyzer or a tandem TOF-TOF.

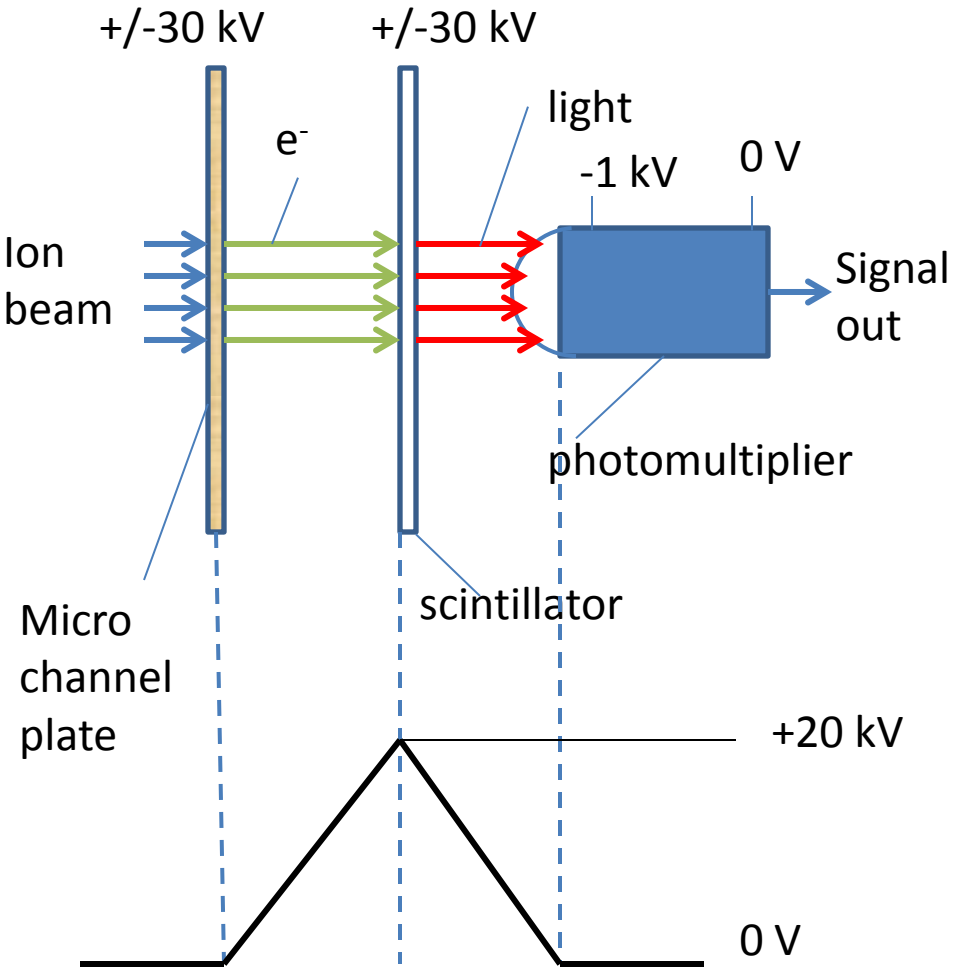

V
V_g
SimulTOF Systems
Velocity and space focus
V_p
100 Linear
detector
V
V_g
V_p
200 Combo
detector
Ion mirror
detector
V
V_g
timed ion
selector
Collision cell
Ion accelerator
V_p
300 Tandem
Ion mirror
detector



SimulTOF Linear @10 kV -- Higher Resolving Power than the old XL Reflector

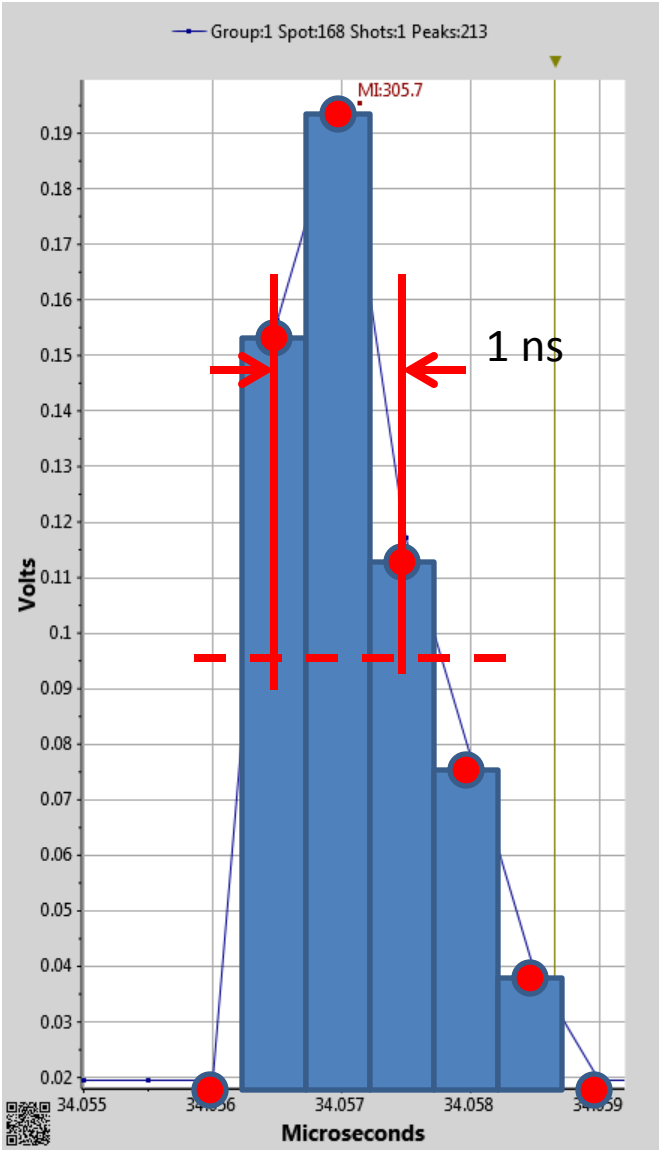
Photonis detector

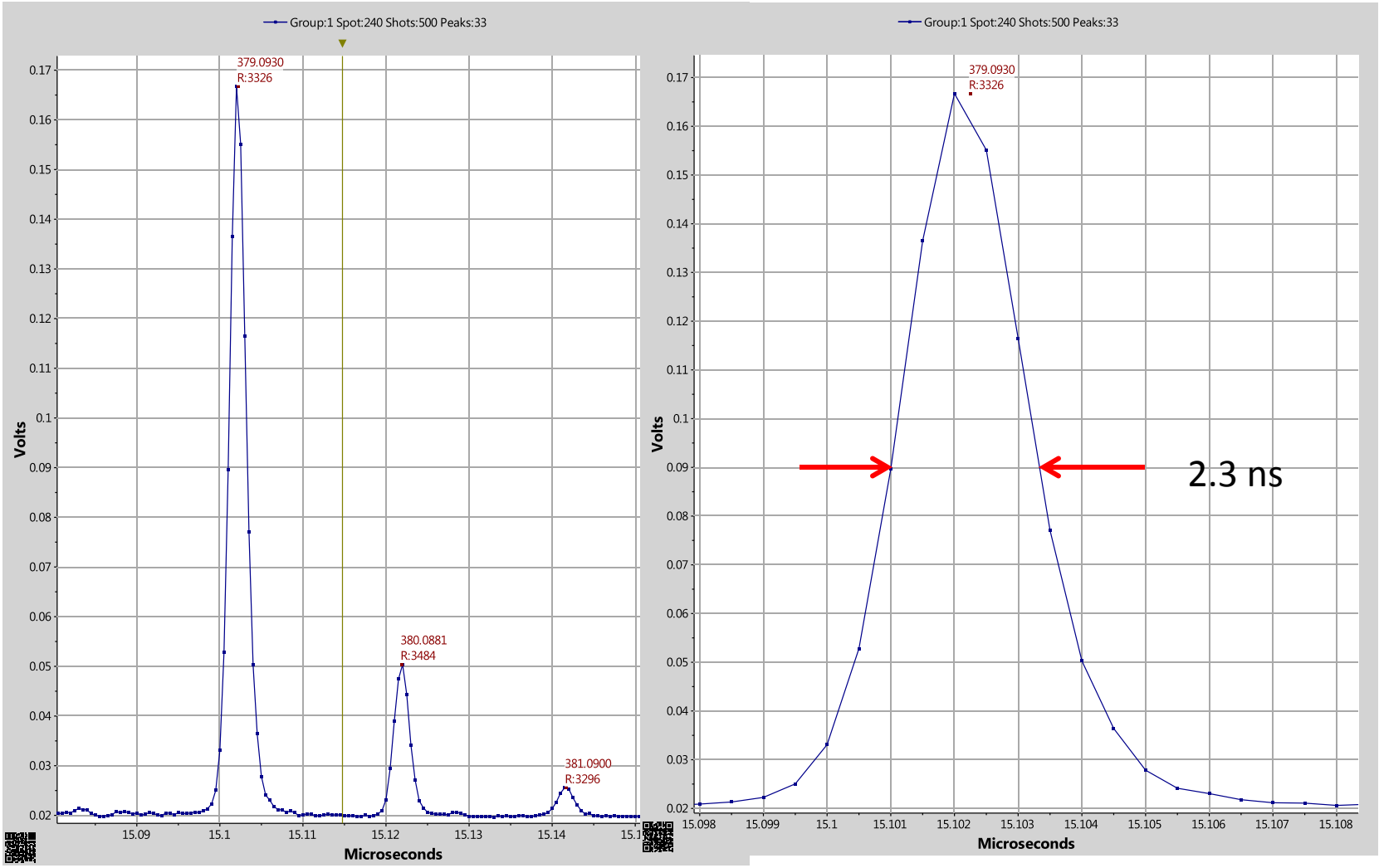
See Ritzau Poster THP 564 for more info



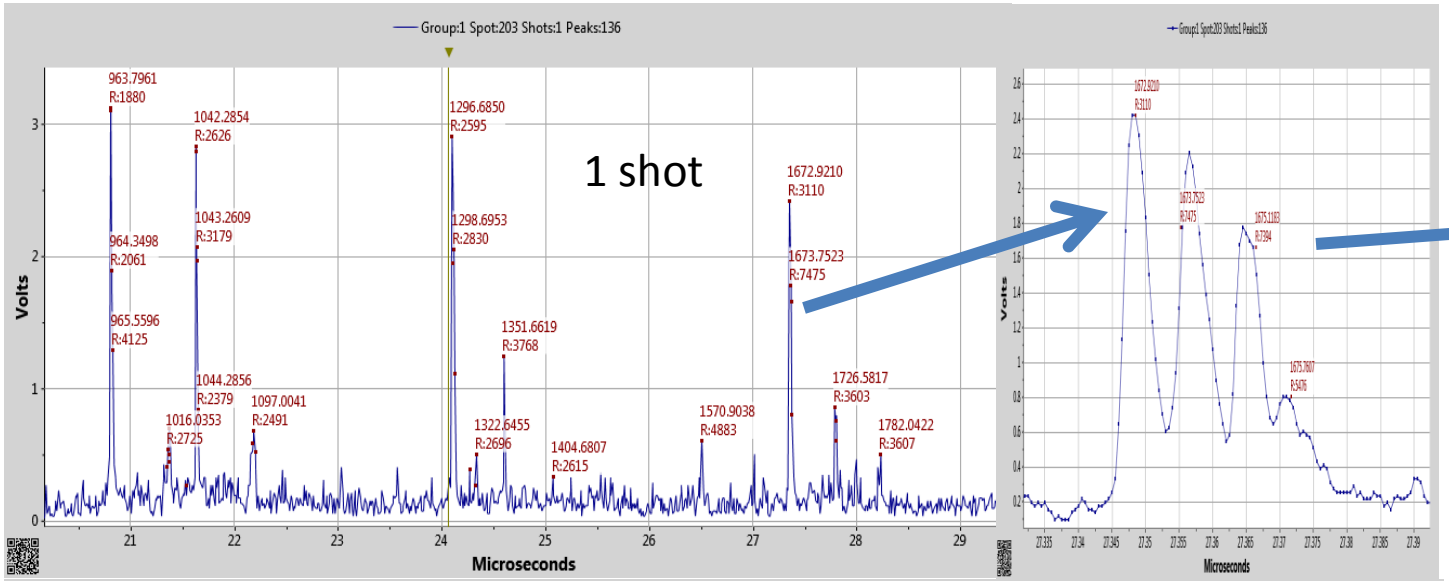
Potential diagram for linear detector

Typical single ion pulse with fast scintillator

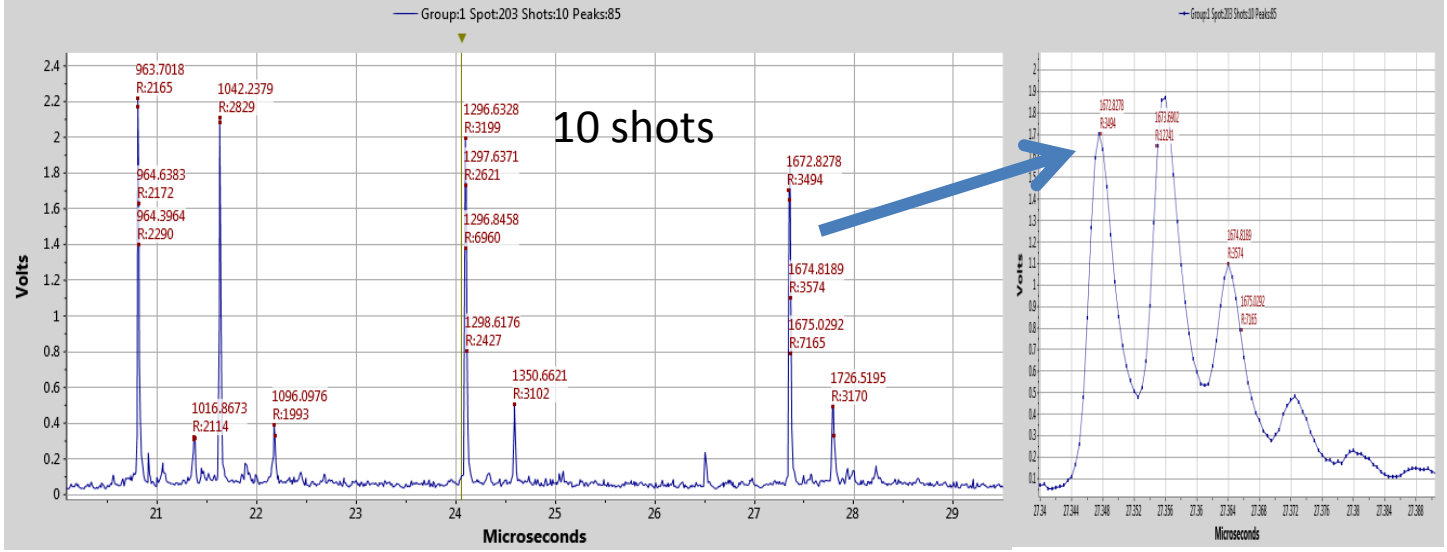




Spectrum of α-cyano matrix dimer measured in SimulTOF 100 Linear MALDI-TOF
At 15 kV energy using Photonis fast hybrid detector

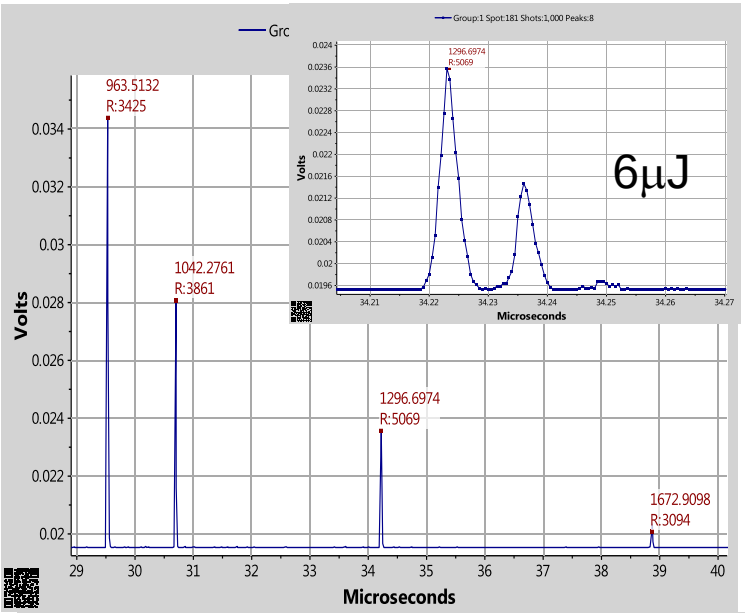


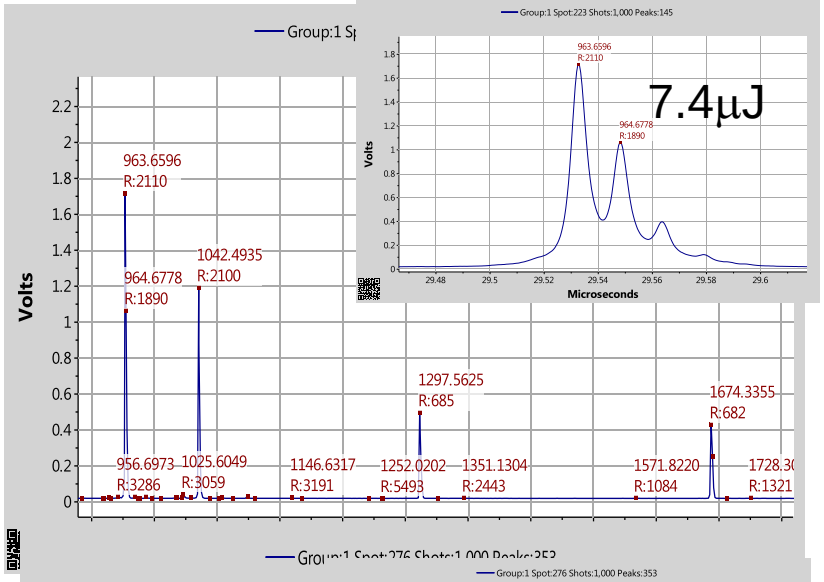
~20,000 ions detected

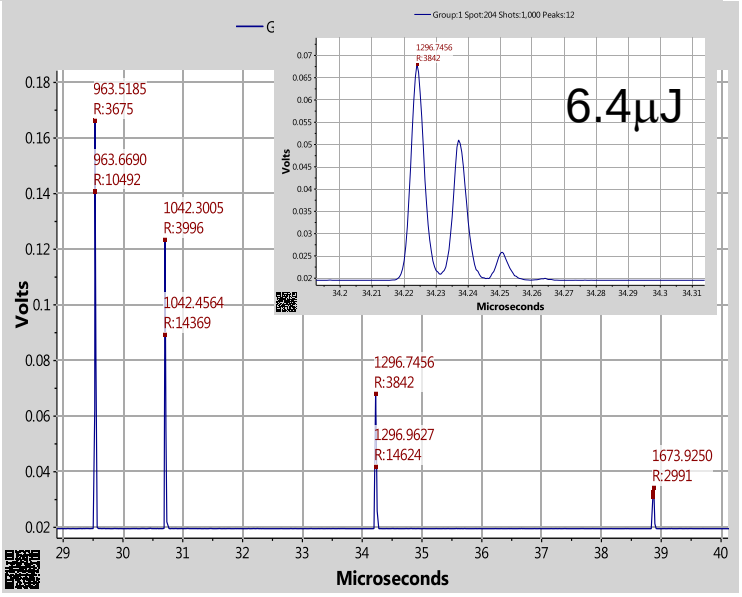


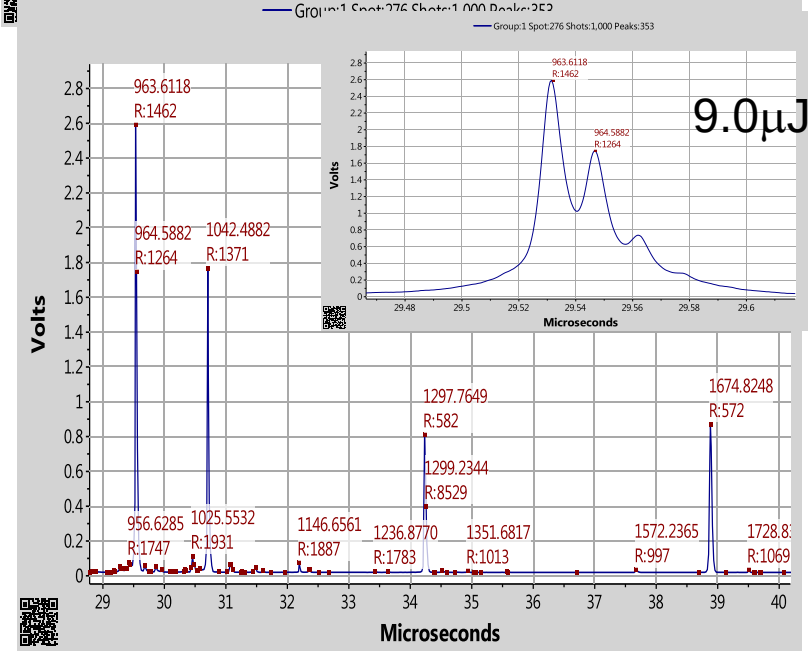
Mixture of peptide standards, 100 femtomole/µL, 2.5 mm spot

Laser spot ca. 50 µm, fluence 1.3x threshold, 0.4 attomole/spot=240,000 molecules

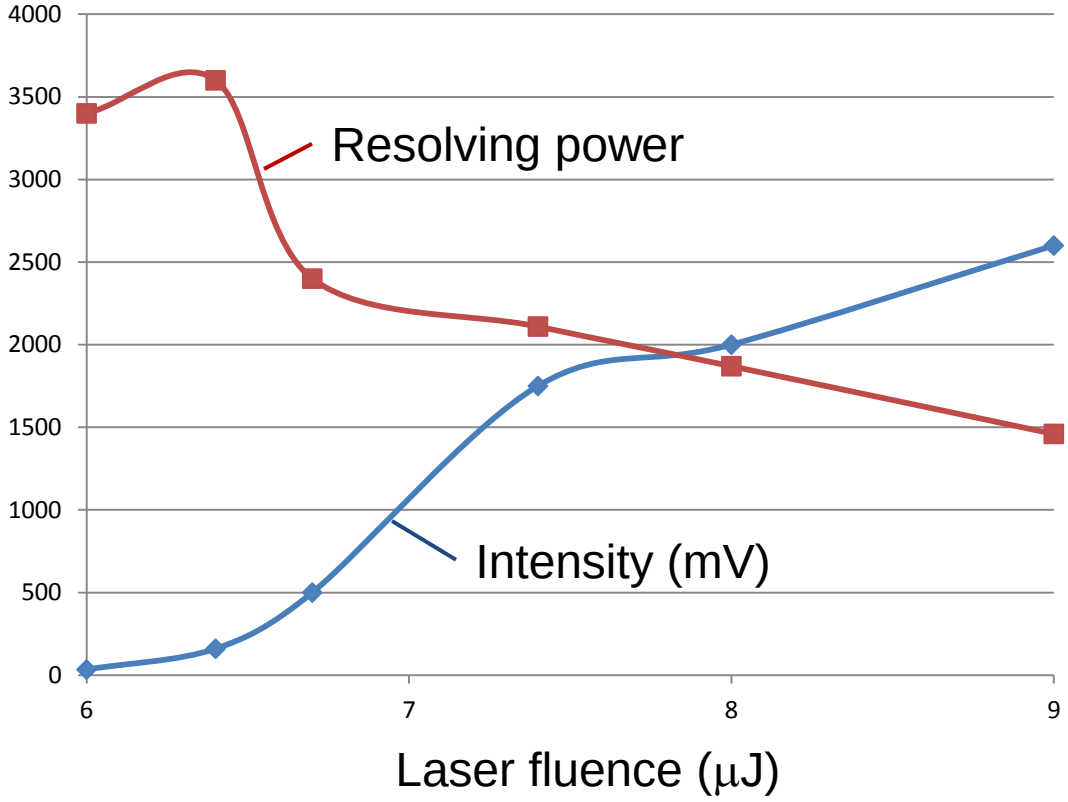




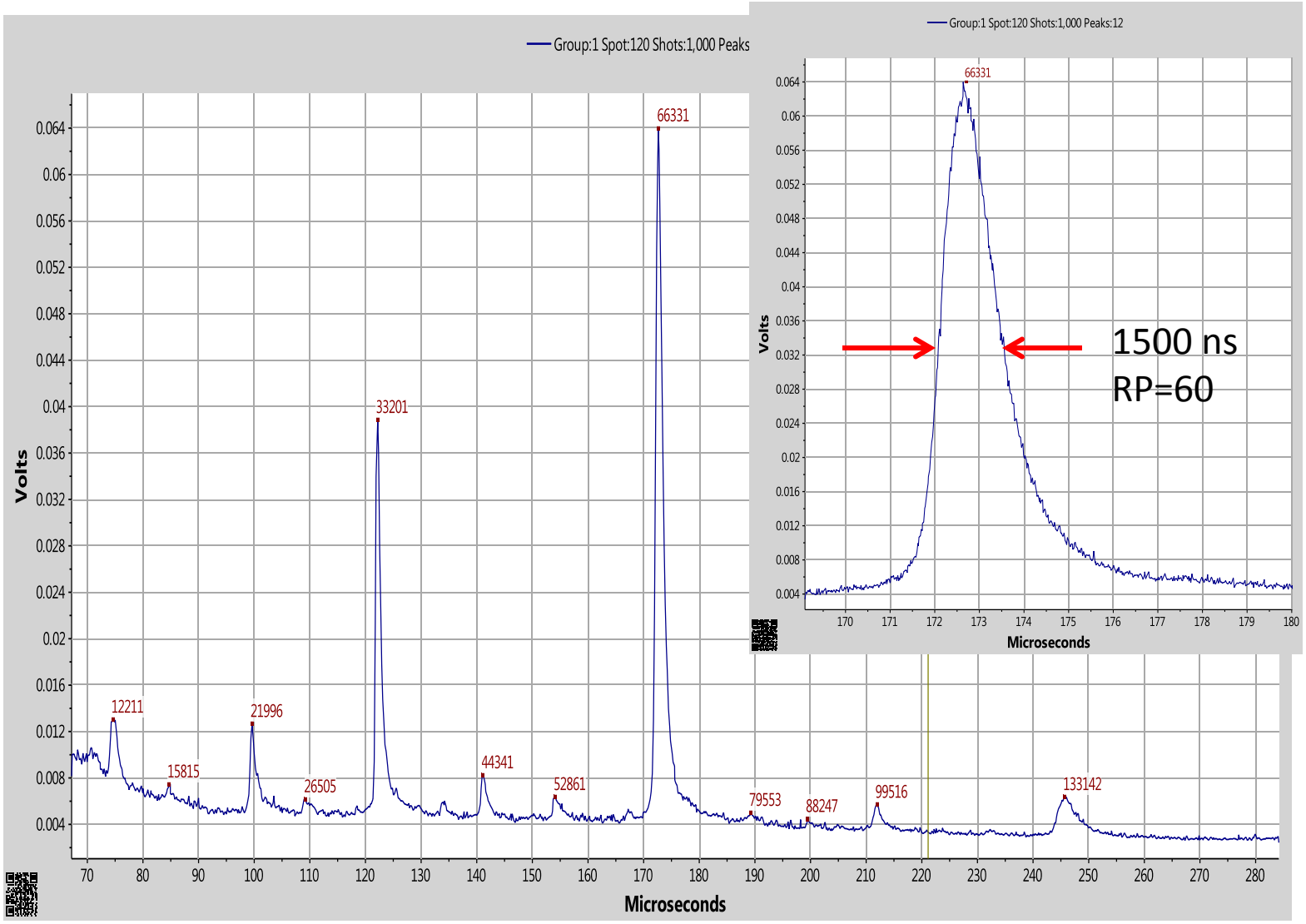




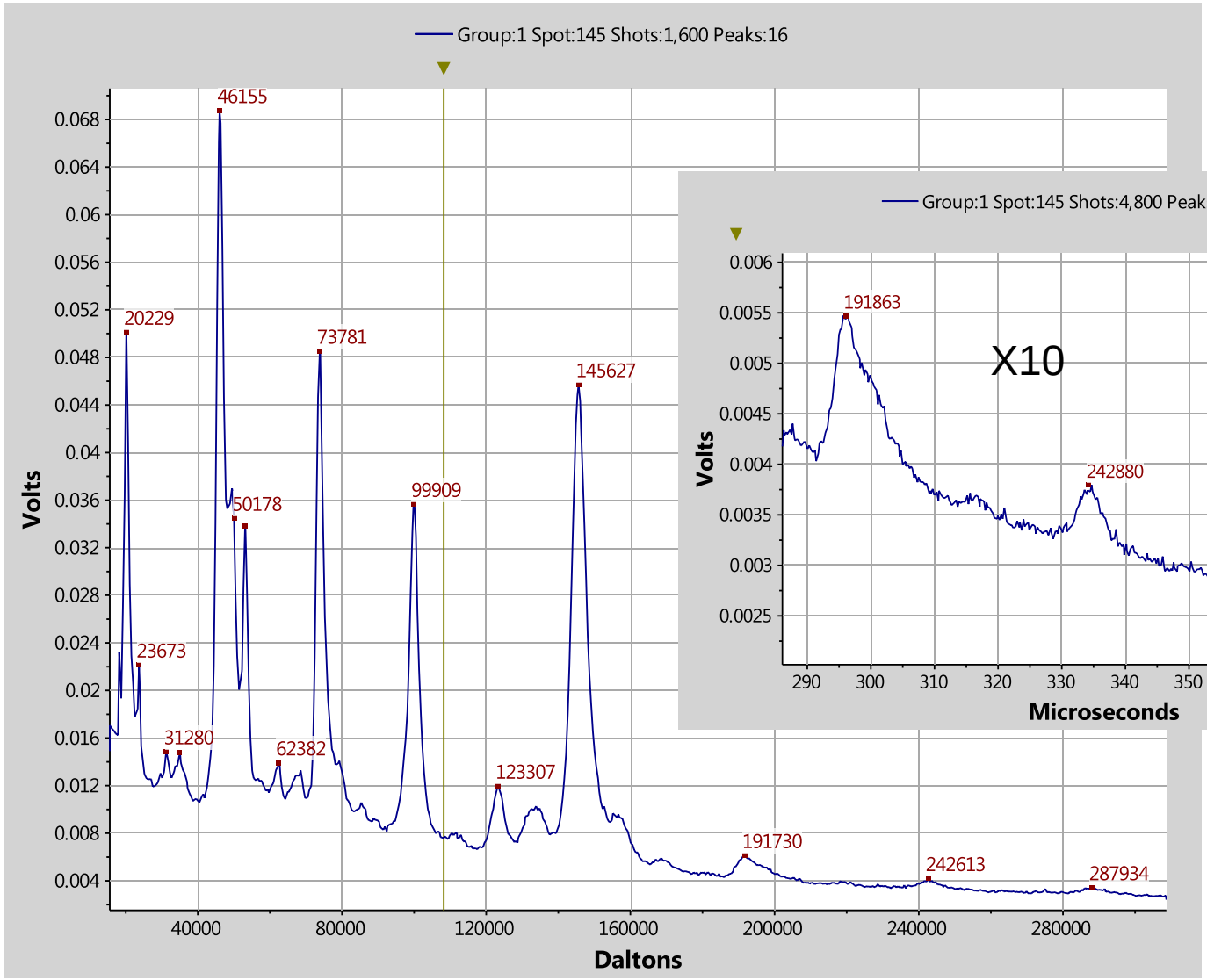
Mixture of peptide standards, 100 femtomole/µL, 2.5 mm spot, 1000 shots as function of laser fluence



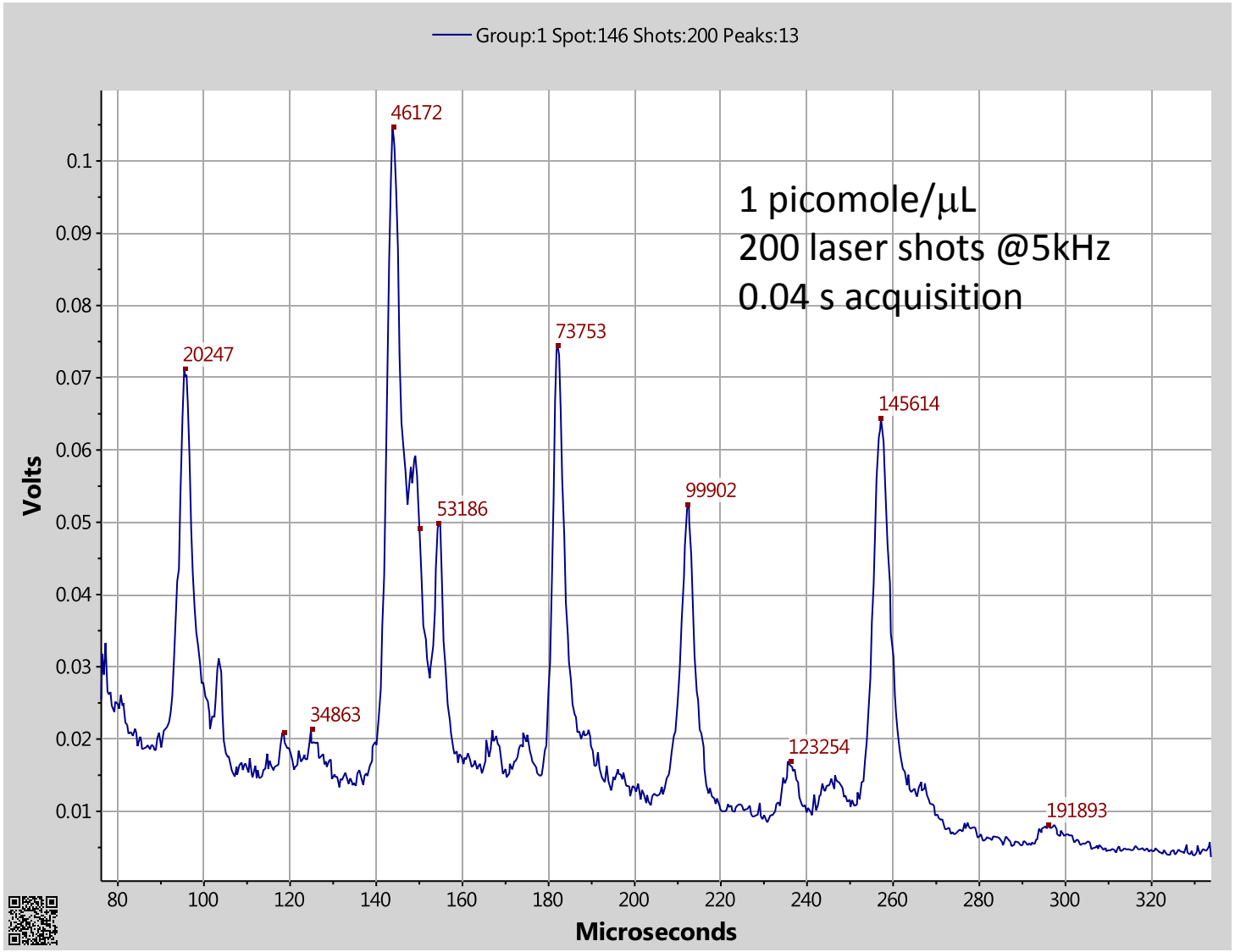
Resolving power and peak intensity for 963.5 in α-cyano matrix



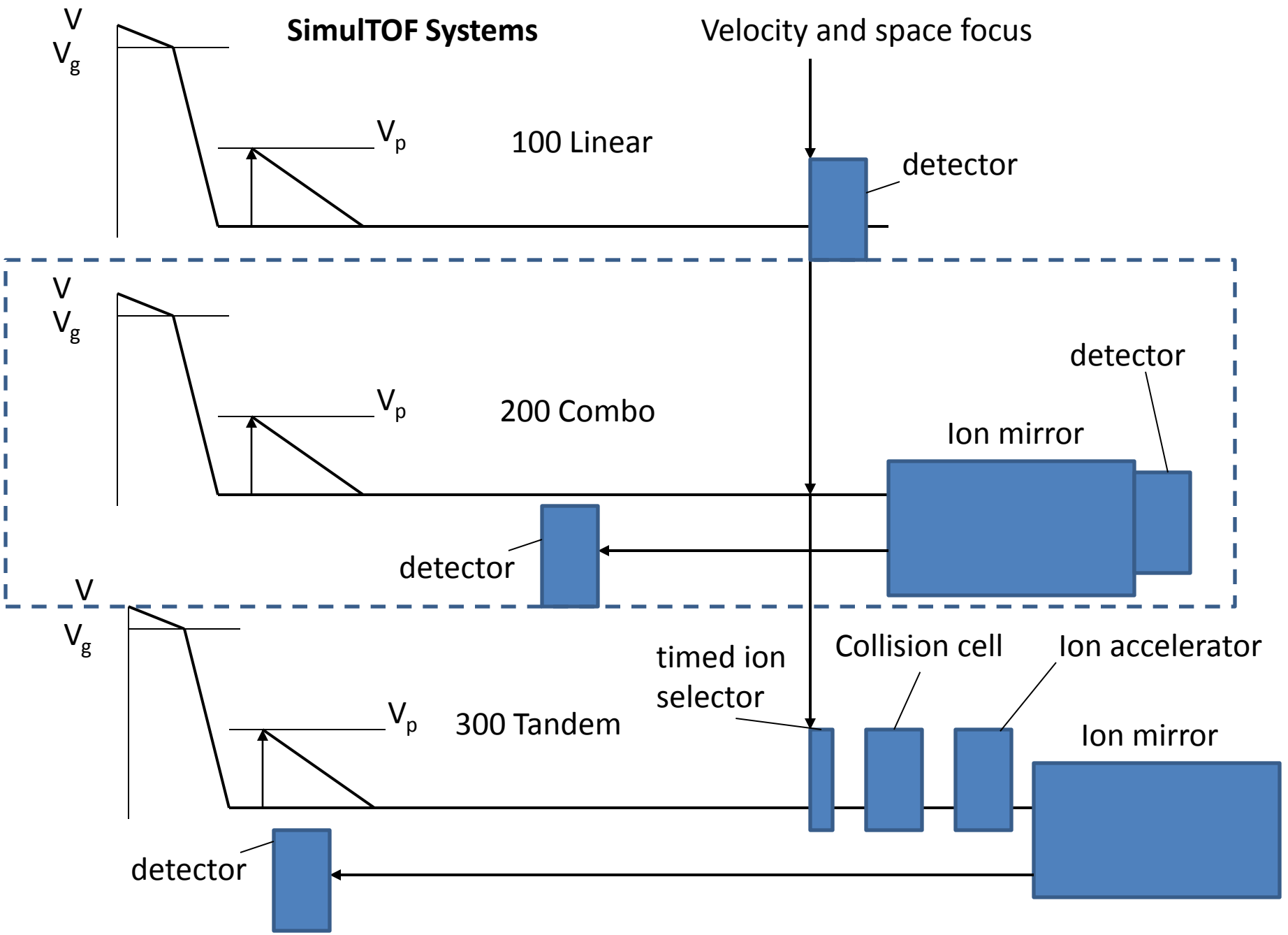
Spectrum of BSA in Sinapinic acid matrix measured in SimulTOF 100 Linear MALDI-TOF at 20 kV energy using Photonis fast hybrid detector with channel plate at ground potential

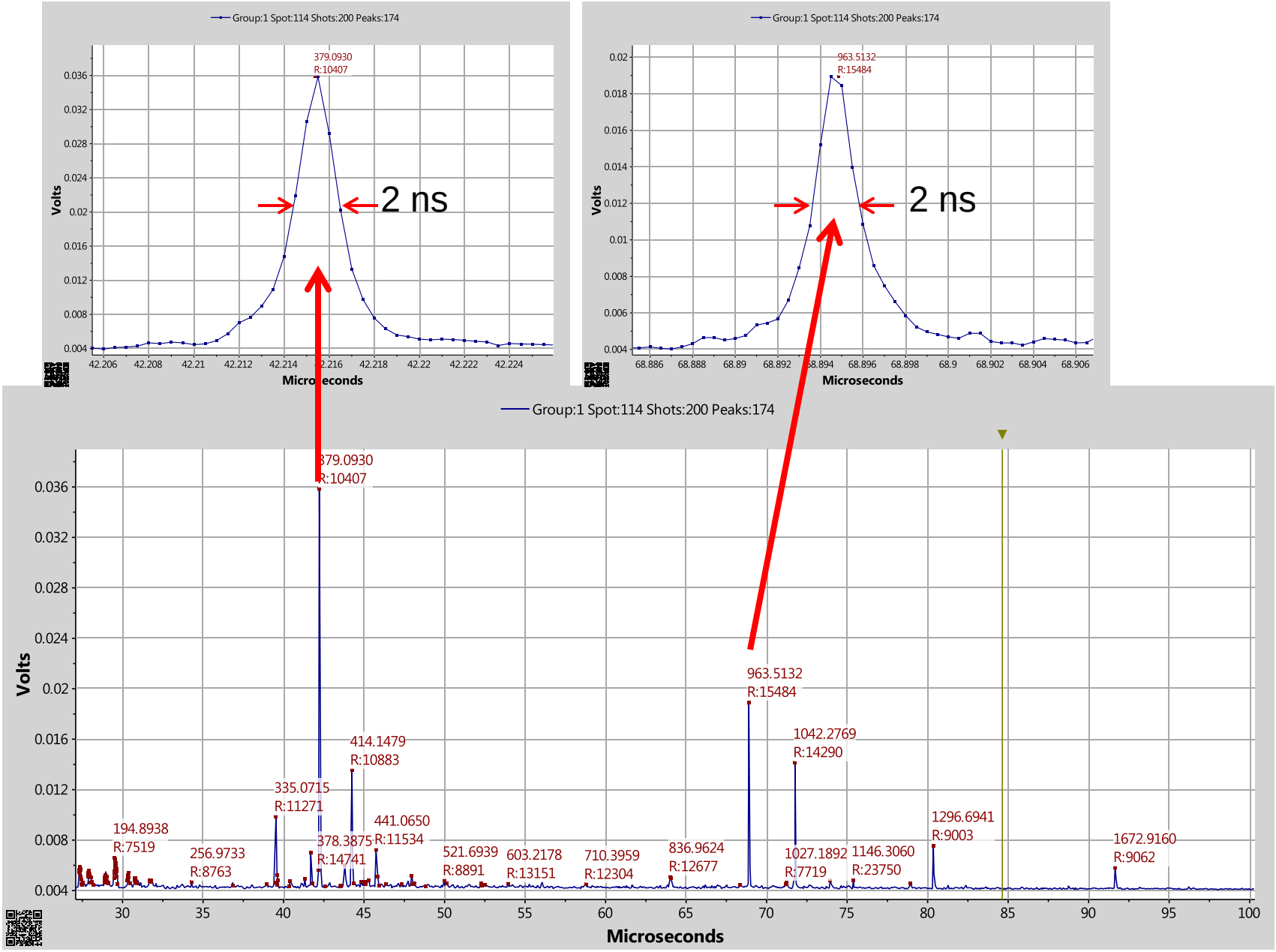


Spectrum of IgG in Sinapinic acid matrix measured in SimulTOF 100 Linear MALDI-TOF at 20 kV energy using Photonis fast hybrid detector with channel plate at ground potential

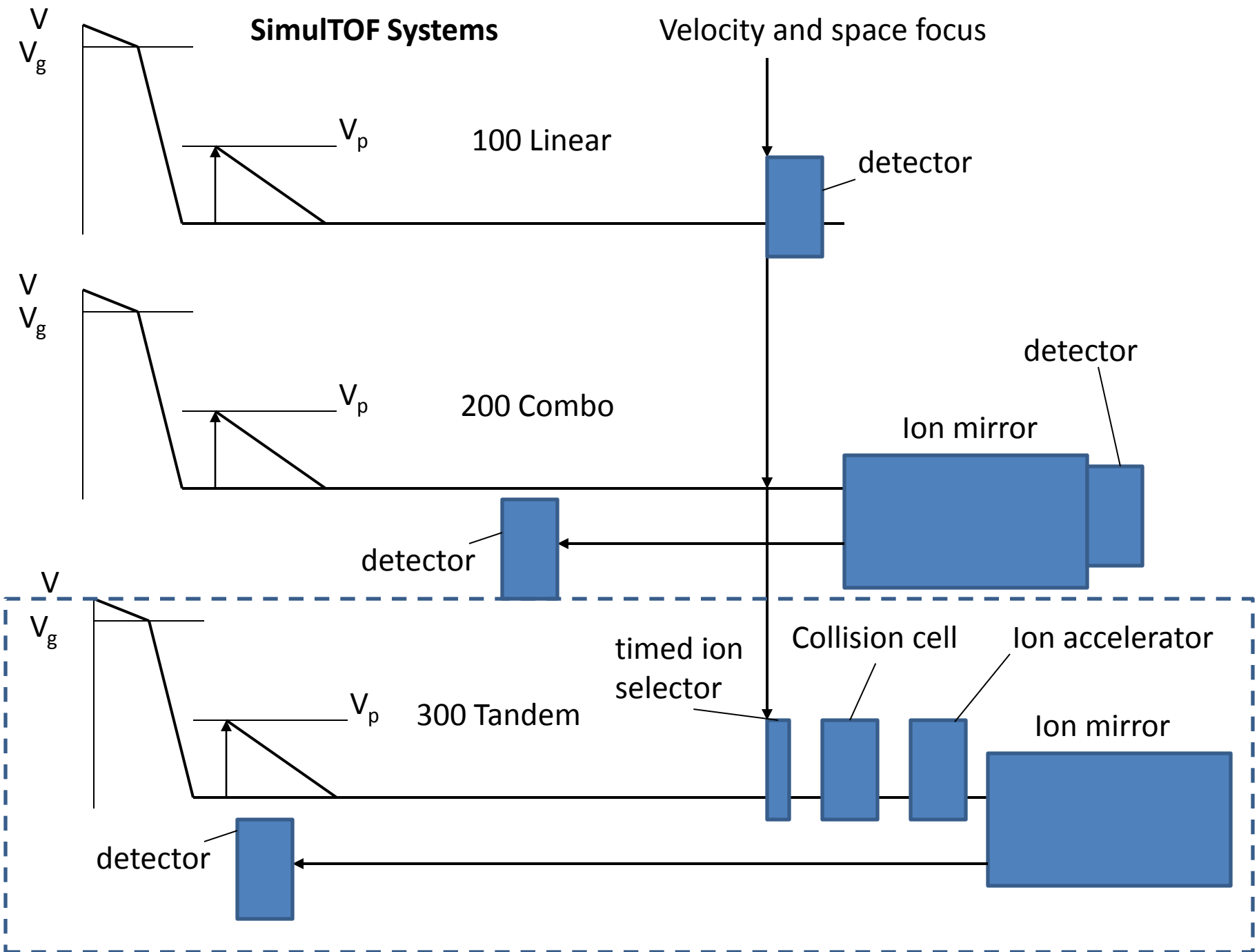


Spectrum of IgG in Sinapinic acid matrix measured in SimulTOF 100 Linear MALDI-TOF at 20 kV energy using Photonis fast hybrid detector with channel plate at ground potential


V
V_g
SimulTOF Systems
Velocity and space focus
V_p
100 Linear
detector
V
V_g
V_p
200 Combo
detector
Ion mirror
detector
V
V_g
V_p
300 Tandem
timed ion selector
Collision cell
Ion accelerator
Ion mirror
detector



200 Combo Reflector Mode, 100 femtomole peptide standards in α-cyano matrix


V
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SimulTOF Systems
Velocity and space focus
V_p
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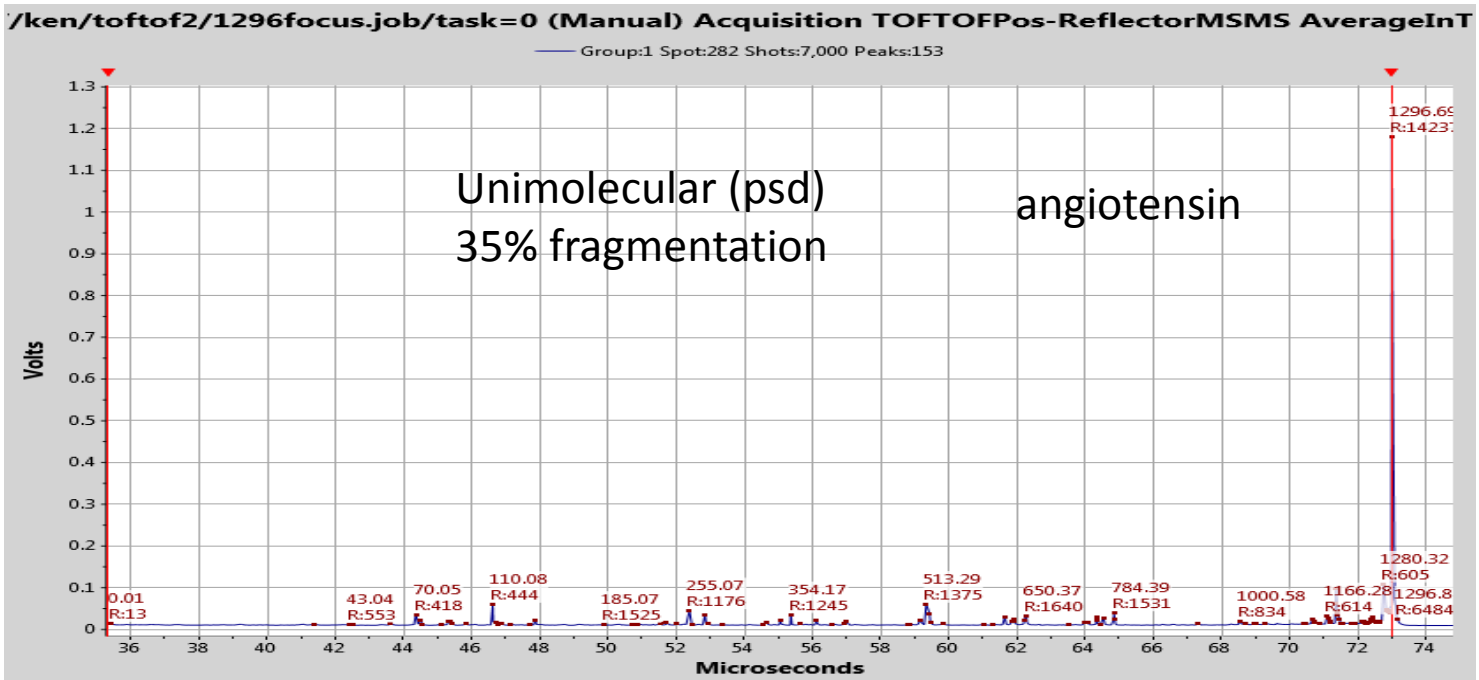
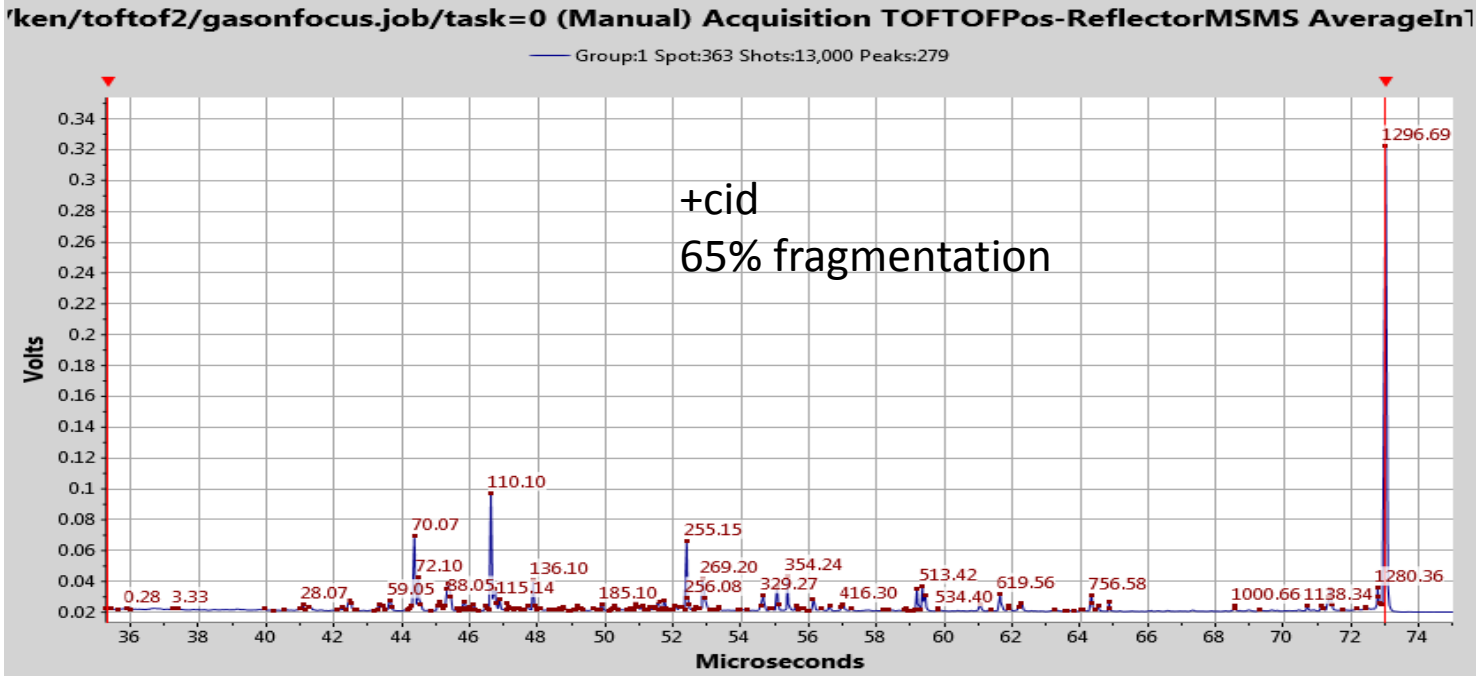
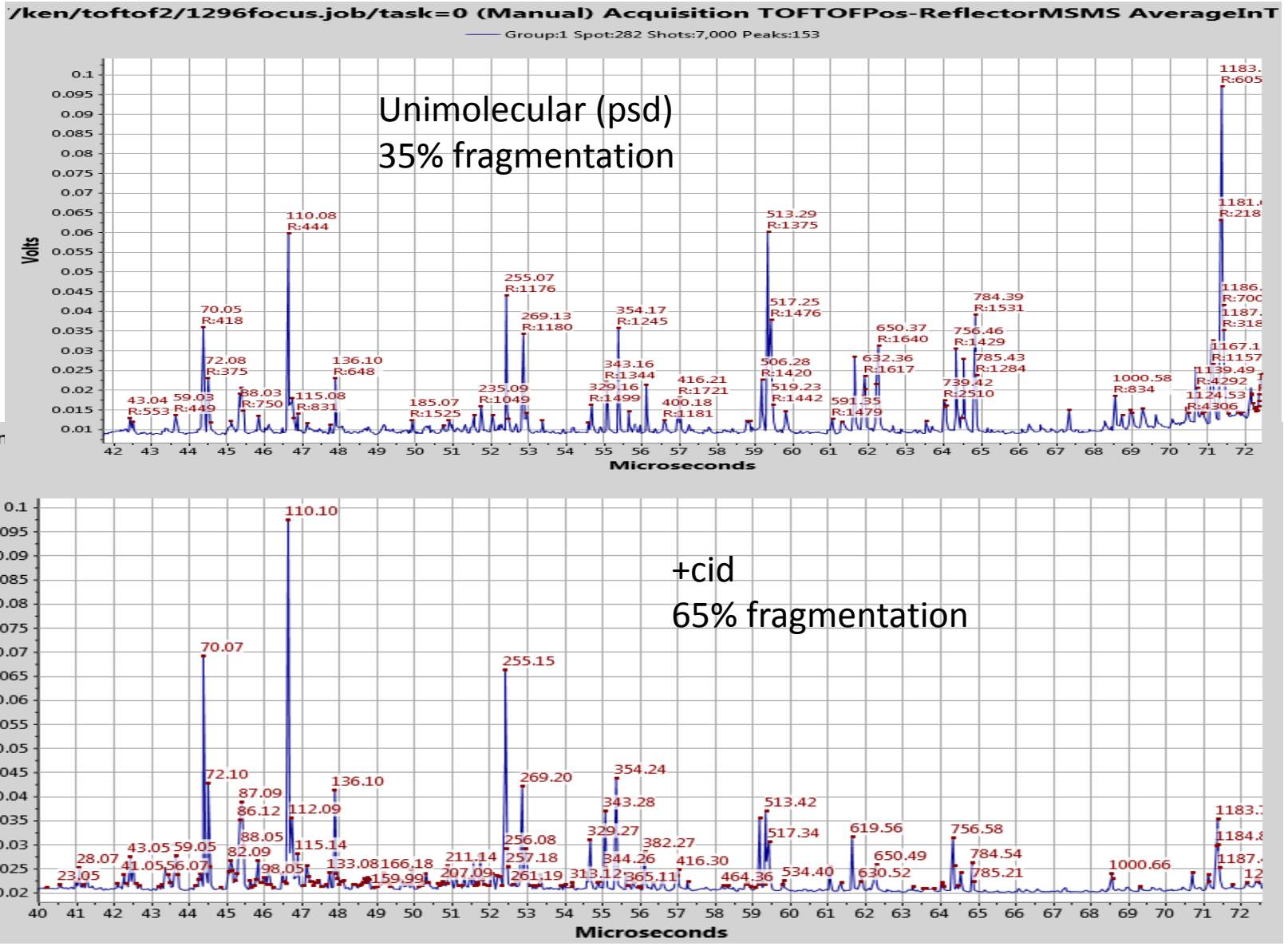

/ken/toftof2/1296focus.job/task=0 (Manual) Acquisition TOFTOFPos-ReflectorMSMS AverageInT
Group:1 Spot:282 Shots:7,000 Peaks:153
Unimolecular (psd)
35% fragmentation
angiotensin
Volts
Microseconds
0.01 R:13
43.04 R:553
70.05 R:418
110.08 R:444
185.07 R:1525
255.07 R:1176
354.17 R:1245
513.29 R:1375
650.37 R:1640
784.39 R:1531
1000.58 R:834
1166.28 R:614
1280.32 R:605
1296.8 R:6484


'ken/toftof2/gasonfocus.job/task=0 (Manual) Acquisition TOFTOFPos-ReflectorMSMS AverageInT
Group:1 Spot:363 Shots:13,000 Peaks:279
+cid
65% fragmentation
Volts
Microseconds
0.28
3.33
28.07
59.05
70.07
72.10
88.05
110.10
115.14
136.10
185.10
255.15
256.08
269.20
329.27
354.24
416.30
513.42
534.40
619.56
756.58
1000.66
1138.34
1280.36
1296.69


/ken/toftof2/1296focus.job/task=0 (Manual) Acquisition TOFTOFPos-ReflectorMSMS AverageInT
Group:1 Spot:282 Shots:7,000 Peaks:153
Unimolecular (psd)
35% fragmentation
Volts
Microseconds
+cid
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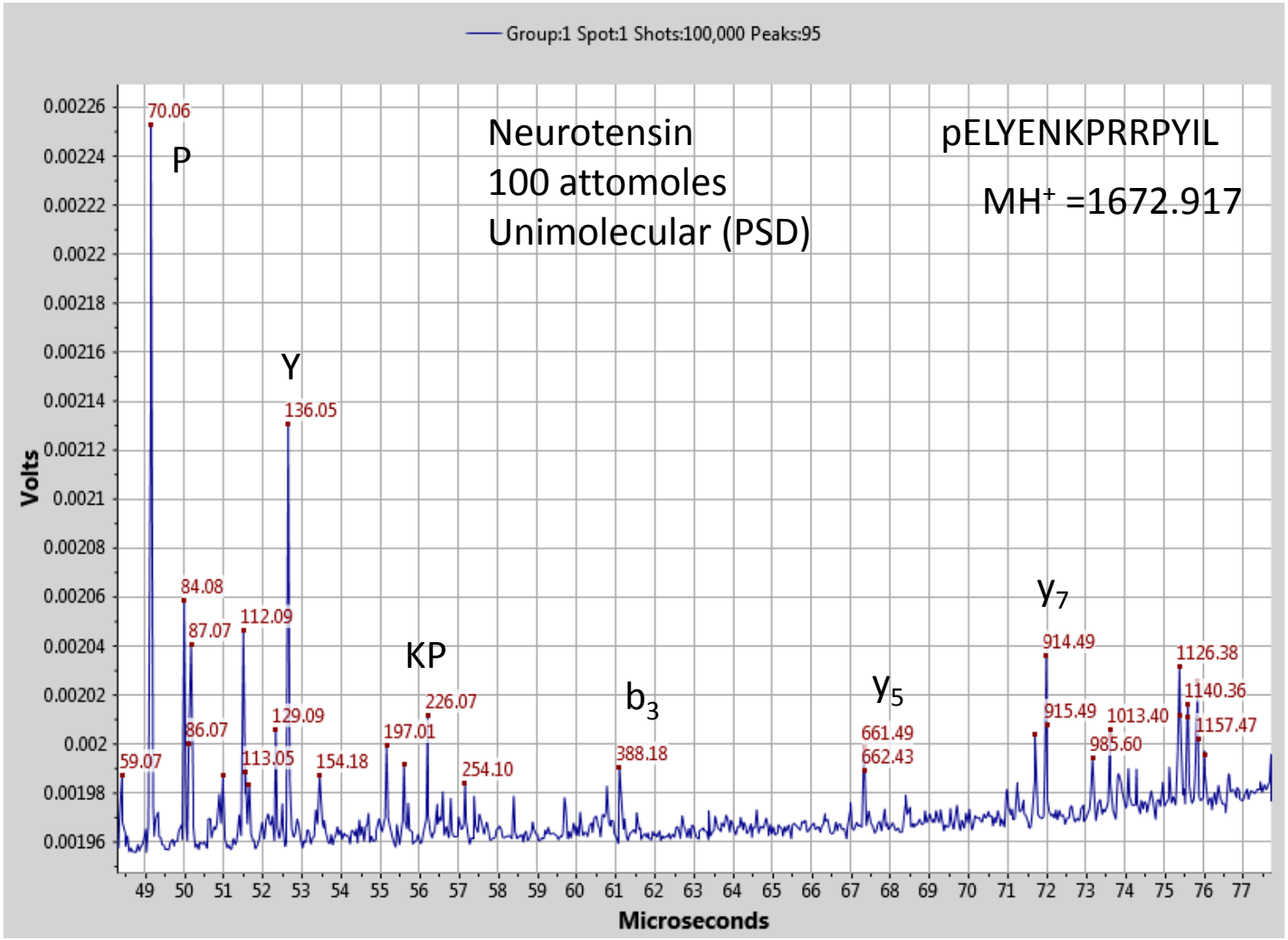
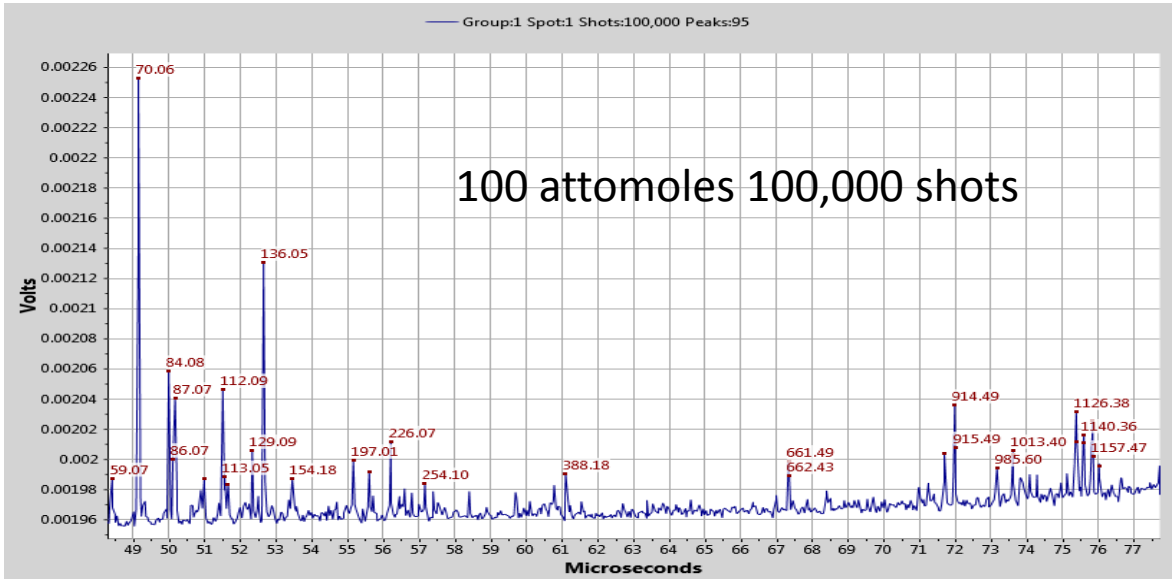
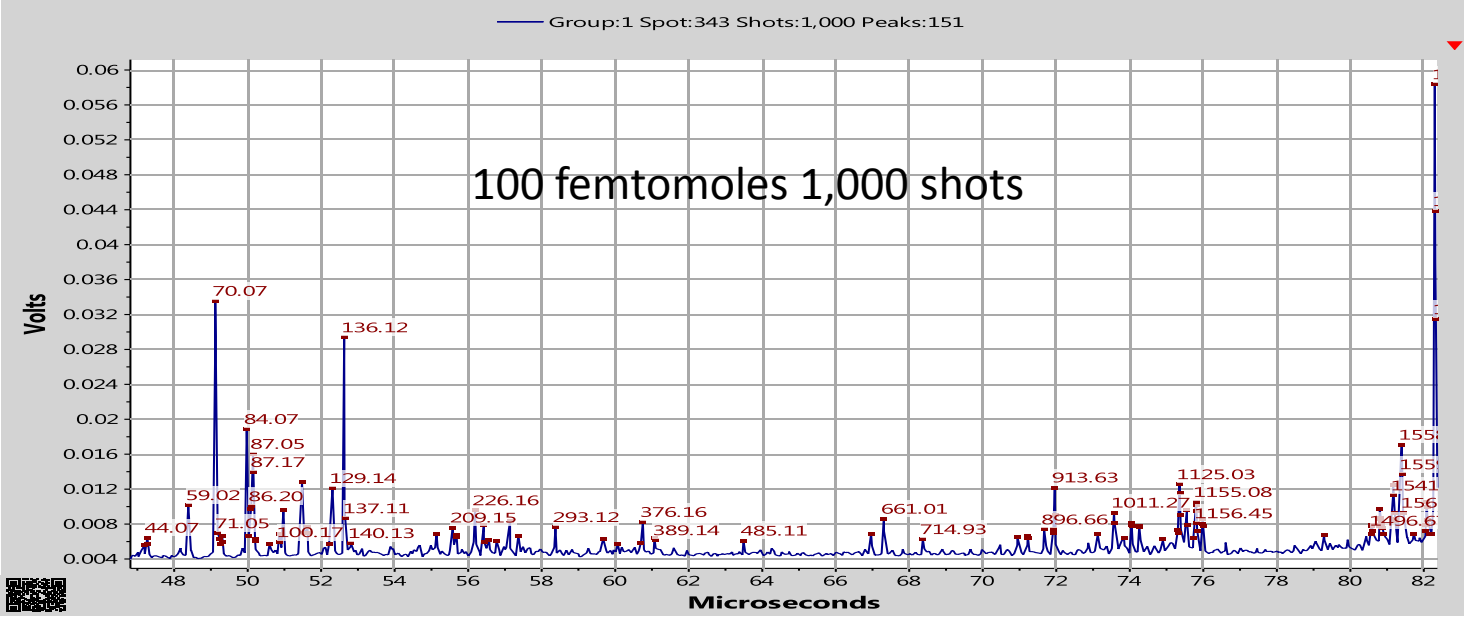
Volts
Microseconds



MS-MS at 100 attomoles/μL on 2.5 mm spot. 100,000 shots, 20 s acquisition at 5 kHz
19 of 30 most intense peaks matched neurotensin using Protein Prospector


Group:1 Spot:1 Shots:100,000 Peaks:95
100 attomoles 100,000 shots
Volts
Microseconds
70.06
136.05
84.08
87.07
112.09
129.09
86.07
59.07
113.05
154.18
197.01
226.07
254.10
388.18
661.49
662.43
914.49
915.49
1013.40
985.60
1126.38
1140.36
1157.47


Group:1 Spot:343 Shots:1,000 Peaks:151
100 femtomoles 1,000 shots
Volts
Microseconds
70.07
136.12
84.07
87.05
87.17
129.14
59.02
86.20
137.11
226.16
209.15
44.07
71.05
100.17
140.13
293.12
376.16
389.14
485.11
661.01
714.93
913.63
896.66
1011.27
1125.03
1155.08
1156.45

Conclusions

- SimulTOF focusing provides high resolving power over broad range in linear analyzer
- Combination with high performance gridless ion optics and hybrid detector provides very high efficiency for ion transmission and detection for both small molecules and proteins
- Combination with two-stage ion mirror provides resolving power comparable to delayed extraction but with higher sensitivity
- Provides efficient first stage for Tandem TOF with both PSD and CID fragmentation

Acknowledgements

- Financial Support
  - NIGMS and NCRR of NIH
  - Christina Hsieh Vestal and the Hsieh Family
- The entire staff at Virgin Instruments
  - Steve Gabeler, Mark Dahl, Joe Valentine electronics
  - George Mills, Matt Gabeler-Lee software
  - Roger Voyer machinist
  - Steve Hattan, Ken Parker scientists
  - Christina Vestal, Bill Gibbs management