Development of tandem mass spectrometry (MS/MS) on miniaturized laser desorption/ionization time-of-flight mass spectrometry (LD-TOF-MS)

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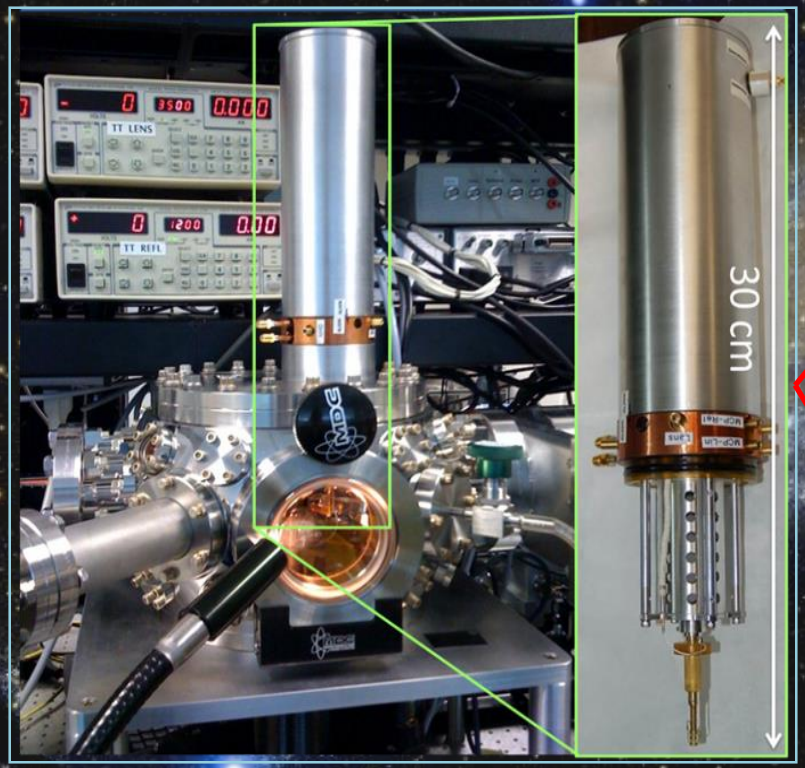
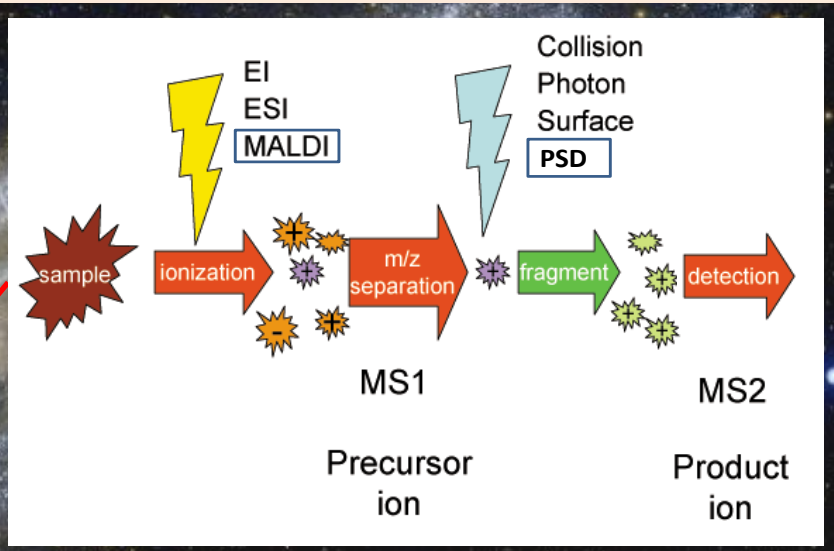
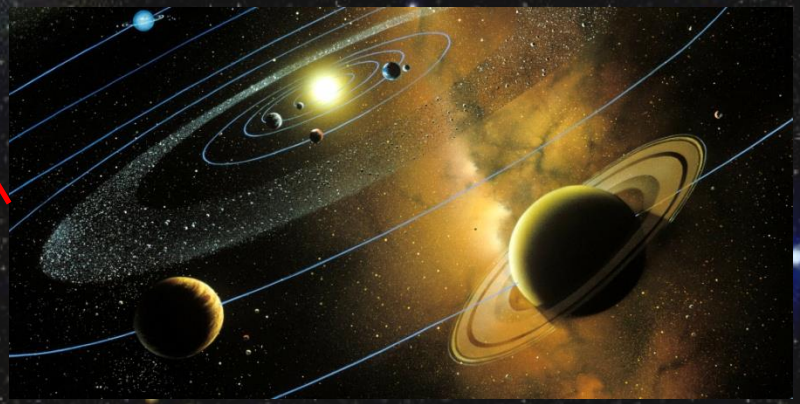
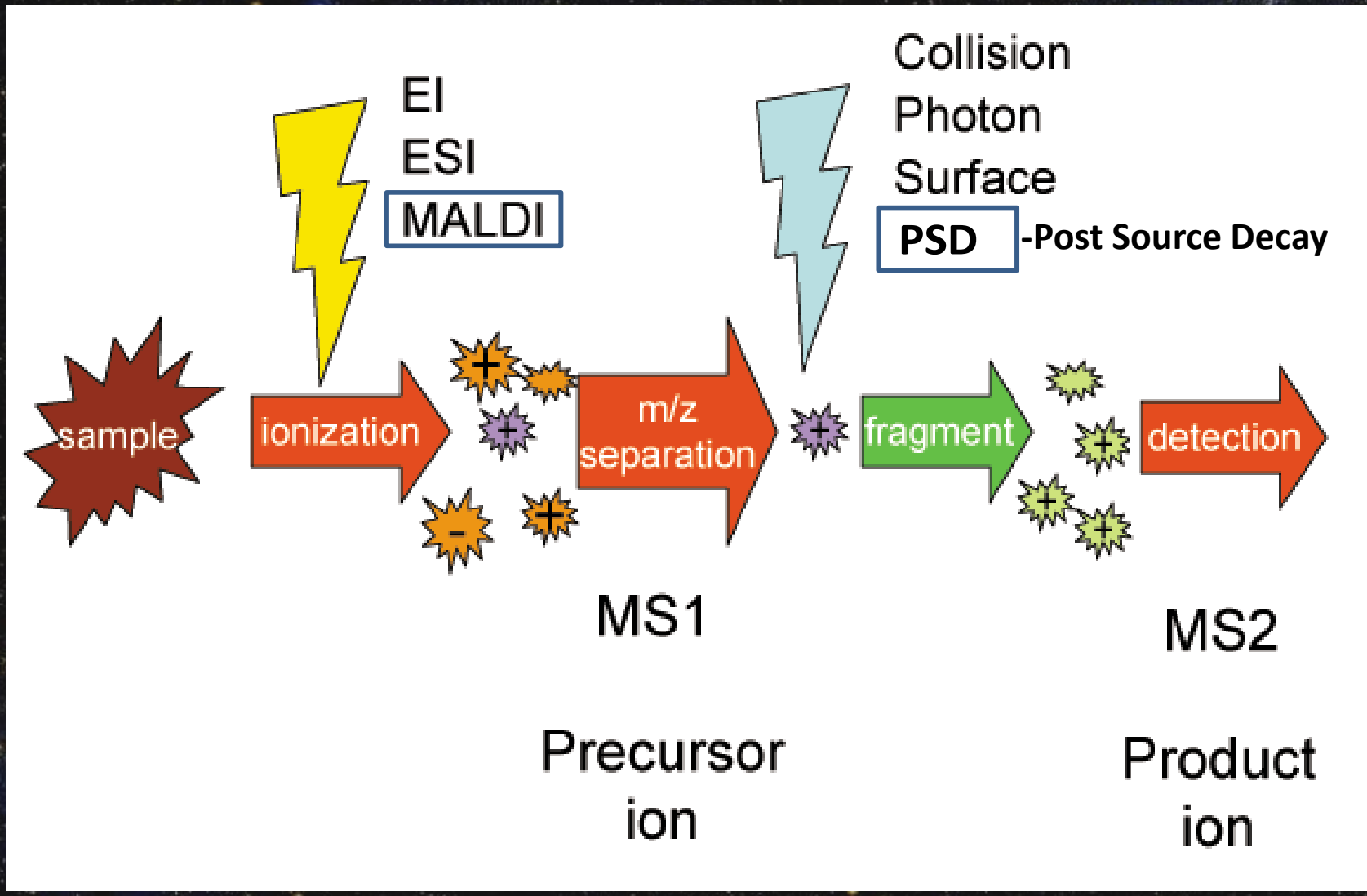






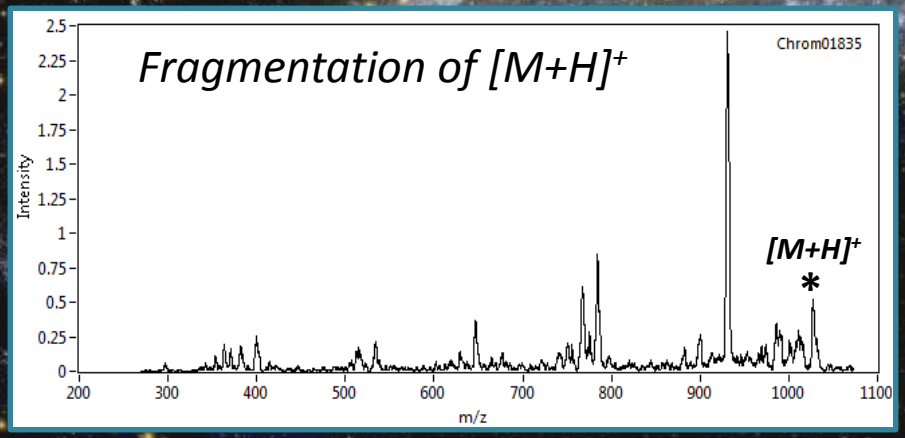
Tandem Mass Spectrometry (MS/MS)

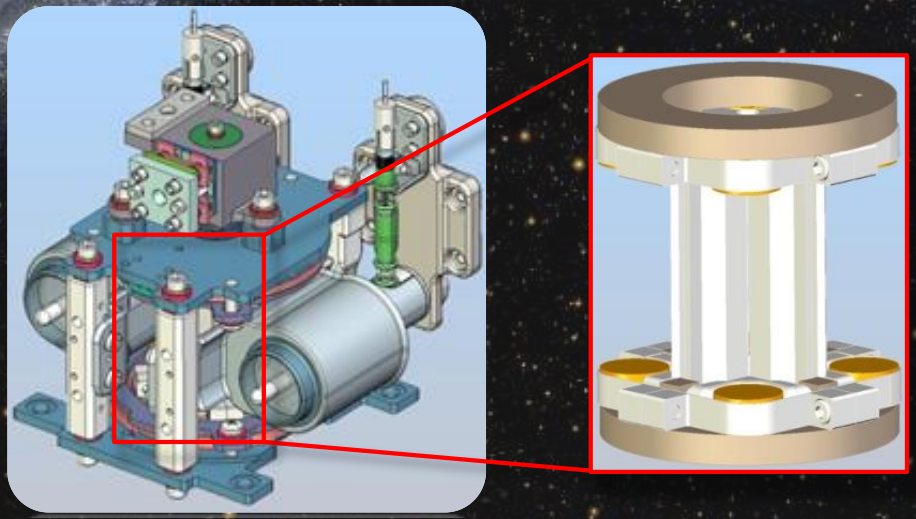
----Molecular structure analysis in MS



ExoMars 2018 mission

The MOMA instrument, as enabled by the ion trap mass analyzer, allows structural characterization of complex molecules via ion isolation using multi-frequency waveforms, and MS/MS.





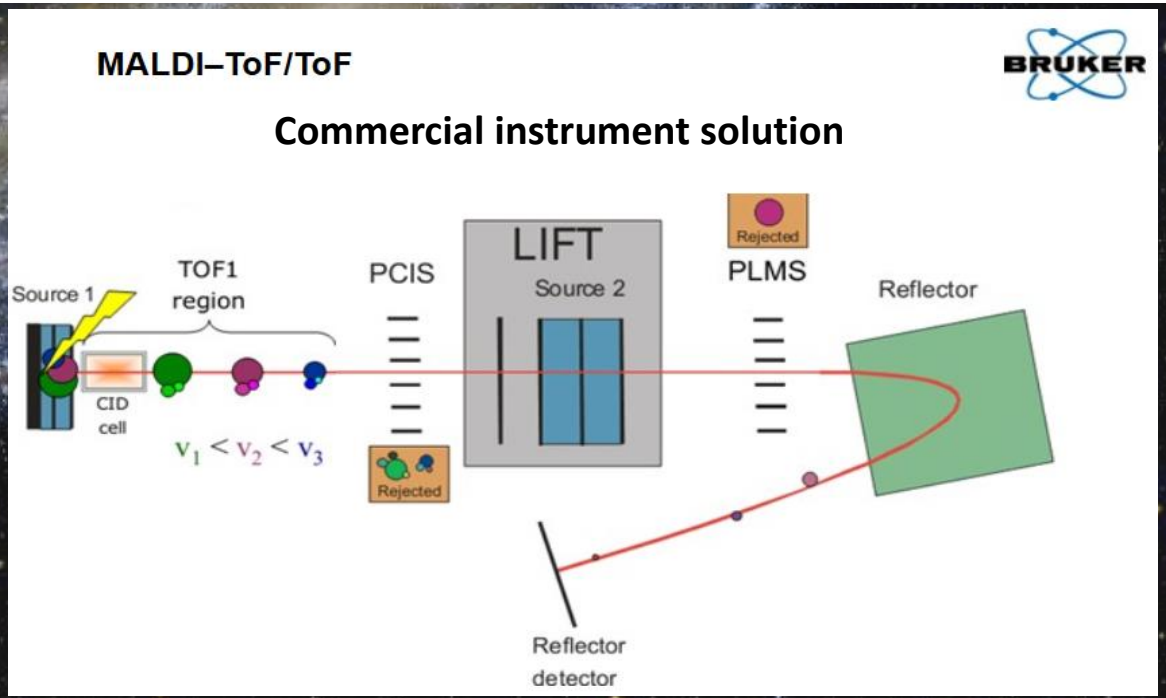
Why TOF?

- For *in situ* planetary mission or field applications, TOF-MS is particularly well suited due to
  - **lightweight packaging**
  - **simple electronics, eg, no RF power supplies**
  - **straightforward development to an instrument system**

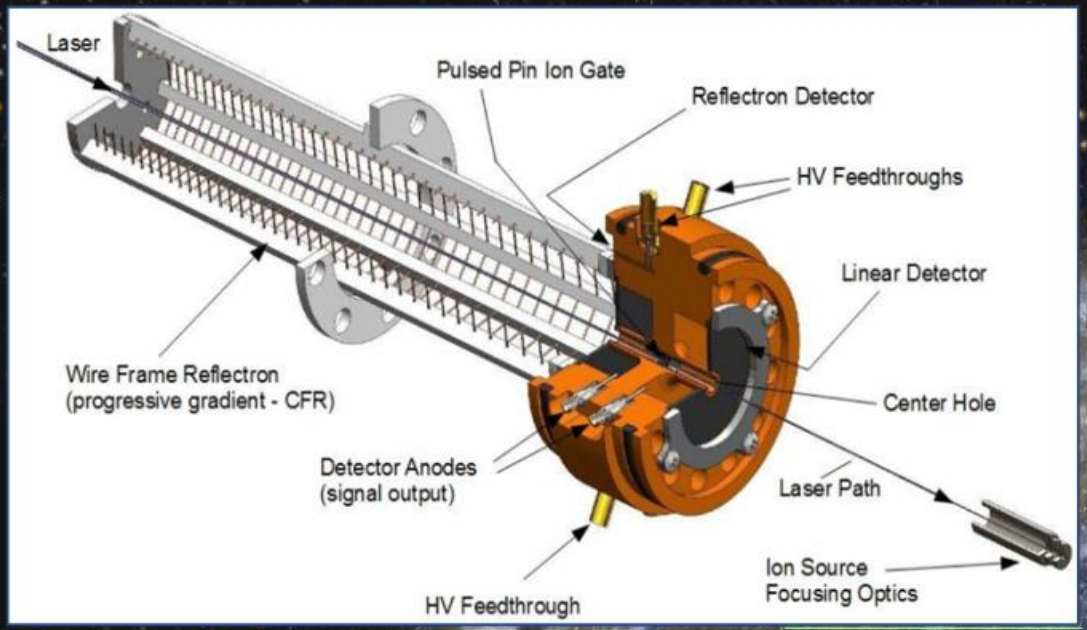
Challenge:

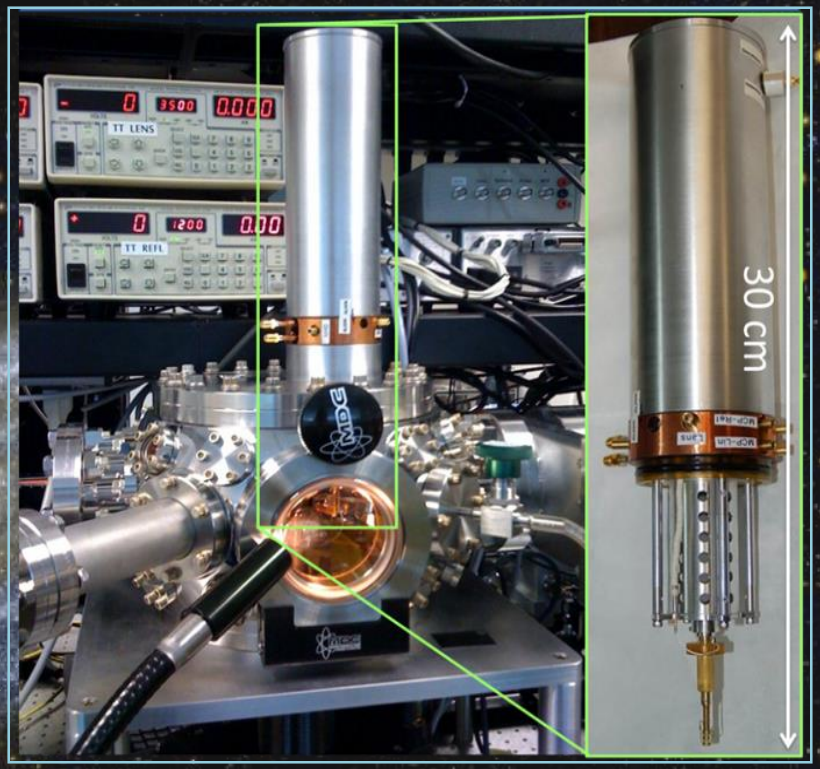
- To include MS/MS capability on TOF, many designs require additional units (e.g., collision cell, LIFT cell) to perform the product ion analysis following fragmentation of the ions, which may induce more weight/volume, more power and new mechanical operations to the instrument.

Commercial MALDI MS



Instrument

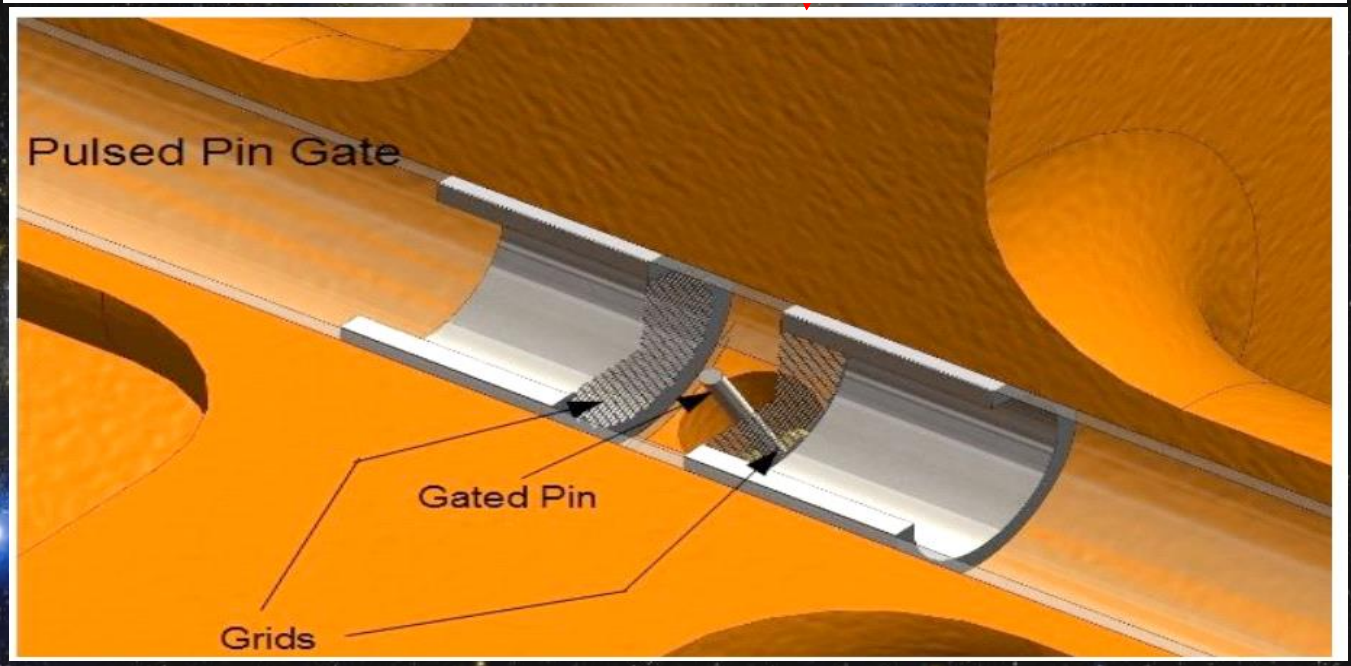




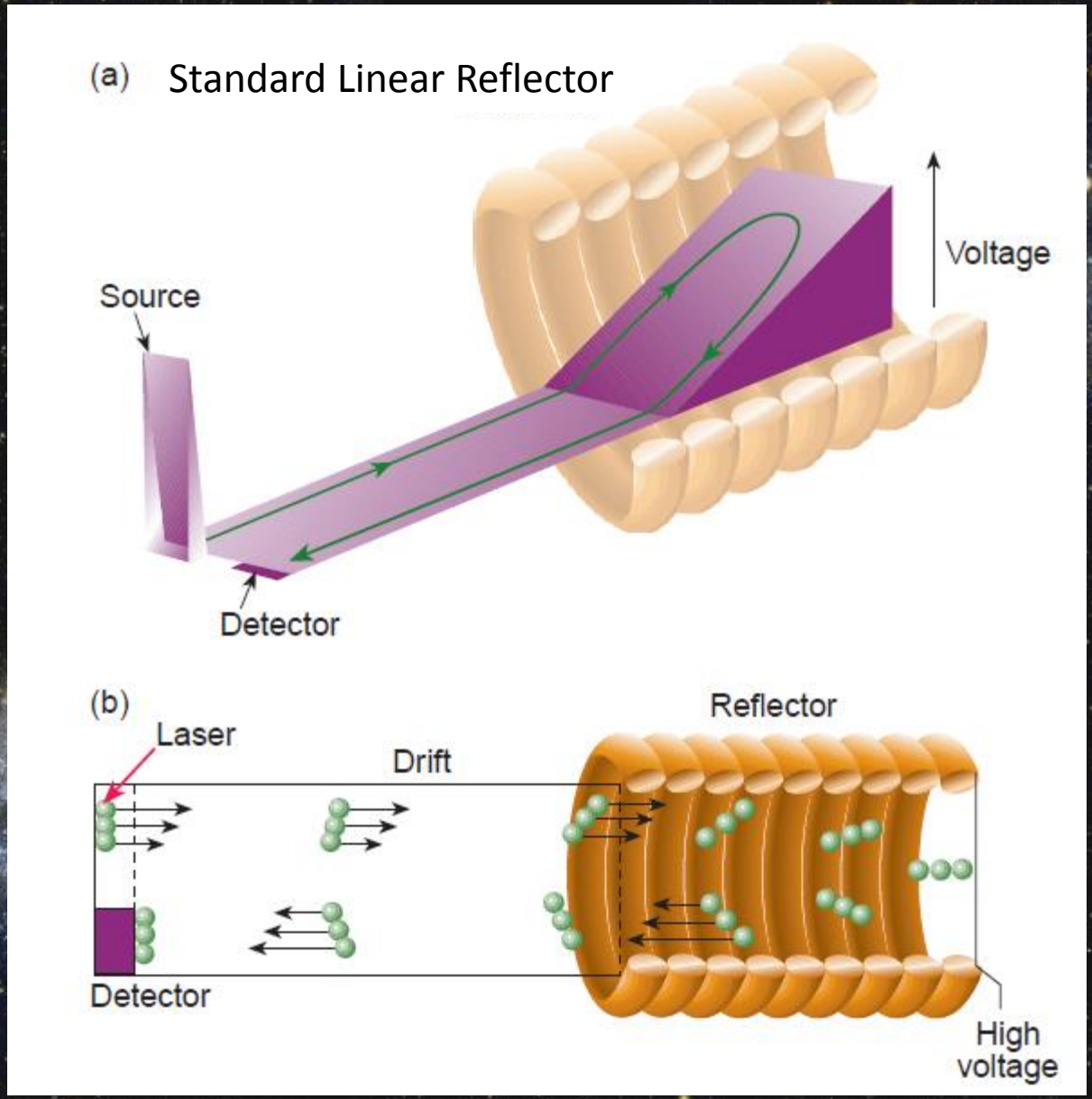
A miniature time-of-flight mass spectrometer (TOF-MS)

● **curved-field reflectron** ● **features a pulsed pin ion gate for precursor ion selection** ● low voltage (<5 kV) and power (<15 W) ● measuring less than 30 cm long ● ~5 kg in mass ● a single UV laser (355nm or 337nm) ● both positive and negative modes ● unit mass resolution at several hundred Da.

- Gate selected precursor ***along with its product ions*** enter the gate *simultaneously* (before dispersion in the reflectron).
- All other ions are deflected from ion beam.
- Precursor and product ions are dispersed in the CFR yielding spectrum of selected parent and associated PSD fragments

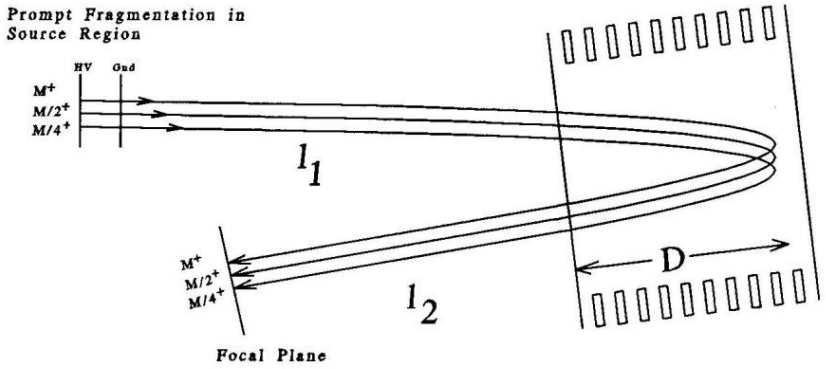


Standard (linear-field) Reflectron TOF



Prompt vs. Post Source Decay (PSD) Focusing

Standard Reflectron TOF
Prompt Fragments

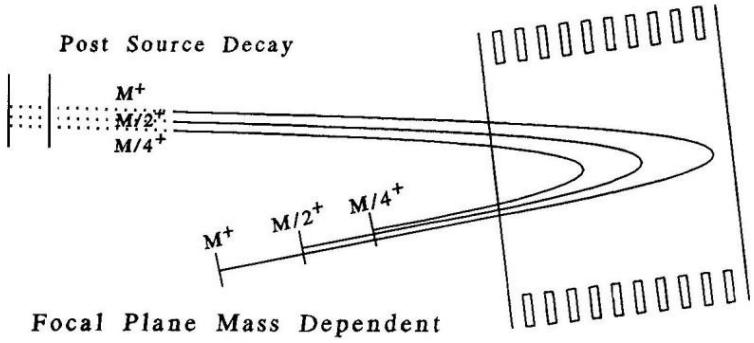


Constant Energy Condition

- Distribution of VELOCITIES
- equal penetration for all ions
- focusing condition: $L = 4xD$ (where $L = l_1 + l_2$)

$$E_{const} = \frac{mv^2}{2}$$

Standard Reflectron
Post Source Decay



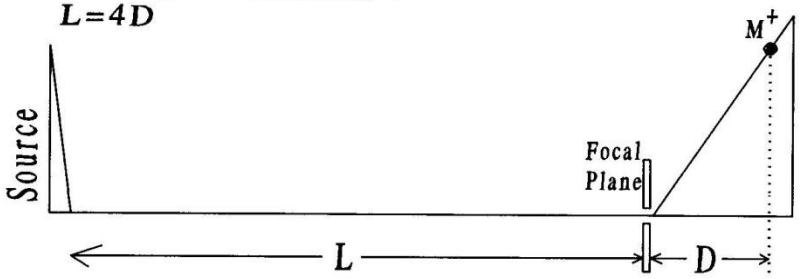
Constant Velocity Condition

- Distribution of ENERGIES
- penetration depth proportional to mass
- each mass follows $L = 4xD$ focusing condition

$$E = \frac{mv_{const}^2}{2}$$

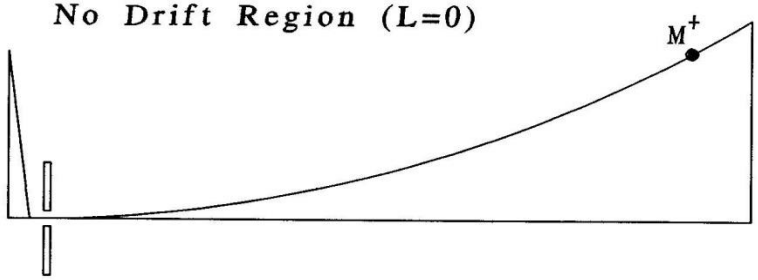
Linear Reflectron

L=4D



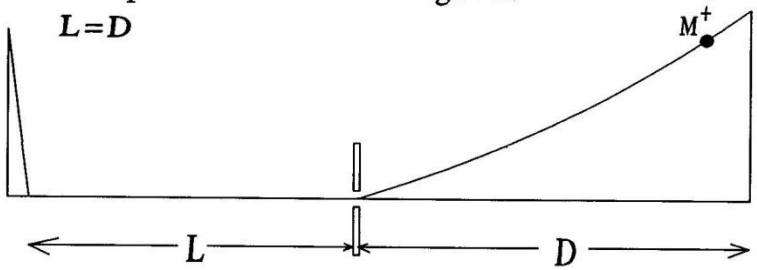
Quadratic Reflectron

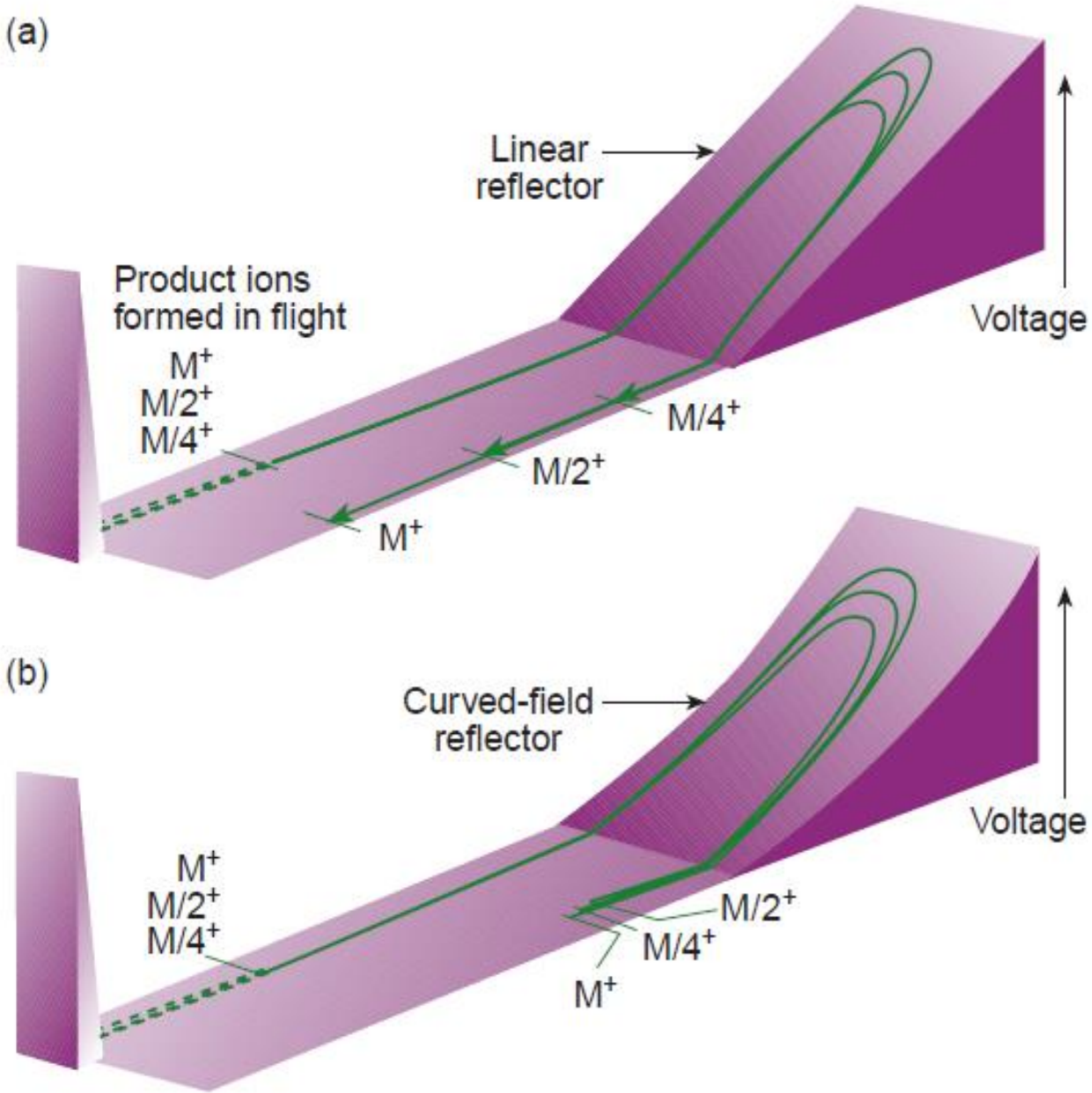
Ideal Energy Correction
No Drift Region (L=0)



Curved Field Reflectron

Ideal energy correction
Incorporates Drift Region:
L=D



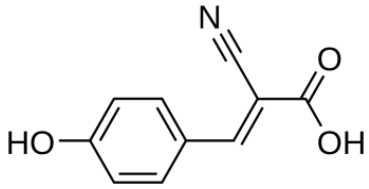


PSD fragment ions focus at different points in space after passage through the reflector. The focal plane of the reflector is dependent on mass.

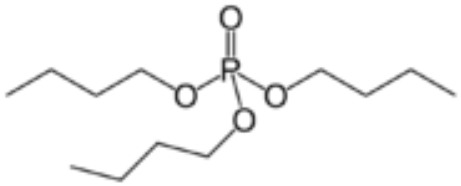
Focal points of all PSD fragments are located at the same point in space after exiting the curved-field reflector.

Samples

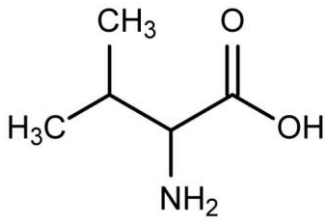
- **CHCHA**: α-Cyano-4-hydroxycinnamic acid, common MALDI matrix.



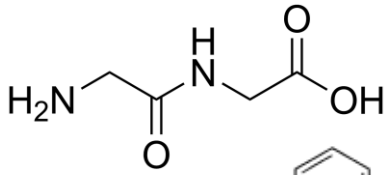
- **TBP**: tributyl phosphate, a component of aircraft hydraulic fluid and as a solvent for extraction and purification of rare earth metals from their ores.

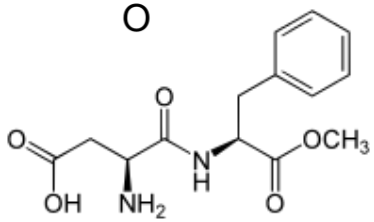


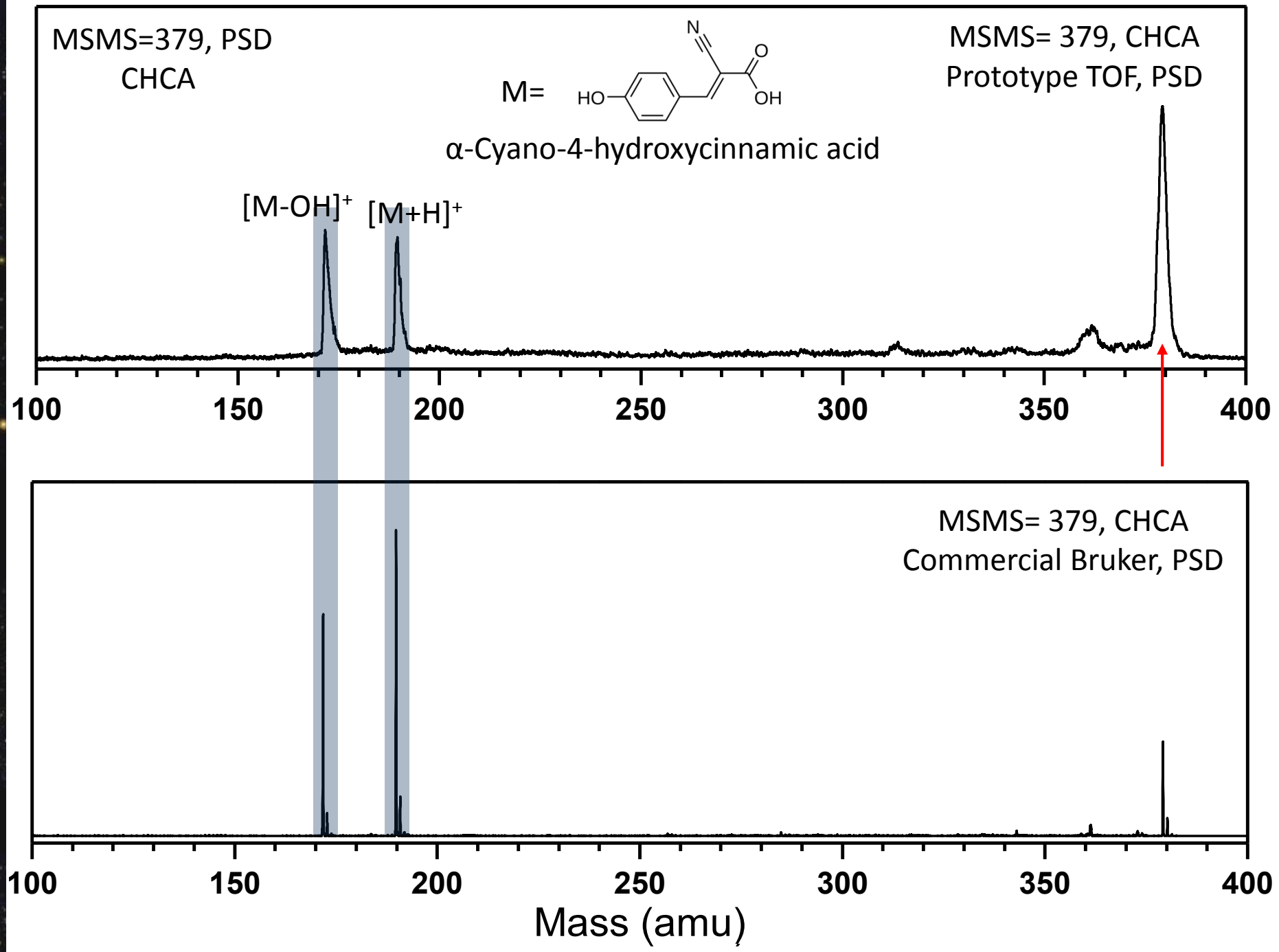
- **Valine**: amino acid, biomarker in meterorite and space.

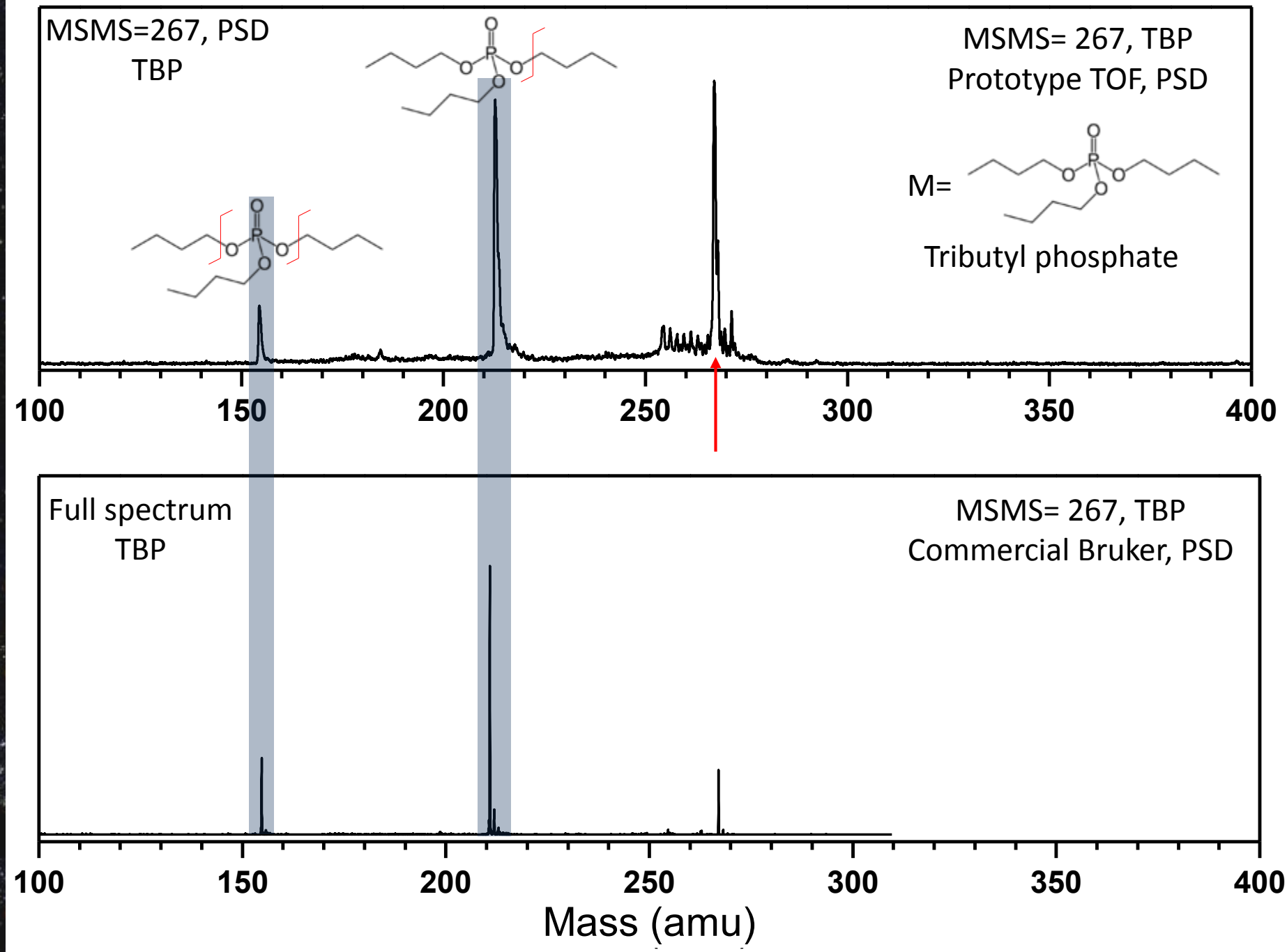


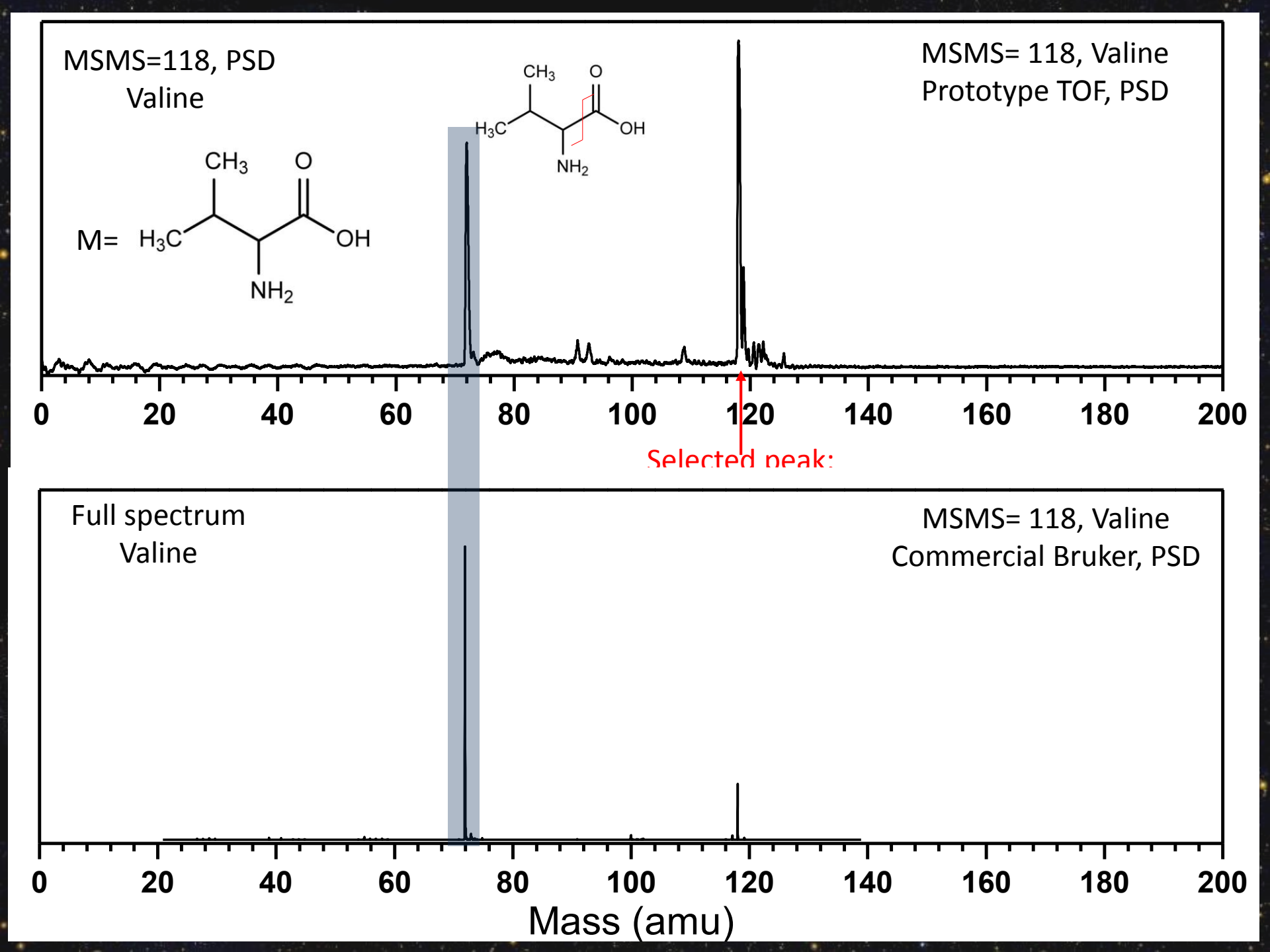
- **Dipeptides**: Glycine-Glycine, Aspartame, target compounds in meteorite and space study.

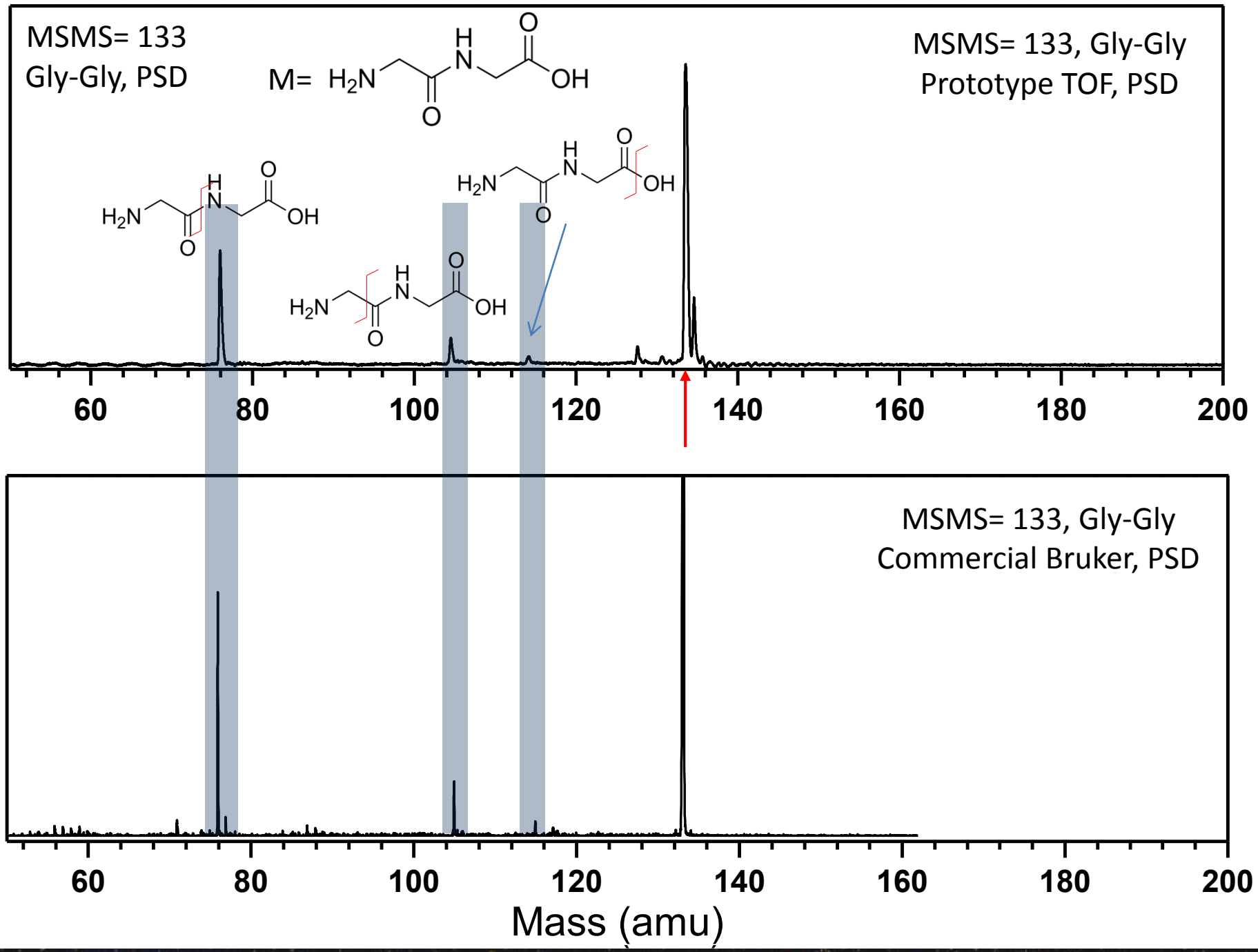


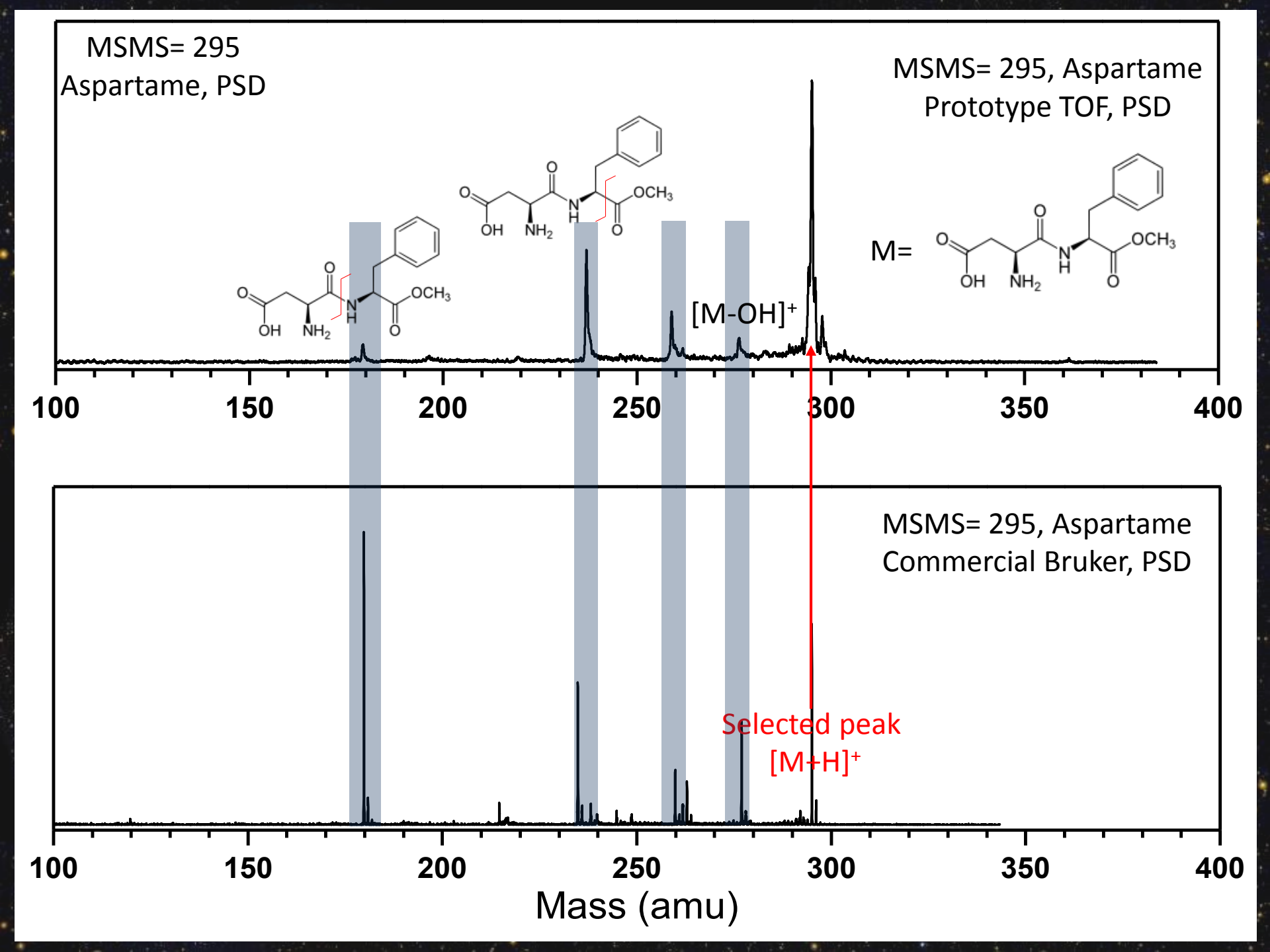



MSMS=379, PSD
CHCA
M=
HO
N
O
OH
α-Cyano-4-hydroxycinnamic acid
MSMS= 379, CHCA
Prototype TOF, PSD
[M-OH]+
[M+H]+
100
150
200
250
300
350
400
MSMS= 379, CHCA
Commercial Bruker, PSD
100
150
200
250
300
350
400
Mass (amu)

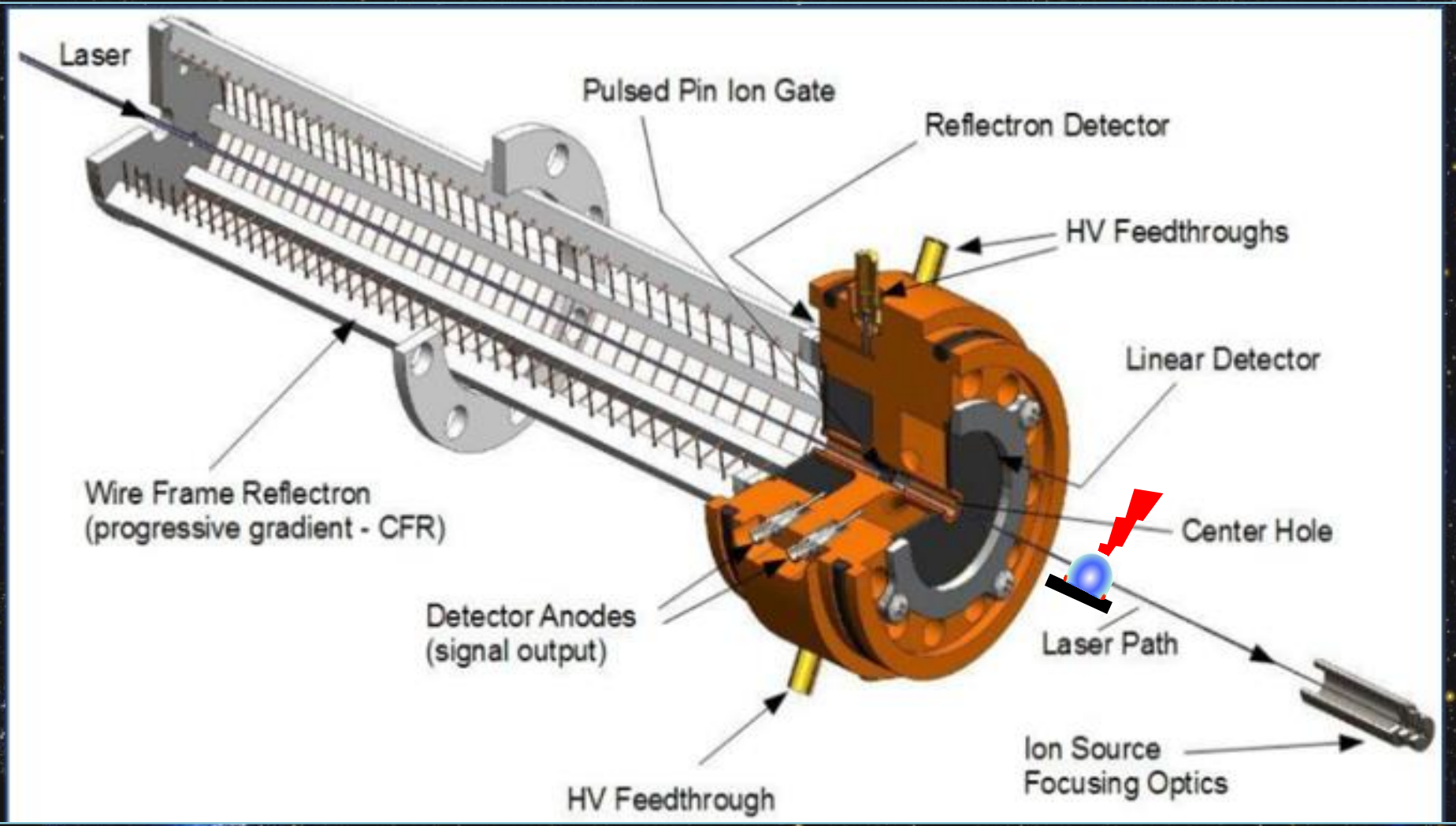

MSMS=267, PSD
TBP
MSMS= 267, TBP
Prototype TOF, PSD
M=
Tributyl phosphate
100
150
200
250
300
350
400
Full spectrum
TBP
MSMS= 267, TBP
Commercial Bruker, PSD
100
150
200
250
300
350
400
Mass (amu)

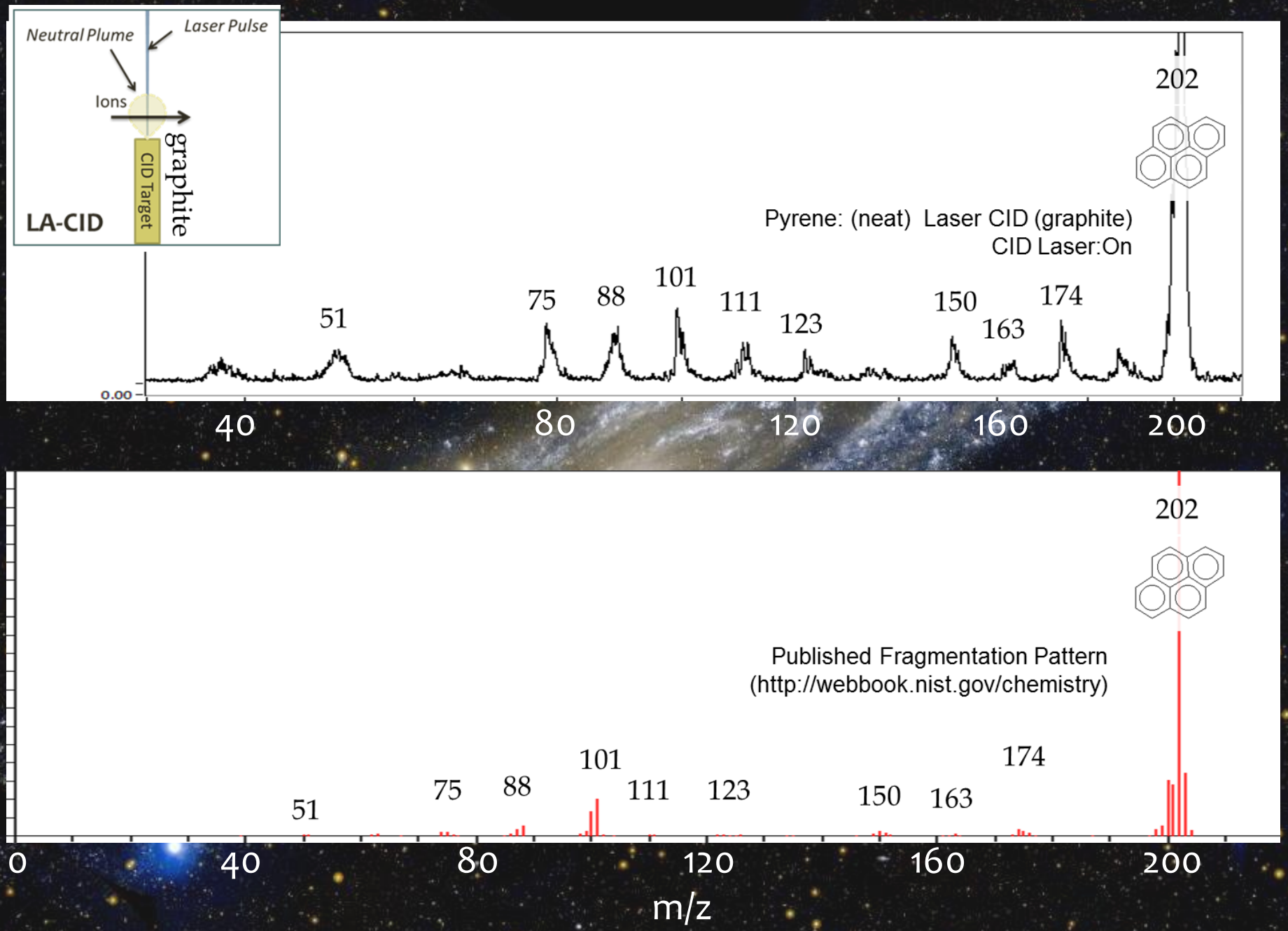

MSMS=118, PSD
Valine
M=
MSMS= 118, Valine
Prototype TOF, PSD
Selected peak:
Full spectrum
Valine
MSMS= 118, Valine
Commercial Bruker, PSD
0
20
40
60
80
100
120
140
160
180
200
Mass (amu)


MSMS= 133
Gly-Gly, PSD
M=
MSMS= 133, Gly-Gly
Prototype TOF, PSD
60
80
100
120
140
160
180
200
MSMS= 133, Gly-Gly
Commercial Bruker, PSD
60
80
100
120
140
160
180
200
Mass (amu)


MSMS= 295
Aspartame, PSD
MSMS= 295, Aspartame
Prototype TOF, PSD
M=
[M-OH]+
MSMS= 295, Aspartame
Commercial Bruker, PSD
Selected peak
[M+H]+
100
150
200
250
300
350
400
Mass (amu)

Local Collision Induced Dissociation (CID)




Neutral Plume
Laser Pulse
Ions
graphite
CID Target
LA-CID
Pyrene: (neat) Laser CID (graphite)
CID Laser:On
202
51
75
88
101
111
123
150
163
174
0.00
40
80
120
160
200
Published Fragmentation Pattern
(http://webbook.nist.gov/chemistry)
202
51
75
88
101
111
123
150
163
174
0
40
80
120
160
200
m/z

Conclusion

- MS/MS capability on miniaturized curved field reflector LD-TOF-MS has been demonstrated.
- In our setup, neglectable additional weight and volume are required to implement MS/MS, thus making the instrument a candidate for use in the analysis of other planetary environments as part of a future spaceflight mission.

Next Step

- MS/MS in the negative mode.
- Develop the miniaturized instrument containing MS/MS capability to higher maturity level for future space missions.

Acknowledgement

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Timothy Cornish
Scott Ecelberger

Thank you!

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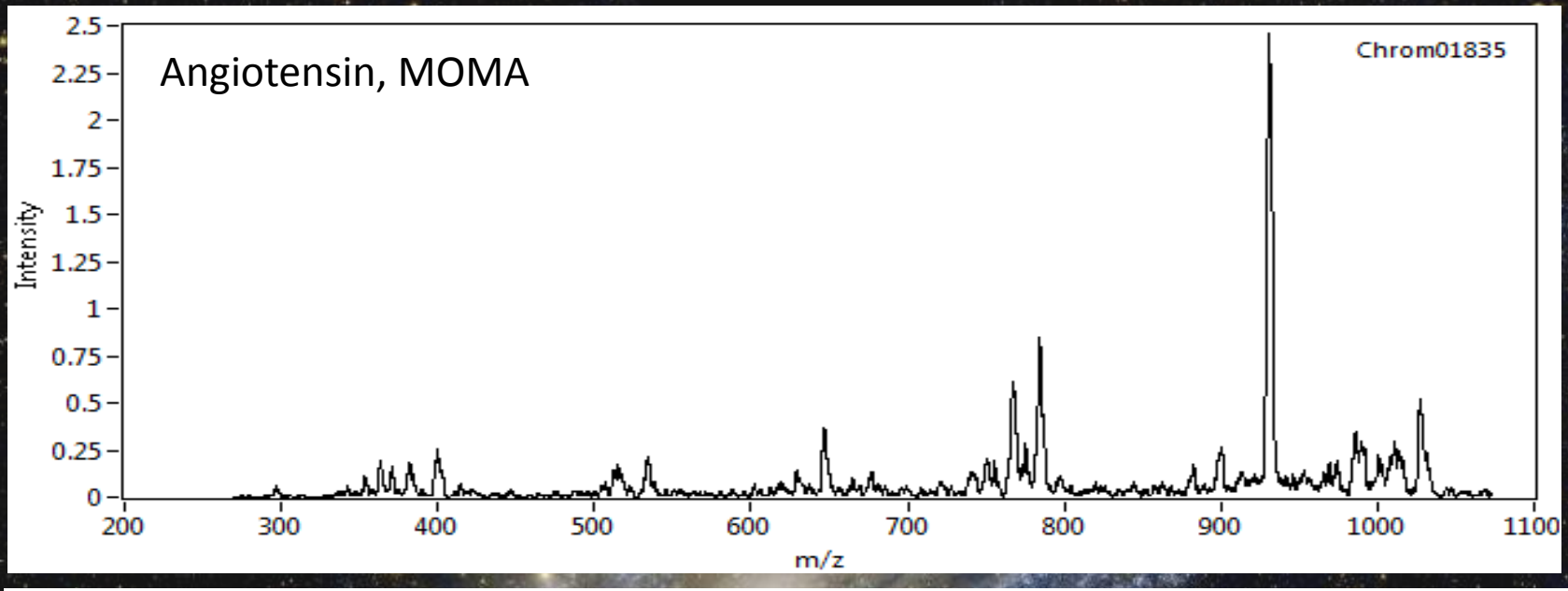
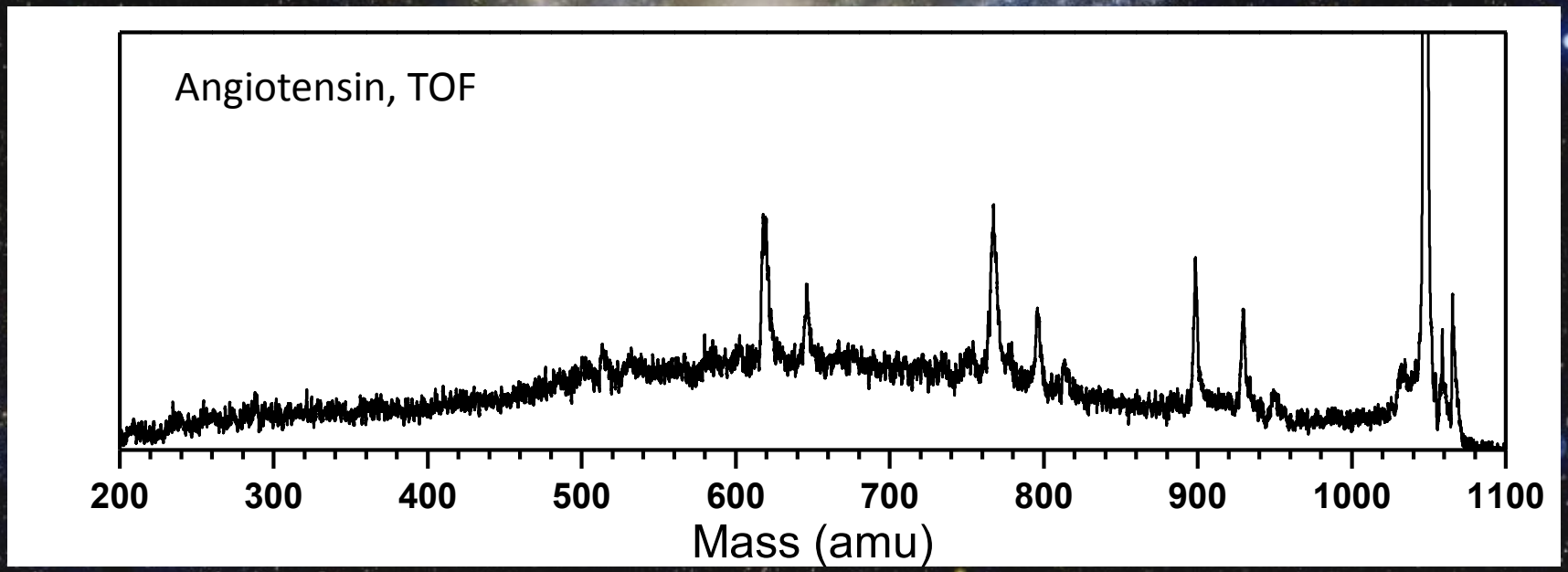
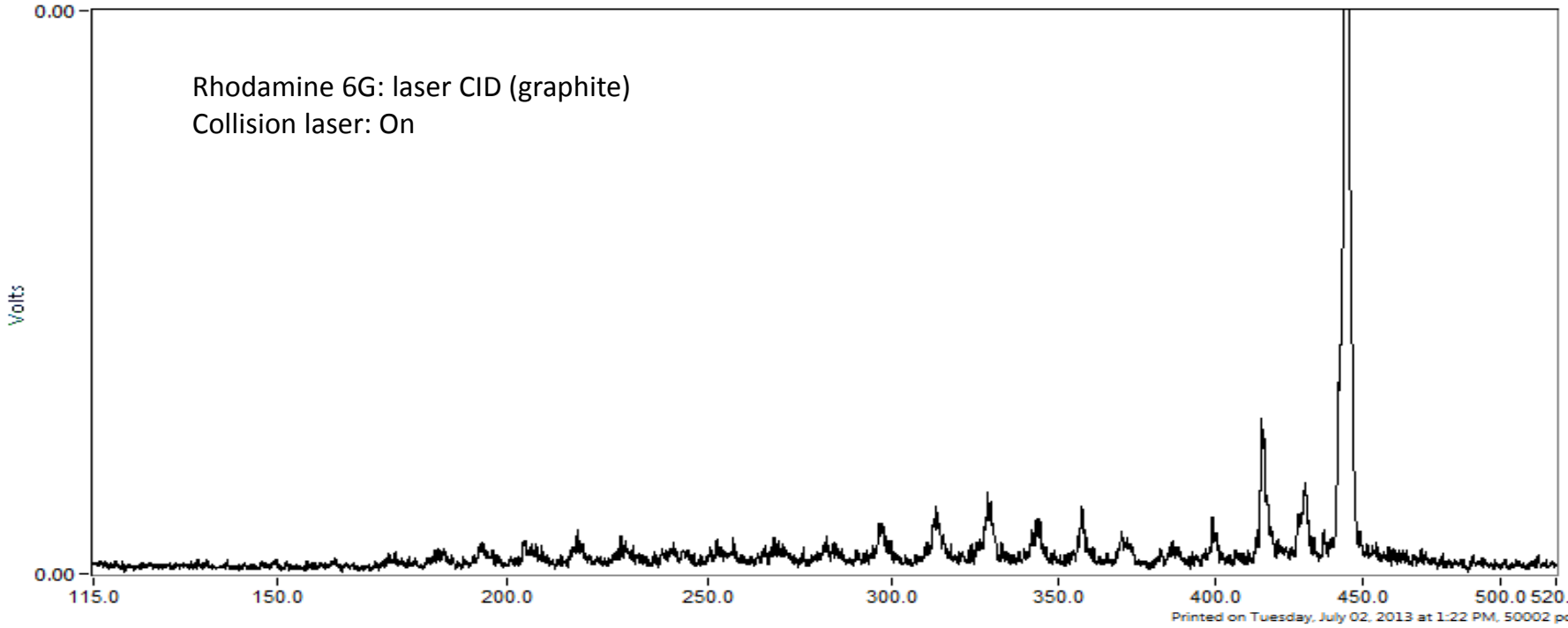
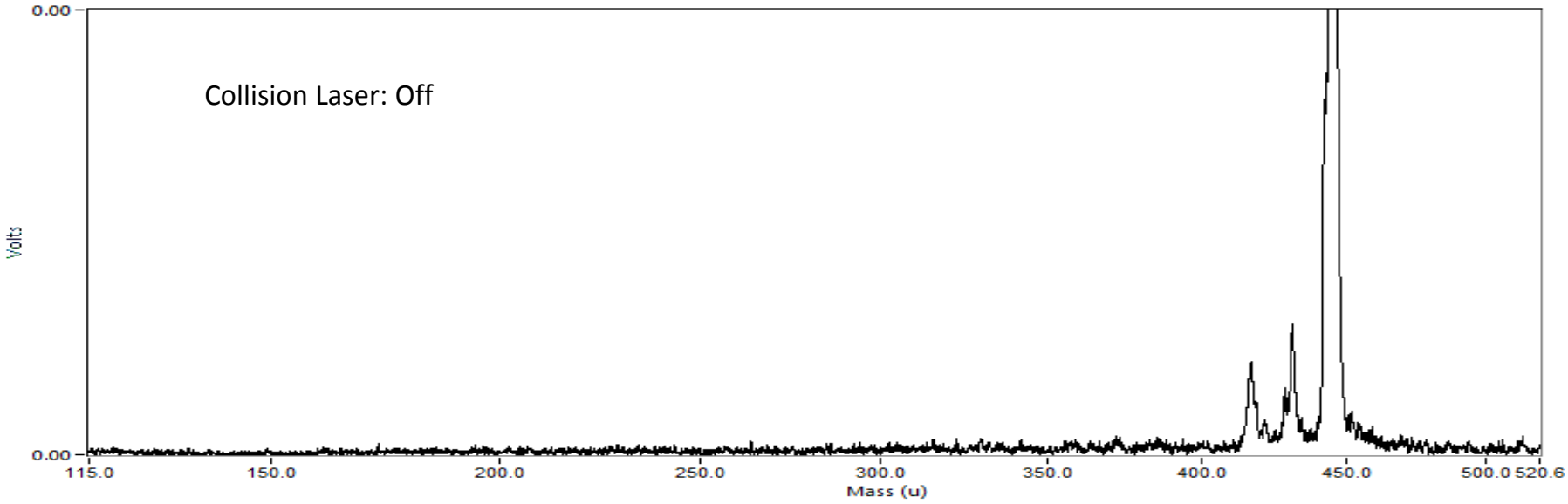
Backup


Angiotensin, MOMA
Chrom01835
Intensity
2.5
2.25
2
1.75
1.5
1.25
1
0.75
0.5
0.25
0
200
300
400
500
600
700
800
900
1000
1100
m/z


Angiotensin, TOF
200
300
400
500
600
700
800
900
1000
1100
Mass (amu)


Rhodamine 6G: laser CID (graphite)
Collision laser: On
Volts
0.00
0.00
115.0
150.0
200.0
250.0
300.0
350.0
400.0
450.0
500.0
520.6


Collision Laser: Off
Volts
0.00
0.00
115.0
150.0
200.0
250.0
300.0
350.0
400.0
450.0
500.0
520.6
Mass (u)

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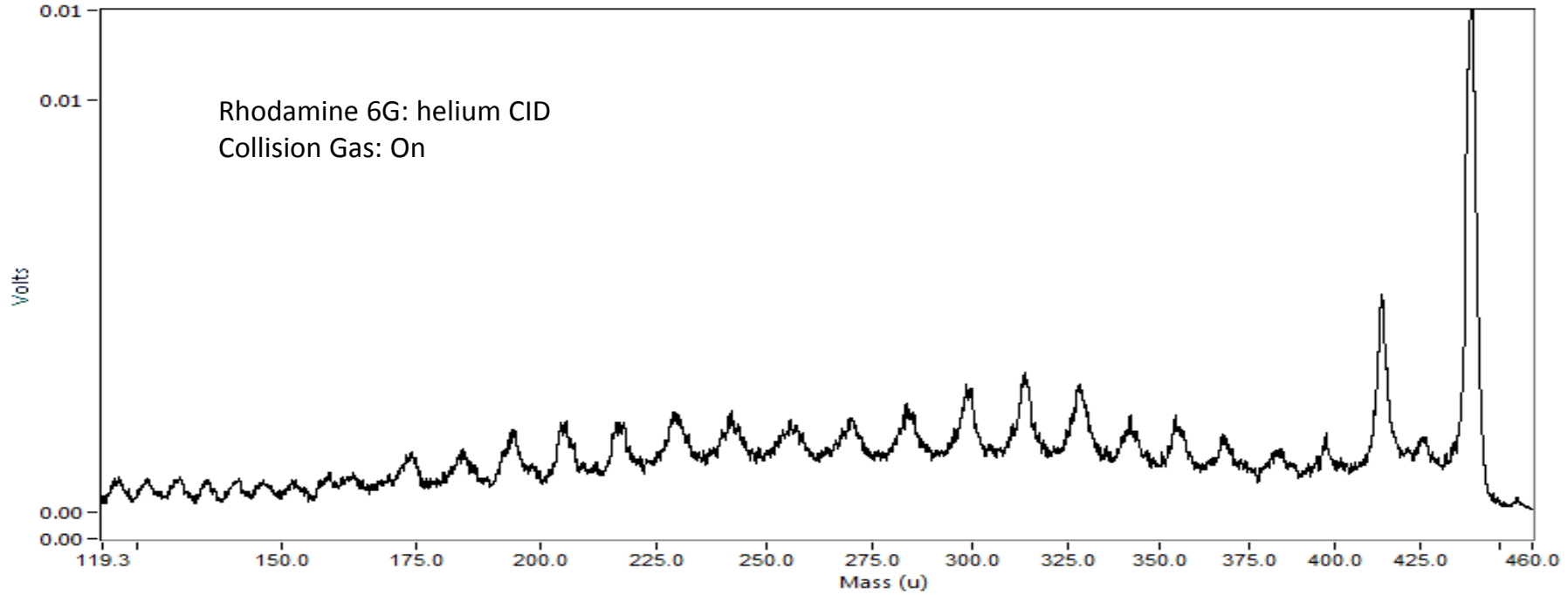

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