A COMPACT, HIGH-RESOLUTION TIME-OF-FLIGHT MASS SPECTROMETER BASED ON AN ELECTROSTATIC ANALYSER.

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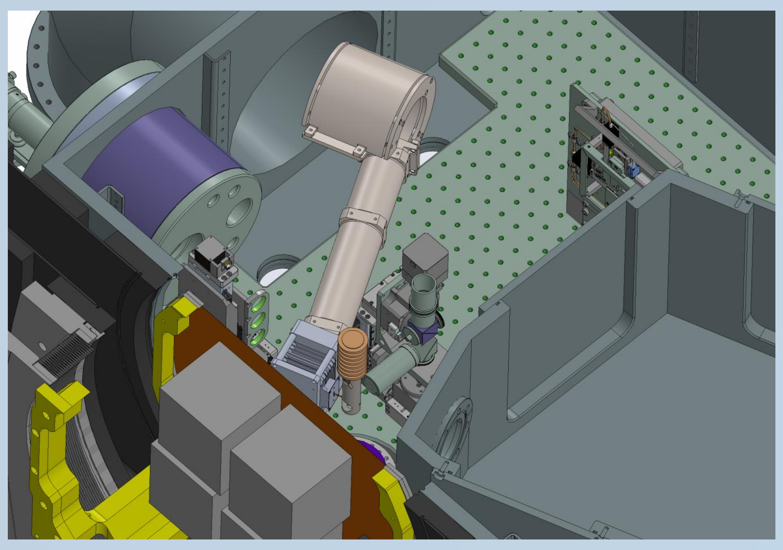
MS SPIDOC

MSVision

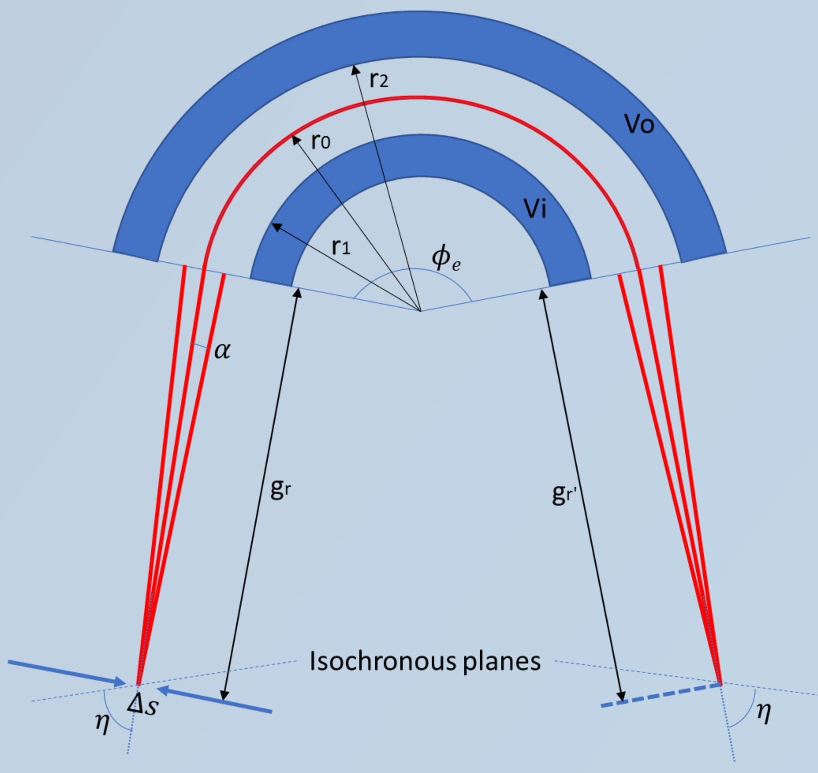
Introduction

Design constraints.

- A diagnostic mass spectrometer was required for the MS-SPIDOC project. Must be able to characterise ion beam containing biomolecular samples including virus capsids.
- Specifications:
  - Fit into small footprint (right).
  - Resolution > 5,000
- Reflectron TOF will not fit ➔ need a different design ➔ ESA.



Cutaway view of MS-SPIDOC chamber showing footprint where TOF must fit.

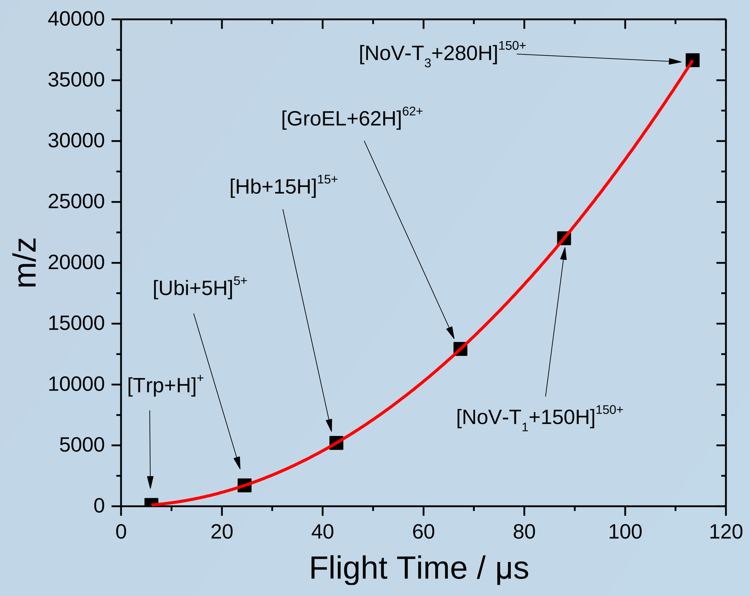


Generalized cylindrical geometry Sector TOF (symmetrical FFR regions).

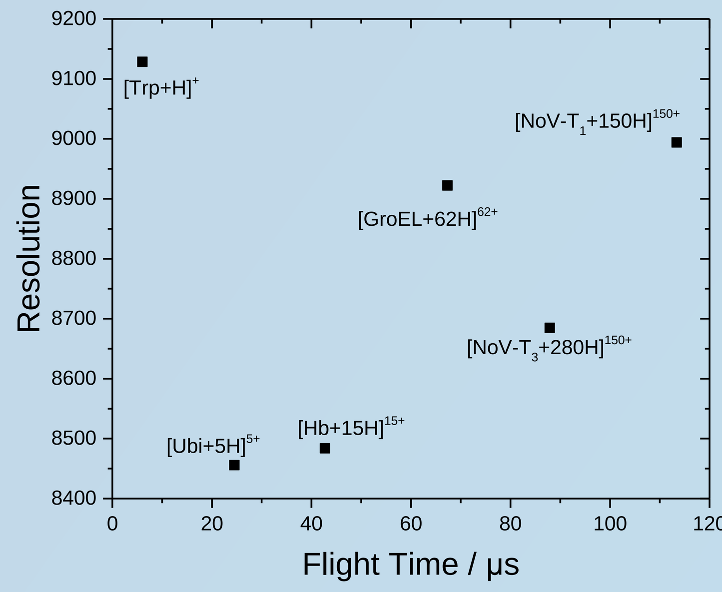
- Time of flight mass spectrometers with electrostatic sectors described theoretically in 1972[1].
- When combined with orthogonal acceleration, can arrange the geometry such that second order energy aberration from pusher and ESA cancel.
- Since the ESA acts as an energy filter, it will inherently reject metastable ions, leading to cleaner signal.
- Flexible design ➔ as long as the $g_r + g_r'$ is kept fixed, free to choose the values of g_r and g_r'.

1. Poschenrider, W.P., Int. J. Mass Spectrom. Ion Processes, 9, 1972, 357-373, https://doi.org/10.1016/0020-7381(72)80020-2

Results: Mass Spectrometry

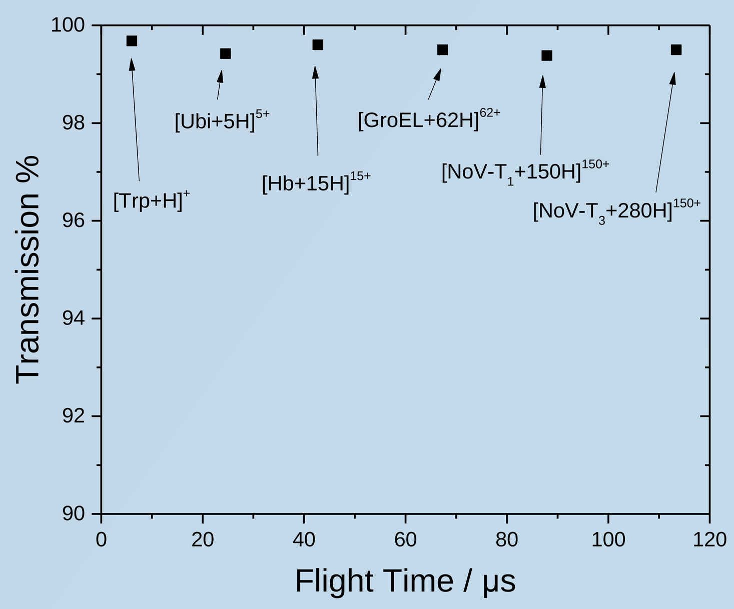


m/z vs flight time for different ions. m/z α TOF², as expected.

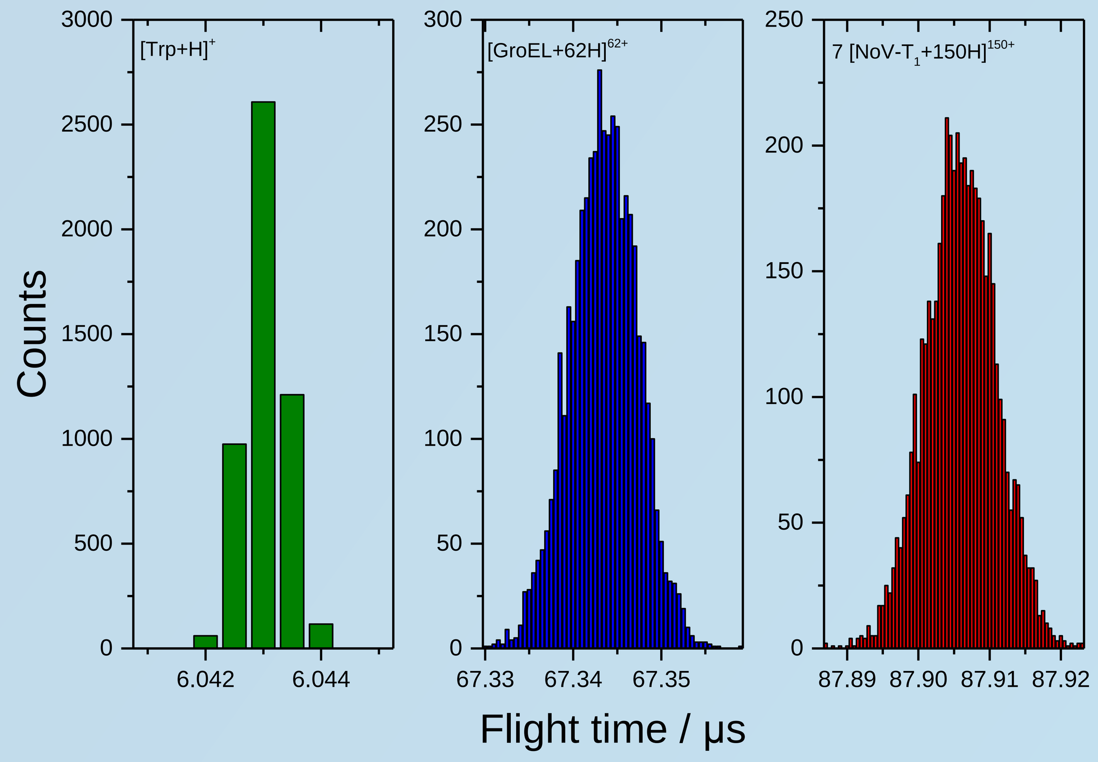


Resolution for ions of different m/z

- Resolution > 8,000 for 23 meV/q energy spread (random).
- For large systems (e.g. viruses), will not be limiting factor in observed resolution.

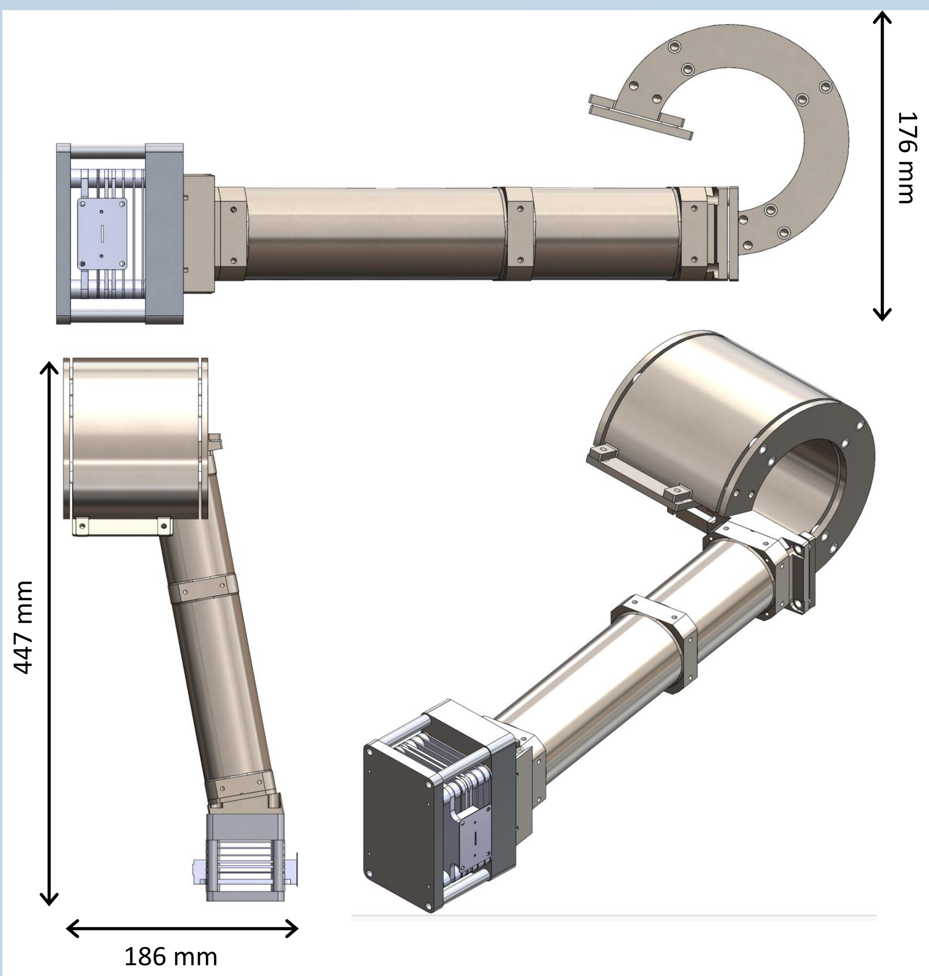


Percentage of ions hitting the detector for different m/z. Transmission > 99% for 23 meV/q energy spread (random). Energy spread in y is main cause for loss of ions on entry to ESA.



Arrival time distributions at time resolution of ADC for monoisotopic ions with 23 meV/q energy spread (random, 5000 ions).

MS-SPIDOC ESA-TOF Design



Design of the ESA-TOF for MS-SPIDOC.

Pusher

- Modified QTOF Ultima pusher stack.
- Ions have 1mm spread and 200 eV/q through pusher
- Ions have 6386 eV/q after pusher and travel at 10° to push direction.

Field Free region

- Total length = 244.4 mm, all before ESA in this configuration.

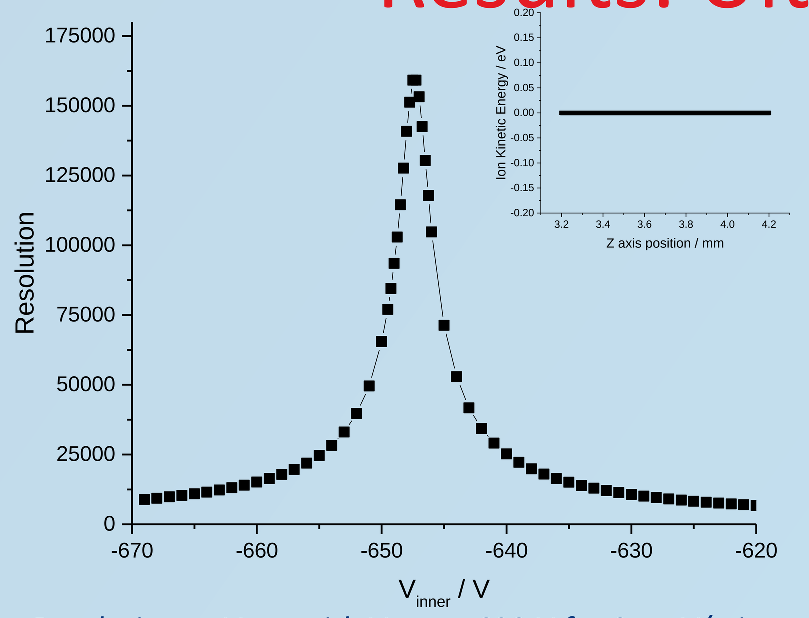
Electrostatic Sector

- r_1 = 52.25 mm, r_2 = 57.75 mm, ϕ = 254.6° (ensure isochronous planes normal to ion trajectories).
- Inner sector has negative voltage relative to FFR, outer sector positive.
- Ion beam traverses 90.4 mm to detector. Ion beam is 25 mm so 27.6 % duty cycle.

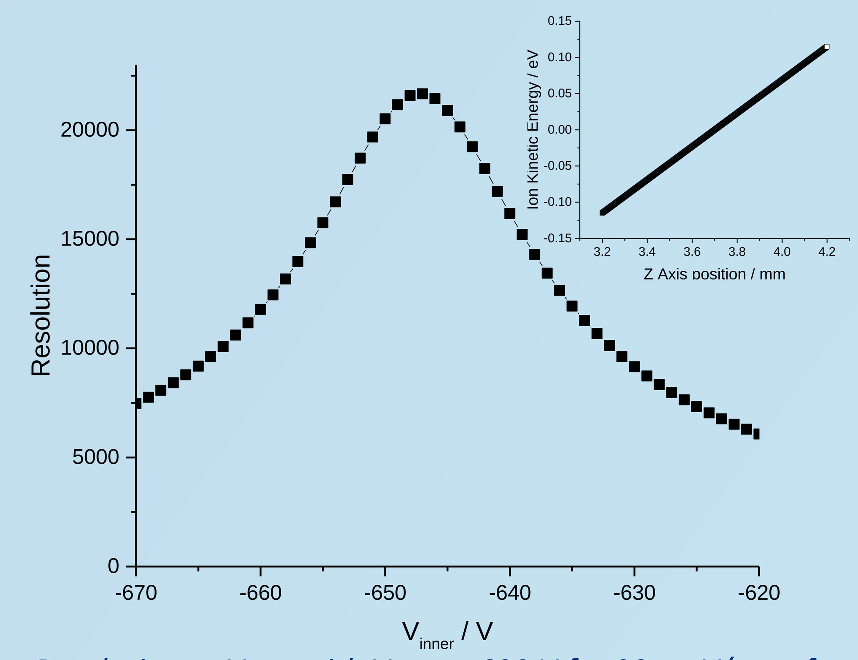
Detector

- Ultrafast electron multiplier detector.
- ADC with 500ps resolution

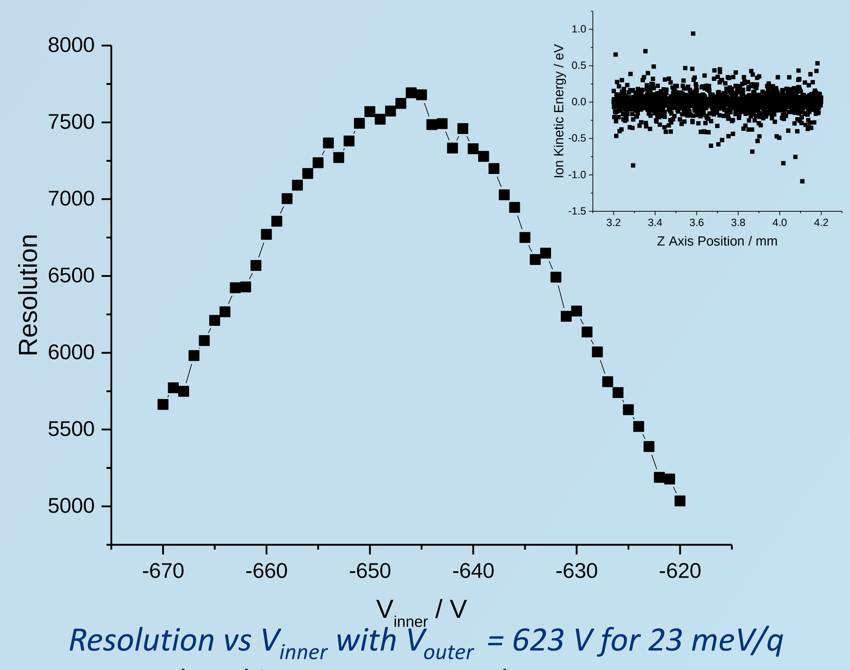
Results: Ultimate Resolution



Resolution vs V_{inner} with V_{outer} = 623 V for 0 meV/q ion energy spread. Inset shows initial ion distribution in Ez/z plane



Resolution vs V_{inner} with V_{outer} = 623 V for 23 meV/q perfect correlation ion energy spread (inset).

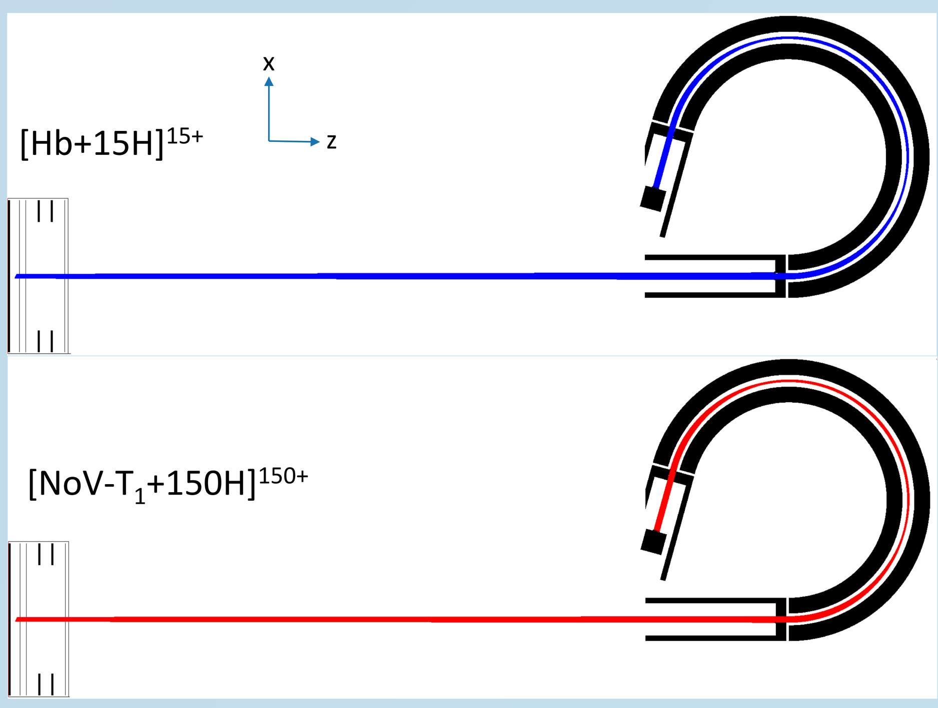


Resolution vs V_{inner} with V_{outer} = 623 V for 23 meV/q uncorrelated ion energy spread.

- Very high resolution without any energy spread ➔ **detector at second space focus.**
- Position and velocity correlated ➔ ions closer to pusher are moving towards & vice versa. **Resolution = 22,500 for perfect correlation.**
- Fully uncorrelated position and velocity ➔ **worst case scenario. Resolution = 7,750.**
- Expected performance somewhere between best and worst case ➔ **7,750 – 22,500.**

Computational Methods

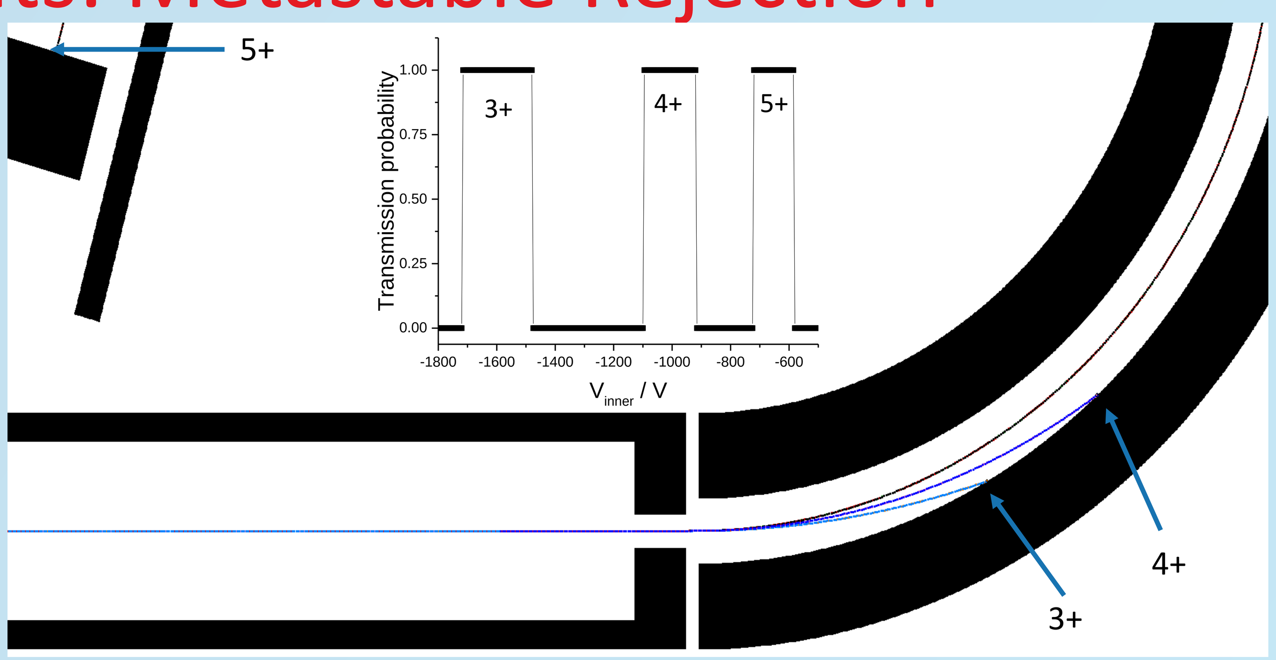
- Models generated with Simion:
  - 0.05 gu/mm for all.
  - Pusher uses symmetry plane
  - ESA extended 2D model covering entire work bench ➔ no fringe plates needed
  - FFR is empty workbench, only drawn near ESA.
- Simulations performed in SIMAX.
- For all simulations, ions have:
  - x = 0 ± 10 mm, E_x = 200 ± 0.023 eV/q
  - y = 0 ± 1 mm, E_y = 0 ± 0.023 eV/q
- 3 ion distributions in z were used (see resolution).
  - z = 0 ± 0.5 mm, E_z = 0 eV/q z = 0 ± 0.5 mm,
  - E_z = 0 ± 0.023 eV/q correlated (i.e. ions at -0.5mm have -0.023eV/q
  - z = 0 ± 0.5 mm, E_z = 0 ± 0.023 eV/q random (i.e. no correlation between energy and position).
- 500 ions used in all simulations.



Typical ion trajectories for haemoglobin 15+ (top) and norovirus T_1 capsids 150+ (bottom). Left shows the pusher stack region. Blank workbench simulated field free region. ESA shown on the right, with field free regions.

Results: Metastable Rejection

- Inherent rejection of metastables will further help resolution
- ESA is energy filter ➔ only metastable fragments of same charge will pass.
- Possibility to scan ESA voltage to probe metastable peaks.



Ion trajectories for different metastable ions. Any change in E/q will prevent ions being detected. The ESA voltage can be scanned to transmit the metastable ions (inset).

Summary and Future

- **Compact ESA-TOF design with a footprint less than 450 x 190 x 180 mm (*lxwxh)*.**
- **Flexible design allows to alter footprint without compromising performance.**
- **Energy filtering of ESA removed metastable ions or allows to study them.**
- **Simulation of mass spectrometry performance shows high ion transmission.**
- **Simulated resolution > 8,000 gives excellent performance for small size.**
- **Prototype currently in final stages of design and ready for manufacturing.**

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