HIGH RESOLUTION MULTI-REFLECTING TIME-OF-FLIGHT MASS ANALYZER WITH FOLDED FLIGHT PATH®

HR MR-TOFMS FFP®

Viatcheslav Artaev

1. Introduction: TOFMS Resolving Power

The time-of-flight (TOF) mass analyzer was first proposed by W. E. Stephens in 1946[1]. With an unlimited mass range, an ability to show all of the masses in each spectrum, and a high spectral generation speed, the advantages of a TOF mass analyzer over the existing mass spectrometer design were immediately recognized. Within a few years, the first experimental mass spectrometers based on a TOF mass analyzer were built[2]. All varieties of time-of-flight mass spectrometers (TOFMS) have three major components: the Extraction Region, where ions are formed or where they are introduced and then extracted as a pulse of ions; the Drift Region, also called a Field-Free Region, where ions fly and separate in time according to their mass-to-charge ratio (m/z); and the ion detector (Figure 1).
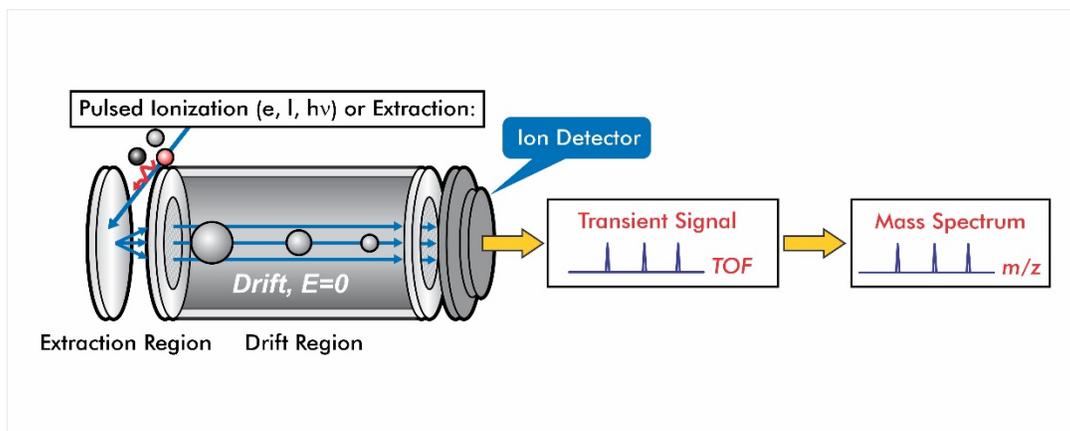

Figure 1. Time-of-flight mass spectrometer concept.

The ions are pushed by an electrical pulse (called the Pulsed Ionization) from the Extraction Region into the Drift Region, where they will obtain the same kinetic energy:

$$K = \frac{mV^2}{2}$$

where K – kinetic energy of ion, m – mass of ion, and V – ion velocity.

TOF utilizes a very simple mass separation concept. All ions will have the same kinetic energy when flying through the Drift Region—their velocity will depend on their mass (from the previous equation), so ions with lower mass will fly faster, and heavy ions will fly slower. Therefore, by measuring the time of each ion's flight, we can define their mass to charge ratios as

$$m/z = B + A * T^2$$

where A and B are constant coefficients characterizing the mass spectrometer, and T is the time-of-flight of the ion with mass m and electrical charge z.

There are several advantages of a TOF mass analyzer:

- Unlimited mass range: The mass analyzer itself is not a limiting factor for the mass range of ions.
- Full mass range spectra: All ion masses present in the extraction region are recorded in the single spectrum.
- No spectral skewing: There is no scan time, as time can be measured extremely fast, which results in no skewing.

An instrument's resolving power, or the ability to separately detect ions with very close m/z values, is one of the most important characteristics of mass analyzers. The general definition of the resolving power R is:

$$R = \frac{m}{\Delta m}$$

where m is the ion mass and Δm is the ion peak width at the corresponding level, as illustrated in Figure 2. High resolving power means a narrower peak, and therefore a more accurate and precise measurement of the top of those peaks.
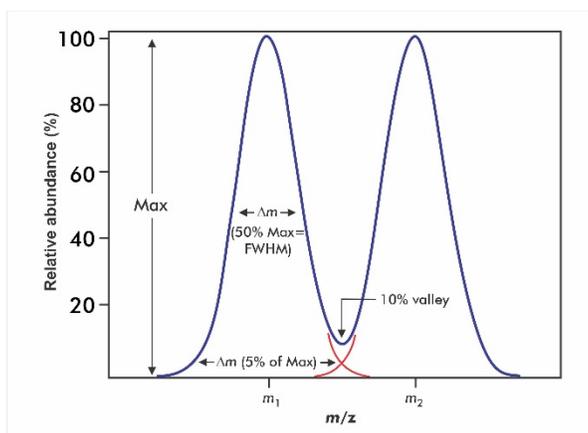

Figure 2. Zoomed in mass spectral peaks.

A peak is identified by an accurate mass assignment which can correspond to a specific chemical formula. This can only be achieved with an adequate resolving power.

As an example, a mass spectrometer with a low (nominal) resolving power will not be able to determine which chemical formula is represented by nominal m/z 28 (Figure 3, top). It could be any one of the three possible formulae based on nominal mass 28, which are called isobars, or even some combination of them. A mass spectrometer with a higher resolving power, such as 3000 or higher, can easily separate those isobaric ions if they are present and measure the m/z value with high mass accuracy, allowing for the assignment of elemental compositions with a high confidence (Figure 3, bottom).
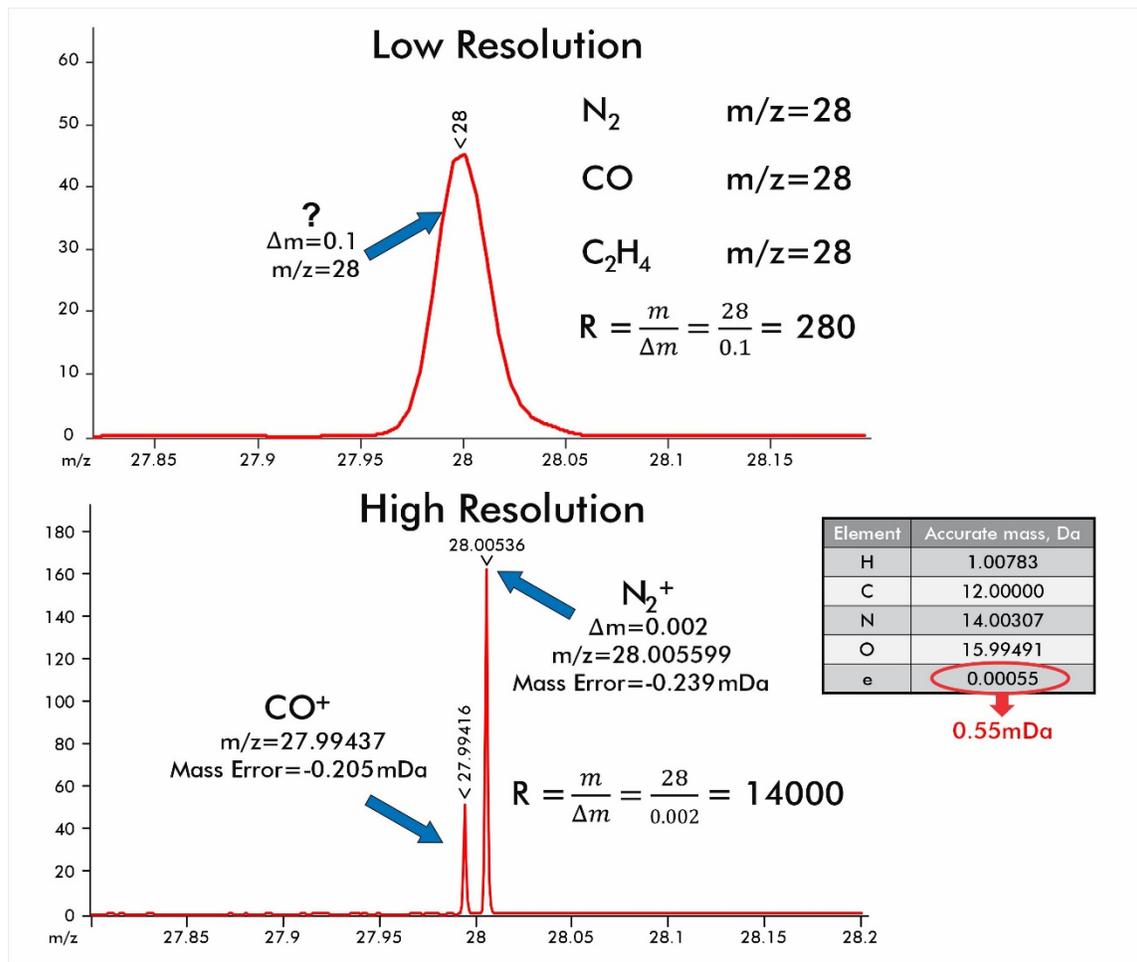

Figure 3. The effect of low vs high resolution on identification.

The resolving power (R) in TOF mass spectrometry is defined by a very simple expression, which is itself derived from the general resolving power definition (Figure 4):

$$R = \frac{TOF}{2*\Delta T}$$

where TOF is the ion's measured time-of-flight and ΔT is the ion peak width, which is usually measured at the half-height (Full Width Half Height, or FWHH).
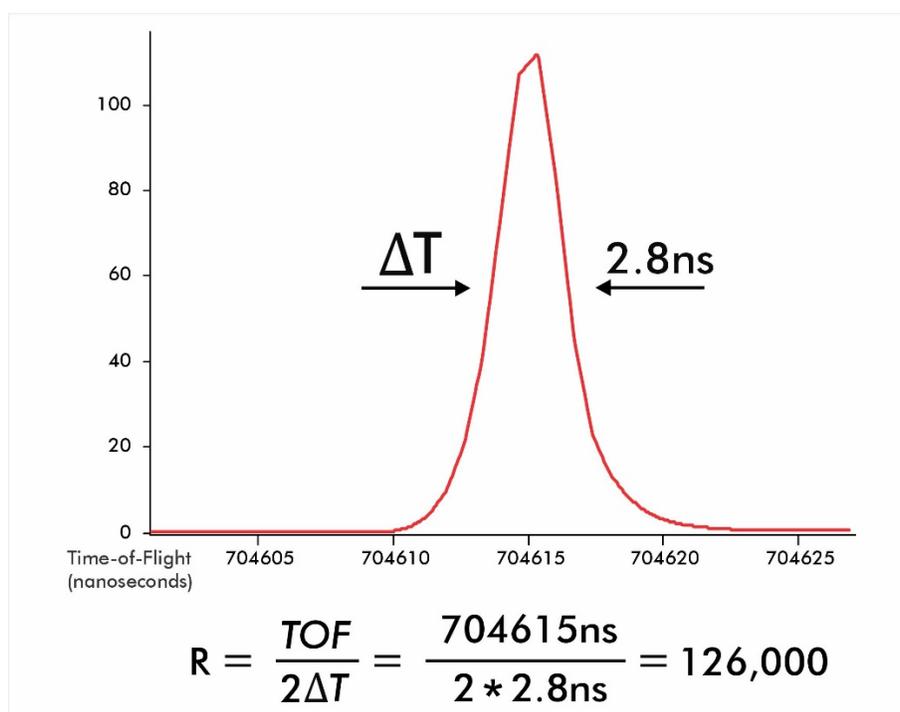

$$R = \frac{TOF}{2\Delta T} = \frac{704615ns}{2*2.8ns} = 126,000$$

Figure 4. Resolving power example.

From this expression, it is obvious that to achieve high resolving power, narrow peaks and large TOF is best. This is precisely the story of high resolution (HR) TOFMS development: make the width narrower, or the flight times longer, or both.

How high does resolving power need to be? It all depends on the applications in question and whether other separation techniques (chromatography, multidimensional chromatography, ion mobility, etc) are available to avoid overlapping peaks from isobaric ions. Figure 5 shows an example of the required resolving power for separating analytes which contain certain isobars. The presented plots show that with the increased m/z of the ions, the demand for resolving power also increases, sometimes to a very challenging level. Some very important pairs (e.g. C_3-SH_4) require a very high resolving power even for relatively low ion masses.

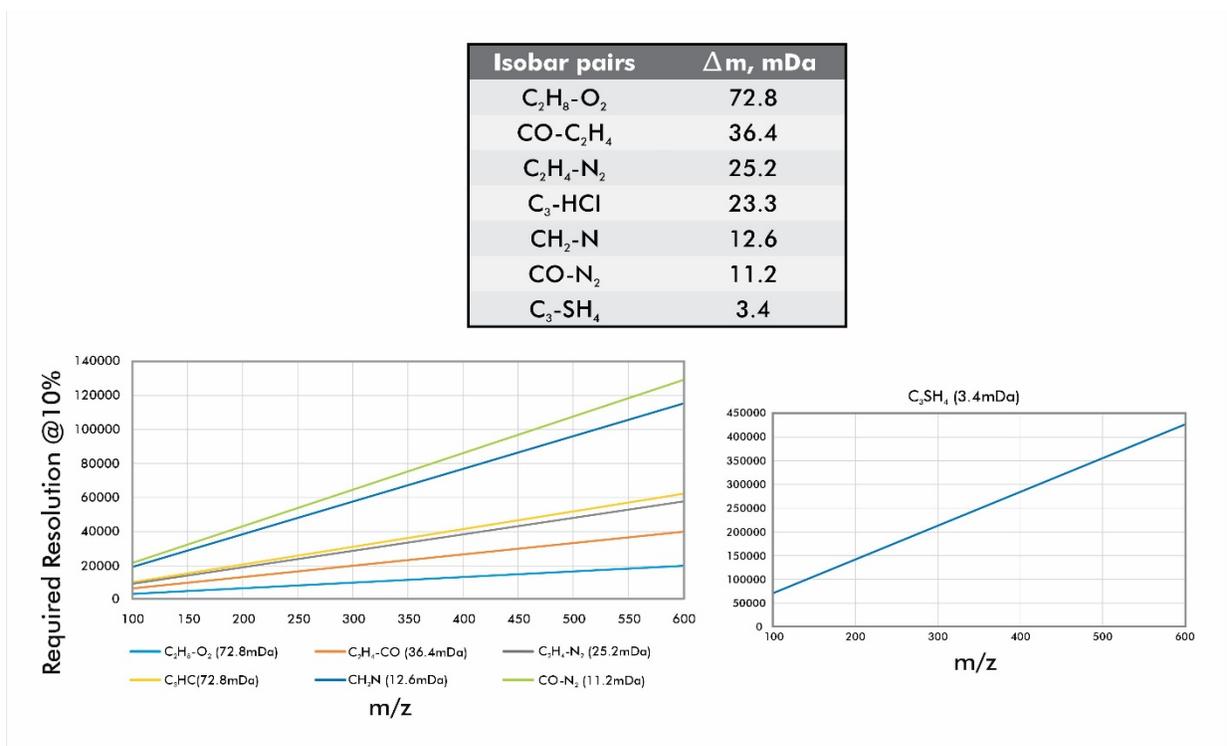| Isobar pairs	Δm, mDa
$C_2H_8-O_2$	72.8
$CO-C_2H_4$	36.4
$C_2H_4-N_2$	25.2
C_3-HCl	23.3
CH_2-N	12.6
$CO-N_2$	11.2
C_3-SH_4	3.4

Figure 5. Required resolving power for separating various isobars.

The ion peak width is defined by many factors, such as the initial conditions of the ions in the Extraction Region and after they leave it, the ion optical characteristics of the system, the repeatability of the power supplies, the mechanical (thermal) stability and tolerances, the ion detector response time, the data acquisition systems' digitizing speed, among many others. At the time of this writing, the smallest measureable peak width is in the range of 1-2 nanoseconds, or slightly shorter, depending on the ionization type, the number of ions in the ion packet, the detectors, the data systems, and several other factors. But, essentially, the peak width is currently limited at this 1-2 ns level and cannot be made significantly narrower.

If the peak width cannot be made smaller, the only meaningful and practically possible method of increasing resolving power would be to increase the TOF for the ions.

2. TOFMS with Long Time-of-Flight of Ions

There are several ways to provide longer TOF for ions in TOFMS.

One method is to reduce the ions' velocity while they fly in the Drift Region. However, reducing the ions' velocity will cause several negative effects, such as increasing the relative energy spread as the ions leave the extraction region and thus the demand for improved time-energy focusing properties of the ion optical system, i.e. after the extraction region, and increasing the scattering of the ions due to collisions with residual gas molecules in the mass analyzer. Good design practice for TOF mass spectrometers suggests having the ion energy as high as it is practical while taking into account various design elements: electrical breakdown distances, availability of stable high voltage power supplies, data acquisition digitizing and data transfer speed, and ion detector properties, to name just a few.

A second method of providing longer TOF for ions in TOFMS is increasing the length of the ion path. Linear mass analyzers with long flight paths up to 10 or more meters in length are known to exist and were used in some early experimental work, but they were not widely used due to their large size and poor ion transmission and resolution.

In 1973, B. Mamyrin and his co-workers proposed[3] a new type of TOF analyzer, which included an electrostatic ion mirror, or reflectron, as it was often called [Figure 6]. Their invention significantly improved the resolving power of TOF analyzers from a couple hundred to several thousand or more significantly by providing time-energy focusing, i.e., making the TOF of ions which enter the reflectron with slightly different kinetic energy almost the same when exiting it. For example, the ions with slightly higher energy spend longer time inside the reflectron because their high energy allows them to penetrate deeper inside the reflecting electrical field of the mirror. The ions with lower energy do not go as deep inside the mirror and spend less time there. In the field-free Drift Region, the situation is reversed: higher energy ions travel through faster, and lower energy ions spend more time there. The dimensions and electrical voltages of this system can be defined such that ions with higher and lower energies will arrive at the detector at the same time, thus achieving time focusing by energy (time-energy focusing). The peak width will become very narrow and the resolving power will be increased. These reflectron-type mass analyzers also increased the TOF of ions by 3 times when compared to the linear analyzers of same size.
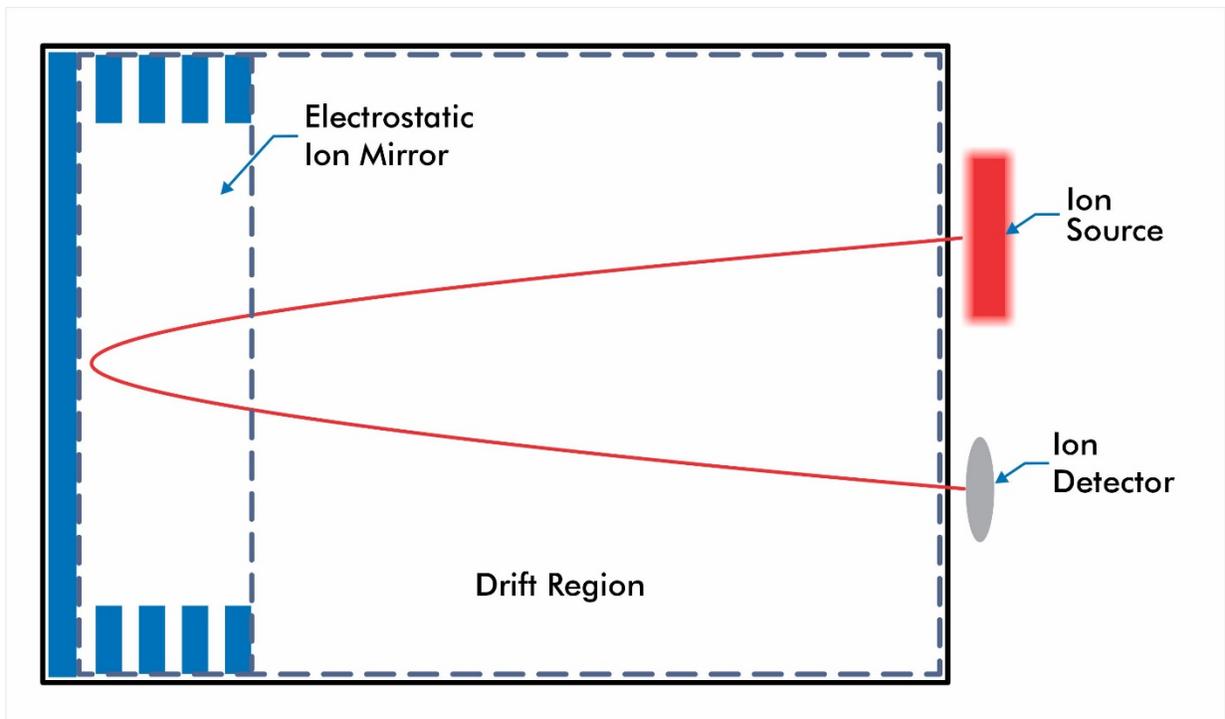
Figure 6. Reflectron mass analyzer concept.

The reflectron concept was widely adopted, and nowadays it is the most popular TOFMS design. However, to increase the resolving power beyond 15,000, manufacturers must increase the linear size of the flight tube significantly, as seen in the example shown in Figure 7, depicting the increased height of the flight tube in order to create resolving powers up to 30,000.
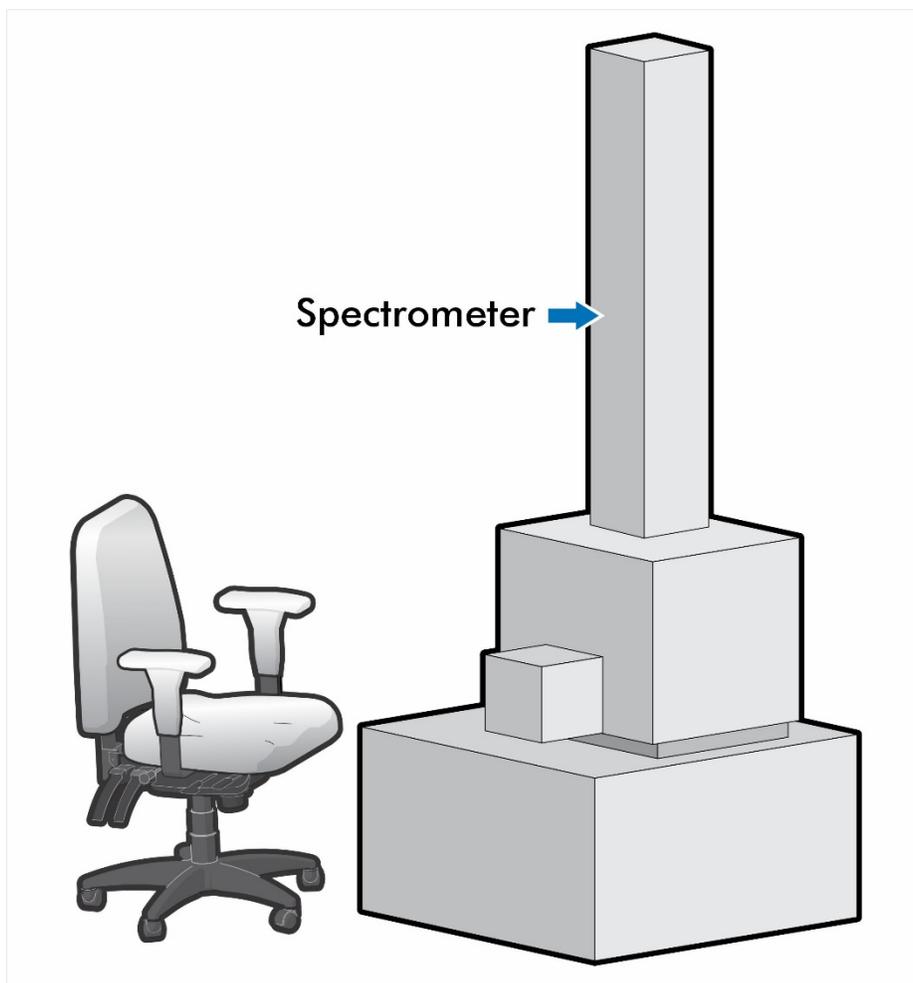
Figure 7. Increased height of the flight tube in a typical high resolution TOFMS.

3. Multi Reflecting Analyzers

An alternative method to improving the resolving power would be by increasing the linear size of the reflectron mass analyzer using a multi-reflection concept (Figure 8). The most common modern configurations of the high-resolution TOF mass analyzers can be described as a V configuration. Ions are ejected from the orthogonal accelerator, reflected by an ion mirror once, and then arrive on the detector.

Alternative analyzers with an elongated ion trajectory in shape of letter N, when ions are reflected twice by two parallel ion mirrors, are also implemented in commercial instruments.

Even a W configuration, elongating the ion path where ions are reflected between two parallel mirrors three times, can be a mechanism to gain resolving power by increasing the TOF of ions while staying within a reasonable analyzer size.

However, increasing resolving power with multi-reflecting configurations doesn't come without tradeoffs. Ions must pass multiple times through the grids (indicated by dashed lines in Figure 8), which define electrical fields with different strengths inside the reflectron. In case of an N-configuration, ions must pass through the grids at least 8 times, and in W-configurations, at least 12 times. Even with most transparent grids, this will lead to significant ion losses of at least a factor of 10. This is why higher numbers of reflections were not implemented commercially, as ion losses become the significant factor limiting application usefulness of such analyzers.
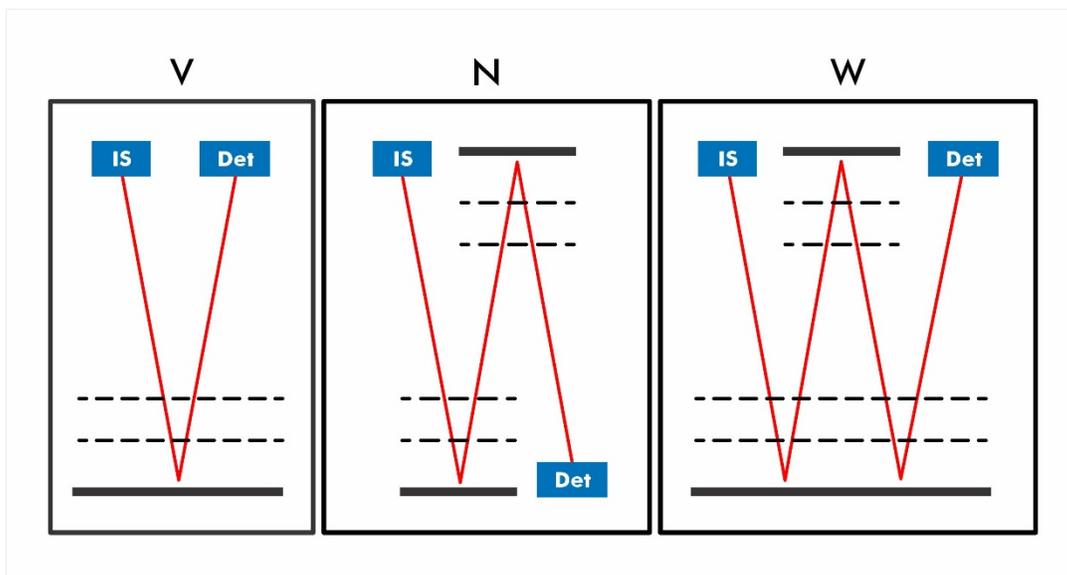

Figure 8. Reflectron analyzers configurations: V-shaped ion trajectory with a single reflection, N-shaped with two reflections, and W-shaped with three reflections. IS – Ion Source, Det – Ion Detector.

4. Planar Gridless Mirror

Various multi-turn and multi-reflecting schemes[4-6] have been explored by many researchers in the past, with most of the designs either being limited by a narrow mass range, poor transmission, or high aberrations. In 1989, E.M. Yakushev and co-workers proposed a novel ion optical design for a TOF mass analyzer based on multiple reflections between planar gridless electrostatic mirrors[7], allowing for multiple ion reflections (i.e., increased ion path length within the practical analyzer dimensions) and improved ion transmission due to the absence of the grids and spatial focusing along the Y-axis (Figure 9) inside the gridless mirror. However, the practical use of that scheme was limited by the ion trajectories divergence in the Z-direction, which created a still-significant loss of ions.
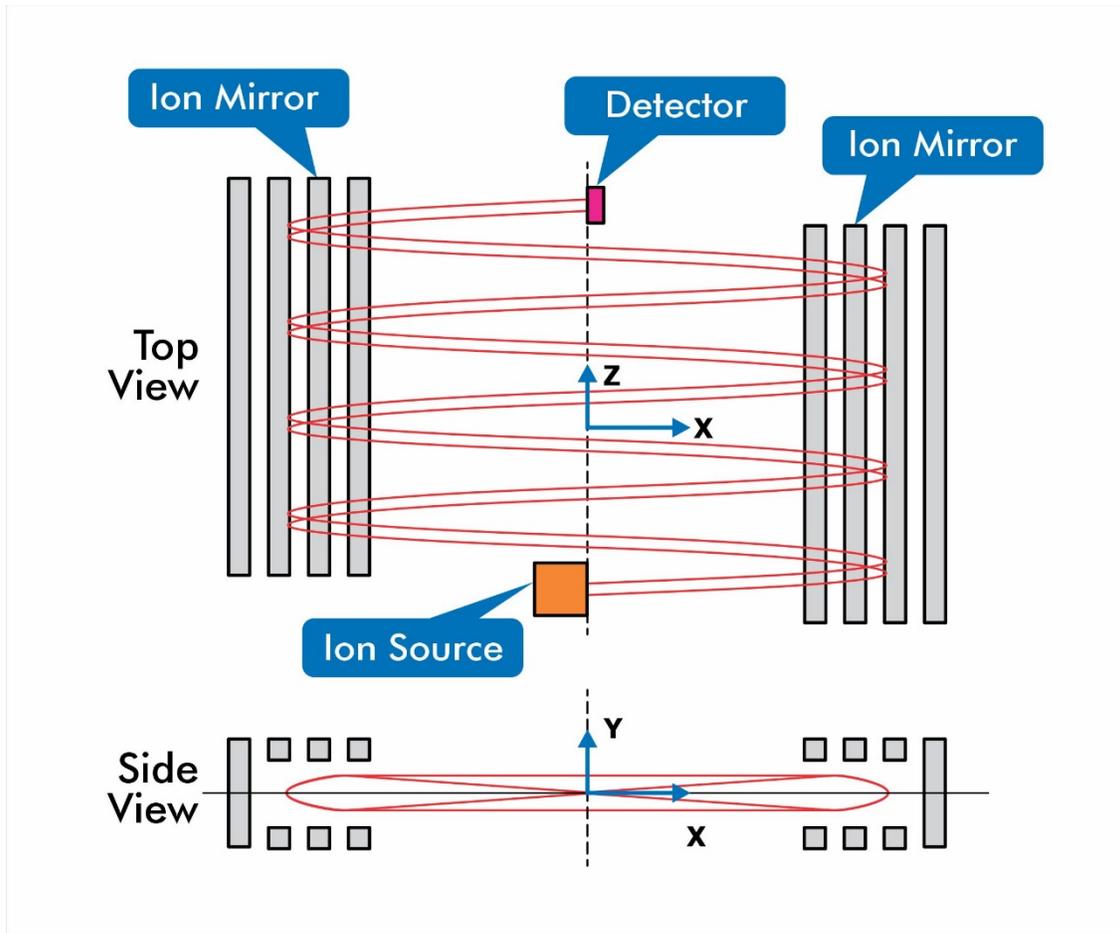
Figure 9. Design concept of the TOF mass analyzer with planar gridless electrostatic mirrors[7].

5. TOF Mass Analyzer Based on the Folded Flight Path (FFP) Concept.

To address the loss of ions in planar gridless mirrors problems due to divergency in the X-Z plane, an array of Einzel focusing electrostatic lenses was placed between the mirrors (Figure 10). In such a configuration, the ions will be spatially focused in the Y-direction (see inset) every time they exit the planar gridless mirror and will be focused in the Z-direction every time they pass through the Einzel lens array. Therefore, over multiple reflections, the trajectory of ions will remain in a zig-zag path, allowing for a long ion flight within a relatively small linear size and with minimal ion losses due to the periodical spatial focusing in both Y- and Z-directions.
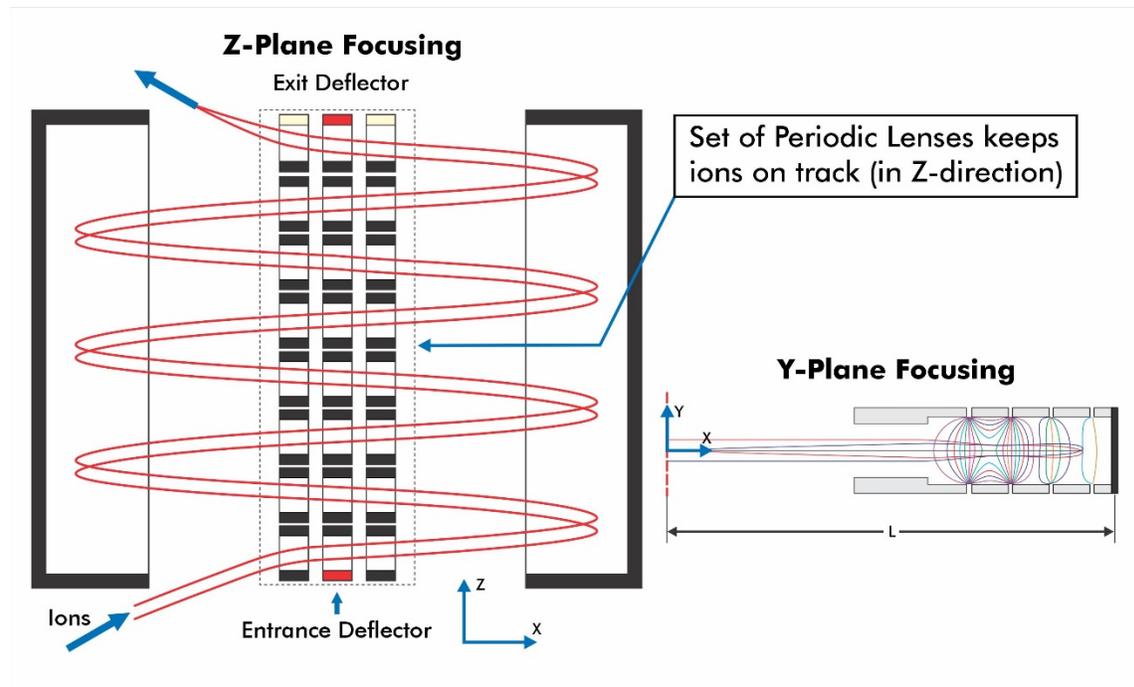
Figure 10. Design concept of the TOF mass analyzer with planar gridless electrostatic mirrors and lens array, placed between the mirrors.

The ion path can be increased even further without increasing the linear size of the mass analyzer if the zig-zag path of the ions could be reversed after the ions reached the analyzer's edge. The ions would then fly the same path in the reversed direction, nearly doubling the ion path length (Figure 11).
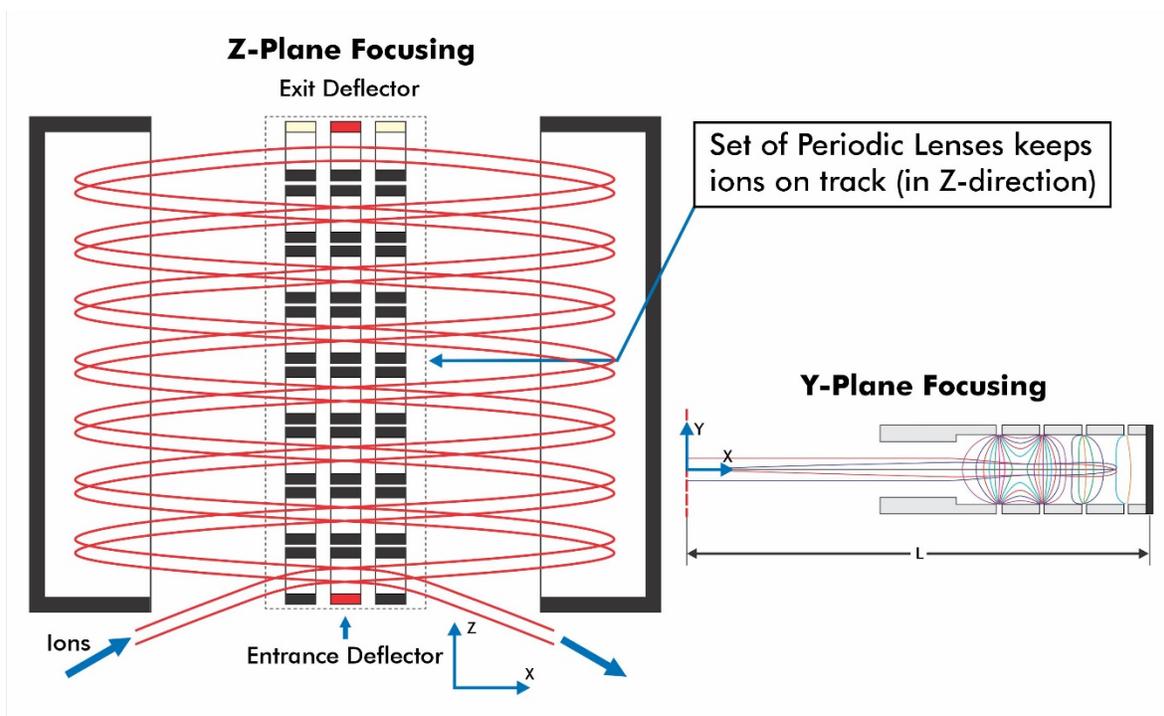
Figure 11. Folded Flight Path TOF mass analyzer concept.

This type of mass analyzer[8] (with either a single path or two-path ion trajectory) was named the Folded Flight Path® (FFP®) and was implemented nearly ten years ago in the family of LECO Pegasus® GC-HRT high resolution mass spectrometers. The major components of the ion optical design of the GC-TOFMS with high resolution *FFP*-based mass analyzers are depicted in Figure 12. The components are: an ion source (EI or Multi-Mode Source™), an ion interface to efficiently transfer the continuous ion beam from the ion source into the orthogonal accelerator, the orthogonal accelerator to form ion packets with the corresponding initial properties, the *Folded Flight Path* mass analyzer for time separation, time and spatial focusing of ions, and an ion detector.
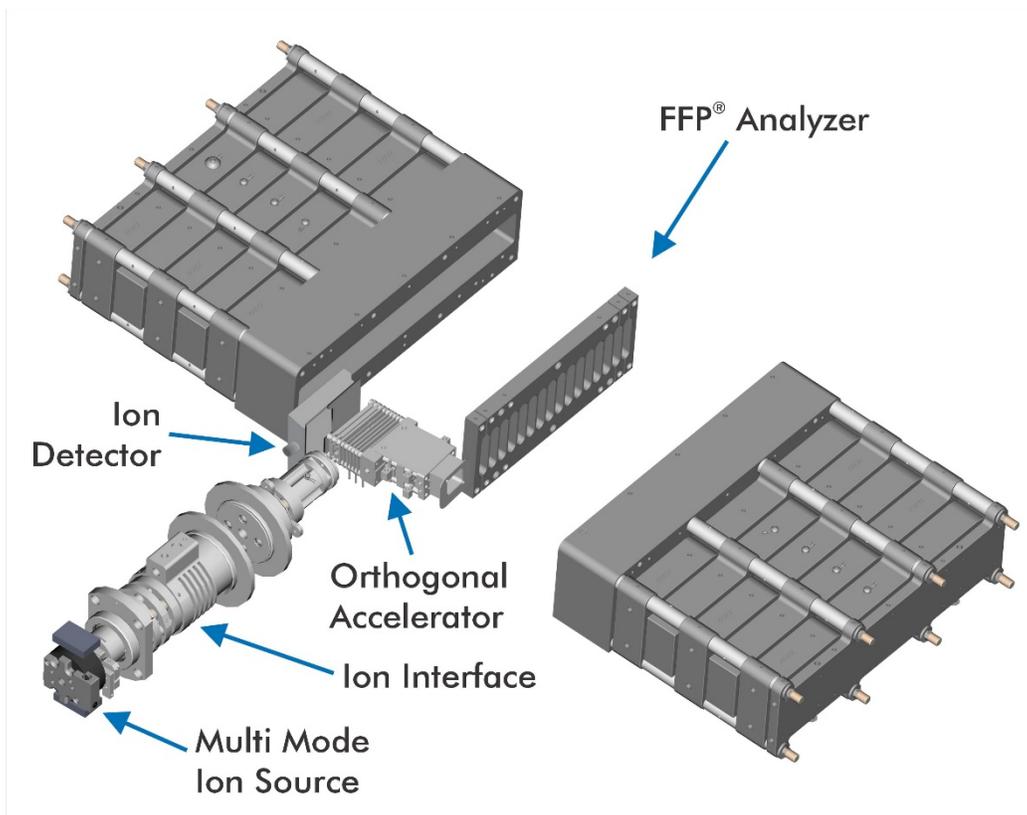
Figure 12. The ion optical CAD representation of the GC-TOFMS with FFP.

After several design iterations, the *FFP* mass analyzer used in the HRT is capable of providing approximately a 20 m ion path within a 30 in x 6 in x 4 in vacuum chamber by using 16 lenses and 32 reflections, resulting in a maximum flight time of 1 ms for an m/z value of 2500 (Figure 13). The selected design has second order time-spatial focusing and third order time-energy focusing with regards to ion-optical performance.
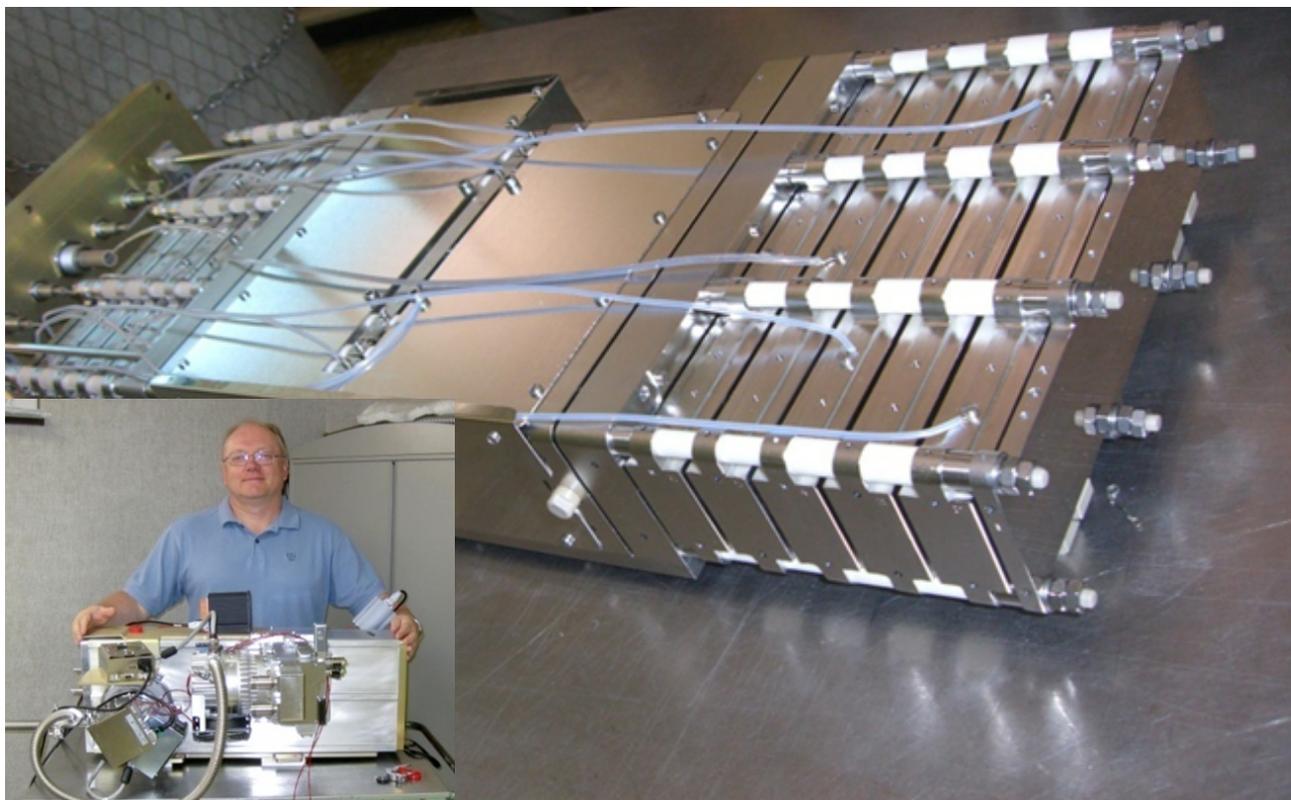
Figure 13. An example of the FFP mass analyzer design. Inset with author for scale.

The mass analyzer was coupled with a gas chromatograph via a heated transferline to directly connect the capillary column and the ion source. The vacuum system consists of two turbomolecular pumps creating the necessary vacuum conditions in the ion source, ion interface, and mass analyzer regions. All of that, as well as the power electronics, custom data acquisition system, and others components were placed inside the original floor-standing model (Figure 14).

Figure 14. Pegasus GC-HRT.

The properties of the mass analyzer, along with the long TOF, allows the *Pegasus* GC-HRT to achieve a resolving power above 25,000 for m/z=219 at FWHH of the peak in High Resolution (HR) mode (Figure 15). In Ultra High Resolution (UHR) mode, the *Pegasus* GC-HRT can achieve a resolving power above 50,000 for m/z=219 at FWHH of the peak (Figure 15).
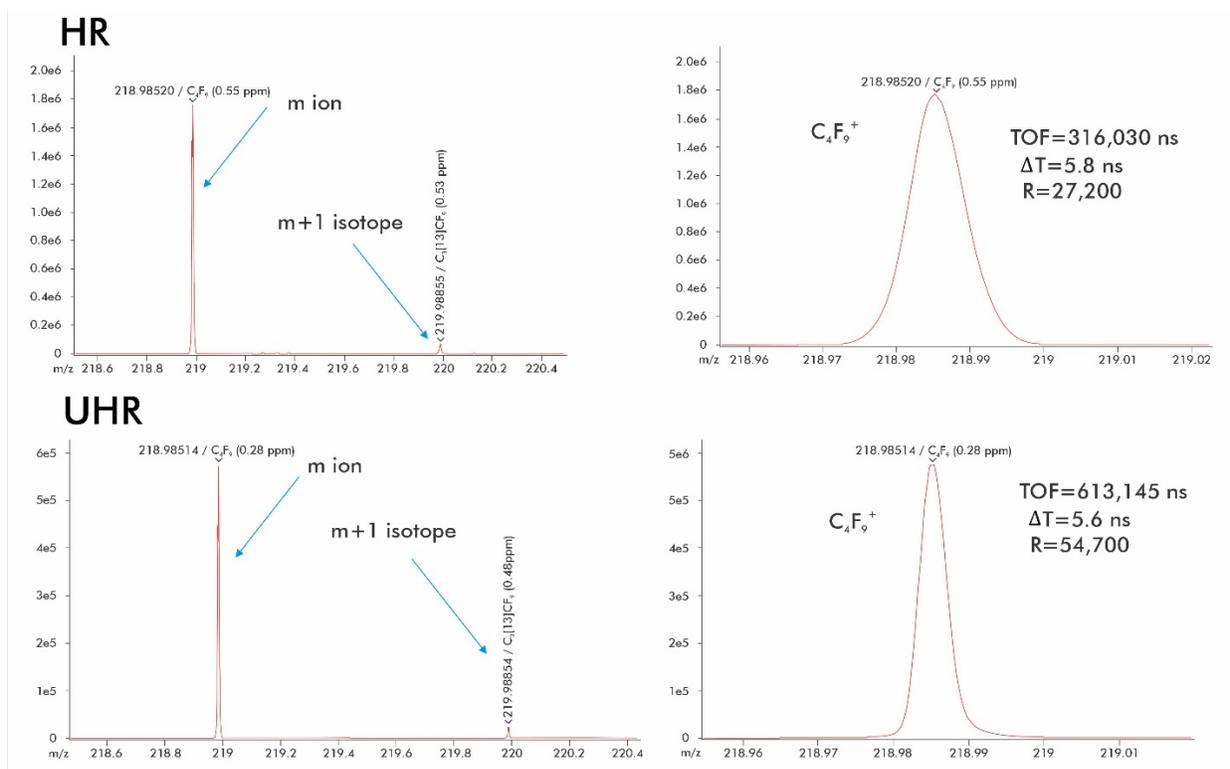
Figure 15. Electron ionization mass spectrum of PFTBA demonstrating separation of ion fragment $C_4F_9^+$ and its first isotope $C_3^{13}CF_9^+$ (left) and $C_4F_9^+$ (m/z=219) (right) ion peak details (TOF, peak width) confirming the resolving power value above 25,000 in High Resolution (HR) mode (top) and confirming the resolving power value above 50,000 in Ultra High Resolution (UHR) mode (bottom).

Figure 16 depicts experimental values of the resolving power vs the m/z obtained by running the GC-HRT mass spectrometer with the *FFP* mass analyzer. This plot is very typical for all of the GC-HRT models, and its shape—increasing with m/z at low values of m/z, rising quickly, and then staying almost constant at the higher m/z—is very normal for TOF mass spectrometers in general and considered one of the very important advantages of TOFMS compared to the other types of mass analyzers. This is in stark contrast to high resolution ion trap mass analyzers, which have the exact opposite relationship (high at low mass and decreasing resolving power as mass increases).
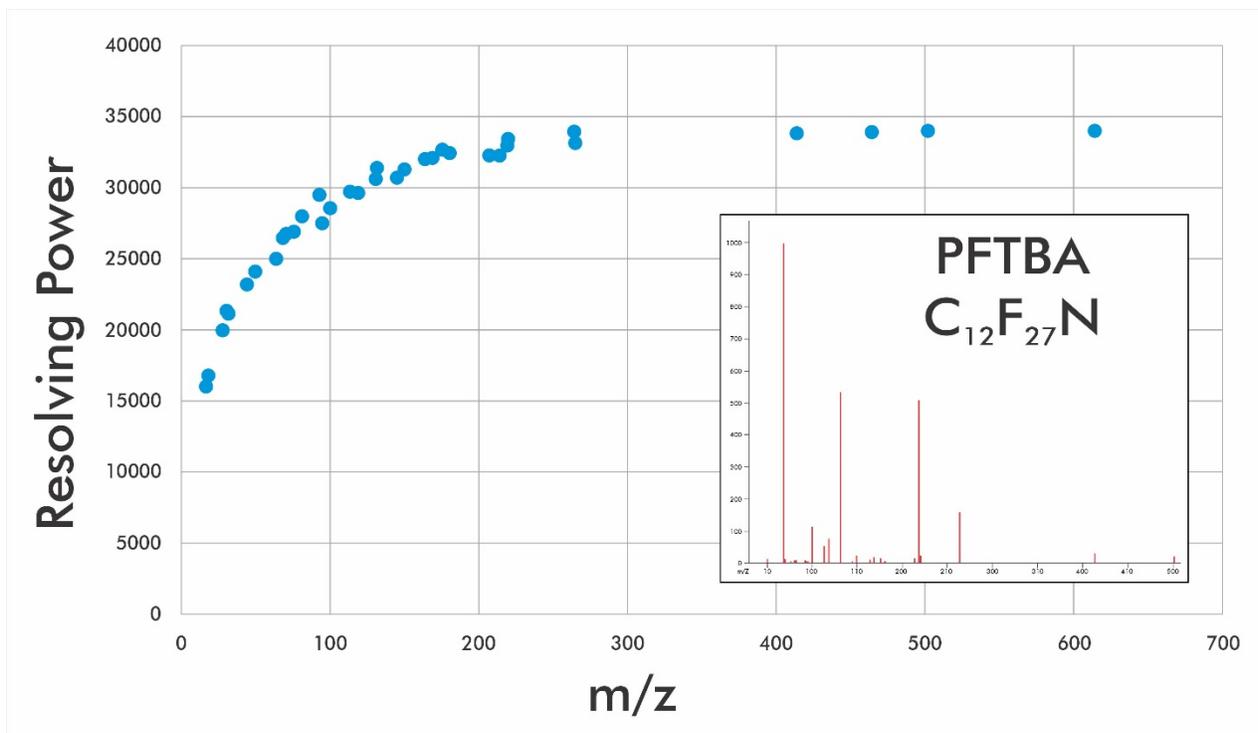
Figure 16. FFP experimental data showing resolving power vs ions' m/z obtained using GC-HRT.

.

The unique configuration of the *FFP* mass analyzer allows for further increases of the resolving power if necessary. Figure 17 shows a schematic of two possible modes for GC-HRT operation: High Resolution (HR) mode and Ultra-High Resolution (UHR) mode. In HR mode, the ions fly in a zig-zag trajectory from left to right and then make another pass by changing drift direction and going right to left before they reach the detector. This mode provides spectral acquisition at full mass range with the resolving power above 25,000 at m/z=219 (at FWHH, Figure 15). This is a standard mode for GC-HRT operation. The UHR mode of operation sends ions for two cycles (N=2) of the *FFP* path, nearly doubling their time-of-flight. The outstanding ion-optical properties of the *FFP* means that the peak width is the same in both HR mode and UHR mode, which results in the resolving power doubling from 25,000 to 50,000 for m/z=219, as shown in Figure 15 above. However, in UHR mode, the mass range that can be collected is reduced to make sure that all of the detected ions make two full cycles through the *FFP* mass analyzer. The theoretical ratio of maximum to minimum m/z that can be acquired in UHR mode is 4. For example, acquisition can start at m/z=100 and stop at m/z=400, which is an acceptable mass range for many applications.
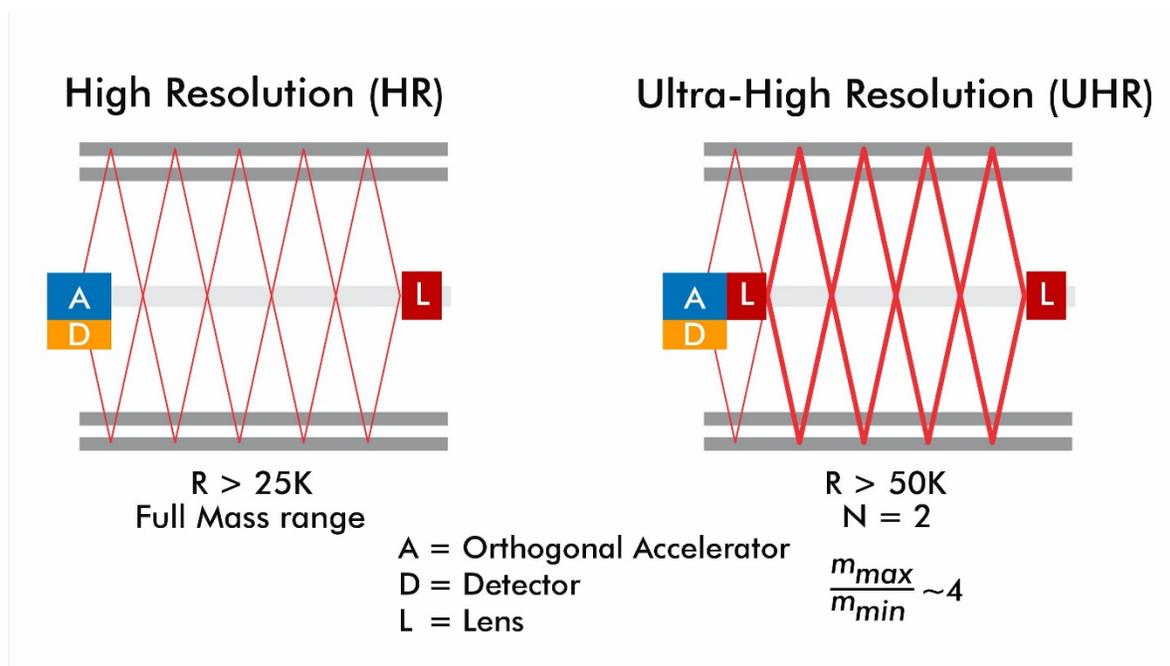
High Resolution (HR)   Ultra-High Resolution (UHR)

A = Orthogonal Accelerator
D = Detector
L = Lens

R > 25K
Full Mass range

R > 50K
N = 2

$$\frac{m_{max}}{m_{min}} \sim 4$$

Figure 17. Modes of operation of the FFP mass analyzer: High Resolution (HR) mode (left) and Ultra-High Resolution (UHR) mode.

6. Improving Duty Cycle with Encoded Frequent Pushing.

The *FFP* mass analyzer provides a significant increase of the flight time of an ion within a very small mass analyzer. In order to achieve high resolving power and high ion transmission, ion packets have to satisfy extremely tight initial energy conditions, including relatively small ion packet dimensions (only few millimeters in length). A long TOF and narrow acceleration region result in a relatively low duty cycle, which is defined as the percentage of the continuous ion beam used for mass analysis. To significantly improve the *FFP* duty cycle, the concept of Encoded Frequent Pushing® (EFP®) was developed and implemented in the latest models of the GC-HRT instruments. The details of *EFP* principles and implementations are described in [9, 10].

The resulting multiplexed mass spectra are deciphered in real time using the knowledge of the pulse sequence implemented for multiplexing. The mass spectra are decoded with the resulting increase in the ion signal by 10 or more times. It must be noted, though, that the *EFP* approach for increasing the TOFMS duty cycle can only be efficiently implemented with high resolving power mass analyzers, like the *FFP* types, as the scarcity of the ion peaks in the mass spectra is one of the main conditions for successful *EFP* implementation.

7. Summary

The High-Resolution Time-of-Flight Mass Spectrometer based on the *Folded Flight Path* analyzer is a novel and unique concept, achieving high resolving power by increasing the ion flight path within reasonable-sized vacuum chambers. The HR-TOFMS with *FFP* easily works with various sample introduction, separation, and ionization techniques, allowing them to take full advantage of TOFMS benefits, such as high analysis speed, high data acquisition rate, wide mass range, and now, with *FFP*, high resolving power and great mass accuracy. The HR-TOFMS with *FFP* is a great addition to the toolbox of modern analysts.

References

1. W. E. Stephens, Phys. Rev. 69 (1946) 691
2. A.E. Cameron, D.F. Eggers. An Ion "Velocitron", Rev. Sci. Instrum. 19 (1948) 605. https://doi.org/10.1063/1.1741336
3. B.A. Mamyrin, V.I. Karataev, D.V. Shmik, Zagulin V.A., The mass-reflectron, a new nonmagnetic time-of-flight mass spectrometer with high resolution. JETP 64 (1973) 82-89
4. Toyoda M, Okumura D, Ishihara M, Katakuse I. Multi-turn time-of-flight mass spectrometers with electrostatic sectors. J. Mass Spectrom 2003; 38: 1125-42. https://doi.org/10.1002/jms.546
5. Satoh T, Tsuno H, Iwanaga M, Kammei Y. The design and characteristic features of a new time-of-flight mass spectrometer with a spiral ion trajectory. J Am Soc Mass Spectrom 2005; 16: 1969-75. https://doi.org/10.1016/j.jasms.2005.08.005
6. Wollnik H, Casares A. An energy-isochronous multi-pass time-of-flight mass spectrometer consisting of two coaxial electrostatic mirrors. Int J Mass Spectrom 2003; 227: 217-22. https://doi.org/10.1016/S1387-3806(03)00127-1
7. L. M. Nazarenko, L. M. Sekunova, E. M. Yakushev, Time-of-flight mass spectrometer with multiple reflections, SU Patent 1725289 A1, 1989
8. Verenchikov A, Yavor M, Mitchell J, Artaev V. US Pat. 7,385,187 (2004)
9. P. Willis, J. Jaloszynski, V. Artaev. Improving duty cycle in the Folded Flight Path high-resolution time-of-flight mass spectrometer. IJMS, 459 (2021) 116467 https://doi.org/10.1016/j.ijms.2020.116467
10. LECO Corporation, Encoded Frequent Pushing: Improving Duty Cycle in the Folded Flight Path (2019) 209-281-006