Introduction

The time-of-flight mass spectrometer (TOFMS) is one of mass spectrometry techniques, which include the quadrupole mass spectrometer, the magnetic sector mass spectrometer, the ion trap mass spectrometer and the Fourier transform ion cyclotron resonance mass spectrometer. In the case of TOFMS, ions of various m/z values, which are generated in the ion source, are accelerated to the detection plane by a pulse voltage applied from a starting time of data acquisition. Since the time-of-flight of ions at the detection plane are proportional to the square root of their m/z values, the ions generated in the ion source can be separated. One of the TOFMS feature is fast measurement, which is due to the unneccessity of scan for any physical parameters such as electric or magnetic fields. Recently, not only a single type mass spectrometer, but also a tandem type mass spectrometer connected with the quadrupole mass spectrometer (Q/TOF) or tandemly connected two TOFMS (TOF/TOF) are available.

The mass resolution of TOFMS is expressed by \( T/2\Delta T \), where \( \Delta T \) is the time-of-flight distribution of the ion group with the same m/z value (ion packet) at the detection plane (that is, spatial distribution of the ion packet in the flight direction at the detection plane) and, T is centroid of the time-of-flight distribution. Since TOFMS was invented in 1964 [1], its mass resolution has been improved by increasing T and decreasing \( \Delta T \). In 1955, a unique acceleration technique was developed, which focuses the initial space and energy distributions at the detector surface in the flight direction. Applying this technique, the mass resolution was increased by decreasing \( \Delta T \) [2]. Furthermore, in the early 1970s, a new technique was developed. In this technique, the focus position defined by the above-mentioned acceleration technique is chosen as the start point, and an ion optical system that is composed of ion mirror [3] or electrostatic sectors [4] is placed at the post stage. This innovation made it possible to increase the time-of-flight T without increasing \( \Delta T \), and led to a dramatic improvement of the mass resolution. Recently, most of commercially available TOFMS instruments use ion mirrors, and their flight paths are 1 to 3 m. For further improvement in the mass resolution of TOFMS, another types of ion optical systems have been proposed. They are the multi-reflecting type [5] and the multi-turn type [6-7] ion optical system where ions flying multiple times on the certain trajectory. These two ion optical systems theoretically achieve an infinitely long flight path in a compact space, and improved the mass resolution. However, they have the limitation of the mass range because ions with large speed (ions with small m/z) lap the ions with small speed (ions with large m/z) when the ions flying on the same trajectory multiple times.

We have developed an original ion optical system that utilizes a spiral ion trajectory. This ion optical system can overcome the "lap" problem present in multi-reflecting and multi-turn type ion optical systems. In addition, it is possible to achieve mass resolution and mass accuracy higher than those of widely used reflectron ion optical systems. In this paper, we describe the design of the spiral trajectory.
Design of the spiral trajectory ion optical system

Multi-turn type ion optical system technique was applied for development of the spiral trajectory ion optical system. Especially, a combination of the “perfect focusing” and “multi-turn” [12] techniques developed at Osaka University, which achieved highest mass resolution in the world, was considered the most suitable for development of the spiral trajectory ion optical system. For conversion of a multi-turn type ion optical system for a spiral trajectory ion optical system, it is necessary to move ion trajectory perpendicular to the orbit plane. In order to achieve this, we have designed the system so that ion injection is slightly tilted to the orbit plane. The advantage of the design is that there is no need for the mechanism to transfer the ions to the next layer. There are concerns about degradation of mass resolution due to the trajectory deviation from a multi-turn type ion optical system. However, the effect should be negligible by keeping the injection angle to several degrees.

Practically, we have designed the spiral trajectory ion optical system based on MULTUM II [7] construction, which consists of four toroidal electrostatic sectors (cylindrical electrodes with two Matsuda plates). The schematic of the ion optical system is shown in Fig. 1. To achieve a spiral trajectory, we have constructed a layered toroidal electric field (TES) by placing (number of cycles +1) Matsuda plates into the cylindrical electrostatic sectors. The Matsuda plates are arranged within certain equal distances $L_1$ in the space $L_x$ between the external and internal electrodes. The three types of voltages applied on TESs 1 to 4 is that of the internal electrode, external electrodes and Matsuda plates. Corresponding voltages are supplied to every Matsuda plates, internal and external electrodes of TES 1 to 4.

Also, four TESs were placed so that they correspond to MULTUM II when looked from the orbit plane. Y direction was set perpendicular to the periodic orbit plane. In development of the MALDI-TOF/TOF, we have made Y direction to horizontal. The TES1 in the Fig. 1 shows the external electrode is removed so that it can be seen the Matsuda plates are equally spaced. Ions fly through the center of the space, formed by $L_x$ and $L_y$. Ion passes the same layer of TESs 1 to 4, and after passing the TES 4, it enters to the next layer of TES 1. The process is repeated for several cycles; the ion thus draws a spiral trajectory and reaches the detector (DET1) (Green line in the Figure 1 represents the ion trajectory). The injection angle $\theta$ into the layered toroidal electric field can be expressed as follows,

$$\tan \theta = (L_y + L_m) / L_c \quad \cdots \cdots \cdots (1)$$

where, $L_m$ is the thickness of a Matsuda plate and $L_c$ is the one cycle length.

As mentioned above, owing to the usage of four TESs of the same structure in its construction, the ion optical system can achieve a complicated trajectory within a simple structure.

Production of MALDI-TOF/TOF utilizing spiral trajectory ion optical system

We have developed MALDI-TOF/TOF utilizing the spiral trajectory ion optical system. It consisted of the first TOFMS using the spiral trajectory ion optical system and the second TOFMS using the reflectron ion optical system. The mass spectrum measurement in the first TOFMS is referred as spiral mode, and the product ion spectrum measurement in the second TOFMS as TOF/TOF mode.

A schematic of the system is shown in Fig. 2 (ion source and the detector DET1 of the first TOFMS are omitted). Spiral trajectory is set to eight cycles of 2.093 m per each. A distance between central trajectories of the adjacent layers is 58 mm, an injection angle is 1.6 degree according to equation (1). Y direction is set as horizontal, so the injection angle is achieved by tilting the extraction direction of the ion source 1.6 degrees from a horizontal plane.

In the spiral mode, ions fly a spiral trajectory and are detected with the spiral mode detector (though not specified in Fig. 2, it is located similarly to DET1 in Fig. 1). Ion gate is placed in the 7th cycle. It allows eliminating high-intensity matrix ions, which are outside of the data acquisition m/z range.

In TOF/TOF mode, selection width of the ion gate is made narrower and monoisotopic ions of precursor ions are selected out of all isotopic ions of them. It is possible to mechanically move the spiral mode detector out of the trajectory so that precursor ions can be introduced into the collision cell. Ions, that entered a collision cell, collide with rare gas inside of the cell with a kinetic energy of approximately 5 eV.

As the injection angle is below 5 degree, the number of the ions surviving the collision is much larger than those for a 90 degree injection in a quadrupole collision cell with no transmission of the collision cell.
20 keV, and generate fragment ions. Precursor ions and fragment ions are mass-separated in a reflectron ion optical system that combines an offset parabolic reflectron (OPR) [13] and a reacceleration mechanism. OPR is a reflectron connecting a linear and parabolic electric fields. It allows simultaneous observation of ions, from low m/z fragment ions up to precursor ions. In addition, in order to increase transmission of ions, fine adjustment of the ion trajectory is enabled by installing two deflectors (DEF1 and DEF2) on both sides of the collision cell.

Evaluation of MALDI-TOF/TOF with spiral trajectory ion optical system utilized

Figure 3 shows mass spectrum of six types of peptide mixtures (in order of m/z increase: Bradykinin fragment 1-7, Angiotensin II, Angiotensin I, P14R, ACTH fragment 1-17, ACTH fragment 18-39). The mass spectrum of Angiotensin II and ACTH fragment 1-17 are also displayed as an enlarged image. Mass resolution is 58000 (FWHM) and 73000 (FWHM) respectively. The mass error of ACTH fragment 1-17 is 0.16 ppm, when internal calibration is performed among five peptides except ACTH fragment 1-17. It became clear from the above mentioned facts that distance of flight for spiral trajectory ion optical system is 17 m, which is 5 times longer than that of the conventional reflectron type ion optical systems. This allows enhancement of mass resolution and mass accuracy.

Figure 4 shows the relation between m/z value and mass resolution when mass resolution is adjusted with ACTH fragment 1-17. Figure 4 shows that it is possible to achieve high mass resolution simultaneously in a wide m/z range. This overcomes the problem of MALDI-TOF MS utilizing conventional reflectron type ion optical system that could achieve high mass resolution only in a narrow m/z range.

Figure 5a shows a product ion spectrum diagram of Poly (oxypropylene), acquired in TOF/TOF mode. Selected precursor ions are monoisotopic ions from [M+Na]+ series with m/z 1027. A numbers of fragmentation channels from sodium ions as fragment ion to precursor ion are observed. The enlarged spectrum around m/z 780 is shown in Fig. 5b. The system is able to select only monoisotopic ions of precursor ions, therefore each fragment channels can be observed as one peak without any isotopic peaks. Two peaks in Fig. 5b indicate different fragmentation channels. It indicates that 2u different fragmentation channels can be clearly separated. Figure 5c displays an image of the same m/z range as in Fig. 5b when measured with conventional MALDI-TOF/TOF. Precursor ion selectivity of traditional TOF/TOF is insufficient so that the fragment ions from all isotopic ions of precursor ions are analyzed in the second TOFMS. Thus every fragmentation channels of product ion spectrum include isotopic peaks. As a result, when m/z values of monoisotopic ions of two fragment channels are close, such as 2 u, their isotopic peaks are overlapped and are impossible to be clearly identified. The high precursor ion selectivity originated from the spiral trajectory ion optical system used in this system makes the structural analysis of chemical compounds much easier.

Conclusion

This paper reports on the development of the spiral trajectory ion optical system. Also, the paper describes the development of MALDI-TOF/TOF, which combines a spiral trajectory ion optical system and reflectron type ion optical system utilizing offset parabolic ion mirrors. Innovative ion optical system introduced to the JMS-S3000 has overcome preexisting problems related to conventional MALDI-TOF and MALDI-TOF/TOF. Thus, the JMS-S3000 is expected to play a significant role in various areas.

References

Fig. 4 Relation between m/z value and mass resolution.

Fig. 5 Product ion spectrum of Poly(oxypropylene).