International Journal of Mass Spectrometry 206 (2001) 251–266

Time-of-flight mass spectrometry (concepts, achievements, and prospects)

B.A. Mamyrin

A.F. Ioffe Physico-Technical Institute, Russian Academy of Sciences, Polytechnicheskaya 26, 194021, St. Petersburg, Russia

Received 3 July 2000; accepted 4 October 2000

Abstract

A brief account is given of the history of dynamic mass spectrometers from the time of their advent. The reasons for their relatively slow development in the 1930s–1940s of the last century are discussed. The general principle underlying the operation of all dynamic mass spectrometers, the difference between the velocities of motion of ions differing in mass but having the same energy, is pointed out. In accordance with its title, the review considers in more detail the history of development of time-of-flight (TOF) mass spectrometers and stresses their two major advantages over the static (magnetic) instruments, namely, the unlimited mass range and the possibility of obtaining extremely rapidly mass spectra over a broad ion mass range. This accounts for the fast progress in their performance and broad application in the period of 1960s–1980s, when investigation of heavy, thermally unstable organic molecules was started and efficient methods of producing their ions were developed. A serious limitation on the resolution of TOF instruments was largely removed after the formulation of the reflectron principle of TOF mass-spectrometer design. The problem of a further increase of the resolution of TOF systems is discussed. The illustrations of TOF reflectron applications are presented, and a possibility of analyzing molecules and clusters with masses of up to millions of daltons is pointed out. These merits have resulted in a sharp increase of production and a broadening of application potential of TOF mass spectrometers compared to the magnetic setups, particularly in the field of biophysics, biochemistry, and organic chemistry. In conclusion the broad horizons opened by the TOF magnetic-resonance mass spectrometers (MRMS) in the area of high-precision mass spectrometric measurements are pointed out. (Int J Mass Spectrom 206 (2001) 251–266) © 2001 Elsevier Science B.V.

Keywords: TOF mass spectrometry; Reflectron; Resolution; Sensitivity; Magnetic resonance mass spectrometer; Application in research

1. Introduction

The history of mass spectrometry started with the work of J.J. Thomson published as far back as 1913 [1], which put forward the principal idea underlying mass spectrometric analysis of the composition of a substance, namely, transformation of all components of the sample to ions, their acceleration by an electric field, and separation of ions with different mass to charge ratios by means of a magnetic field. E.W. Aston built a prototype of modern static magnetic mass spectrometers in 1919 [2]. Thomson and Aston were the first to make by mass spectrometry a great discovery by revealing the existence of isotopes of stable elements.

Subsequent progress in the development of static

---

* Corresponding author. E-mail: mamyrin.mass@pop.ioffe.rssi.ru

PII S1387-3806(01)00392-4

instruments due to A.J. Dempster [3], A.O. Nier [4], J. Mattauch and H. Herzog [5], K.T. Bainbridge and E.B. Jordan [6], G.P. Barnard [7], V.M. Kelman, I.V. Rodnikova, and L.M. Sekunova [8]; the enormous number of publications dealing only with the improvement of analyzers, ion sources, ion detection techniques; reviews and monographs on the application of mass spectrometry—all this has raised the mass spectrometer to the level where it may be considered one of the most universal instruments for compositional analysis of substances, and the mass spectrometry, one of the most important tools of research in nuclear and atomic physics, chemistry, and biology.

The wealth of scientific achievements amassed in the nearly 90 years of continuous improvements and application of static mass spectrometers, as well as their mass production organized by many instrument-making companies in all technologically advanced countries, became eventually an obstacle to development of dynamic mass spectrometers.

Progress in the field of dynamic mass spectrometers during the first decades after their advent was impeded also by the fact that their principal analytical parameters, such as the resolution and the sensitivity, were inferior to those of the static instruments. This was partially due to the poor level of rf and pulsed technology at the time.

It should be pointed out that many potential merits of magnet-free dynamic instruments, such as, for instance, the unlimited ion mass range they were capable of analyzing, could not be appropriately recognized, because even the methods of obtaining ions of complex thermally unstable molecules were unknown in the 1950s–1960s.

The separation of ions with different mass/charge ratios (m/q) at an equal energy (qU) in static mass spectrometers is based on the difference of the radii of their trajectories in a uniform dc magnetic field. No combination of static electric fields is capable of separating a flux of such ions in mass. This can be done only by applying periodically changing (in particular, sine wave) or pulsed fields.

The basic idea consists here in that monoenergetic ions with different m/q ratios have different velocities, and, hence, they take different times to traverse a given path in the instrument. By applying a periodically varying or a pulsed electric field in certain parts of the path, one can impart different energies to ions with different velocities, thus making possible their separation. If the electric field varies periodically, ions with a given m/q (i.e. a given time taken by them to pass a certain path) will acquire the largest (or the smallest) increment of energy (provided the field frequency was chosen accordingly). By properly varying the frequency, one can measure consecutively the whole mass spectrum. By applying a pulse one can create a short ion packet, and ions with different velocities will separate in their subsequent propagation in individual packets, so that their consecutive arrival to the detector can be recorded in the form of a mass spectrum.

Dynamic (similar to static) instruments make use of various methods of focusing angularly divergent ions. In contrast to the static devices, however, in dynamic instruments one can employ many methods of producing output signals (a narrow slit with a collector or microchannel plate, energy analyzer, method of induced ac potential, Fourier analyzer, absorption of driving ac field energy).

The rich diversity of possible ways to combine ion separation, focusing, and detection in dynamic mass spectrometers accounts for the large number of instrument designs proposed. The monograph by E.W. Blauth, for instance, considered more than 50 such arrangements [9]. Although most of them did not find application because of the limited range of their analytical and operating characteristics, some ideas turned out to be feasible and enjoy an ever increasing use.

In accordance with the main idea underlying ion separation in dynamic instruments, namely, using differences in the time taken to pass a certain path in the instrument, they all can be called “time-of-flight,” however this term has stuck in the literature only to the mass spectrometers, in which short ion packets are produced by a pulsed source and the ions with different mass/charge ratios are separated due to their different flight times to the detector in the field-free drift space and in the correcting parts of the static fields.

It is such instruments that we are going to discuss in the following.

2. Simple time-of-flight mass spectrometer

The first TOF instrument with a mass-spectrum display was built by A.E. Cameron and D.F. Eggers in 1948 [10]. It contained all components of a simple time-of-flight instrument, namely, a pulsed ion source, a field-free drift space, and an oscillograph as detecting device. However the resolution of the instrument was extremely low (the Hg^+, Hg^{++}, and Hg^{+++} ions were barely detectable). Therefore this work played to a certain extent a negative role in development of the concept of TOF instruments, which happens quite frequently in technology with radically novel ideas.

The first publication on a TOF mass spectrometer with a resolution of practical significance (above 50) appeared in 1953 [11]. It was followed by a number of studies reporting TOF mass spectrometer resolutions above 100, where all xenon isotopes were well resolved [12–15]. The approaches aimed at improving the resolution of TOF instruments were suggested in Wiley and McLaren publication. (1) A possibility of focusing packets of ions with a given *m/q* ratio near the detector although they may have been created at different points in the source ionization chamber (and, hence, may have different energies and velocities), which was demonstrated experimentally in [15]. (2) The effective depth of the electron multipliers was shown [12] to influence strongly the resolution of all TOF instruments, because it increases the effective thickness of the packet. The use of an electron multiplier with a planar input and a magnetic field [16] permitted one to increase the resolution to 300. (3) It was shown also that even small initial thermal energies ($\leq$0.1 eV) of ions, that were generated in the same source plane but had oppositely directed velocities along the instrument axis, can degrade dramatically the resolution, and this factor should be taken into account when calculating such systems. The method recommended in [12] to combat this phenomenon can hardly be accepted as correct, because it is valid only for a narrow ion-mass interval.

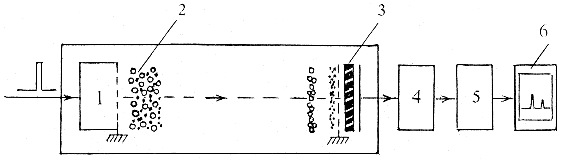

Fig. 1. Linear time-of-flight mass spectrometer. 1—pulsed ion source; 2—ion packet near the source; 3—secondary electron multiplier; 4—wide band amplifier of the output signal; 5—computer; and 6—display.

TOF instruments of a fairly simple construction were manufactured by Bendix in USA. One of the first industrial instruments developed at our laboratory (A.F. Ioffe Physico-Technical Institute, Russian Academy of Sciences, Russia) was a pulsed mass spectroscope (with spectra displayed on the oscillographic screen) was demonstrated at the World Exhibition in Brussels in the Atomium pavilion (1958). After the first launchings of satellites, the Scientific Instruments Company in USSR manufactured a series of TOF mass spectrometers for investigation of the upper layers of the atmosphere by rockets and satellites (MX6407P).

Fig. 1 presents the scheme of a TOF instrument with a pulsed ion source, with the functions of its components given in the caption.

The width of the ion packet near the detector, which determines the instrument resolution, depends on the following aberration factors: Δl_1—inaccuracy of focusing in the double-gap source because of the finite thickness of the ion formation zone or other reasons resulting in an ion energy spread in sources of any kind; Δl_2—broadening due to the angular spread in ion trajectories; Δl_3—deviation of the source and detector planes from perpendicularity to the instrument axis; Δl_4—effective depth of the microchannel plate; Δl_5—effect of the initial velocities of ions that formed in the same source plane but have oppositely directed velocity components parallel to the instrument axis (the “turn-around” effect); Δl_6—the slopes of the leading edge and top of the withdrawal source pulse; Δl_7—broadening of the detector output-current pulses induced by electron avalanches in the microchannel plate (MCP) and in the course of amplification by a broad-band amplifier; Δl_8—effect of stray fields in the field electrode grids; Δl_9—laser pulse length; Δl_{10}—influence of the space charge created by ions of the same species.

These factors have to be taken into account in the calculation of any TOF mass spectrometer system. As follows from calculations carried out for a simple TOF instrument, at the present-day level of electronics the resolution depends primarily on Δl_1 and Δl_5, which are determined by the ion energy spread and the initial, oppositely directed ion velocities.

The effect of Δl_1 can be estimated in the following way. The ion flight time can be written

$$T = \frac{L}{v} = L\sqrt{\frac{m}{2qU}} \tag{1}$$

where L is the length of the drift space, and v is the ion velocity. The resolution determined only by the energy spread ΔU

$$R_{\Delta U} = \frac{m}{\Delta m} = \frac{U}{\Delta U} \tag{2}$$

is independent of the drift length L. For instance, for $U = 2000$ V and $\Delta U = 5$ V, $R_{\Delta U} = 400 = L/2\Delta l_1$, which for $L = 1000$ mm corresponds to $\Delta l_1 = 1.25$ mm.

The effect of Δl_5 for a double-gap source can be estimated from a readily derivable expression

$$\Delta l_5 = \frac{4}{E_1}\sqrt{\Delta U_0 U_2} \tag{3}$$

where ΔU_0 is the potential difference corresponding to oppositely directed initial ion velocities, E_1 is the electric field in the first source gap, and U_2 is the second-gap potential difference accelerating the ions. For $E_1 = 400$ V/cm, $U_2 = 1000$ V, and $\Delta U_0 = 0.1$ V, the packet broadening $\Delta l_5 = 1$ mm.

Eqs. (2) and (3) permit an important conclusion that the resolution of a simple TOF instrument is governed primarily by the energy spread (and is independent of L at $L \geq 1$ m) and the initial ion velocities, because the effect of all the other above-mentioned factors degrading the resolution can be made substantially smaller in the present state of technology.

Increasing the accelerating voltage U for a given energy spread reduces naturally the effect of the latter, thus permitting one to increase strongly the resolution when analyzing heavy ions. One has succeeded in reaching in a TOF instrument a resolution of 4600 for ion masses (3–6) 10^3 a.u. [17].

This has required, however, a considerable complication of the ion source design. The ion packets were produced by a laser operating with ~5 ns long pulses, and the ions were accelerated in three gaps to 44 keV. Also, the last section generated an additional pulse to accelerate the ions having a lower energy. This places a limit on obtaining the whole mass spectrum at a given instrument setting. It was, however, rightfully pointed out [18] that “it is impossible to develop a universal mass spectrometer appropriate for any study.” As indeed one certainly could not design a car equally superior as a lorry and a racer.

3. TOF instruments with compensation of ion energy spread on the resolution (TOF reflectrons)

To increase the resolution of TOF mass spectrometers, many scientists in the 1950s–60s tried to design ion sources with a smaller energy spread, however no substantial progress has been reached in this field. My analysis of the problem has led to the conclusion that one should devote efforts not to combating the energy spread (particularly after the advent of laser ionization techniques) but rather to neutralization of their effect outside the source. Recollection of children’s games (whose ball thrown upward would fly the longest) led me to an investigation of the effect of reflecting (decelerating) electric fields on the increase of the flight time of ions leaving the source with a higher energy. As followed from calculations, if the ions of a packet enter immediately a decelerating field whose potential grows as $U = ax^2$, where a is a constant, and x is the coordinate reckoned from the beginning

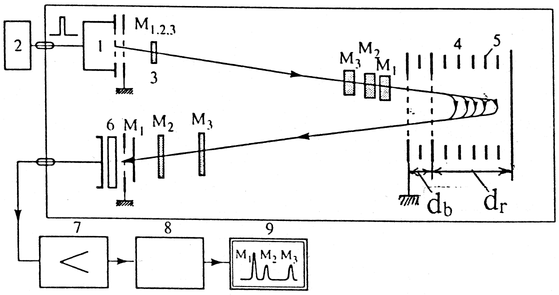

Fig. 2. TOF mass spectrometer with a two-section reflector with plane electric fields. 1—pulsed ion source; 2—power supply (laser); 3—focused ion packet near the ion source; 4—double sectional reflector; 5—electrodes for creation of plane electric fields; 6—detector; 7—wide band amplifier; 8—computer; 9—display; d_b—the ion deceleration section; and d_r—the ion reflection section.

of the decelerating field, the time required to stop an ion with energy qU in this field will be

$$t = \int_0^{x_{\max}} \frac{dx}{\sqrt{\frac{2q(U - ax^2)}{m}}} = \frac{\pi}{2\sqrt{\frac{2qa}{m}}},$$

where $x_{\max} = \sqrt{U/a}$ is the coordinate of the ion stop.

Hence the ion flight time in such a decelerating field, reckoned from the instant the ion enters it to that of its leaving (equal to $2t$) does not depend on the initial ion velocity at all. In this case if a thin packet confining ions of a given mass but having different energies impinges on the detector immediately on exiting this field, the instrument resolution should be determined only by other aberration factors.

Unfortunately, it appears next to impossible to generate such a plane field with a quadratically increasing potential, however in principle one could try to approximate this situation. This was shown in my thesis of 1966 and mentioned also in [19]. (In 1984 Y. Yoshida was issued a US Patent No. 4625112 for such an instrument.)

Further calculations [19–21] showed that even a uniform double-gap decelerating field (combined with the flight in the field-free drift space) provides second-order focusing in ion energy spread and the angle of ion emission from the source (triple second-order focusing) [19,21,23] (Fig. 2). Note that in the case of an ideally thin packet and ideal grids bounding the two decelerating-field gaps the resolution may reach hundreds of thousands at an ion energy spread in the packet of a few percent. It should be stressed that unlike the conventional TOF mass spectrometer without reflector the resolution of an instrument with reflector increases proportionally to the drift length (provided the other aberration factors listed in Sec. 2 are fixed). Using the notation of the caption to Fig. 2, the ion TOF can be written as

$$t = A_0\left[\frac{A_1}{\sqrt{k}} + A_2(\sqrt{k} - \sqrt{k - p})\right] = A_0 F \tag{4}$$

where $k = U/U_0$; qU_0 is the mean ion energy and qU the ion energy corresponding to the ion velocity components parallel to the instrument axis; $k_0 = 1$, $p = U_b/U_0$;

$$A_0 = \frac{4d_r}{\sqrt{\frac{2qU}{m}}}\frac{U_0}{U_r};$$

$$A_1 = \frac{L_1 + L_2}{4d_r U_0};$$

$$A_2 = \frac{d_b}{d_r}\frac{U_r}{U_b}.$$

U_b is the potential difference in the decelerating gap d_b; U_r is the potential difference in the reflecting gap d_r.

As seen from Eq. (4), variation of the ion energy qU (i.e. of k) affects only F, whereas A_0 in independent of the ion energy (i.e. k) variation. By analyzing the expression for $dF/dk = 0$ and $d^2F/dk^2 = 0$ one can find the optimum expressions relating the geometric dimensions and the potential differences in the instrument which provide maximum TOF focusing under variation of the ion energy (i.e. the maximum resolution).

In 1971 we measured experimentally the curves relating the ion TOF variation ($\Delta t/t$) to the variation of ion energy $\Delta U/U_0$) [22]. As evident from Fig. 3, the ion TOF through an optimally adjusted system and for $\Delta U/U_0 = \pm 12\%$ practically did not vary (within the accuracy of measurement). The pattern changed dramatically when the potential difference U_b in the decelerating (first) gap of the reflector was changed by a few percent (Fig. 3). The same figure shows by a dashed line the variation of the ion flight time in a TOF instrument without reflector for equal lengths of the drift space.

[23] quotes the characteristics of the first TOF reflectron and presents a mass spectrum of rhenium bromide obtained with a resolution $R_{50\%} \approx 5000$.

In 1980 the Scientific Instruments Company (Russian Academy of Sciences) manufactured MX 5302 TOF reflectrons designed for analysis of organic molecules with $R \approx 5600$. A special lock permitted sample replacement without impairing vacuum. The total length of the analyzer with ion source was ~1.3 m. Fig. 4 presents a spectrum of a mixture of two organometallic compounds [24] and Fig. 5 displays the general view of the instrument.

The 1970s [23,24] were highlighted by a fast spread of reflectron TOF instruments, particularly

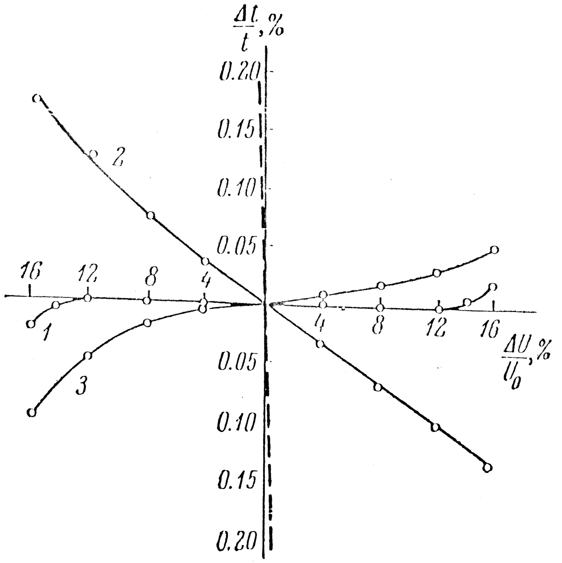

Fig. 3. Experimental curves of the relative time-of-flight change of ions $\Delta t/t$ as a function of ions energy change $\Delta U/U_0$. 1—optimal adjustment of the instrument $U_b = (U_b)_0$; 2—$\Delta U_b/(U_b)_0 = +6\%$; 3—$\Delta U_b/(U_b)_0 = -4\%$; and 4—$\Delta t/t_0$—for linear instrument of the same ion drift length but without reflector.

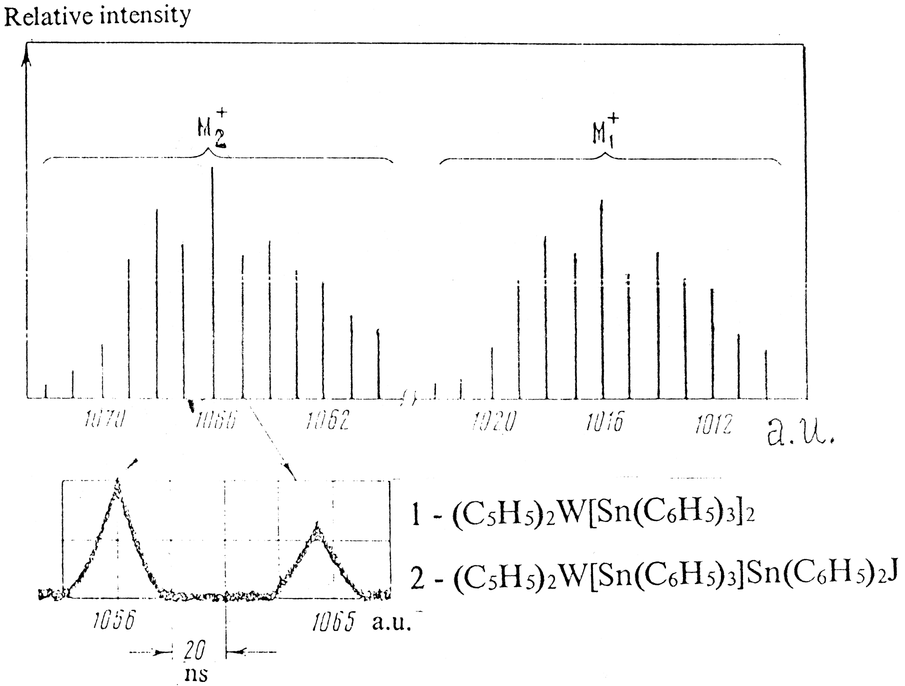

Fig. 4. Mass spectrum of mixture of two metalloorganic compounds. 1—$(C_5H_5)_2W[Sn(C_6H_5)_3]_2$; $m_1 = 1016$ a.u. and 2—$(C_5H_5)_2W[Sn(C_6H_5)_3]Sn(C_6H_5)_2J$; $m_2 = 1066$ a.u. $R_{50\%} \approx 5600$.

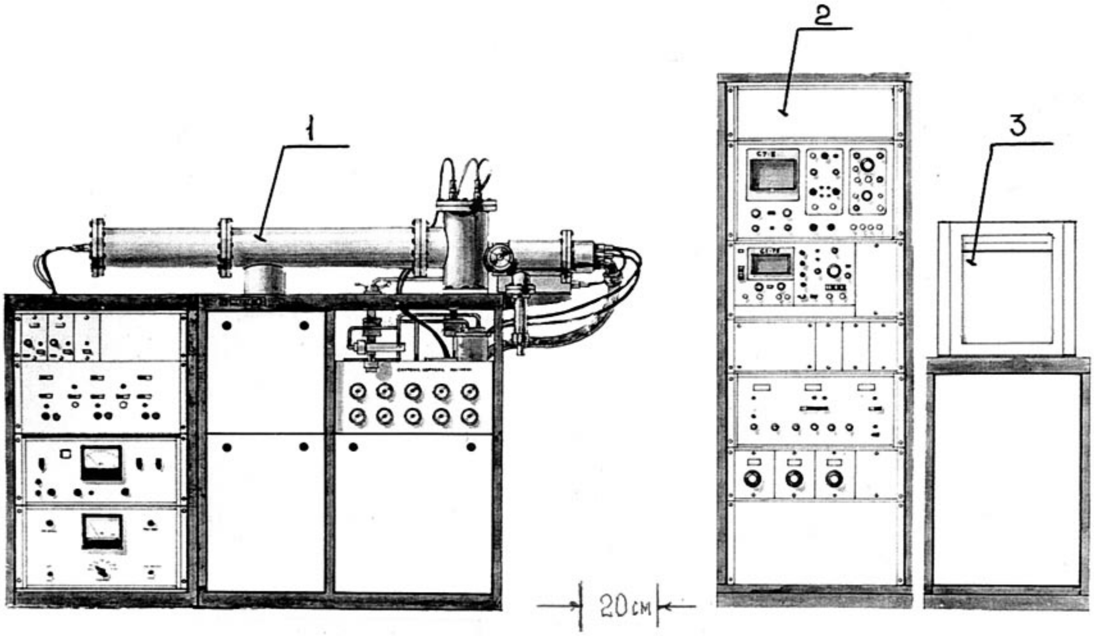

Fig. 5. General view of the first world TOF reflectron. 1—analyzer with ion source; 2—electronics post; and 3—display.

after the introduction of laser-based techniques of obtaining large, thermally unstable biomolecules. Their production on an industrial scale started in 1980 with Leybold-Heraeus Co. (LAMMA-500, LAMMA-1000), Bruker Co. (TOF-1), Finnigan Mat Co. (VISION 2000) and so on.

A substantial progress in achieving of a high resolution and broadening the possibilities of detection of large-mass ions was reached in the works of T. Bergman, T.P. Martin, and H. Schaber [25–28]. These studies demonstrated clearly the role of the micro-optics of the grids bounding the reflector gaps. A resolution of 35×10^3 combined with a high sensitivity was attained in an instrument ~3 m long [25]. This high sensitivity was achieved by focusing the ion beam by a quadrupole doublet. It was shown that increasing the ion energy before the MCP detector to 16 keV permits efficient enough detection of cluster ions with masses of up to 2×10^6 a.u. [29].

[28] presents the characteristics of a gridless reflector, however one has in this case to limit the ion beam in diameter. Nevertheless BRUKER manufactured TOF-1 equipped with such a reflector for $R =$ 10 000 [30–32]. An obvious merit of such reflectors is not only the absence of grids but also the possibility of simultaneously focusing the reflected ions in angle, which increases the absolute sensitivity of the instrument.

V.M. Doroshenko and R.J. Cotter [33] proposed a method of calculation of reflectron TOF systems taking into account the ion source parameters. It was shown that by introducing a slight nonlinearity in the last plane-field reflector gap one can improve the resolution of the system as a whole. This facilitates substantially the possibility of experimental realization of such a field. Unfortunately, the article does not illustrate the calculation of the parameters of such a high-resolution system (with all aberration factors taken into account). C.A. Flory et al. [34] proposed such an introduction of a small nonlinearity in the plane reflector field to improve the resolution. However in this case the ideal ion TOF focusing also requires correction with inclusion of all aberration factors.

The extent to which practical results may deviate from calculations can be judged from the paper of M.

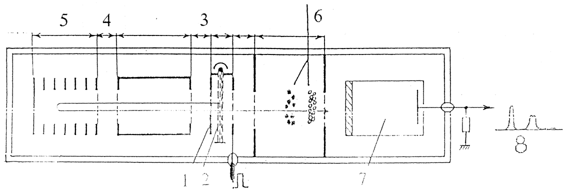

Fig. 6. Linear TOF reflectron. 1—transparent ion source with grid electrodes; 2—pulsed electron beam; 3—acceleration gap; 4—deceleration gap; 5—reflector; 6—focused ion packet; and 7—detector.

Yang and J.P. Reilly [35], who quoted an experimental figure $R = 1.1 \times 10^4$ against the calculated resolution $R > 10^6$. At the same time this article and the review [36] present a comprehensive analysis of the magnitude of the aberration factors involved.

Besides the TOF reflectron scheme depicted in Fig. 2, there are presently a variety of modifications in which the basic idea underlying the TOF reflectron has been realized to date. Fig. 6 presents the scheme of a “linear” TOF reflectron [37], which is convenient for some applications.

The ions exiting the chamber of a pulsed source bounded by transparent grids move toward the reflector on the instrument axis and, after reflection, are propagated downstream to the detector through the source (at this instant the withdrawal pulse has already come to an end) to fall onto the detector. This version is convenient for small-size technological sensors. For instance, linear TOF reflectrons ~16 cm long with a diameter of 5 cm vacuum chamber providing a resolution of about 300 were developed for analysis of technical gases. With a chamber 90 cm long, such an instrument had a resolution $R_{50\%} = 1200$.

Our laboratory developed a TOF reflectron to study laser-assisted isotope separation [38]. The source of this instrument included a supersonic pulsed jet which fed molecules containing the two isotopes to be separated into the chamber (Fig. 7). Pulses delivered by a high-power laser were directed perpendicular to the instrument axis. The laser light frequency was chosen so as to ensure breakdown of the molecules containing only one of the isotopes. The molecules were ionized by an electron beam. Only ions of the isotope of interest were admitted to the detector, and this was done by applying a synchronized pulse to the retarding grid electrodes in front of the detector. The electronics provided synchronous operation of the electromagnetic valve of the supersonic jet, laser, electron beams, and detector valve. The instrument resolution was ≥1000.

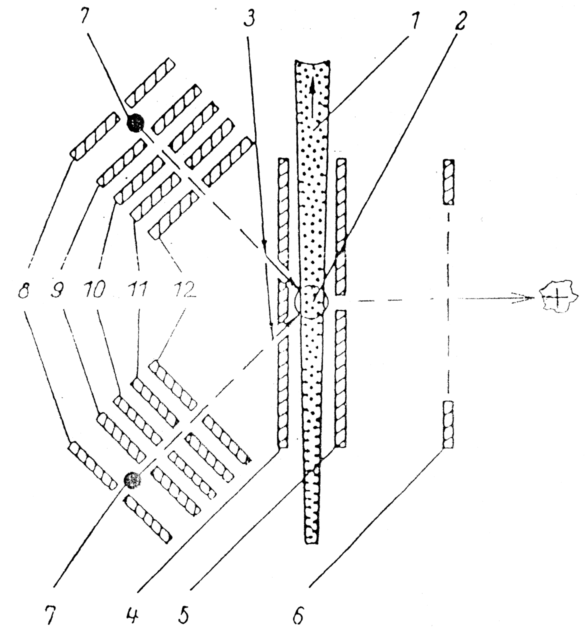

Fig. 7. Ion source of TOF reflectron for investigation of isotopes obtained by laser. 1—pulsed supersonic jet; 2—pulsed laser beam; 3—electron beams for ionization of neutrals; 4, 5—ionization chamber walls; 6—grid electrode of ion source (grounded); 7—cathodes emitting electrons; and 8–12—focusing electrodes.

A miniature laser TOF reflectron with a close-to-quadratic reflecting-field distribution was designed [39]. A 52-mm long cylindrical resistor electrode with a diameter of 38 mm housed an endcap adjusting the reflector length. The sample illuminated by laser pulses passing along the instrument axis was placed in the beginning of the cylinder (at its center). The reflected ions were intercepted by a detector located in the sample plane. The instrument is designed for rapid monitoring of low-mass organic volatiles.

TOF reflectrons with laser-pulse power densities $\geq 10^9$ W/cm^2 can be used for elemental and isotope analysis of practically any substance (metals, ceramics, semiconductors, and solid organic compounds) (LAMMA-1000, Leybold-Heraeus Co.).

In conclusion to this section on TOF reflectrons consider the merits of these systems. (1) Unlimited mass range (up to millions of daltons) [29]; (2) possibility of using all kinds of pulsed ion production [electron impact, laser evaporation and ionization, sources with ^{252}Cf, desorption by a strong electric field, electrospray ionization (ESI), MALDI, etc.]; (3) high resolution even for large ion-energy spreads (tens of thousands [25], with 10^5 realized in practice); (4) high sensitivity (down to single atoms when using laser resonant excitation in an electric field [40–42]; (5) fast measurement of the full mass spectrum (ion composition in the source can be determined in down to a few nanoseconds); (6) possibility of separating ions of isomers (molecules with the same ion composition) through resonant excitation of neutrals evaporated by a tunable laser [43–45]; (7) a good mass-line shape with limited tails; (8) automatically obtainable mass spectrum scan without application of additional scanning devices; (9) possibility of noise suppression in ion detection for a known spectrum by using the time gate technique (by opening the signal store in the detector channel only for the time of arrival of the ions of interest [61]; (10) absence of expensive mechanical units (compared to magnetic mass spectrometers) and no requirement on a high precision of component manufacture and adjustment (compared to quadrupole instruments and traps) for the same resolution.

4. Progress in TOF spectrometry

Although TOF mass spectrometers without reflectors had a resolution only of a few hundreds, they found broad application in research already starting with the late 1950s, because they made possible obtaining without any inertia the full mass spectrum of the ions produced in the ionization chamber of the source. This permitted one to use them to advantage in studies of the sorption and desorption processes on various surfaces (the flash-filament technique) [46,47]. The oxidation of high-melting metals was investigated successfully [48,49]. These instruments were employed to investigate the destruction of polymers subjected to mechanical and thermal loading [50,51]. Measurements of the absolute cross sections of two-photon excitation of atoms made use of a pulsed laser, also in combination with a TOF mass spectrometer [52].

The first studies of Macfarlain into the formation of ions of nondestructed organic molecules by means of ^{252}Cf fragments were made with a linear TOF mass spectrometer, where the sensitivity was enhanced by drawing the ions to the instrument axis by an electric field perpendicular to the latter [53].

Linear TOF instruments manufactured by Bendix were employed for rapid gas analysis in many technological processes (electrical remelting of metals etc.).

As already mentioned in Sec. 2, one could attain resolutions above 4000 with a linear TOF analyzer by applying a high accelerating voltage [17]. This was found convenient when studying the processes occurring in the ion drift space.

Development of TOF reflectrons broadened substantially the application of mass spectrometry in science and technology, because the resolution of such instruments increased sharply, and also because for a resolution of the order of 10^3 these devices became noticeably smaller and less expensive whereas offering a high reliability.

TOF reflectrons began to be employed in space research. A TOF reflectron with a source providing silver foil transport was designed to measure the composition of Halley cometary-tail particles. The particles of the cometary tail hit with a very high velocity (up to 80 km/s) the foil and entered in the form of atomic ions the analyzer [54]. The instrument operated successfully on the VEGA spacecraft. The description of the results of this space experiment can be found in [55].

Our laboratory developed a miniature TOF reflectron (a linear version) to study the upper atmospheric layers on rockets and satellites. The system of the source and of a special corrector (with an open window and a hitting flow velocity of 2 to 20 km/s)

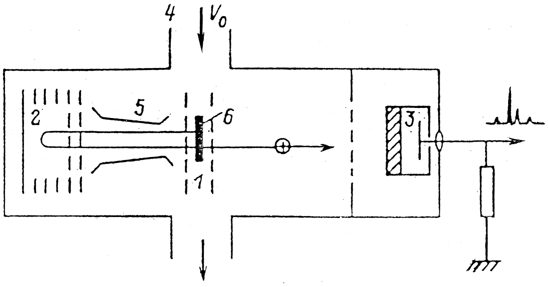

Fig. 8. TOF reflectron for investigation the upper atmosphere with the aid of rocket and satellite. 1—ion source; the ionization space is surrounded by grids; 2—two-section reflector with the ion retardation section; 3—ion detector (MCP); 4—flux of molecules entering from the atmosphere; 5—correction plates; and 6—electron beam.

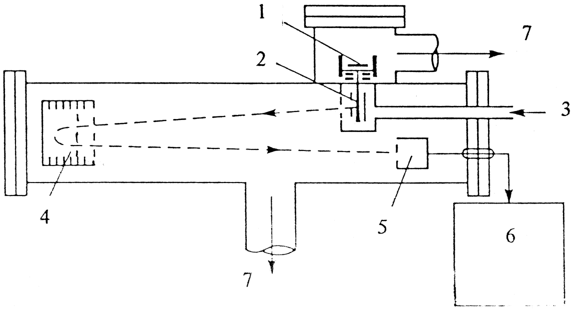

Fig. 9. TOF reflectron for gas analysis with a separate chamber for the hot cathode. 1—cathode; 2—electron beam; 3—gas; 4—reflector; 5—electron multiplier; 6—wide band amplifier; and 7—to vacuum pump.

excluded distortion of the information obtained [56] (Fig. 8).

A TOF reflectron to study the surface of Phobos (the Martian satellite) was developed at the Space Research Institute (Moscow). In passing at a distance of 30–80 m above the surface, the spacecraft was intended to emit laser pulses with a power density high enough to initiate emission of ions from the surface. A reflectron analyzer with a $\sim$30 cm^2 window mounted on the spacecraft had to receive ion packets propagating in the vacuum of space. The scheme of the instrument can be found in [20]. Laboratory experiments confirmed the possibility of obtaining a resolution $M/\Delta M \approx 200$. Unfortunately, the two space experiments did not produce any results because of the failure of the communication system.

Application [57] of a TOF reflectron in the atomic probe of Müller-Zong [58] permitted one to measure the masses of atoms emitted from a desired point in the atomic image of a unit cell of metal-alloy crystallites with a high resolution. The resolution is $\sim$500 for a 40% ion-energy spread.

TOF reflectron instruments are employed in monitoring fast processes both in research (combustion, explosions, reactions occurring in pure inert gases, etc.) and in industry (converter production of metals, vacuum refining of steel alloys, chemical industry).

Our laboratory used the TOF reflectron scheme to develop FTIAN-3 gas analysis systems put subsequently in mass production. These systems permit the converter operator to monitor with a time delay of only a few seconds the process of steel smelting, to stop the process at the preset melt temperature and carbon content, and to prevent explosion hazards. FTIAN-3 systems operate at iron and steel works in Russia, Ukraine, Kazachstan, China and other countries. A FTIAN-5 system has recently been developed [59,61], which permits determination of impurities in industrial gases with a sensitivity of up to 10^{-10} in 1 s, which is very important for new methods of melt temperature determination [60,61]. The systems are capable of autonomous operation for a long time in the conditions prevailing in metallurgical industry. The high accuracy of analysis was achieved by using a special detection system. To exclude the processes occurring at a hot cathode, the ion source cathode is located in a separate evacuated chamber (Fig. 9). This permitted one to drop calibration even after periodic checks of the impurity content in oxygen, extended the service life to more than a year of continuous operation, and made possible an increase of the mass spectrometer sensitivity.

TOF reflectrons are used in studies of many-atomic clusters, of the properties and methods of production of fullerenes. Our laboratory has completed a series of studies with TOF reflectrons with laser evaporation of fullerenes and their thermal evaporation from a crucible. The mass spectrum of pure, laser-evaporated graphite revealed the C_{60} and C_{70} fullerenes and weaker-intensity clusters with C_n increasing continuously in steps of two carbon atoms [62]. Laser evaporation of porous graphite can produce cluster ions consisting of many thousands of carbon atoms. When working with laser sources one has to bear in mind possible association and destruction of the sample components, particularly if the composition of the sample is not known [63].

TOF reflectron with a resolution of 5000 was used to study fullerenes under thermal evaporation and electron-impact ionization [64]. A series of $^{12}C_n{}^{13}C_m$ isotope peaks was obtained for $n + m = 60, 70$, and 84. A good agreement was demonstrated with calculated peak intensities corresponding to the natural $^{12}C/^{13}C$ abundance.

The ion charge was found to depend strongly on the energy of the ionizing electrons within the 10–100 eV range. A high yield of fullerenes enriched strongly in the ^{13}C isotope (up to 17%) was reached in arc discharge in an atmosphere containing $^{13}C_2$ [65], which is important for NMR medico-biological research.

Metal-containing fullerites were investigated [66]. It was shown that Gd atoms are captured by C_{82} fullerenes to form Gd at C_{82} complexes, whereas fullerenes made up of a smaller or larger number of carbon atoms do not capture Gd at all.

A study was made [67] of the formation of carbon “cluster out of clusters” $(C_{60})_n^+$, $(C'60)_n^{++}$, and $(C_{70})_n^+$ with masses of up to 2×10^5 a.u., in which n, the number of fullerenes contained in such a many-fullerene molecule, reached as high as 150! One observed “magic” n numbers, at which the mass spectrum exhibited the largest peaks. The problem of detecting such heavy ions was solved by introducing postacceleration and increasing the ion charge state.

Na and Cs clusters with masses of up to 2×10^6 a.u. have been investigated [29]. The possibility of detecting such ions by post acceleration at up to 16 kV was demonstrated.

TOF reflectrons tailored for solution of specific physical, chemical, and biological problems are designed in laboratories of many countries. Instruments for rapid monitoring of stable hydrocarbons [39] and investigation of laser-assisted isotope separation [38] have been mentioned in Sec. 3.

However the most vigorous growth was observed in TOF mass spectrometry in the 1980s–1990s, the years of explosive progress in biophysical and biochemical research associated with development of experimental genetics, modern pharmacology, and synthesis of complex bioorganic compounds of many-atomic clusters. This naturally required a considerable broadening of the mass range covered by analytical equipment up to thousands and millions of daltons [68–70] (interest in biomolecular ions with masses of up to 110×10^6 daltons has recently been announced [71]).

The decisive role of analytical equipment in this research is stressed by the fact that a group of scientists in Russia headed by the academicians D.V. Shemyakin and Yu.A. Ovchinnikov (N.S. Shwitsov, N.S. Wulfson, B.W. Rosinov, and others) were the first to propose the mass spectrometric method of deciphering the aminoacid sequences in peptides (Nature, 1966 [72]) but could not develop these ideas to the experimental stage because no equipment with the required analytical parameters was available at the time.

TOF reflectrons provided a possibility of analyzing molecules with a practically unlimited mass range with a fairly high resolution and a high sensitivity. Methods of evaporation and ionization of thermally unstable biomolecules were soon developed due to the brilliant works of F. Hillenkamp and M. Karas [73], A. Brown and J. Lennon (MALDI) [74], I. Macfarlain and B. Sundqvist (^{252}Cf fragments) [75,76], R.J. Cotter with co-workers [77], E.W. Schlag with co-workers, K.G. Standing with co-workers; one should also mention here the proposal of the ESI and other ionization techniques [78–80].

The highest achievement in biophysics and biochemistry is certainly the deciphering of more than 50% of the human genome, establishment not only of the major part played by individual genes but of their interaction as well, locating the genes whose damage is responsible for predisposition of some people to certain diseases, unraveling of the chemical formulas of many proteins, and synthesis of some biopolymers and enzymes. While it is not only the mass spectrometry, TOF reflectrons, and their combination in tandem systems with other mass spectrometric instruments and chromatographs that have to be given credit for these achievements, but nevertheless the time-of-flight mass spectrometry has played an important part in all this.

In this connection it appears appropriate to cite here the words said by I.E. Tamm, the Nobel Laureate for 1958, at a lecture at the Leningrad University in the 1960s: “Many years ago, when I was confronted by the problem of choosing the future profession, I did not doubt for a minute that there is nothing more interesting than physics. I have to confess, however, that if I had to choose the road now, I am not sure anymore that I would make the same decision. I believe that the future belongs to biology.” [81].

5. Conclusion

The objective pursued by this paper has been not to make an exhaustive account of the history of development of time-of-flight mass spectrometry up to the year 2000, because the wealth of publications on improvements in instruments and on the studies made with them is so large that such a task would have required a monograph. This is evidenced by the thick volumes containing Proceedings of Conferences of the American Society for Mass Spectrometry (ASMS), which cover thousands of papers. The comparatively specific subject of application of the TOF mass spectrometry to investigation of the fullerenes in only the 15 years of its development has grown to virtually thousands of publications. I have attempted only to relate the key steps passed by the idea of TOF-based separation of ions in its development and to demonstrate the possibility of using this method to advantage in the various areas of scientific research and in monitoring technological processes.

The most prolific fields where TOF mass spectrometry is presently employed are undoubtedly biophysics, biochemistry, and biomedicine, which require analysis of large, thermally unstable molecules with masses reaching millions of daltons. This subject is covered by the monograph of R.J. Cotter, TOF Mass Spectrometry. Instrumentation and Application in Biological Research [82].

In this connection the issue naturally arises of the possibility of increasing the resolution of TOF mass spectrometers, and of reaching and surpassing the resolution of 10^5.

Three ways of solving this problem can be conceived. (1) Application in TOF reflectrons of additional correcting pulsed voltages, which would allow reaching a high resolution at the given instrument setting only within the mass interval of interest for the researcher; (2) improvement of resolution over the whole mass range by reducing the effect of aberration factors and using “ideal” methods of ion energy focusing [33,34]; and (3) increasing the ion-drift path length in the instrument at a good electrostatic angle focusing.

The third way appears to be the most interesting approach, because an appreciable reduction of the sum of the aberration factors is extremely difficult. Indeed, a resolution of 10^5 for a reasonable length of the instrument of 2–3 m would require, all aberrations included, a packet a few tens of microns thick, which is anything but a simple task even when using high-precision adjustments and special microchannel plates.

I believe therefore that the most promising way lies in a substantial increase of the drift length by folding the ion trajectory in some compact spatial figure, with which one could increase the drift path by an order of magnitude or more within a fairly small gabarits of instrument.

In a vacuum of 10^{-7} Torr, the mean free path of particles is about 500 m and, hence, collisions would not be a problem. A.A. Makarov [83,84] presents an illustration of increasing the effective path in a nonmagnetic system with overall dimensions of a few cm. Our laboratory is developing other approaches to substantially increasing the ion drift length for instruments of a reasonable size.

Finally, it should be pointed out that science abounds in specific problems where one requires not analysis of large masses but rather an anomalously high resolution, a high accuracy of ion mass determination, and measurement of extremely low concentrations of impurities at the isotopic, atomic, or molecular level. In these cases magnetic focusing of the ion TOF permits one to reach very high analytical characteristics.

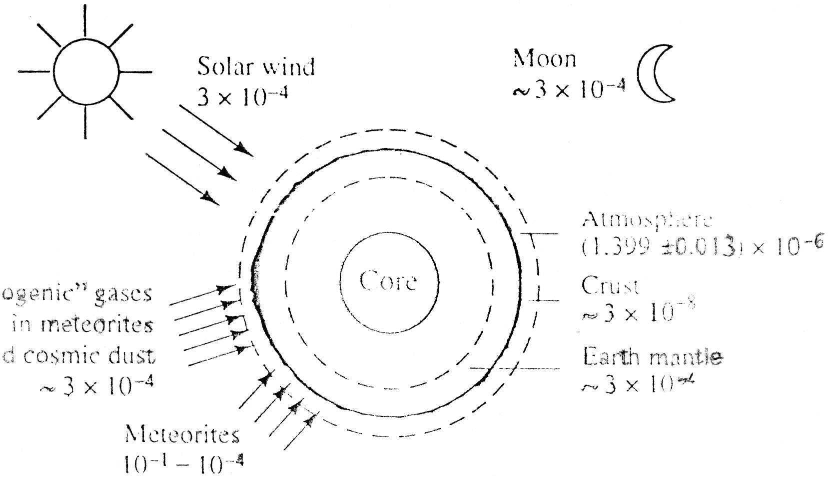

Fig. 10. ^{3}He/^{4}He isotope ratios in geospheres and near space.

The impressive progress in ICR mass spectrometry is public knowledge. I shall dwell here on a less known TOF magnetic resonance method developed at our laboratory (the MRMS instrument). In moving from the source (which operates continuously) to the detector, the ions in this instrument make two turns in one magnet gap plane and are accelerated twice at the same point of the trajectory (the modulator) by a rf voltage. Depending on the actual phase at which it enters the modulator, the radius of the trajectory changes so dramatically that if a harmonic of the ion cyclotron frequency ω_c is at resonance with the modulator voltage frequency $\omega_m = n\omega_c$ ($n \approx 100$), one can produce ion packets $\approx 10^{-11}$ s long. This is achieved by displacing the ion jet past narrow slits [85,86]. The instrument resolution achieved here is $R_{50\%} = 350 \times 10^3$ for a trajectory radius ≈ 100 mm. For $R = 20 \times 10^3$, the high sensitivity and a very good peak shape [the resolution at 10^{-10} (!) of peak height drops only by a factor of 5!] permits one to measure isotope ratios down to 10^{-11}, i.e. where the content of the poor isotope in a sample is $\sim 10^4$ atoms and one has to separate the interfering multiplet peaks.

Such instruments produced by the industry (MI 9303) have made possible a number of fundamental discoveries in geochemistry and geophysics (their results are discussed in our book [85] and accounted briefly in [61]).

Before the advent of the MRMS, the He isotope distribution in the earth and in near space was practically impossible to measure, because the ^{3}He/^{4}He isotope ratio varies over a tremendously broad range from 10^{-1} (in some meteorites) to 10^{-10} (uranium minerals), with the most interesting objects having ^{3}He/^{4}He $= 10^{-4}$–10^{-10}.

A joint work of our laboratory with geochemists has for the first time yielded the pattern of the ^{3}He/^{4}He distribution, which is shown in Fig. 10. The most interesting result here is the discovery in the earth's mantle of the "primeval helium" with an isotope ratio ^{3}He/^{4}He $= 3 \times 10^{-4}$ (over the whole of the earth!), with the ^{3}He content in the mantle exceeding its mean level in the earth's crust by $\sim 10^3$ times. This discovery has explained the ^{3}He/^{4}He paradox of the earth's atmosphere, ($\cong 1.399 \pm 0.013$) $\times 10^{-6}$ (first measured by us with such precision), offered a possibility of locating deep rifts in the crust where the main ore deposits are concentrated, provided a basis for developing an isotope method of measuring the heat flux distribution in the earth's crust on the continents, as well as established helium isotope criteria in the search for uranium–thorium and lithium–beryllium ore deposits.

The MRMS instrument permitted a discovery of a new, athermal kind of gas diffusion in solids, the so-called “dislocation dynamic diffusion,” that takes place even at 1.6 K [87,88]!

The high accuracy with which the ion cyclotron frequency was measured on the instrument with $R_{50\%} = 350 \times 10^3$ permitted determination with metrological precision of the most important physical constant, namely, the ratio of the proton magnetic moment to the nuclear magneton [89], which resulted in a substantial refinement of the values of many fundamental physical constants (the Planck and Faraday constants, nuclear magnetic moments, etc.) [89].

A MRMS with $R = 10^6$ is being presently assembled at our laboratory with the purpose to increase the precision of nuclide masses and fundamental constants of physics.

The recent work done on the MRMS, which was associated with a precise measurement of the tritium molecule halfperiod [90], permitted development for the first time of a helium-isotope method to measure the differences in the tritium decay halfperiod induced by different electronic environment of its nucleus [91,92]. This offered a possibility, likewise for the first time, to measure the halfperiod of the tritium atom and nucleus decay [93]. These data are being currently used to calculate the neutron decay halfperiod nowadays.

Accumulation of data on the halfperiod of tritium atoms in different hydrogen-containing molecules (with tritium substituted for hydrogen) will provide a basis for development of a new method of experimental investigation of the electronic density distribution in hydrogen-containing molecules by means of nuclear-sized probes located directly at the site of the substituted hydrogen atom.

The time and the frequency are parameters which are measured by modern instrumentation with the highest precision. Therefore the time-of-flight and TOF magnetic-resonance mass spectrometry will play an important part in future physical and biochemical measurements.

Acknowledgements

Professor Jürgen Grotemeyer, who kindly proposed to me to write this manuscript for a special issue of the International Journal Mass Spectrometry, suggested a broad freedom in my selecting the material to be included. I express to him my deep gratitude for this proposal and ask him to excuse me bigheartedly if I have used this freedom with too large a liberty.

References

[1] J.J. Tomson, Nature 90 (1913) 645; 90 (1913) 663; 91 (1913) 333.

[2] F.M. Aston, Philos. Mag. 38 (1919) 707.

[3] A.J. Dempster, Phys. Rev. 20 (1922) 631.

[4] A.O. Nier, Phys. Rev. 50 (1936) 1041; 52 (1937) 933.

[5] J. Mattauch, H. Herzog, Z. Phys. 89 (1934) 786.

[6] K.T. Bainbridge, E.B. Jordan, Phys. Rev. 50 (1936) 282.

[7] G.P. Barnard, Modern Mass Spectrometry, Institute of Physics, London, 1953.

[8] V.M. Kelman, I.V. Rodnikova, L.M. Sekunova, Static Mass Spectrometers, Nauka, Alma-Ata (1985) (in Russian).

[9] E.W. Blauth, Dynamische Massenspektrometer, Friedr. Vieweg und Sohn, Braunschweig, 1965.

[10] A.E. Cameron, D.F. Eggers, Rev. Sci. Instrum. 19 (1948) 605.

[11] N.I. Ionov, B.A. Mamyrin, Zh. Tekh. Fiz. 23 (1953) 2101.

[12] W.C. Willey, I.H. McLaren, Rev. Sci. Instrum. 26 (1955) 1150.

[13] H.S. Katzenstein, S.S. Friedland, Rev. Sci. Instrum. 26 (1955) 324.

[14] E.I. Agishev, N.I. Ionov, Zh. Tekh. Fiz. 28 (1958) 1775; Sov. Phys. Tech. Phys. 3 (1958) 1638.

[15] E.I. Agishev, N.I. Ionov, Zh. Tekh. Fiz. 26 (1956) 203; Sov. Phys. Tech. Phys. 1 (1956) 201.

[16] L.G. Smith, Rev. Sci. Instrum. 22 (1951) 166.

[17] J.M. Grundwüzner, M. Bönisch, G.R. Kinsel, J. Grotemeier, E.W. Schlag, Int. J. Mass Spectrom. Ion Processes 131 (1994) 139.

[18] C. Brunne, Int. J. Mass Spectrom. Ion Processes 76 (1987) 125.

[19] B.A. Mamyrin, Author’s Abstract of Doctorate, A.F. Ioffe Physico-Technical Institute, Leningrad, 1966.

[20] B.A. Mamyrin, Int. J. Mass Spectrom. Ion Processes 131 (1994) 1.

[21] B.A. Mamyrin, Russian Patent No. 198034 (1966).

[22] V.I. Karataev, B.A. Mamyrin, D.V. Shmikk, J. Tech. Phys. 16 (1971) 1498 (in Russian).

[23] B.A. Mamyrin, V.I. Karataev, D.V. Shmikk, V.A. Zagulin, Sov. Phys. JETP 37 (1973) 45.

[24] B.A. Mamyrin, V.I. Karataev, in Mass Spectrometry and Chemical Kinetics, Nauka, Moscow, 1985, p. 202.

[25] T. Bergman, T.P. Martin, H. Schaber, Rev. Sci. Instrum. 60 (1989) 347.

[26] T. Bergman, T.P. Martin, H. Schaber, Rev. Sci. Instrum. 60 (1989) 214.

[27] T. Bergman, H. Goehlich, T.P. Martin, H. Schaber, G. Malegiannakis, Rev. Sci. Instrum. 61 (1990) 2585.

[28] T. Bergman, T.P. Martin, H. Schaber, Rev. Sci. Instrum. 61 (1990) 2592.

[29] V. Zimmerman, U. Näher, S. Frank, T.P. Martin, Large Clusters of Atoms and Molecules, Kluwer Academic, Dordrecht, The Netherlands, 1996, pp. 511–530.

[30] K.W. Walter, V. Boesl, E.W. Schlag, Z. Naturforsch. 33a (1978) 1546.

[31] J. Grotemeyer, V. Boesl, K.W. Walter, E.W. Schlag, J. Am. Chem. Soc. 108 (1986) 4239.

[32] J. Grotemeyer, V. Boesl, K.W. Walter, E.W. Schlag, Org. Mass Spectrom. 21 (1986) 595.

[33] V.M. Doroshenko, R.J. Cotter, J. Am. Soc. Mass Spectrom. 10 (1999) 992.

[34] C.A. Flory, R.C. Taber, G.E. Yefchak, H. Pac. Lab. Tech. Rep. 95 (1995) 105.

[35] M. Yang, J.P. Reilly, Int. J. Mass Spectrom. Ion Processes 75 (1987) 209.

[36] U. Boesl, R. Wenkauf, E.W. Schlag, Int. J. Mass Spectrom. Ion Processes 112 (1992) 121.

[37] B.A. Mamyrin, D.V. Shmikk, Sov. Phys. JETP 49 (1979) 762.

[38] M.A. Ivanov, B.N. Kozlov, B.A. Mamyrin, D.V. Shmikk, V.G. Shchebelyn. Zh. Tekh. Fiz. 53 (1983) 2039 (in Russian).

[39] R.J. Cotter, T.J. Cornish, W. Bryden, Cyber Congress on Analytical BioSciences (CCAB97) Vol. 1, 21 August 1997.

[40] V.S. Antonov, I.N. Knyazev, V.S. Letokhov, V.M. Matiuk, V.G. Movshev, V.K. Potapov, Opt. Lett. 3 (1978) 37.

[41] G.P. Bekov, V.S. Letokhov, O.I. Matveev, V.I. Mishin, Zh. Eksp. Teor. Fiz. 75 (1978) 2092 (in Russian).

[42] V.S. Letokhov, Laser Photoionization Spectroscopy, Academic, Orlando, FL, 1987, Chap. 4.

[43] U. Boesl, H.J. Neusser, E.W. Schlag, Z. Naturforsch. 33a (1978) 1546.

[44] L. Zandee, R.B. Bemstein, D.A. Lichtin, J. Chem. Phys. 69 (1978) 3427.

[45] V.S. Letokhov, Laser Photoionization Spectroscopy, Academic, Orlando, FL, 1987, Chap. 2.

[46] J.A. Becker, C.D. Hartman, J. Phys. Chem. 57 (1953) 157.

[47] V.N. Ageev, N.I. Ionov, Extended Abstracts, International Symposium on Sorption–Desorption Phenomena, Rome, 1967, 112, 8.

[48] V.N. Ageev, S.N. Solovyev, Kinetika Kataliz, 22 (1981) 1019 (in Russian).

[49] V.N. Ageev, N.I. Ionov, Studies of Adsorption by Electron Stimulated Desorption and Flash-Filament Methods, Progress in Surface Science, Pergamon, New York, 1974, Vol. 5, p. 1.

[50] O.F. Pozdnyakov, B.P. Redkov, F.Sh. Tabarov, Plaste Kautschuk 29 (1982) 148.

[51] O.F. Pozdnyakov, V.S. Undin, B.P. Redkov, Fiz. Tverd. Tela 32 (1990) 1356 (in Russian).

[52] N.A. Cherepkov, A.Yu. Elizarov, J. Phys. B: At. Mol. Opt. Phys. 24 (1991) 4169.

[53] R.D. Macfarlaine, D.F. Torgerson, Int. J. Mass Spectrom. Ion Processes 21 (1976) 81.

[54] R.Z. Sagdeev, S.R. Tabaldyev, V.B. Leonas, Mass Spectrometry and Chemical Kinetics, Nauka, Moscow, 1985 (in Russian).

[55] J. Kissel, R.Z. Sagdeev, J.L. Bertaux, V.N. Angarov, J. Audouze, J.E. Blamont, K. Buchler, E.N. Evlanov, H. Fechtig, M.N. Fomenkova, H. von Hoerner, N.A. Inogamov, V.N. Khromov, W. Knabe, F.R. Krueger, Y. Langevin, V.B. Leonas, A.C. Levasseur-Regourd, G.G. Managadze, S.N. Podkolozin, V.D. Shapiro, S.R. Tabaldyev, B.V. Zubkov, Nature 321 (1986) 280.

[56] B.A. Mamyrin, A.A. Pozhunkov, B.M. Dubenskii, S.P. Parinov, A.G. Fedorov, Zh. Tekh. Fiz. 63, 200 (1993); Tech. Phys. 38 (1993) 1033.

[57] A.N. Kudryavzev, N.V. Nikonenkov, B.M. Dubensky, D.V. Shmikk, Pribory Tekhn. Eksperim. 2 (1990) 140 (in Russian).

[58] E.W. Müller, T.T. Tsong, Field Ion Microscopy and Field Evaporation, Progress in Surface Science, Pergamon, New York, 1979, Vol. 4, No. 1.

[59] M.I. Ivanov, B.A. Mamyrin, I.L. Fedichkin, Russian Patent No. 1690023, 1993.

[60] M.I. Ivanov, V.G. Smorodin, V.V. Chifonenko, Russian Patent No. 2063005, 1996.

[61] B.A. Mamyrin, in Ioffe Institute 1918–1998, Development and Research Activities, St. Petersburg, 1998, pp. 221–232.

[62] B.N. Kozlov, B.A. Mamyrin, Tech. Phys. 44 (1999) 1073.

[63] B.A. Mamyrin, V.I. Karataev, B.N. Kozlov, Mol. Mat. 7 (1996) 69.

[64] V.I. Karataev, B.A. Mamyrin, Mol. Mat. 4 (1994) 195.

[65] D.V. Afanas'ev, G.A. Baranov, G.A. Dyuzev, V.I. Karataev, Tech. Phys. Lett. 25 (1999) 722 (in Russian).

[66] V.I. Karataev, Tech. Phys. Lett. 24 (1998) 167.

[67] T.P. Martin, T. Bergmann, U. Näher, H. Schaber, U. Zimmerman, Nucl. Instrum. Methods Phys. Res. B 88 (1994) 1.

[68] W. Nelson, P. Williams, Proceedings of the International Conference on Secondary Ions Mass Spectrometry, Monteray, 4–8 September 1989, Wiley, Chichester, 1989, p. 215.

[69] M. Karas, U. Bahr, Trends Anal. Chem. 9 (1990) 423.

[70] I. Baranov, S. Jarmiychik, S. Kirillov, V. Obnorskii, K. Wien, C. Reimann, Nucl. Instrum. Methods Phys. Res. B 157 (1999) 167.

[71] R. Chen, J.E. Bruce, X. Cheng, D.W. Mitchell, S.A. Hoftadler, G.A. Anderdon, R.D. Smith, Proceedings of the 43rd ASMS Conference on Mass Spectrometry, Atlanta, GA, 1995, p. 800.

[72] M.M. Schemyakin, Yu.A. Ovchinnikov, A.A. Kiryushkin, E.I. Vinogradova, A.I. Miroshnikov, Yu.B. Alakhov, V.M. Lipkin, Yu.B. Shvitsov, Yu.V. Wulfson, B.V. Rosinov, V.N. Bochkarev, Y.M. Burikiv, Nature 211 (1966) 361.

[73] M. Karas, F. Hillenkamp, Anal. Chem. 60 (1988) 2299.

[74] R.S. Brown, J.J. Lennon, Anal. Chem. 67 (1995) 1998.

[75] B. Sundqvist, R.D. Macfarlane, Mass Spectrometry Reviews, Wiley, New York, 1985, Vol. 4, pp. 421–460.

[76] P.W. Geno, R.D. Macfarlane, Int. J. Mass Spectrom. Ion Processes 77 (1987) 75.

[77] R.J. Cotter, Anal. Chem. 56 (1984) 485A.

[78] M.L. Alexandrov, L.N. Gall, N.V. Krasnov, V.I. Nikolaev, V.I. Pavlenko, V.A. Shkurov, B.A. Baram, M.A. Gratchev, V.D. Knorre, Yu.S. Kusner, Bio-Organ. Khim. 10 (1984) 710 (in Russian).

[79] C.V. Whitehous, R.N. Dreyer, M. Yamashita, J.B. Fenn, Anal. Chem. 57 (1985) 675.

[80] V.L. Talrose, A.F. Dodonov, I.V. Chernushevich, Ecological Mass Spectrometry, Conference on Analytical Chemistry and Applied Spectroscopy, Chicago, 1991.
[81] V. Gubarev, Farewell to the XX Century, Moscow, Nauka, 1999, p. 286 (in Russian).
[82] R.J. Cotter, Time-of-Flight Mass Spectrometry: Instrumentation and Application in Biological Research, American Chemical Society, Washington, DC, 1997.
[83] A.A. Makarov, Mass Spectrometer, US Patent No. 6686346, 1999.
[84] A.A. Makarov, Proceedings of the 47th ASMS Conference on Mass Spectrometry, Dallas, January 1999.
[85] B.A. Mamyrin, I.N. Tolstikhin, Helium Isotopes in Nature, Elsevier, Amsterdam, 1984, pp. 1–273.
[86] B.A. Mamyrin, S.A. Alekseenko, N.N. Aruev, Zh. Exp. Theor. Phys. 80 (1981) 2125 [Sov. Phys. JETP 53 (1981) p. 1109.
[87] O.V. Klyavin, B.A. Mamyrin, L.V. Khabarin, Yu.M. Tchernov, Fiz. Tverd. Tela 18 (1976) 1281 (in Russian).
[88] O.V. Klyavin, B.A. Mamyrin, L.V. Khabarin, Yu.M. Tchernov, Fiz. Tverd. Tela 24 (1982) 2001 (in Russian).
[89] B.A. Mamyrin, N.N. Aruev, S.A. Alekseenko, Zh. Eksper. Teor. Fiz. 63 (1972) 3 [Sov. Phys. JETP 36 (1973) 1].
[90] Yu.A. Akulov, B.A. Mamyrin, L.V. Khabarin, V.S. Yudenich, N.N. Ryazantseva, Sov. Tech. Phys. Lett. 14 (1988) 416.
[91] Yu.A. Akulov, B.A. Mamyrin, P.M. Shikhaliev, Tech. Phys. Lett. 19 (1993) 594.
[92] Yu.A. Akulov, B.A. Mamyrin, JETP Lett. 68 (1998) 175.
[93] Yu.A. Akulov, B.A. Mamyrin, Zh. Tekh. Fiz. Lett. 26 (2000) 23 (in Russian).