ISSN 0868–5886 НАУЧНОЕ ПРИБОРОСТРОЕНИЕ, 2018, том 28, № 4, с. 151–160

РАЗРАБОТКА ПРИБОРОВ И СИСТЕМ

УДК 338.001.36 + 338.012; 543.51; 577.112.5 + 621.384.8

THE INNOVATIVE DIRECTION OF THE DEVELOPMENT OF SCIENTIFIC INSTRUMENTATION — TIME-OF-FLIGHT MASS SPECTROMETERS

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The breakthrough scientific research in the field of development of analytical instrumentation, one of the areas of analytical instrumentation — time-of-flight mass spectrometry is being described. The creation of domestic time-of-flight mass spectrometers implements the task of import substitution of foreign equipment, and refers to significant, risky for state organizations financing. The scientific instruments that do not have domestic analogues and illustrate the development of one of the most promising areas of scientific instrumentation are being presented. Time-of-flight mass spectrometry makes it possible to create the most powerful in terms of sensitivity, informativity and speed small-sized analytical systems with modern software for qualitative and accurate quantitative analysis of the composition and structure of chemical compounds.

Keywords: mass spectrometry, ion source, electrospray fluid, ion flow, space charge

A PROMISING DIRECTION IN THE DEVELOPMENT OF ANALYTICAL INSTRUMENTATION IS THE CREATION OF INNOVATIVE INSTRUMENTS FOR IMPORT SUBSTITUTION

The Institute of Analytical Instrumentation of the Russian Academy of Sciences (IAI RAS) has for decades worked by conducting fundamental and applied scientific research and developed unique competences in the field of analytical instrumentation, and now produces prototypes of competitive instruments, organizing their small-scale or serial production.

One of the main tasks of analytical instrumentation IAI RAS sees in solving the problem of import substitution of instruments and equipment necessary for performing works on priority scientific directions, taking into account the needs of domestic and foreign markets, and also an annual increase in sales of devices [1, 2].

Mass spectrometry is practically the most powerful method of analyzing the composition, structure and quantities of chemical compounds in terms of sensitivity, informativeness and speed. The mass spectrometry method is used in modern high-tech scientific fields, having the ability to analyze various substances: isotopes of chemical elements, complex biopolymers such as proteins and nucleic acids, distinguish microorganisms, detect compounds at nano-dimensional levels, carry out qualitative and quantitative analysis of various mixtures consisting of thousands of organic compounds without their prior separation.

Instruments of the IAI RAS using the method of mass spectrometry have found their application: in chemistry, in physics, in biology, in medicine, in pharmaceutics, in ecology, in criminalistics, in antiterrorist activity, in control of the quality of food products, in nuclear research and other areas of scientific research [3–5].

The IAI RAS as well as foreign companies such as Agilent Technologies, Bruker Scientific Instruments, Thermo Fisher Scientific, LECO Corporation, Danaher Corporation, creates mass-spectrometric express diagnostics devices at the world level, solving the problem of diagnosing early stages of various diseases: oncology, cardiovascular, genetic.

In modern clinics, the instruments realizing molecular genetic methods and methods of ionization time-of-flight mass spectrometry, based on the use of physical innovative technologies, have replaced cultural diagnostics. World experience in the use of mass-spectrometric express diagnostics for the species identification of microorganisms extracted from clinical material confirms the high value of the method and the potential opportunity for direct indication of bacteria in the clinical material, which significantly shortens the time of analysis and opens up new resources for use in various sections of the microbiological diagnostics [6].

Modern mass spectrometry is based on the elemental base of a high level of integration, which allows to miniaturize equipment, using the latest technologies, contributing to the increase of the innovation level of the devices being created.

THE BENCHTOP TIME-OF-FLIGHT MASS SPECTROMETER MX5310 (11)

The benchtop time-of-flight mass spectrometer MX5310(11) [7] is designed for solving a wide range of research and applied problems of medicine, biotechnology, pharmacology, environmental protection, criminology, and agricultural industry (Fig. 1).

The instrument operation principle is based on the method of producing ions from the solutions of substances under analysis.

Since instrument MX5310 (11) ensures high-sensitive analysis of solutions of samples of various natures, it is possible: to diagnose diseases at early stages; to perform proteomic investigations; to control drug production and storage; to develop new drugs; to control food purity.

The instrument is produced in two modifications: MX5310 with the electrospray ion source (the liquid sample bulk velocity of up to 1 ml/min) and MX5311 with the nanoelectrospray ion source (the liquid sample bulk velocity of several nanoliters per minute). MX5310 (11) can be equipped with a liquid chromatograph.

ADVANTAGES

Advantages of the mass spectrometer MX5310 (11): analytical characteristics of instrument MX5310 (11) are comparable with the world-best ones in this instrument class; the instruments can work in both the "on-line" and "off-line" modes; the original software

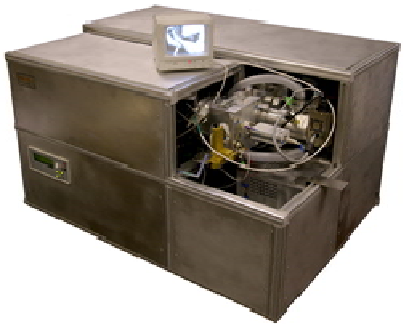

Fig. 1. The mass spectrometer MX5310 (11)

(TOF+) allows continuous monitoring of the analysis and high-speed data compression; since the instrument can work with domestic consumables, operating costs are; 15 times lower than in working with foreign analogues; in case of small-batch production, the instrument cost is considerably lower than that of foreign analogues of the same class.

BASIC PERFORMANCE CHARACTERISTICS OF THE MASS SPECTROMETER MX5310 (11)

The basic performance characteristics of the mass spectrometer MX-5310 (11) are presented at Table 1. Purity analysis of the insulin pharmaceutical form produced by different companies by using instrument MX5310 was performed. The comparison of insulin from different manufacturers (Fig. 2–4) for the presence of foreign impurities shows that the most pure is French insulin, and that Ukrainian insulin contains the greatest amount of impurities. The instrument is used for cancer diagnostics (Fig. 5).

Table 1. Basic performance characteristics of the mass spectrometer MX5310 (11)

Mass-spectrometric detection of the presence of the goal substance and impurities with the sensitivity no less than, M		10^{-15}
Resolution at the peak half-height, minimum		7 000
Detectable mass number	extreme range, up to, daltons	10 000
	range, up to, daltons	20 000
Mass measurement accuracy, with internal calibration, %		10^{-15}
Mass stability for 30 min, maximum, %		2×10^{-3}
Overall dimensions, mm		1040 × 760 × 600

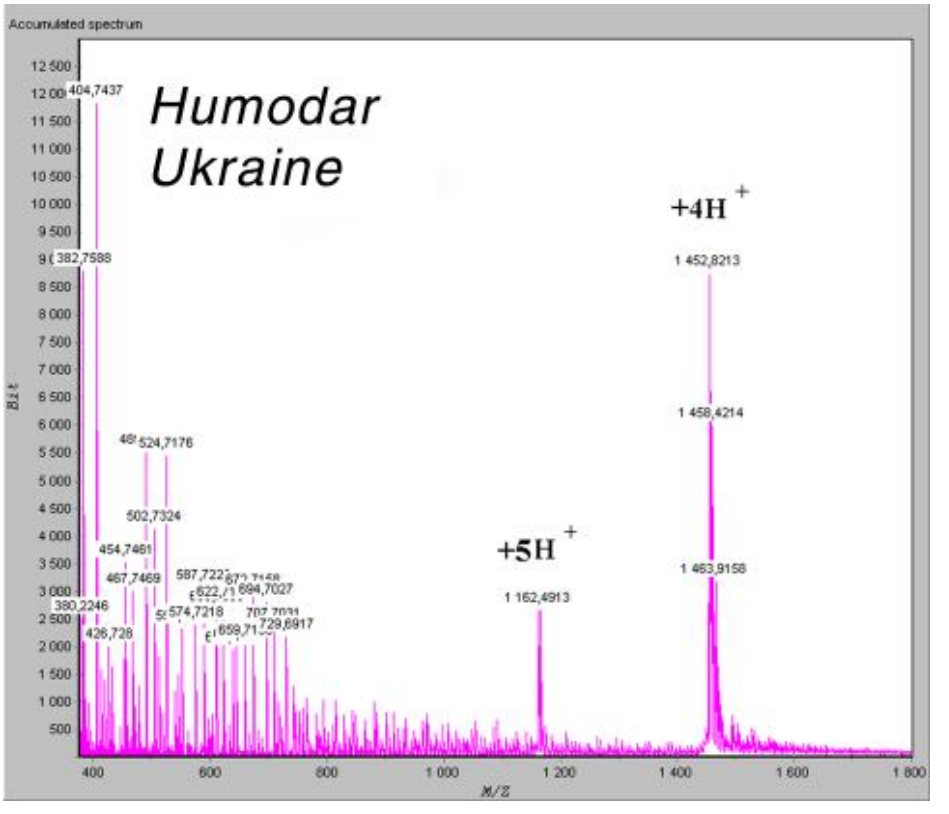

Fig. 2. Control of the purity of insulin in the Ukrainian pharmaceutical industrial company

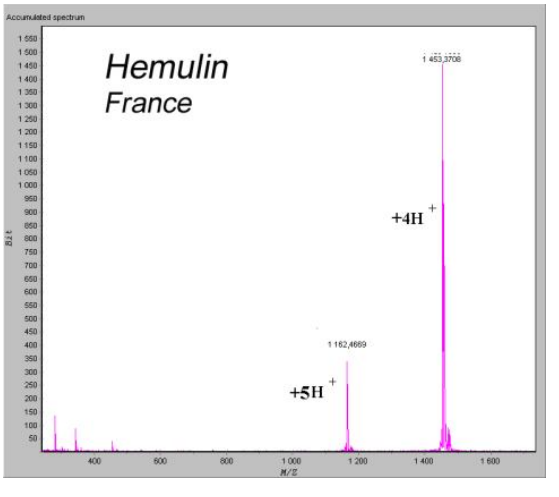

Fig. 3. Control of the purity of insulin in the French pharmaceutical manufacturing company

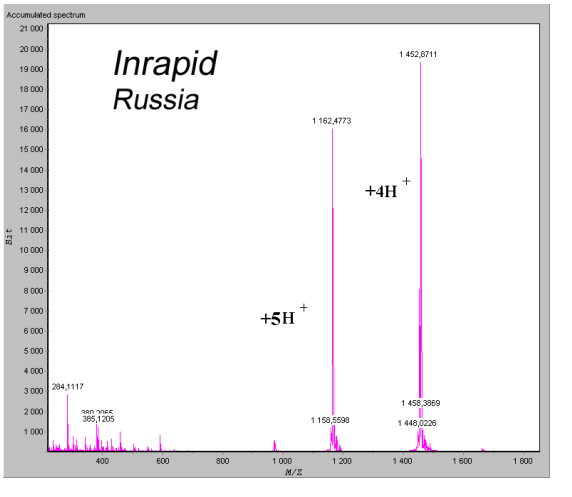

Fig. 4. Control of Russian pharmaceutical industrial company

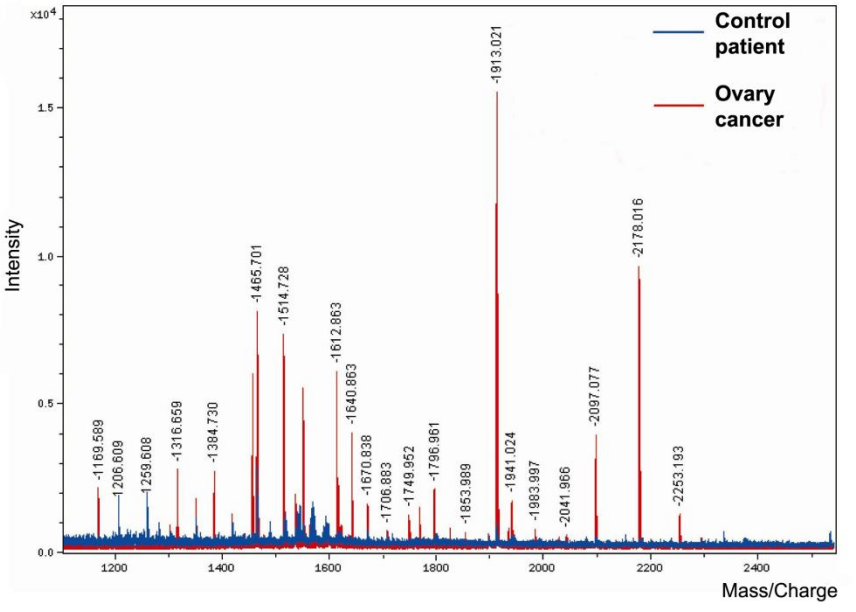

Fig. 5. Diagnostics of cancer by using instrument MX5310

MASS SPECTROMETRIC COMPLEX MX5313

The domestic analytical complex MX5313 [8–14] is a highly sensitive world-class device (Fig. 6). The use of instrument complexes MX5313 allows to determine the composition of complex mixtures of various substances with high accuracy.

The analytical complex MX5313 allows to significantly reduce operating costs and speed up the maintenance of the device [15, 16].

Analytical complex MX5313 is designed for the quantitative analysis of complex (more than 50 components) mixtures of volatile and semi-volatile compounds. The analytical complex MX5313 allows for the quantitative analysis of most drugs, poisonous substances, explosives, pesticides, steroids and drugs.

The analytical complex consists of the following devices: a time-of-flight mass analyzer of the reflectron type with orthogonal injection of a continuous ion beam from a source that has an electron impact; a heated interface in the form of a gas chromatograph ("Crystal 5000") and a vacuum evacuation system based on the use of high-vacuum turbomolecular pumps [17–21].

The method of diagnostics of complex mixtures, using the Analytical Complex MX5313, allows to reliably detect hazardous substances for humans at enterprises that have harmful production. Dangerous to humans substances, as a rule, are not diagnosed by any other methods. The use of the MX5313 Analytical Complex in the course of environmental monitoring increases the reliability of the analysis results by accurately determining the mass of the analyte [22].

Fig. 6. Mass spectrometer complex MX5313

SOFTWARE FOR THE MX5313 ANALYTICAL COMPLEX

The software of the Analytical Complex MX5313 allows: control and management of the operation of the complex; registration of mass spectra; search by name and chemical formulas of substances stored in the National Institute of Standards and Technology (NIST) database; viewing structural formulas of substances stored in the NIST database; viewing the mass spectra of substances stored in the NIST database; search on demand in the NIST database of substances which mass spectra correspond to the registered mass spectrum by the Analytical Complex MX5313; determination of peaks on the graph of the total ion current "TotalIonCurrent" (TIC). The determination of the

peaks in the TIC graph allows: allocation of the peaks on the TIC spectrum; mapping of the peak mass center; scaling of TIC graph fragments; output of the peak parameters as a separate window.

MAIN TECHNICAL CHARACTERISTICS OF THE MX5313 ANALYTIC COMPLEX

The basic performance characteristics of the mass spectrometer MX5313 are presented at Table 2. According to the recorded mass spectrum of the electron impact of PFTBA the results on the accuracy of determination of ion masses are given in Table 3. Results on the accuracy of determination of ion masses were determined at a voltage of 2100 V, 1000 scans at the detector.

The accuracy of the masses of the registered ions up to 5 ppm allows to improve the probability of recognition of the analytes.

Analytical characteristics of the MX5313 manufactured in the IAI RAS, at the level of the world's best samples in this class of devices. The device does not have any domestic analogues. The MX5313 analytical complex was developed by order of the Federal Medical and Biological Agency of Russia.

Table 2. Main technical characteristics

Resolution for mass 614 Yes, Perfluorotributylamine (PFTBA)	5000
Range of scanned masses, atomic mass unit (u)	30–1000
Scanning speed, spectra per second	200
Sensitivity, hexachlorobenzene at a signal-to-noise ratio	$2\ 10^{-12}$, 30:1
Version of the analytical complex performance	desktop
Power consumption, no more, kW	3
From AC power	220 V

Table 3. Results on the accuracy of determination of ion masses

N n / a	Type	Formula	Neutral	Theoretical	Observed	Error Yes	Error ppm
1	PFTBA 69	CF3	68.9952096	68.994661	68.994661	0	0
2	PFTBA 69	C2F4	99.9936128	99.9930642	99.993074	0.0098	0.09800679
3	PFTBA 69	C2F4N	113.996687	113.996138	113.996069	0.069	0.60528366
4	PFTBA 69	C2F5	118.992016	118.991467	118.991974	0.507	4.26080972
5	PFTBA 69	C3F5	130.992016	130.991467	130.991944	0.477	3.64145856
6	PFTBA 69	C3F7	168.988822	168.988274	168.988923	0.649	3.84050315
7	PFTBA 69	C4F9	218.985629	218.98508	218.985257	0.177	0.80827424
8	PFTBA 69	C5F10N	263.987106	263.986557	263.986068	0.489	1.85236705
9	PFTBA 69	C8F16N	413.977525	413.976977	413.976126	0.851	2.05566987
10	PFTBA 69	C9F18N	463.974332	463.973783	463.974128	0.345	0.74357649
11	PFTBA 69	C9F20N	501.971138	501.970589	501.970589	0	—

TIME-OF-FLIGHT MASS SPECTROMETER WITH ELECTROSPRAY MX5303

The mass spectrometer is designed for the analysis of thermally unstable substances of organic and bioorganic origin directly from solutions.

The device can work in conjunction with a liquid chromatograph.

The new generation MX5303 mass spectrometric complex (Fig.7) is based on the method of obtaining ions from solutions of bioorganic compounds. The MX-5303 mass spectrometer with electrospray can be used to solve a wide range of biochemical problems [23–29].

Examples of such problems solved with the help of mass spectrometry with "soft" ionization methods areas follows: research of cellular and molecular bases of carcinogenesis, analysis of protein-protein interactions in DNA repair complexes, search for disease markers (cell pathology, study of protein composition).

The device uses electrospray ionization of the analyzed solution at atmospheric pressure, which makes it possible to obtain quasimolecular ions of thermolabile compounds directly from the solution. Ions are transported from the ionization region at atmospheric pressure through the differential pumping system to the high-vacuum region of the mass analyzer. As a mass analyzer, a time-of-flight analyzer with orthogonal ion input is used. When the instrument is operated in combination with a liquid chromatograph, a mass chromatogram is obtained by summing the total intensity of the ion current in each mass spectrum. The amount of substance required for such an analysis and introduced into the column of the chromatograph is 1 pg [30–35].

THE MAIN TECHNICAL CHARACTERISTICS OF THE ANALYTICAL COMPLEX MX5313

The main technical characteristics of the analytical complex MX5313 are presented in Table 4.

Fig. 7. Time-of-flight mass spectrometer with electrospray MX5303

Table 4. The main technical characteristics of the Analytical Complex MX5313

Resolution of the mass spectrometer at 50% of the peak height of the mass spectrum	10 000
The range of recorded mass numbers of the mass spectrometer (taking into account multiply charged ions), Yes	Up to 10 000
Accuracy of mass determination (with internal calibration), %	10^{-4}
The speed of full spectrum recording, spectra per second, not less than	10
The detection limit for gramicidin C at a flow of 1 μl / min, M	10^{-15}

APPLICATION OF MX5303 IN COMBINATION WITH A LIQUID CHROMATOGRAPH FOR THE ANALYSIS OF INSULIN SYNTHESIS PRODUCTS

Mass spectrometer MX5303, manufactured by IAI RAS, has high analytical characteristics of similar world-class devices (Fig. 8, 9). The MX5303 mass spectrometer operates both on-line and off-line. Mass spectrometer MX5303 is equipped with original software TOF-Plus, which allows continuous monitoring of the analysis procedure and high-speed compression of data without information loss. The MX5303 mass spectrometer has no domestic counterparts.

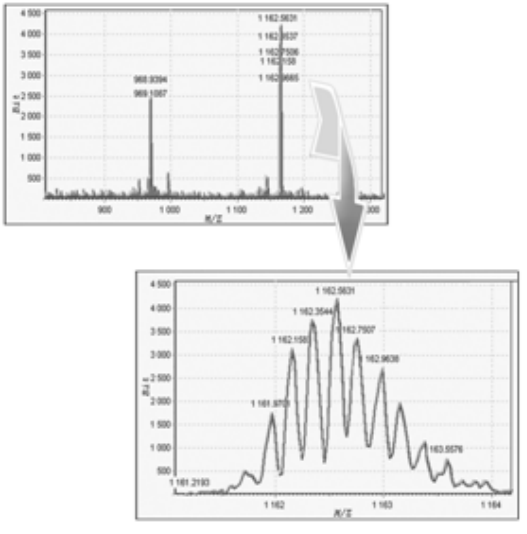

Fig. 8. Analysis of hydrolyzate products of the hybrid protein "off-line"

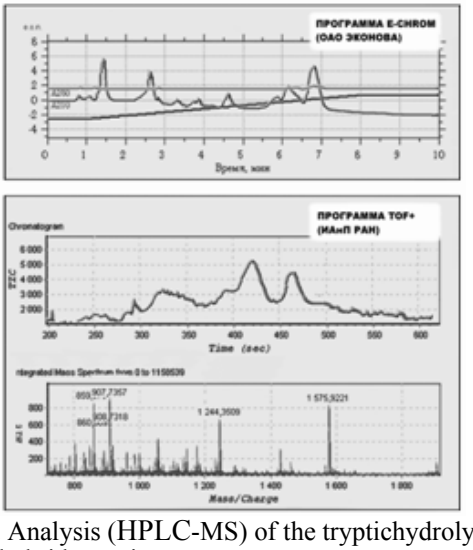

Fig. 9. Analysis (HPLC-MS) of the tryptichydrolyzate of the hybrid protein

TIME-OF-FLIGHT MASS SPECTROMETERS MX5310 (11), MX5303 AND MASS-SPECTROMETRIC COMPLEX MX5313, PRODUCED BY IAI RAS, ON THE MARKET OF SCIENTIFIC INSTRUMENT MAKING

Time-of-flight mass spectrometers MX5310 (11); MX5303 and MX5313 mass spectrometry serially produced by IAI RAS successfully compete in the domestic and foreign markets for scientific instrumentation with the following foreign companies: Thermo Fisher Scientific; LECO Corporation; Waters Corporation; JEOL USA, Inc. (Table 5).

Time-of-flight mass spectrometers MX5310 (11); MX5303 and MX5313 mass spectrometry have been used in research organizations, institutions of higher professional education and institutions of the Russian Academy of Sciences. Time-of-flight mass spectrometers MX5310 (11); MX5303 and MX5313 mass spectrometry are operated by organizations working, in particular, in the field of creating new methods for diagnostics of diseases at an early stage — oncology, cardiovascular diseases, genetic diseases; in the field of creation, control of medicinal preparations, both in the production process and in the composition of finished medicines for compliance with their certificate; in the field of criminalistics — the trace analysis of drugs in biological fluids. Mass spectrometric complexes MX5313 can be used in the following areas: analytical chemistry, chemical synthesis, toxicology, forensic and clinical analysis of toxic preparations, analysis of pesticides in food and drinking water quality control, analysis of dioxins and nitrofurans, metabolism of drugs, control of psychotropic drugs, analysis of explosives, analysis of oil and oil products [36].

Domestic time-of-flight mass spectrometers implement a method for processing mass spectra of peptides to extract information on the masses of sample molecules based on analysis and decomposition of the structure of the mass spectrum using statistical data on the form of isotope distributions of molecular ions of peptides, as well as a method for controlling the production of genetically engineered insulin of ahuman with the help of tandem of HPLC-MS in the direct injection mode of the sample [37, 38].

SIMION 7.0 software with original modules developed in the IAI RAS was used for development of time-of-flight mass spectrometers manufactured by IAI RAS and for optimizing its ion-optical parameters.

IAI RAS developed a theory and carried out experimental studies of a planar multi-reflective time-of-flight mass analyzer, a theory of time-of-flight mass analyzers of a new type that allows to realize a fundamentally new tandem mass spectrometric (MS-MS) analysis in the "nested time" mode has been created.

Table 5. Comparison of analytical characteristics of mass spectrometric analyzers

Characteristics	Mass Spectrometers						
	Pegasus	TruTOF	AccuTOF GC	GCT	H-TOF	AutoSpec	DSF
Manufacturer	LECO	LECO	JEOL	Waters	Thermo	Waters	Thermo
Analyzer type	Time-of-flight (TOF)	Time-of-flight (TOF)	Time-of-flight (TOF)	Time-of-flight (TOF)	Quadrupole (Q)	Magnetic sector (EBE)	Magnetic sector (EBE)
Resolution	1000	2000	5000	7000	1000	80 000	60 000
Detection limit	1 nr HCB (s/n > 10)	2 nr HCB (s/n > 10)	2 nr OFN (s/n > 100)	3 nr OFN (s/n > 50)	1 nr OFN (s/n > 400)	100 фг OFN (s/n > 400)	100 фг OFN (s/n > 300)
Recordings peed of spectra	500 cps / sec	80 cps / sec	25 cps / sec	10 cps / sec	1–10 cps / sec	0.1–1 cps / sec	0.1–1 cps / sec
Arrangement	Floor	Desktop	Floor	Desktop	Desktop	Floor	Floor

The IAI RAS implements the creation of time-of-flight mass spectrometers that perform the function of import substitution in the market of scientific instrument making.

The Ministry of Science and Higher Education of Russia, defending the interests of the subordinate institutions of science, implements one of the types of state economic policy to replace imports with domestic products during the period of anti-Russian sanctions, thereby protecting the domestic producer by replacing imported scientific instruments and technologies with scientific instruments of national production.

A positive scenario for the development of domestic instrumentation provides for financing by the Ministry of Science and Higher Education of Russia of fundamental scientific research on promising areas of scientific instrumentation in order to increase the competitiveness of domestic products through the development of high-tech, science-intensive products with relatively high added value.

REFERENCES

1. Slepak K.B. *Razvitie nauki, obrazovaniya i innovacionnyh tekhnologij v regionah Rossii kak faktor obespecheniya nacional'noj bezopasnosti: monografiya* [The development of science, education and innovative technologies in the regions of Russia]. Saint Petersburg, Publishing house of Polytechnic University, 2014. 192 p. (In Russ.).
2. Slepak K.B. [The development of the scientific and educational potential of Russia in the process of innovative import substitution]. *Ekonomika i upravlenie* [Economics and Management], 2015, no. 7, pp. 84–91. (In Russ.).
3. Slepak B.S., Slepak K.B. [Management of Innovations in Scientific Instrumentation]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2017, vol. 27, no. 4, pp. 107–117. URL: http://iairas.ru/mag/2017/abst4.php#abst13.
4. Slepak B.S., Slepak K.B. [The innovative direction of scientific instrumentation is the Mössbauer spectroscopy as a factor in the improvement of the branches of the Russian economy. Part 1. Breakthrough scientific research in the field of Mossbauer spectroscopy]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2018, vol. 28, no. 1, pp. 79–92. URL: http://iairas.ru/mag/2018/abst1.php#abst10.
5. Slepak B.S., Slepak K.B. [The innovative direction of scientific instrumentation is Mössbauer spectroscopy as a factor in the improvement of the branches of the Russian economy. Part 2. Creation of the national research equipment in the field of Mössbauer spectroscopy]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2018, vol. 28, no. 2, pp. 75–88. URL: http://iairas.ru/mag/2018/abst2.php#abst11.
6. Polushin Y.S., Levshankov A.I., Lakhin R.E., Pashchinin A.N., Bezrukova E.V., Piskunovich A.L., Kostyuchek D.F., Belozerova A.K., Gaidukov S.N., Shapkayts V.A., Belozerova L.A., Krasnov N.V. [Prospects of using the antioxidant analyzer in clinical practice for assessing nonspecific resistance of the organism under various critical conditions and for forecasting obstetric complications]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 3, pp. 5–12. URL: http://iairas.ru/mag/2013/abst3.php#abst1. (In Russ.).
7. Bublyaev R.A., Golikov Y.K., Krasnov N.V. *Time-of-flight Mass Spectrometer*. Patent RF no. 2295797. Prioritet 6.06.2005. (In Russ.).
8. Alekseev D.N., Gavrik M.A., Monakov A.G., Muradymov M.Z., Prisyach S.S., Yavor M.I., Krasnov N.V. *Ustrojstvo vremyaproletnogo mass-spektrometra dlya razde-*

leniya i registracii ionov analiziruemyh veshchestv. Patent RF for useful model № 137381. [The device of a time-of-flight mass spectrometer for separation and registration of ions of analytes]. Prioritet 10.02.2014. (In Russ.).
9. Nazimov I.V., Muradymov M.Z., Bublyaev R.A., Gavrik M.A., Prisyach S.S., Krasnov N.V. *Metod mass-spektrometricheskogo sekvenirovaniya peptidov i opredelenie ih aminokislotnyj posledovatel'nostej*. Patent RF no. 2498443. [Method of mass-spectrometric sequencing of peptides and determination of their amino acid sequences]. Prioritet 10.11.2013. (In Russ.).
10. Muradymov M.Z., Semenov S.Y., Krasnov N.V. *Ustrojstvo nepreryvnogo stabil'nogo ehlektroraspyleniya rastvorov v istochnike ionov pri atmosfernom davlenii*. Patent RF no. 2587679. [Device for continuous stable electrospray of solutions in the ion source at atmospheric pressure]. Prioritet 27.05.2016. (In Russ.).
11. Krasnov M.N., Krasnov N.V. *Ustrojstvo istochnika ionov-ehlektrosprej dlya polucheniya beskapel'nogo stabil'nogo ionnogo toka analiziruemyh veshchestv iz rastvorov v techenie dlitel'nogo vremeni*. Patent RF for useful model no. 169146. [Device ion source-electrospray to obtain a steady-state stable ion current of analytes from solutions for a long time]. Prioritet 07.03.2017. (In Russ.).
12. Arseniev A.N., Monakov A.G., Krasnov M.N., Krasnov N.V. *Ustrojstvo dvuhpolyarnogo maloshumyashchego istochnika pitaniya*. Patent RF for useful model no. 174218. [The device of a bipolar low-noise power source]. Prioritet 09.10.2017. (In Russ.).
13. Krasnov M.N., Krasnov N.V. *Sposob obrazovaniya beskapel'nogo ionnogo potoka pri ehlektroraspylenii analiziruemyh rastvorov v istochnikah ionov s atmosfernym davleniem*. Patent RF no. 2613429. [Method for the formation of a dripless ionic stream during electrospraying of the solutions under analysis in ion sources with atmospheric pressure]. Prioritet 16.03.2017. (In Russ.).
14. Krasnov M.N., Muradymov M.Z., Krasnov N.V. *Sposob nepreryvnogo stabil'nogo ehlektroraspyleniya rastvorov v istochnike ionov pri atmosfernom davlenii*. Patent RF no. 2612324. [Method for continuous stable electrospraying of solutions in a source of ions at atmospheric pressure]. Prioritet 07.03.2017. (In Russ.).
15. Arseniev A.N., Monakov A.G., Krasnov M.N., Krasnov N.V. [Adjustable bipolar highly stable power supplies]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2017, vol. 27, no. 3, pp. 8–17. URL: http://iairas.ru/mag/2017/abst3.php#abst2. (In Russ.).
16. Arseniev A.N., Monakov A.G., Krasnov M.N., Krasnov N.V. *Ustrojstvo dvuhpolyarnogo maloshumyashchego istochnika pitaniya*. Patent RF for useful model no. 174218. [The device of a bipolar low-noise power source]. Prioritet 09.10.2017. (In Russ.).
17. Pomozov T.V., Yavor M.I. [A non-grid orthogonal accelerator for multireflection time-of-flight mass analyzers]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2012, vol. 22, no. 1, pp. 113–120. URL: http://iairas.ru/mag/2012/abst1.php#abst17. (In Russ.).
18. Pomozov T.V., Yavor M.I., Verenchikov A.N. [Reflectrons with orthogonal ion acceleration on the basis of planar mesh mirrors]. *Zhurnal tekhnicheskoj fiziki* [Journal of Applied Physics], 2012, vol. 82, no. 4, pp. 130–136. (In Russ.).
19. Samokish V.A., Muradymov M.Z., Krasnov N.V. Electrospray ion sourse with a dynamic liquid flow splitter. *Rapid Commun. mass spectrometry*, 2013, no. 27, vol. 8, pp. 904–908. Doi: 10.1002 / rcm 6524.
20. Golikov Y.K., Krasnova N.K., Nikolaev V.I., Soloviev K.V. [Separation of ions in a combination of stationary fields — electric quadrupole and magnetic homogeneous]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 1, pp. 52–60. URL: http://iairas.ru/mag/2013/abst1.php#abst6. (In Russ.).
21. Krasnova N.K., Golikov Y.K., Elokhin V.A., Nikolaev V.I. [A new dynamic mass spectrometer with an electric shock]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 1, pp. 68–73. URL: http://iairas.ru/mag/2013/abst1.php#abst8. (In Russ.).
22. Alekseev D.N., Arseniev A.N., Belchenko G.V., Gavrik M.A., Monakov A.G., Muradymov M.Z., Prisyach S.S., Yavor M.I., Zvereva A.V., Zinin A.V., Myaldzin Sh.U., Nikitina S.N., Pomozov T.V., Turtya S.B. [Analytical complex GC-MS on the basis of a time-of-flight mass spectrometer with a source of "electron impact" ions]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 4, pp. 95–103. URL: http://iairas.ru/mag/2013/abst4.php#abst13. (In Russ.).
23. Arseniev A.N., Muradymov M.Z., Krasnov N.V. [Field desorption of ions from the tip at the meniscus of liquid during EHD-sputtering]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2014, vol. 24, no. 3, pp. 3–8. URL: http://iairas.ru/mag/2014/abst3.php#abst1. (In Russ.).
24. Koryakin P.S., Krasnov I.A., Krasnov N.V., Muradymov M.Z., Krasnov M.N. [Ion-drift spectrometer with an electrospray ion source as a liquid chromatograph detector]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2015, vol. 25, no. 2, pp. 34–39. URL: http://iairas.ru/mag/2015/abst2.php#abst3. (In Russ.).
25. Pashkov O.V., Muradymov M.Z., Krasnov M.N., Krasnov N.V. [Characteristics of an electrospray torch with a dynamic division of the liquid flow at atmospheric pressure]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2015, vol. 25, no. 3, pp. 3–9. URL: http://iairas.ru/mag/2015/abst3.php#abst1. (In Russ.).
26. Kuzmin D.A., Muradymov M.Z., Pomozov T.V., Arseniev A.N., Krasnov N.V. [Transportation of ions in sources with ionization at atmospheric pressure. I. Substantive geometry]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2017, vol. 27, no. 4, pp. 8–16. URL: http://iairas.ru/mag/2017/abst4.php#abst2. (In Russ.).
27. Arseniev A.N., Muradymov M.Z., Krasnov M.N., Kuzmin D.A., Pomozov T.V., Krasnov N.V. [Transportation of ions in sources with ionization at atmospheric pressure. II. Inverse geometry]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2017, vol. 27, no. 4, pp. 17–23. URL: http://iairas.ru/mag/2017/abst4.php#abst3. (In Russ.).
28. Krasnov M.N., Krasnov N.V. *Ustrojstvo obrazovaniya beskapel'nogo ionnogo potoka pri ehlektroraspylenii analiziruemyh rastvorov v istochnikah ionov s atmosfernym davleniem*. Patent RF no. 2608361. [The device for the

formation of a dripless ion flux during electrospraying of the solutions under analysis in ion sources with atmospheric pressure]. Prioritet 2015. (In Russ.).
29. Muradymov M.Z., Pashkov O.V., Krasnov N.V. *Ustrojstvo stabil'nogo ehlektroraspyleniya pri atmosfernom davlenii rastvorov veshchestv dlya istochnikov ionov*. Patent RF no. 2608362. [Device of stable electrospray at atmospheric pressure of solutions of substances for ion sources]. Prioritet 2015. (In Russ.).
30. Alexandrov M.L, Gall L.N. Krasnov N.V., Nikolaev V.I., Pavlenko V.A., Shkurov V.A. Extraction of ions from solutions under atmos-pheric pressure as a method for mass spec-trometric analysis of bioorganic compounds. *Rapid communications in mass spectrometry*, 2008, no. 22, pp. 267–270. Doi: 10.1002/rcm.3113.
31. Polushin Y.S., Levshankov A.I., Lakhin R.E., Pashchinin A.N., Bezrukova E.V., Piskunovich A.L., Kostyuchek D.F., Belozerova A.K., Gaidukov S.N., Shapkayts V.A., Belozerova L.A., Krasnov N.V. [Prospects of the use of the antioxidant analyzer in clinical practice for assessing nonspecific resistance of the organism under various critical conditions and for forecasting obstetric complications]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 3, pp. 5–12. URL: http://iairas.ru/mag/2013/abst3.php#abst1. (In Russ.).
32. Al-Tawil E.A., Muradymov M.Z., Krasnov M.N., Krasnov N.V. [Electrospraying of conducting solutions under normal conditions over a wide range of volumetric velocities]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2017, vol. 27, no. 2, pp. 3–12. URL: http://iairas.ru/mag/2017/abst2.php#abst1.
Doi: 10.18358 / np-27 -2-i312. (In Russ.).
33. Muradymov M.Z., Krasnov N.V. *Sposob stabil'nogo ehlektroraspyleniya rastvorov v istochnike pri atmosfernom davlenii*. Patent RF no. 2608366. [A method of stable electrospraying of solutions in a source at atmospheric pressure]. Prioritet 10.01.2017. (In Russ.).
34. Muradymov M.Z., Monakov A.G., Krasnov N.V. *Ustrojstvo vremyaproletnogo mass-spektrometra s istochnikom ionov s ionizaciej pri atmosfernom davlenii dlya razdeleniya i registracii ionov analiziruemyh veshchestv*. Patent RF no. 158343. [The device of the time-of-flight mass spectrometer with ion source with ionization at atmospheric pressure for separation and registration of ions of the analytes]. Prioritet 07.12.2015. (In Russ.).
35. Muradymov M.Z., Krasnov N.V. *Istochnik ionov s fotoionizaciej pri atmosfernom davlenii*. Patent RF no. 2572358. [Source of ions with photoionization at atmospheric pressure]. Prioritet 08.12.2015. (In Russ.).
36. Arseniev A.N., Muradymov M.Z., Krasnov N.V. Investigation of Electrospray Stability with Dynamic Liquid Flow Splitter. *Analytical Chemistry*, 2014, vol. 69, no. 14, pp. 30–32.
37. Nazimov I.V., Novikov A.V., Bublyaev R.A., Fironov S.I., Prisyach S.S., Muradymov M.Z., Krasnov N.V. [Analytical complex for the determination of the amino acid sequence of peptides]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2011, vol. 21, no. 4, pp. 22–26. URL: http://iairas.ru/mag/2011/abst4.php#abst2. (In Russ.).
38. Krasnov I.A., Bobkov D.E., Zaitseva M., Prisyach S.S., Krasnov N.V. [Development of HPLC-MS method for the analysis of ursodeoxycholic acid in the mode of registration of positively charged ions]. *Nauchnoe Priborostroenie* [Scientific Instrumentation], 2013, vol. 23, no. 1, pp. 44–51. URL: http://iairas.ru/mag/2013/abst1.php#abst5. (In Russ.).

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Article received in edition 17.08.2018

ISSN 0868–5886 НАУЧНОЕ ПРИБОРОСТРОЕНИЕ, 2018, том 28, № 4, с. 151–160

РАЗРАБОТКА ПРИБОРОВ И СИСТЕМ

УДК 338.001.36 + 338.012; 543.51; 577.112.5 + 621.384.8

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ИННОВАЦИОННОЕ НАПРАВЛЕНИЕ РАЗВИТИЯ НАУЧНОГО ПРИБОРОСТРОЕНИЯ — ВРЕМЯПРОЛЕТНЫЕ МАСС-СПЕКТРОМЕТРЫ

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Описаны прорывные научные исследования в области развития аналитического приборостроения, одного из направлений аналитического приборостроения — времяпролетной масс-спектрометрии. Создание отечественных времяпролетных масс-спектрометров реализует задачу импортозамещения зарубежного оборудования, и относится к значительному, рискованному для государственных организаций финансированию. Представлены не имеющие отечественных аналогов научные приборы, которые иллюстрируют развитие одного из наиболее перспективных направлений научного приборостроения. Времяпролетная масс-спектрометрия позволяет создавать самые мощные по чувствительности, информативности и быстроте малогабаритные аналитические системы с современным программным обеспечением для качественного и точного количественного анализа состава и структуры химических соединений.

Кл. сл.: масс-спектрометрия, источник ионов, электрораспыление жидкости, ионный поток, объемный заряд

СПИСОК ЛИТЕРАТУРЫ

1. *Слепак К.Б.* Развитие науки, образования и инновационных технологий в регионах России как фактор обеспечения национальной безопасности. Монография. СПб.: Издательство Политехнического университета, 2014. 192 с. ISBN 978-5- 7422-4577-3.
2. *Слепак К.Б.* Развитие научно-образовательного потенциала регионов России в процессе инновационного импортозамещения // Экономика и управление. 2015. № 7. С. 84–91.
3. *Слепак Б.С., Слепак К.Б.* Инновации в научном приборостроении // Научное приборостроение. 2017. Т. 27, № 4. С. 107–117.
URL: http://iairas.ru/mag/2017/abst4.php#abst13.
4. *Слепак Б.С., Слепак К.Б.* Инновационное направление научного приборостроения — мёссбауэровская спектроскопия как фактор совершенствования отраслей российской экономики. Ч. 1. Прорывные научные исследования в области мёссбауэровской спектроскопии // Научное приборостроение. 2018. Т. 28, № 1. С. 79–92.
URL: http://iairas.ru/mag/2018/abst1.php#abst10.
5. *Слепак Б.С., Слепак К.Б.* Инновационное направление научного приборостроения — мёссбауэровская спектроскопия как фактор совершенствования отраслей российской экономики. Ч. 2. Создание национального исследовательского оборудования в области мёссбауэровской спектроскопии // Научное приборостроение. 2018. Т. 28, № 2. С. 75–88.
URL: http://iairas.ru/mag/2018/abst2.php#abst11.
6. *Полушин Ю.С., Левшанков А.И., Лахин Р.Е., Пащинин А.Н., Безрукова Е.В., Пискунович А.Л., Костючек Д.Ф., Белозерова А.К., Гайдуков С.Н., Шапкайц В.А., Белозерова Л.А., Краснов Н.В.* Перспективы использования анализатора антиоксидантов в клинической практике для оценки неспецифической резистентности организма при различных критических состояниях и для прогнозирования акушерских осложнений // Научное приборостроение. 2013. Т. 23, № 3. С. 5–12.
URL: http://iairas.ru/mag/2013/abst3.php#abst1.
7. *Бубляев Р.А. Голиков Ю.К., Краснов Н.В.* Time-of-flight Mass Spectrometer. Патент на изобретение РФ № 2295797 от 6.06.2005.
8. *Алексеев Д.Н., Гаврик М.А., Монаков А.Г., Мурадымов М.З., Присяч С.С., Явор М.И., Краснов Н.В.* Устройство времяпролетного масс-спектрометра для разделения и регистрации ионов анализируемых веществ. Патент РФ на полезную модель №137381 от 10.02.2014.
9. *Назимов И.В., Мурадымов М.З., Бубляев Р.А., Гав-*

рик М.А., Присяч С.С., Краснов Н.В. Метод масс-спектрометрического секвенирования пептидов и определение их аминокислотных последовательностей. Патент на изобретение РФ № 2498443 от 10.11.2013.
10. *Мурадымов М.З., Семенов С.Ю., Краснов Н.В.* Устройство непрерывного стабильного электрораспыления растворов в источнике ионов при атмосферном давлении. Патент РФ на изобретение № 2587679 от 27.05.2016.
11. *Краснов М.Н., Краснов Н.В.* Устройство источника ионов-электроспрей для получения бескапельного стабильного ионного тока анализируемых веществ из растворов в течение длительного времени. Патент РФ на полезную модель № 169146 от 07.03.2017.
12. *Арсеньев А.Н., Монаков А.Г., Краснов М.Н., Краснов Н.В.* Устройство двухполярного малошумящего источника питания. Патент РФ на полезную модель № 174218 от 09.10.2017.
13. *Краснов М.Н., Краснов Н.В.* Способ образования бескапельного ионного потока при электрораспылении анализируемых растворов в источниках ионов с атмосферным давлением. Патент РФ на изобретение № 2613429 от 16.03.2017.
14. *Краснов М.Н., Мурадымов М.З., Краснов Н.В.* Способ непрерывного стабильного электрораспыления растворов в источнике ионов при атмосферном давлении. Патент РФ на изобретение № 2612324 от 07.03.2017.
15. *Арсеньев А.Н., Монаков А.Г., Краснов М.Н., Краснов Н.В.* Регулируемые двухполярные высокостабильные источники питания // Научное приборостроение. 2017. Т. 27, № 3. С. 8–17.
URL: http://iairas.ru/mag/2017/abst3.php#abst2.
16. *Арсеньев А.Н., Монаков А.Г., Краснов М.Н., Краснов Н.В.* Устройство двухполярного малошумящего источника питания. Патент РФ на полезную модель № 174218 от 09.10.2017.
17. *Помозов Т.В., Явор М.И.* Бессеточный ортогональной ускоритель для многоотражательных времяпролетных масс-анализаторов // Научное приборостроение. 2012. Т. 22, № 1. С. 113–120.
URL: http://iairas.ru/mag/2012/abst1.php#abst17.
18. *Помозов Т.В., Явор М.И., Веренчиков А.Н.* Рефлектроны с ортогональным ускорением ионов на основе планарных бессеточных зеркал // ЖТФ. 2012. Т. 82, вып. 4. С. 130–136.
19. *Samokish V.A., Muradymov M.Z., Krasnov N.V.* Electrospray ion sourse with a dynamic liquid flow splitter // Rapid Commun. mass spectrometry. 2013. Vol. 27, no. 8. P. 904–908. Doi 10.1002/rcm 6524.
20. *Голиков Ю.К., Краснова Н.К., Николаев В.И., Соловьев К.В.* Разделение ионов в комбинации стационарных полей — электрического квадрупольного и магнитного однородного // Научное приборостроение. 2013. Т. 23, № 1. С. 52–60.
URL: http://iairas.ru/mag/2013/abst1.php#abst6.
21. *Краснова Н.К., Голиков Ю.К., Елохин В.А., Николаев В.И.* Новый динамический масс-спектрометр с электрическим ударом // Научное приборостроение. 2013. Т. 23, № 1. С. 68–73.
URL: http://iairas.ru/mag/2013/abst1.php#abst8.
22. *Алексеев Д.Н., Арсеньев А.Н., Бельченко Г.В., Гаврик М.А., Монаков А.Г., Мурадымов М.З., Присяч С.С., Явор М.И., Зверева А.В., Зинин А.В., Мяльдзин Ш.У., Никитина С.Н., Помозов Т.В., Туртиа С.Б.* Аналитический комплекс ГХ-МС на базе времяпролетного масс-спектрометра с источником ионов "электронный удар" // Научное приборостроение. 2013. Т. 23, № 4. С. 95–103.
URL: http://iairas.ru/mag/2013/abst4.php#abst13.
23. *Арсеньев А.Н., Мурадымов М.З., Краснов Н.В.* Полевая десорбция ионов из острия на мениске жидкости при ЭГД-распылении // Научное приборостроение. 2014. Т. 24, № 3. С. 3–8.
URL: http://iairas.ru/mag/2014/abst3.php#abst1.
24. *Корякин П.С., Краснов И.А., Краснов Н.В., Мурадымов М.З., Краснов М.Н.* Ион-дрейфовый спектрометр с электрораспылительным источником ионов как детектор жидкостного хроматографа // Научное приборостроение. 2015. Т. 25, № 2. С.34–39.
URL: http://iairas.ru/mag/2015/abst2.php#abst3.
25. *Пашков О.В., Мурадымов М.З., Краснов М.Н., Краснов Н.В.* Характеристики факела электрораспыления с динамическим делением потока жидкости при атмосферном давлении // Научное приборостроение. 2015. Т. 25, № 3. С. 3–9.
URL: http://iairas.ru/mag/2015/abst3.php#abst1.
26. *Кузьмин Д.А, Мурадымов М.З., Помозов Т.В., Арсеньев А.Н., Краснов Н.В.* Транспортировка ионов в источниках с ионизацией при атмосферном давлении. I. Субстантивная геометрия // Научное приборостроение. 2017. Т. 27, № 4. С. 8–16.
URL: http://iairas.ru/mag/2017/abst4.php#abst2.
27. *Арсеньев А.Н., Мурадымов М.З., Краснов М.Н., Кузьмин Д.А., Помозов Т.В., Краснов Н.В.* Транспортировка ионов в источниках с ионизацией при атмосферном давлении. II. Инверсная геометрия // Научное приборостроение. 2017. Т. 27, № 4. С. 17–23.
URL: http://iairas.ru/mag/2017/abst4.php#abst3.
28. *Краснов М.Н., Краснов Н.В.* Устройство образования бескапельного ионного потока при электрораспылении анализируемых растворов в источниках ионов с атмосферным давлением. Патент РФ на изобретение № 2608361 от 2015.
29. *Мурадымов М.З., Пашков О.В., Краснов Н.В.* Устройство стабильного электрораспыления при атмосферном давлении растворов веществ для источников ионов. Патент РФ на изобретение № 2608362 от 2015.
30. *Alexandrov M.L, Gall L.N.. Krasnov N.V., Nikolaev V.I., Pavlenko V.A., Shkurov V.A.* Extraction of ions from solutions under atmos-pheric pressure as a method for mass spec-trometric analysis of bioorganic compounds // Rapid communications in mass spectrometry. 2008. No. 22. P. 267–270. Doi: 10.1002/rcm.3113.
31. *Полушин Ю.С., Левшанков А.И., Лахин Р.Е., Пащинин А.Н., Безрукова Е.В., Пискунович А.Л., Костючек Д.Ф., Белозерова А.К., Гайдуков С.Н., Шапкайц В.А., Белозерова Л.А., Краснов Н.В.* Перспективы использования анализатора антиоксидантов в клинической практике для оценки неспецифической резистентности организма при различных критических состояниях

и для прогнозирования акушерских осложнений // Научное приборостроение. 2013. Т. 23, № 3. С. 5–12. URL: http://iairas.ru/mag/2013/abst3.php#abst1.
32. *Аль-Тавил Е.А., Мурадымов М.З., Краснов М.Н., Краснов Н.В.* Электрораспыление проводящих растворов при нормальных условиях в широком диапазоне объемных скоростей // Научное приборостроение. 2017. Т. 27, № 2. С. 3–12.
URL: http://iairas.ru/mag/2017/abst2.php#abst1.
33. *Мурадымов М.З., Краснов Н.В.* Способ стабильного электрораспыления растворов в источнике при атмосферном давлении. Патент РФ на изобретение № 2608366 от 10.01.2017.
34. *Мурадымов М.З., Монаков А.Г. Краснов Н.В.* Устройство времяпролетного масс-спектрометра с источником ионов с ионизацией при атмосферном давлении для разделения и регистрации ионов анализируемых веществ. Патент РФ на изобретение № 158343 от 07.12.2015.
35. *Мурадымов М.З., Краснов Н.В.* Источник ионов с фотоионизацией при атмосферном давлении. Патент РФ на изобретение № 2572358 от 08.12.2015.
36. *Арсеньев А.Н., Краснов Н.В., Мурадымов М.З.* Исследования стабильности электрораспыления при динамическом делении потока жидкости // Масс-спектрометрия. 2014. Т. 11, № 1. С. 36–38.
37. *Назимов И.В., Новиков А.В., Бубляев Р.А., Фиронов С.И., Присяч С.С., Мурадымов М.З., Краснов Н.В.* Аналитический комплекс для определения аминокислотной последовательности пептидов // Научное приборостроение. 2011. Т. 21, № 4. С. 22–26.
URL: http://iairas.ru/mag/2011/abst4.php#abst2.
38. *Краснов И.А., Бобков Д.Е., Зайцева М., Присяч С.С., Краснов Н.В.* Разработка ВЭЖХ-МС-метода для анализа урсодезоксихолевой кислоты в режиме регистрации положительно заряженных ионов // Научное приборостроение. 2013. Т. 23, № 1. С. 44–51.
URL: http://iairas.ru/mag/2013/abst1.php#abst5.

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Материал поступил в редакцию: 17.08.2018