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(54) **Title**: A DUAL SOURCE MASS SPECTROMETRY SYSTEM

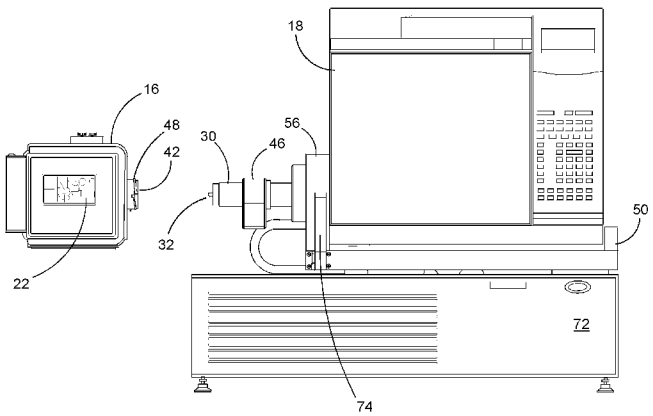

FIGURE 3

(57) **Abstract**: In or for a dual source mass spectrometer system (10) operable in a first mode with an LC source [LC/MS] (12) and in a second mode with a GC source [GC/MS] (18). The GC source input into an ion source chamber (22) for delivering the ionized output from the GC source to the mass spectrometer, a GC source unit (18) comprising a GC interface probe (30). The GC source unit is retractably mounted to take the GC interface probe from a retracted position in which it is disengaged from the mass spectrometer of the system, (whereby the system is operable in said first LC/MS mode) into a deployed position in which the GC interface probe is operatively connected to the ion source chamber of the mass spectrometer (whereby the system is operable in said second GC/MS mode). The GC interface probe has docking means (42, 46, 48) for releasable engagement with complementary docking means provided by a housing of the ion source chamber to allow operation with a GC ion source chamber in the second mode.

WO 2010/100509 A1

A DUAL SOURCE MASS SPECTROMETRY SYSTEM

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is directed generally to scientific laboratory analytical equipment, and more particularly, to the combination of Chromatography Systems and Mass Spectrometers.

2. Background of the Related Art

Scientific laboratories commonly need to analyse samples by the use of Chromatography in order to separate different constituents within the samples. Once the samples have been separated, they may need further analysis in order to identify what the different constituents are. Normally the most effective way of performing the analysis of the separated constituents is the use of mass spectrometers.

Chromatography can be performed either on gaseous samples or on liquid samples. However, the apparatus required to perform Liquid Chromatography and Gas Chromatography are rather different, so much so that different machines are required to perform the different analyses.

Mass spectrometers can be used to measure the mass of ions and analyse the structure of these ions, by studying fragmentation of the ions that may occur within the mass spectrometer. Chromatography systems typically produce molecules rather than ions, so the mass spectrometer needs to produce ions from the molecules that are delivered to it. This typically is performed in an ion source. There are many ways of ionizing the molecules that are injected into an ion source. Atmospheric Pressure Chemical Ionisation [APCI] is one of these methods. In this method, the molecules are sprayed into an ion source chamber and the spray is subjected to a corona discharge that creates ions.

APCI is a desirable fragmentation technique because it typically produces singly charged ions, and so the results of the analysis are easier to interpret. Furthermore

APCI is a method of ionization that is possible to use for samples that are both liquid and gaseous.

Mass Spectrometers are precise instruments, and so are expensive and delicate. Until recently, they have always been specifically designed for one of LCMS or GCMS and not for interchangable use. In the past also instruments have been designed to swap between GCMS and LCMS. However, the changeover has been time consuming and often the dual instruments compromised the performance on one or the other of the two techniques. This is especially true for Vacuum GCMS systems utilizing Electron Impact Ionization. The advantage of using APCI is that both LCMS and GCMS are operated at the same pressure and there is no need to change the MS other than to put an ion chamber on in place of a cone gas nozzle.

An attempt to provide a dual source mass spectrometry system comprises a mass spectrometer that has an ion source capable of being used for either LCMS or GCMS. However the design of the source is such that both an LCMS interface probe and a GCMS interface probe are permanently connected to an API source housing. This arrangement is an improvement over the use of separate LCMS and GCMS machines but is inefficient, and so cannot easily identify small quantities of analytes that may be present in the sample.

It would therefore be desirable to produce a Mass Spectrometer that is capable of efficiently analysing the output of either liquid or gas chromatography systems with easy transfer between the two different inputs, and with easy and minimal alterations required as now provided by the present invention.

It is envisaged that the dual source mass spectrometry system of the present invention has applications for example in synthetics confirmation and impurity profiling, natural products research, and in the fields of flavours and fragrances, nutraceuticals, petrochemicals, metabolomics, environmental screening, pesticide residue analysis and some forensic applications. The combination of LCMS and GCMS allows a wider range of compounds to be analyzed on a single instrument platform.

SUMMARY OF THE INVENTION

The present invention provides in or for a dual source mass spectrometer system operable in a first mode with an LC source [LC/MS] and in a second mode with a GC source [GC/MS], said GC source inputting into an ion source chamber for delivering the ionized output from the GC source to the mass spectrometer, a GC source unit comprising a GC interface probe wherein the GC source unit is retractably mounted to take the GC interface probe from a retracted position in which it is disengaged from the mass spectrometer of the system, whereby the system is operable in said first LC/MS mode, into a deployed position in which the GC interface probe is operatively connected to the ion source chamber of the mass spectrometer whereby the system is operable in said second GC/MS mode.

According to a feature of the invention, the GC interface probe may have docking means for releasable engagement with complementary docking means provided by a housing of the ion source chamber to allow operation with a GC ion source chamber in said second mode and to allow substitution of the GC ion source housing by an LC ion source housing to allow operation with the LC ion source housing in said first mode. Preferably, the docking means of the GC interface probe allows the probe to be progressively drawn into a docking port provided by the ion source housing and releasably locked in position. Preferably, the docking port comprises a screw-threaded nozzle incorporating sealing means and the GC interface probe comprises a complementary screw-threaded locking lever to releasably engage the nozzle whereby the probe can be sealingly coupled with the nozzle.

According to another feature of the invention, the GC source unit may incorporate a lockable rail system to allow slidable movement of the unit over the rail system so that it can be offered up to, and retracted from, the mass spectrometer of the system.

DESCRIPTION OF THE DRAWINGS

An embodiment of the invention will now be described, by way of example, with reference to the accompanying drawings, in which:-

Figure 1 is a perspective view of the dual source mass spectrometry system comprising an LC source unit, an MS unit and a GC unit;

Figure 2 is a cross-sectional view of the GC ion source housing and the GC interface probe;

Figure 2A is a schematic view of the GC transfer line showing the ion source enclosure or housing and the GC oven in the GC unit.

Figure 3 is a perspective view of the GC unit and the GC ion source housing with the GC interface probe in a retracted position;

Figure 4 is a view similar to Figure 3 but showing the GC interface probe offered up to the GC ion source housing;

Figure 5 is a view similar to Figure 4 but showing the GC interface probe engaged with the GC ion source housing in a deployed position;

Figure 6 is a perspective view of a slidable carriage which receives the GC unit and is mounted on rails to a base unit; and

Figure 7 is an exploded perspective view of the carriage, rail system and base unit.

SPECIFIC DESCRIPTION

Referring to the drawings there is shown a dual source mass spectrometry system 10 which comprises a liquid chromatography [LC] unit 12, a mass spectrometer [MS] unit 14, an ion source housing 16 which may be suitable for use with the LC unit or with the GC unit and a gas chromatography [GC] unit 18.

When it is required for the system to operate in LC/MS mode, the ion source housing 16 is one which is appropriate for use with a LC column of the LC unit 12 in which case the GC unit 18 is disengaged and retracted from the MS unit 14. In order to operate the system in GC/MS mode, the LC ion source housing (not shown) is substituted by a GC ion source housing and the GC unit 18 is put into a deployed position in which it is operatively connected to the MS unit.

Referring now to Figure 2 of the drawings, the GC ion source housing 16 incorporates an ion source chamber 22. The chamber 22 has at least one outlet port 24, at least one gas inlet (not shown), a sample port 26, and at least one corona pin port 28.

The housing 16 is made of a structural material such as plastics, metal, glass or ceramic. A preferred metal is stainless steel, titanium, aluminium, copper, brass and other alloys.

The sample port 26 is constructed and arranged to receive a GC interface probe 30 comprising a gas chromatographic column 32. The column is surrounded by a heated sheath gas tube 34. The gas chromatographic column 32 is for placing the analyte molecules in the chamber 22. The analyte molecules are suspended or dissolved in gas. The column has a mobile phase and a stationary phase and is used to separate components based upon their vapour pressure. When compounds elute from the column into the chamber they are in the vapour phase. Gas chromatographic columns are known in the art and are available from several venders. For example, without limitation, gas chromatographic columns are sold by Varian, Inc. (Palo Alto, California, USA) under several trademarks including FactorFour™, CP-Sil, and Select™.

Referring to Figure 2A, the sample port 26 receives the inner tube 27 of a transfer line 29 and transfer line tip 31 from which the column 32 protrudes. It is not a close fit but has a reasonable clearance with the transfer line to prevent the chamber from grounding on the metal transfer line. The outside wall of the column 32 and the inner diameter of the sample port cooperate to form a close fit. However, the fit need not be airtight. A gap allows excess gas in chamber 22 to vent and be carried off by a vent structure of the atmospheric pressure ionization housing. Thereby the chamber is swept out in the timescale of a chromatographic peak.

The gas inlet is constructed and arranged to be placed in fluid communication with a source of an inert gas [not shown] for placing the inert gas into the chamber 22. Inert gases comprise any substantially non-reactive gas, such as nitrogen. Such gases are sold by numerous venders under pressure in tanks.

The outlet port 24 is constructed and arranged to be received on or about an opening 36 of a vacuum region 38 of a mass spectrometer generally designated by the numeral 40. The opening 36 normally interfaces between the vacuum region 38 and an atmospheric pressure region of the atmospheric pressure ionization housing 16. The

atmospheric region may deviate slightly from atmospheric but is substantially near atmospheric pressure.

Opening 36 is formed in an inlet cone 42 which substantially fills the outlet port 24 to form a substantially closed chamber 22. The chamber 22 has a volume of 0.5 to 5.0 cc when the outlet port 24 is received on or about the opening 36 of the vacuum region 38.

The opening 36 of the vacuum region 38 defines a sample axis. A preferred sample port 24 is constructed and arranged to introduce analyte molecules 33 within sixty degrees of a line perpendicular to the sample axis.

The corona pin port 28 is constructed and arranged for receiving a corona discharge pin for discharging electrons. The discharged electrons place a charge on analyte molecules 33 (Figure 2) as the analyte molecules leave the gas chromatographic column 32. These charged and uncharged analyte molecules are circulated around the chamber 22 by the gas introduced through the gas inlet and received in the opening 36 of the vacuum region for mass analysis.

Preferably, the corona discharge port is constructed and arranged to place the corona discharge pin within the flow of the sample discharged from the gas chromatographic column 32. Usually, the corona discharge port is aligned with the sample axis allowing gases to circulate around the corona discharge pin.
Plasma formed by corona discharge into a gas consists of the carrier gas in combination with make-up gas supplied through the transfer inner tube 27 through a connecting line 35.

In the case of N2 make-up gas $N2^+$ and $N4^+$ are formed in the plasma then
$N2^+ + M > M^{+\cdot} + N2$
$N4^+ + M > M^{+\cdot} + 2N2$
In addition with trace amounts of moisture $H30^+$, then
$H30^+ + M > MH^+ + H20$
With higher concentrations of water $H^+ (H20)_n$, then
$H^+ (H20)_n + M > MH^+ + nH20$

Selective ionization can also be performed by photo-ionization.

The removal of the GC ion source housing 16 allows the mass spectrometer to receive liquid samples from an LC atmospheric pressure ionization source [not shown] in a conventional manner.

Referring to Figures 2, 3 and 4, the GC ion source housing 16 includes a nozzle 42 which forms part of complementary docking means for detachably receiving the GC interface probe 30 which incorporates the GC column 32. The nozzle includes a sealing O-ring 44 (Figure 2) by which the GC interface probe is sealingly engaged in the nozzle. Referring back to Figures 3 and 4, the GC interface probe 30 has another part of the complementary docking means which includes a rotatable screw-threaded locking lever 46 which co-operates with a mating screw-threaded portion 48 of the docking nozzle such that when the probe is offered up to the nozzle, engagement of the complementary screw-threaded parts by manipulation of the locking level causes the probe, and hence the GC column, to be progressively docked in the chamber 22 of the GC ion source housing 16.

In order to take the GC interface probe 30 from a retracted position in which it is disengaged from the GC ion source chamber, whereby the system is operable in a first LC/MS mode, into a deployed position in which the GC interface probe 30 is operatively connected to the GC ion source chamber, whereby the system is operable in a second GC/MS mode, as shown in Figure 5, the GC unit is slidably mounted on a rail system.

Referring now to Figures 6 and 7 of the drawings, details of the GC unit rail system are shown. The GC unit 18 (see Figures 1 to 5) is received in a carriage 50 which includes a floor 52 having a keel portion 54 and end walls 56, 58 respectively by which the GC unit 18 is secured to the carriage 50. End wall 56 includes an opening 60 through which the GC interface probe extends from the GC unit. The keel portion 54 is furnished with a pair of parallel rails 62, 64 (which operate in a manner similar to those found in office filing cabinets) which have runners fixed to opposed walls 66, 68 of a channel 70 formed in the upper face of a base unit 72 so that the keel portion sits with clearance in the channel. Thus the carriage (together with the GC unit 18)

can slide to and fro with respect to the base unit. A locking handle 74 is provided by the carriage to assist in the sliding movement of the carriage but also for manipulation to lock the rail 66 against the channel to prevent movement of the carriage relative to the base unit.

The travel of the carriage relative to the base unit is such that when the GC unit is retracted, the GC transfer probe is drawn clear of the MS unit and, at the extremity of its travel in the opposite direction, the GC transfer probe is presented to the docking nozzle so that the complementary docking means can progressively draw in the probe and hence the GC column for operative connection to the chamber.

CLAIMS

1. In or for a dual source mass spectrometer system operable in a first mode with an LC source [LC/MS] and in a second mode with a GC source [GC/MS], said GC source inputting into an ion source chamber for delivering the ionized output from the GC source to the mass spectrometer, a GC source unit comprising a GC interface probe wherein the GC source unit is retractably mounted to take the GC interface probe from a retracted position in which it is disengaged from the mass spectrometer of the system, whereby the system is operable in said first LC/MS mode, into a deployed position in which the GC interface probe is operatively connected to the ion source chamber of the mass spectrometer whereby the system is operable in said second GC/MS mode.

2. A GC source unit according to claim 1, wherein the GC interface probe has docking means for releasable engagement with complementary docking means provided by a housing of the ion source chamber to allow operation with a GC ion source chamber in said second mode and to allow substitution of the GC ion source housing by an LC ion source housing to allow operation with the LC ion source housing in said first mode.

3. A GC source unit according to claim 2, wherein the docking means of the GC interface probe allows the probe to be progressively drawn into a docking port provided by the ion source housing and releasably locked in position.

4. A GC source unit according to claim 3, wherein the docking port comprises a screw-threaded nozzle incorporating sealing means and the GC interface probe comprises a complementary screw-threaded locking lever to releasably engage the nozzle whereby the probe can be sealingly coupled with the nozzle.

5. A GC source unit according to any of the preceding claims wherein the GC source unit incorporates a lockable rail system to allow slidable movement of the unit over the rail system so that it can be offered up to, and retracted from, the mass spectrometer of the system.

6. A dual source mass spectrometer system substantially as hereinbefore described with reference to and as shown in the accompanying drawings.

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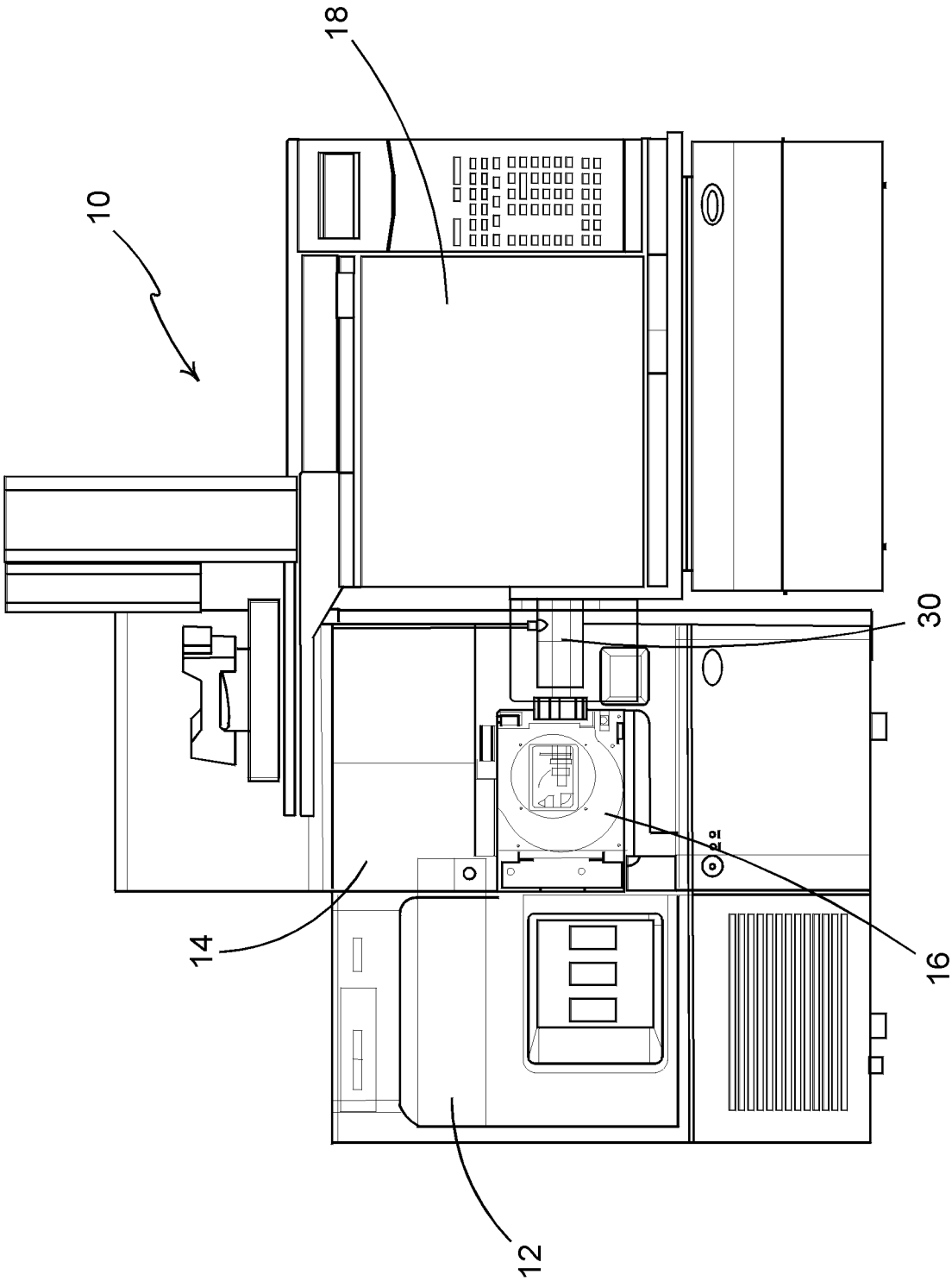

FIGURE 1

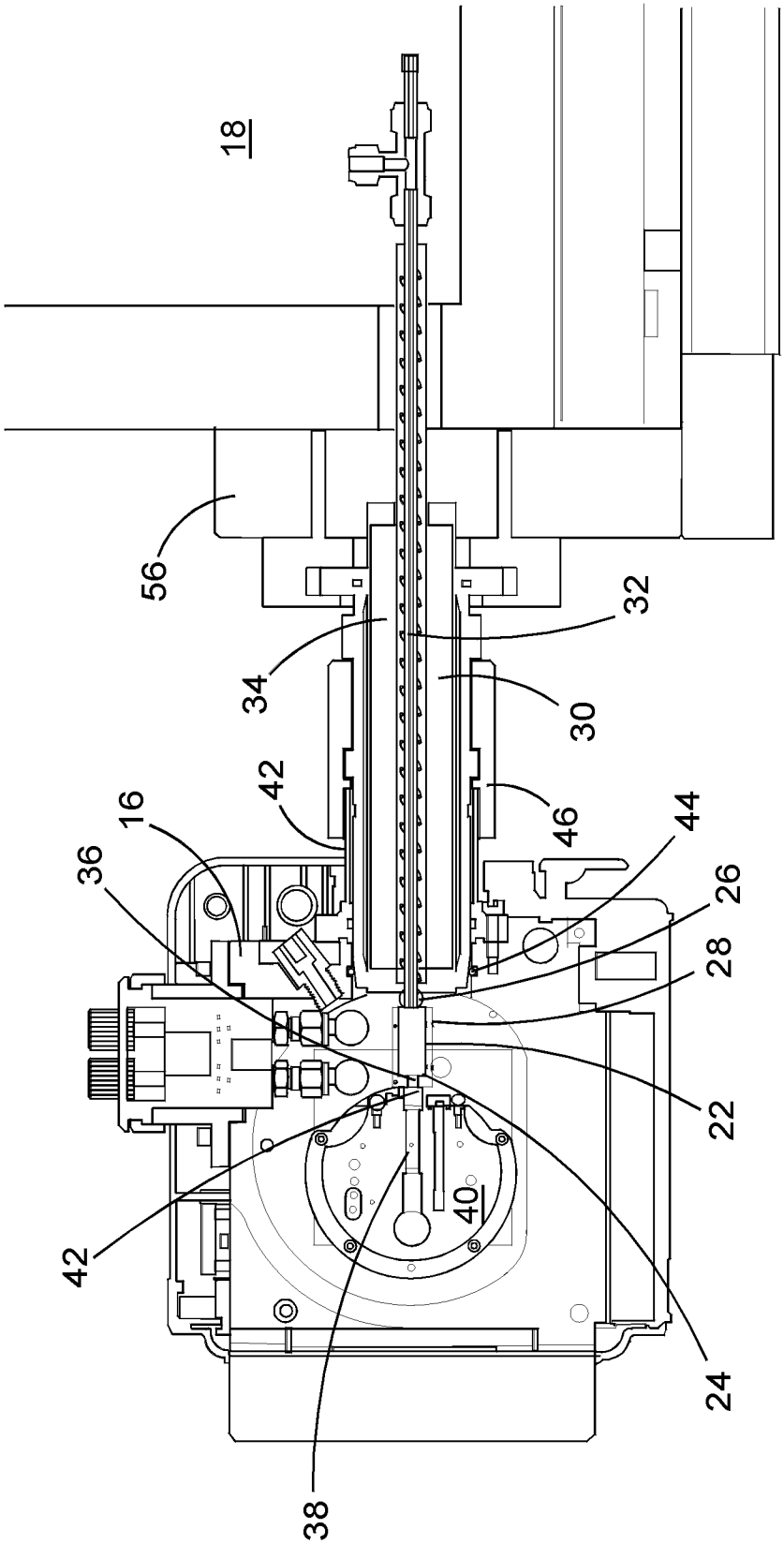

FIGURE 2

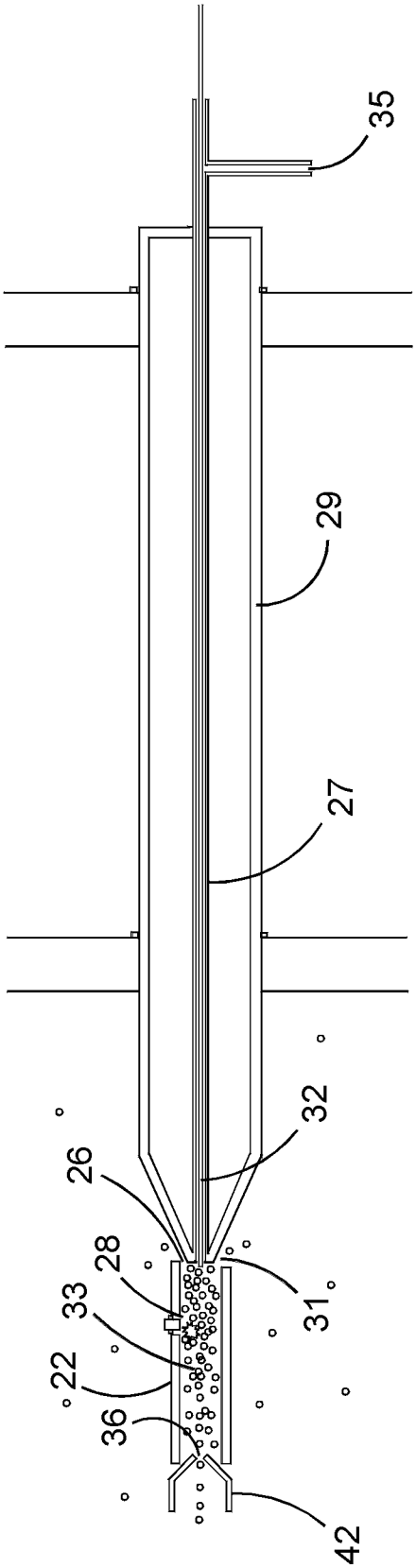

FIGURE 2A

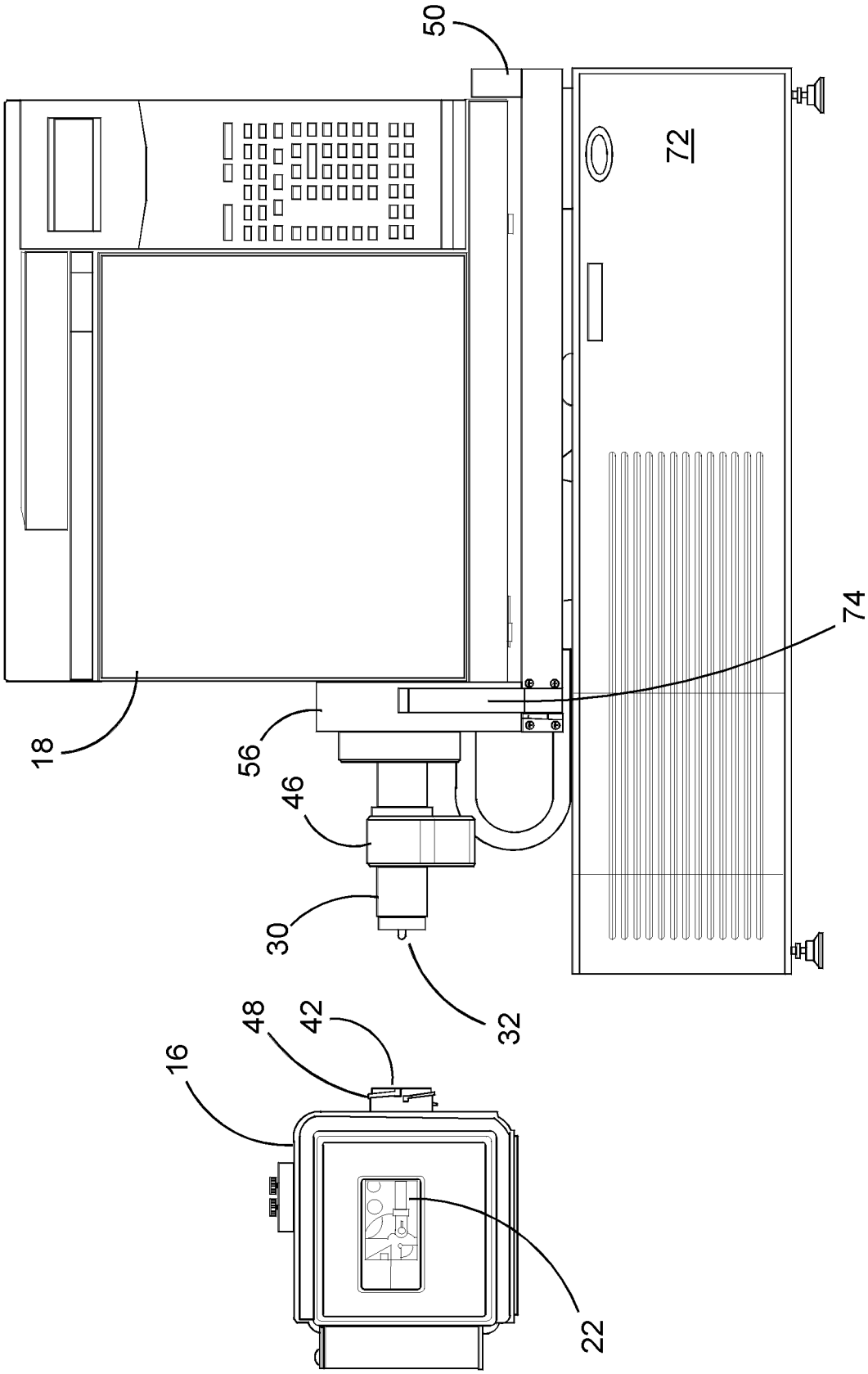

FIGURE 3

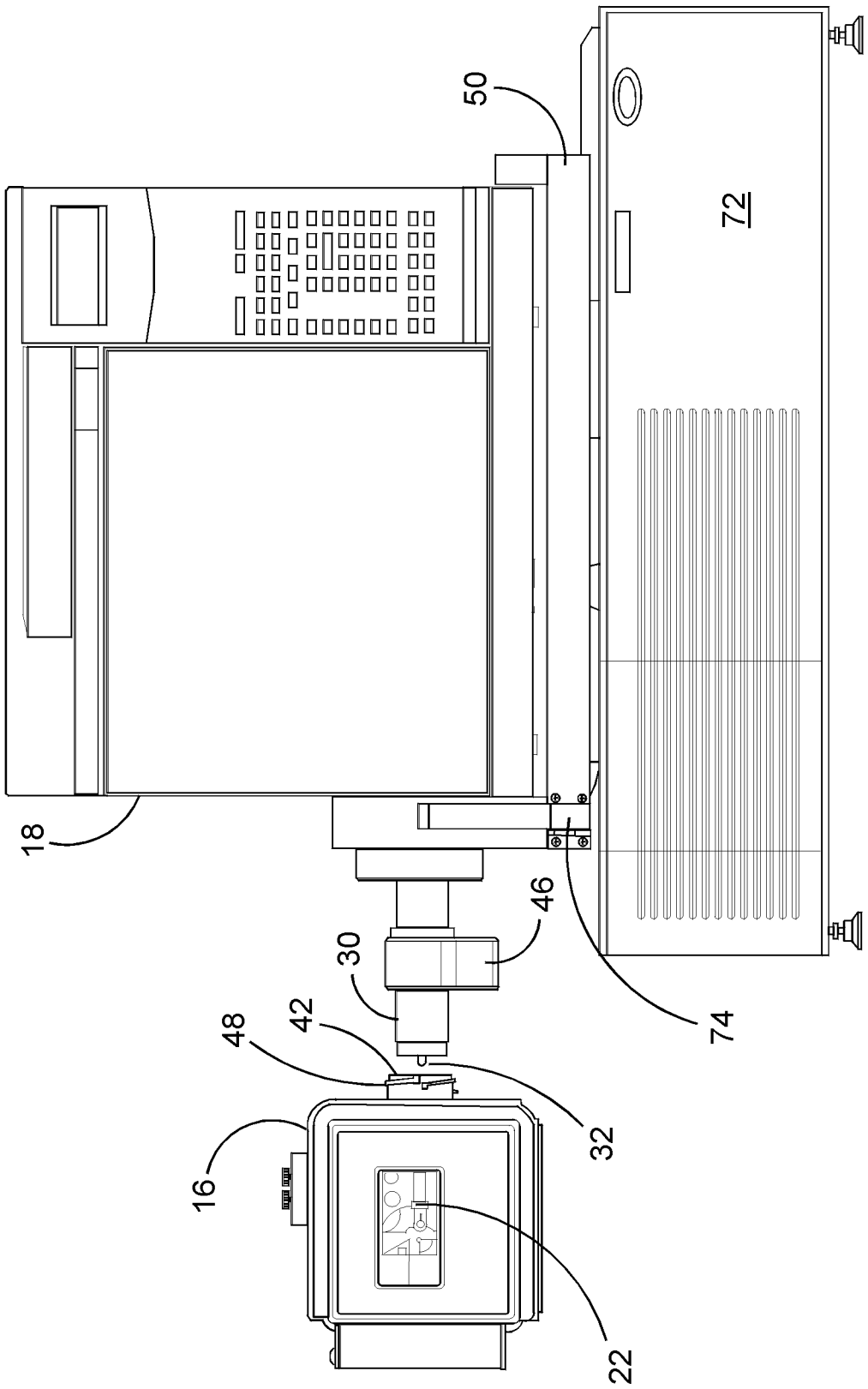

FIGURE 4

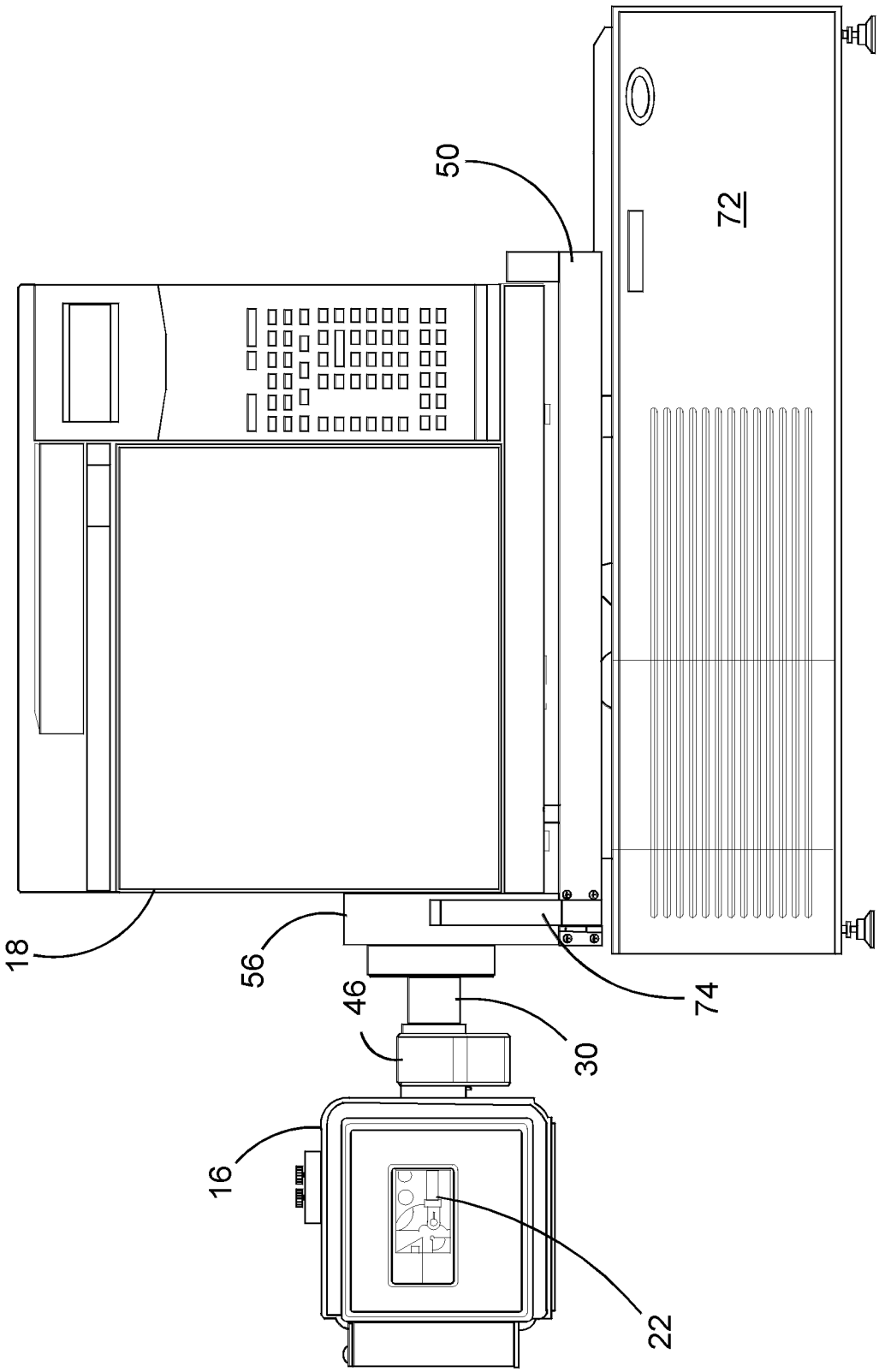

FIGURE 5

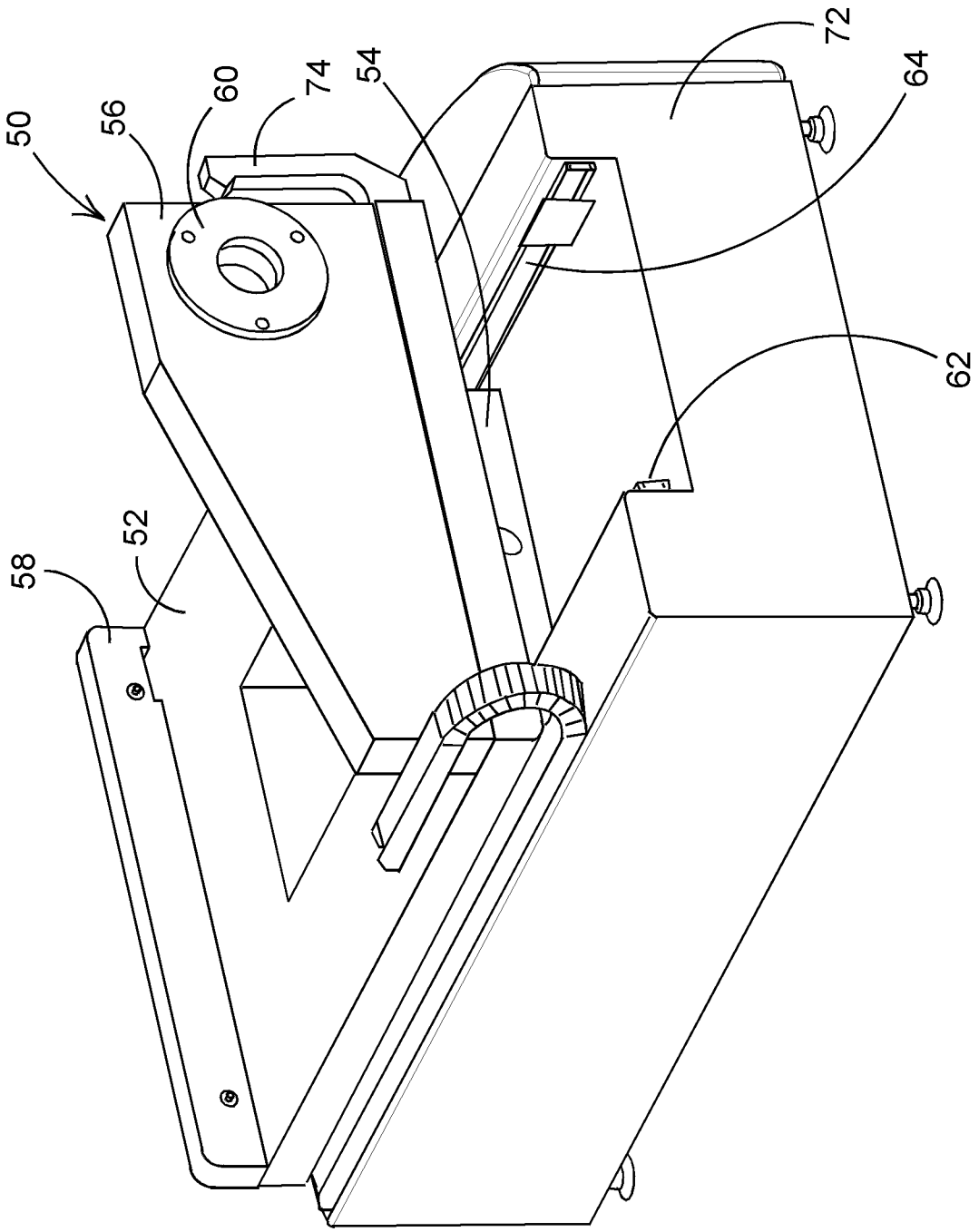

FIGURE 6

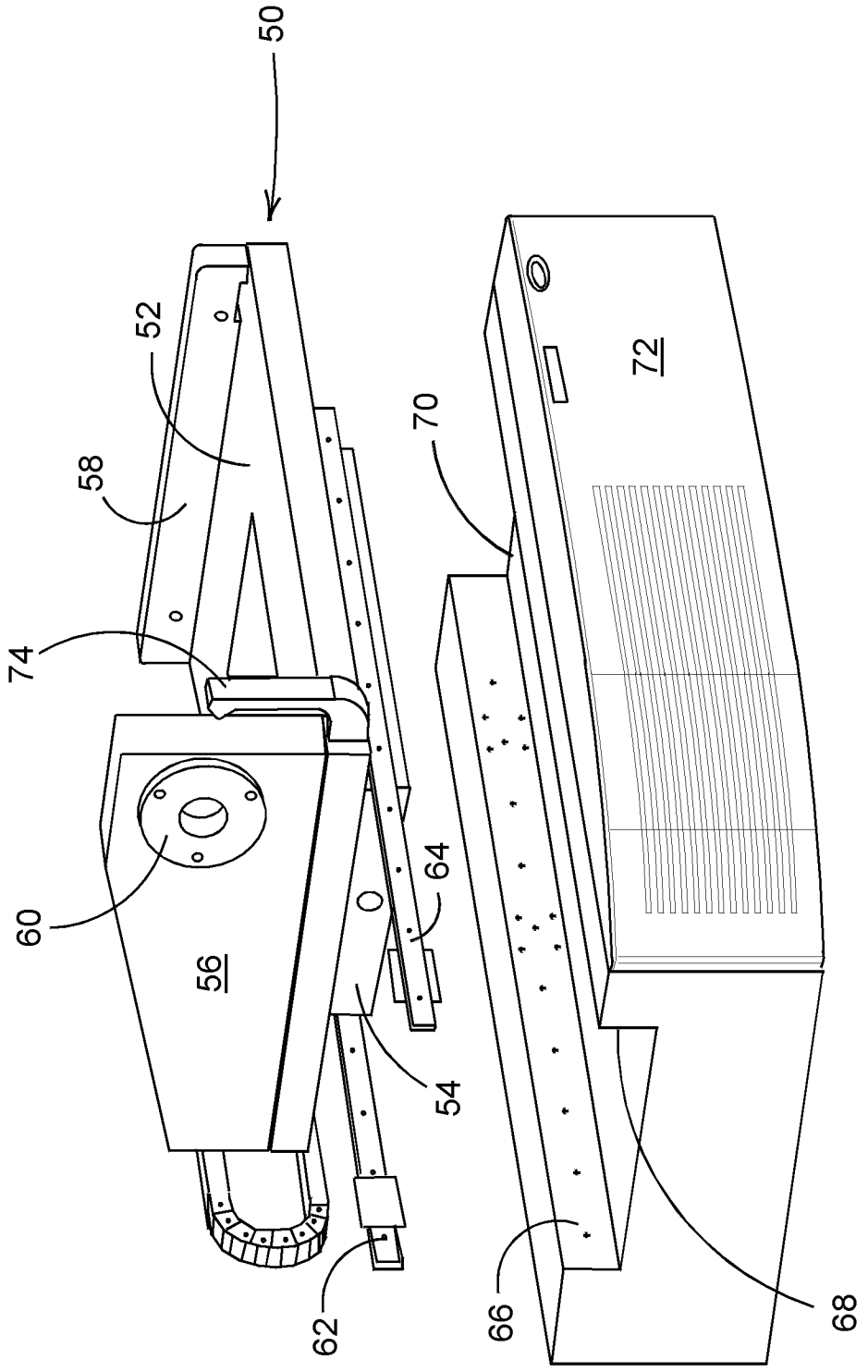

FIGURE 7

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2010/050393

A. CLASSIFICATION OF SUBJECT MATTER
INV. H01J49/04 G01N30/72
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
H01J G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/048107 A1 (MCEWEN CHARLES NEHEMIAH [US]) 28 February 2008 (2008-02-28) paragraphs [0003], [0005], [0012] paragraphs [0016], [0030] paragraph [0041] - paragraph [0049] paragraph [0055] - paragraph [0058] figure 1	1-6
X,P	WO 2009/137463 A1 (WATERS TECHNOLOGIES CORP [US]; JARRELL JOSEPH A [US]) 12 November 2009 (2009-11-12) page 5, line 19 - line 27 page 6, line 27 - line 29 page 9, line 4 - line 19	1-6
A	US 6 646 257 B1 (FISCHER STEVEN M [US] ET AL) 11 November 2003 (2003-11-11) the whole document	1-6

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[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 June 2010	06/07/2010

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2010/050393

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2008/296485 A1 (BENTER THORSTEN [DE] ET AL) 4 December 2008 (2008-12-04) the whole document	1-6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2010/050393

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2008048107 A1	28-02-2008	NONE	
WO 2009137463 A1	12-11-2009	NONE	
US 6646257 B1	11-11-2003	CN 1681579 A	12-10-2005
		EP 1539332 A1	15-06-2005
		JP 2005539358 T	22-12-2005
		WO 2004026448 A1	01-04-2004
		US 2004079881 A1	29-04-2004
US 2008296485 A1	04-12-2008	DE 102004025841 A1	15-12-2005
		WO 2005117062 A2	08-12-2005