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(54) **METHOD AND APPARATUS FOR MASS ANALYSING A FIRST SAMPLE**

(57) The invention relates to a method for mass analysing a first sample by ionising the first sample to first sample ions and obtaining mass spectra from the first sample ions with a mass analyser (207), wherein two or more assays are obtained from the first sample and each one of the assays is transferred to another first ion source (205.1, 205.2) and ionised by the respective first ion source (205.1, 205.2) to first sample ions. Thereby, the first sample is mass analysed in cycles, wherein in each cycle, consecutively for each one of the first ion sources (205.1, 205.2), the first sample ions ionised by the respective one of the first ion sources (205.1, 205.2) are transferred to the mass analyser (207) and at least one mass spectrum is obtained with the mass analyser (207) from the first sample ions ionised by and transferred from the respective one of the first ion sources (205.1, 205.2), the at least one mass spectrum being assigned to the respective one of the first ion sources (205.1, 205.2). The invention further relates to an apparatus (201) for mass analysing a first sample by executing the method according to the invention. This apparatus (201) includes an

assay obtaining device (203) for obtaining two or more assays from the first sample, first ion sources (205.1, 205.2) for ionising the assays to first sample ions, an assay guiding arrangement for transferring each one of the assays from the assay obtaining device to the corresponding one of the first ion sources for ionising the respective one of the assays to the first sample ions. Furthermore, the apparatus (201) includes a mass analyser (207) for mass analysing said first sample ions, and an ion guiding arrangement (206) for transferring from each one of the first ion sources (205.1, 205.2) the first sample ions ionised by the respective one of the first ion sources (205.1, 205.2) to the mass analyser (207) for obtaining with the mass analyser (207) at least one mass spectrum from the first sample ions ionised by and transferred from the respective one of the first ion sources (205.1, 205.2), the at least one mass spectrum being assigned to the respective one of the first ion sources (205.1, 205.2).

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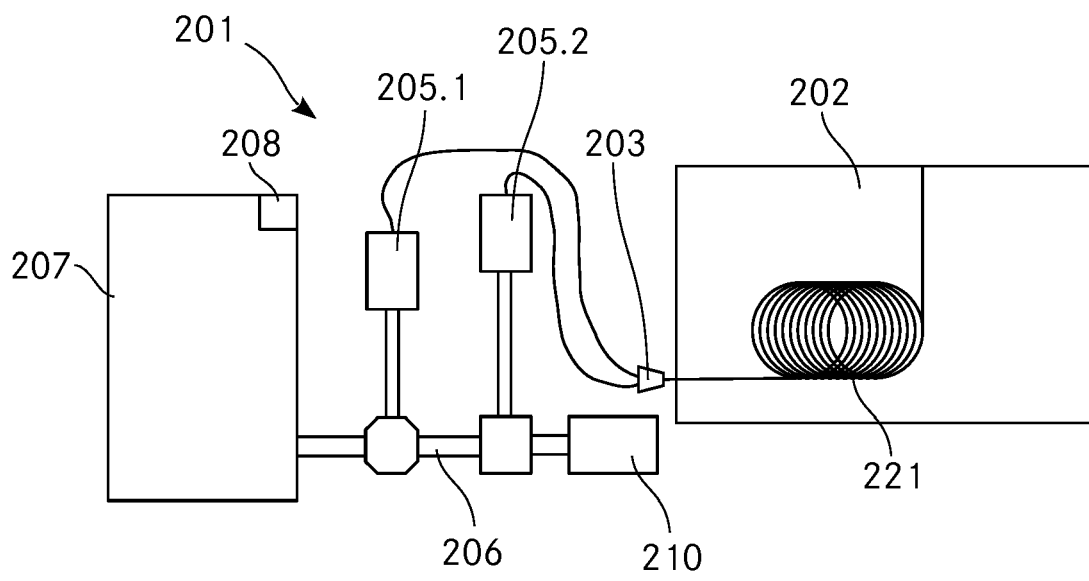


Fig. 3

Description

Technical Field

[0001] The invention relates to a method for mass analysing a first sample by ionising the first sample to first sample ions and obtaining mass spectra from the first sample ions with a mass analyser. Furthermore, the invention relates to an apparatus for mass analysing the first sample by executing the method according to the invention.

Background Art

[0002] Shared across many domains of analysis like food safety, environmental research, clinical research, forensic toxicology and doping control, the requirement to detect and determine very high numbers of known and unknown substances in a wide variety of sample matrices is essential. The levels of substance abundance within a single sample is thereby often ranging from sub $\mu\text{g/kg}$ level to low mg/kg level which makes the simultaneous detection of the different substances challenging.

[0003] In the literature, the analysis of such samples is broadly shown to be a very difficult task. In almost every case, unknown compounds can exist in such a sample in high concentration and/or in severe toxic potential. Nowadays, many scientists in the mentioned fields even believe that the concentration of unknown compounds exceed by far the concentration of the known compounds.

[0004] In case of targeted analysis, where the analysis is focused on specific, known and thus targeted compounds, the information about the unknown and thus untargeted compounds is often lost. Therefore, these targeted methods have to be expanded to include the information about non-targeted substances.

[0005] Methods and apparatuses pertaining to the technical field have been employed when it came to extend targeted analysis methods to non-targeted analysis methods. For example, since the end of the 20th century, the application of soft ionisation methods like electrospray ionisation (ESI) and atmospheric pressure ionization (APCI) in mass spectrometry have shown to maintain higher sensitivities as well as more limited fragmentation of molecules to be detected. Furthermore, more robust and more sensitive high resolution mass spectrometers (HRMS) have become available. These high resolution mass spectrometers allow the separation of substances with smaller mass differences. Furthermore, the high-speed-internet opened up completely new possibilities for researchers to exchange and process data. Since the 2010s, the development of online mass spectral libraries like for example *MassBank*, *METLIN* and *mzCloud* and analysis software packages have enabled processing huge amounts of data generated by the new techniques.

[0006] All these factors enable a broader, non-targeted analysis of samples. Nonetheless, non-targeted analysis

is still difficult and unknown compounds in a sample can often not be identified as desired.

Summary of the invention

[0007] It is the object of the invention to create a method and an apparatus for analysing a first sample by ionising the first sample to first sample ions and obtaining mass spectra from the first sample ions with a mass analyser, the method and apparatus pertaining to the technical field initially mentioned, that enable an improved non-targeted analysis of the first sample.

[0008] The solution of the invention is specified by the features of claim 1. According to the invention, two or more assays are obtained from the first sample and each one of the assays is transferred to another first ion source and ionised by the respective first ion source to first sample ions. Furthermore, the first sample is mass analysed in cycles, wherein in each cycle, consecutively for each one of the first ion sources, the first sample ions ionised by the respective one of the first ion sources are transferred to the mass analyser and at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the respective one of the first ion sources, the at least one mass spectrum being assigned to the respective one of the first ion sources.

[0009] For the solution according to the invention, the first sample can be of any type of sample. The first sample can be a gaseous sample, a liquid sample, a solid sample or a mixture of those. Furthermore, the first sample can be a confined sample which can be stored and transported in some sample container like a bottle, a box or the like. Or, the first sample can be a non-confined sample like for example ambient air, water in a waterway or aerosol particles and/or liquid particles dispersed in gas emerging from an exhaust of a machine or factory.

[0010] In the solution according to the invention two or more assays obtained from the first sample preferably comprise essentially the same distribution of constituent parts as the first sample. Particular preferably, the two or more assays obtained from the first sample comprise the same distribution of constituent parts as the sample. In order to obtain the two or more assays from the first sample, the assays are divided from the first sample. Thereby, after dividing the assays from the sample, there may be some part of the sample remaining. This remaining part preferably comprises essentially the same distribution of constituent parts as the first sample, particular preferably the same distribution of constituent parts as the first sample. This remaining part of the sample is however not referred to in the present text as assay because it is not transferred to one of the first ionisation sources and ionised by the respective first ion source. In case no such part of the sample is remaining after the assays are divided from the first sample, the first sample is divided into the two or more assays. This latter variant has the advantage that the entire first sample is transferred to

the first ion sources, ionised to the first sample ions and subsequently mass analysed with the mass analyser.

[0011] According to the invention, each one of the assays is transferred to another first ion source and ionised by the respective first ion source to first sample ions. Thus, a same number of first ion sources is employed as the number of assays obtained from the first sample. Consequently, since two or more assays are obtained from the first sample, two or more first ion sources are employed. Thereby, it is irrelevant whether these two or more first ion sources are of a same type or of a different type.

[0012] According to the invention, the first sample is mass analysed in cycles. Preferably, the first sample is thereby mass analysed by consecutively executing the same cycle twice or more times.

[0013] According to the invention, in each cycle, consecutively for each one of the first ion sources, the first sample ions ionised by the respective one of the first ion sources are transferred to the mass analyser and at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the respective one of the first ion sources, the at least one mass spectrum being assigned to the respective one of the first ion sources. Thus, each one of the at least one mass spectrum obtained from the first sample ions is obtained from first sample ions which have been ionised by one of the first ion sources, wherein the respective at least one mass spectrum is assigned to the respective one of the first ion sources. Thereby, the assignment of the respective at least one mass spectrum to the respective one of the first ion sources can for example be achieved by storing information on the respective one of the first ion sources together with the respective mass spectrum or by storing the respective mass spectrum in a memory or data storage assigned to mass spectra from the respective one of the first ion sources.

[0014] According to the invention, during each cycle, consecutively for each one of the first ion sources, at least one mass spectrum is obtained and assigned to the respective one of the first ion sources. Thus, during each cycle, at least a same number of mass spectra is obtained with the mass analyser as the number of first ion sources that are employed and as the number of assays that are obtained from the first sample. Thereby, to each one of the first ion sources, at least one of the obtained mass spectra is assigned.

[0015] Since the first sample is mass analysed in cycles, during each cycle, preferably a sequence is performed wherein each element of the sequence is linked to one of the first ion sources in that the respective element begins with starting transferring the first sample ions ionised by the corresponding one of the first ion sources to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the first sample ions ionised by and transferred from the corresponding one of the first ion sources and in that the respective element ends with stopping transferring the first

sample ions ionised by the corresponding one of the first ion sources to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the first sample ions ionised by and transferred from the corresponding one of the first ion sources. Thus, in this picture of a sequence with elements, each element is linked to one of the first ion sources.

[0016] In a preferred variant, in each cycle, consecutively for each one of the first ion sources, exactly once for one continuous period of time the first sample ions ionised by the respective one of the first ion sources are transferred to the mass analyser and at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the respective one of the first ion sources, the at least one mass spectrum being assigned to the respective one of the first ion sources. In the before mentioned picture of the sequence being performed during each cycle, in this preferred variant, the sequence comprises a same number of elements as assays are obtained from the first sample. Thereby, each element is linked to another one of the first ion sources.

[0017] In a further preferred variant, the sequence comprises more elements than assays are obtained from the first sample. Thereby, to each one of the first ion sources, at least one element of the sequence is linked. At least two elements of the sequence however are linked to a same one of the first ion sources. In this variant, preferably the at least two elements of the sequence which are linked to the same one of the first ion sources are separated in the sequence by at least one other element of the sequence.

[0018] Since the first sample is mass analysed in cycles, wherein in each cycle, consecutively for each one of the first ion sources, the first sample ions ionised by the respective one of the first ion sources are transferred to the mass analyser, the first sample ions are preferably transferred from the different first ion sources to the mass analyser in a pulsed manner. Thereby, in a first variant, for each one of the first ion sources, the first sample ions ionised by the respective one of the first ion sources are ionised in pulses, in particular in the pulses in which the first sample ions are transferred to the mass analyser. In a second variant, for each one of the first ion sources, the first sample ions ionised by the respective one of the first ion sources are ionised continuously, wherein the first sample ions are transferred in pulses to the mass analyser. In this second variant, the first sample ions are accumulated in an ion trap from where they are transferred in pulses to the mass analyser or are transferred in a continuous beam of first sample ions originating from the respective continuous first ion source, the continuous beam being repeatedly directed into an entrance of the mass analyser and subsequently away to miss the entrance of the mass analyser for transferring the first sample ions ionised by the respective continuous first ion source to the mass analyser in a pulsed manner. This can for example be achieved by switching the ion optics

in the path of the first sample ions from the respective continuous first ion source to the mass analyser.

[0019] The solution of the invention is further specified by an apparatus for mass analysing a first sample by executing the method according to the invention. This apparatus includes an assay obtaining device for obtaining two or more assays from the first sample, first ion sources for ionising the assays to first sample ions, an assay guiding arrangement for transferring each one of the assays from the assay obtaining device to the corresponding one of the first ion sources for ionising the respective one of the assays to the first sample ions. Furthermore, the apparatus includes a mass analyser for mass analysing the first sample ions, and an ion guiding arrangement for transferring from each one of the first ion sources the first sample ions ionised by the respective one of the first ion sources to the mass analyser for obtaining with the mass analyser at least one mass spectrum from the first sample ions ionised by and transferred from the respective one of the first ion sources, the at least one mass spectrum being assigned to the respective one of the first ion sources.

[0020] The method and the apparatus according to the invention have the advantage that mass spectra from ions ionized by two or more different first ion sources but originating from one and the same sample, i.e. the first sample, can be obtained quasi-simultaneously, wherein each mass spectrum comprises only information about the ions ionised with one of the first ion sources. Thus, a broader range of information can be gathered from one and the same first sample in one measurement run because different types of ionisation sources can be used for the different first ion sources. This is particular advantageous in case the first sample changes over time on a timescale slower than a time required by the mass analyser for obtaining one mass spectrum. Thereby, the timescale over which the first sample changes is not required to be slower by many orders of magnitude than the time required by the mass analyser for obtaining one mass spectrum but can be in the same order of magnitude as the time required by the mass analyser for obtaining one mass spectrum.

[0021] Independent of whether the first sample changes over time or not, an improved non-targeted analysis of the first sample is enabled with the method and apparatus according to the invention because a broader range of information can be gathered from one and the same first sample in one measurement run.

[0022] Advantageously, during each cycle, for each one of the first ion sources, at least five, particular advantageously at least ten mass spectra are obtained from the first sample ions transferred from and ionised by the respective one of the first ion sources. Particular advantageously, during each cycle, for each one of the first ion sources the at least five or at least ten mass spectra are obtained in direct succession from each other from the first sample ions transferred from and ionised by the respective one of the first ion sources. In a variant however,

during each cycle, for each one of the first ion sources, less than five mass spectra are obtained from the first sample ions transferred from and ionised by the respective one of the first ion sources. In a further variant, during each cycle, for each one of the first ion sources, exactly one mass spectrum is obtained from the first sample ions transferred from and ionised by the respective one of the first ion sources.

[0023] In case during each cycle, for each one of the first ion sources more than one mass spectra is obtained with the mass analyser from the first sample ions transferred from the respective one of the first ion sources, preferably during each cycle, the more than one mass spectra obtained with the mass analyser from the first sample ions transferred from and ionised by the respective one of the first ion sources are added up to one mass spectrum assigned to the respective first ion source. This has the advantage that the obtained mass spectra provide statistically more significant information.

[0024] Alternatively, however, during each cycle, for each one of the first ion sources more than one mass spectra are obtained with the mass analyser from the first sample ions transferred from the respective one of the first ion sources, during each cycle, the more than one mass spectra obtained with the mass analyser from the first sample ions transferred from and ionised by the respective one of the first ion sources are maintained separately.

[0025] In a preferred variant, each one of the at least one mass spectrum is obtained from the first sample ions that have been ionised by a one of the first ion sources, wherein the respective at least one mass spectrum is assigned to the respective one of the first ion sources and to the cycle in which the respective mass spectrum has been recorded. This has the advantage that a time evolution of the first sample during the mass analysis can easily be analysed because for each mass spectrum, the cycle in which it was recorded is known while at the same time, the first ion source from which the first sample ions used for obtaining the respective mass spectrum is known, too.

[0026] Alternatively, the mass spectra obtained from the first sample ions are not assigned to the cycle in which they have been recorded.

[0027] Advantageously, the first ion sources with which the assays are ionised to the first sample ions are switched in parallel with respect to each other. This has the advantage that different types of ion sources using different ionisation conditions like for example different gas pressures in a region where the respective assay is ionised to first sample ions can be employed as first ion sources. Alternatively, the first ion sources with which the assays are ionised to first sample ions are switched in series with respect to each other.

[0028] Preferably, each one of the cycles has a duration in time of 1 second or less, particular preferably 0.1 seconds or less, most preferably 0.01 seconds or less. This has the advantage that changes in the first sample

can easily be detected and analysed with a time resolution of the mentioned duration of the individual cycles. Thus good analysis of changing samples is enabled.

[0029] Preferably, a repetition rate of the cycles is 1 Hz or more, particular preferably 10 Hz or more, most preferably 100 Hz or more. In a variant, however, the repetition rate of the cycles is less than 1 Hz.

[0030] Alternatively, at least one of the cycles has a duration in time of more than 1 seconds.

[0031] Preferably, during each cycle, consecutively for each one of the first ion sources, the first sample ions ionised by the respective one of the ion sources are transferred to the mass analyser and the at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the respective one of the first ion sources during a time of less than 0.5 seconds, particular preferably less than 0.05 seconds, most preferably less than 0.005 seconds.

[0032] Alternatively, one of the at least one mass spectrum is obtained from the first sample ions ionised by and transferred from the respective one of the first ion sources during a time of 0.5 seconds or more.

[0033] Advantageously, in the present text, a mass spectrum refers to an array of data points and represents the ions of the mass analysed sample ordered in accordance with their mass per charge ratio, wherein each data point is assigned to a particular mass per charge ratio or a particular range of mass per charge ratios and each data point indicates the number of ions which have a mass per charge ratio matching the particular mass per charge ratio or being within the particular range of mass per charge ratios assigned to the respective data point. Thereby, the data points are not required to provide the exact number of ions which have a mass per charge ratio matching the particular mass per charge ratio or being within the particular range of mass per charge ratios assigned to the respective data point. As the data points indicate the number of ions which have a mass per charge ratio matching the particular mass per charge ratio or being within the particular range of mass per charge ratios assigned to the respective data point, it is sufficient if the data points provide a measure proportional to the number of ions which have a mass per charge ratio matching the particular mass per charge ratio or being within the particular range of mass per charge ratios assigned to the respective data point.

[0034] Advantageously, the mass analyser provides mass spectra each with at least 5'000 data points, particular advantageously each with at least 8'000 data points, most advantageously with at least 10'000 data points. The higher the number of data points in the mass spectra is, the more detailed the mass analysis is. Alternatively however, the mass analyser provides mass spectra each with less than 5'000 data points.

[0035] Preferably, at least one of the first ion sources is a continuous ion source. Thereby, a continuous ion source is advantageously an ion source to which the sample or assay to be ionised can be transferred continuously

and which provides a continuous beam of ions of the ionised sample or assay. At least one of the first ion sources being a continuous ion source has thus the advantage that the respective assay is continuously ionised to first sample ions whenever the respective assay is transferred to the first ion source being a continuous ion source.

[0036] Particular preferably, all of the first ion sources are continuous ion sources.

[0037] In case one or more of the first ion sources are continuous ion sources, preferably a continuous beam of first sample ions originating from the respective continuous first ion source is repeatedly directed into an entrance of the mass analyser and subsequently away to miss the entrance of the mass analyser in order to transfer the first sample ions ionised by the respective continuous first ion source to the mass analyser in a pulsed manner, wherein whenever the beam is directed away to miss the entrance of the mass analyser, the beam is directed to an ion detector for detecting a number of the first sample ions in the beam during the time the beam is directed away to miss the entrance of the mass analyser. Thereby, a Faraday Cup, an electron multiplier or a micro-channel plate (MCP) detector can for example be employed as ion detector. Independent of the type of ion detector, detecting the number of first sample ions in the beam during the time the beam is directed away to miss the entrance of the mass analyser has the advantage that a quantification of the mass spectra assigned to the corresponding continuous first ion source is simplified and improved.

[0038] In a variant however, the beam of first sample ions is not directed to an ion detector for detecting a number of the first sample ions in the beam during the time the beam is directed away to miss the entrance of the mass analyser.

[0039] Alternatively to these variants, none of the first ion sources is a continuous ion source.

[0040] Preferably, one of the first ion sources is a chemical ionisation ion source. This has the advantage that with the one of the first ion sources being a chemical ionisation ion source, a soft ionisation of the respective assay to first sample ions can be achieved. Consequently, in case the first sample comprises molecules as constituent parts, these molecules are maintained to a large extent without fragmentation during their ionisation to first sample ions. Consequently, in the mass spectra assigned to the one of the first ion sources being the chemical ionisation ion source comprise information about the mass to charge ratio of the molecules.

[0041] Alternatively, none of the first ion sources is a chemical ionisation ion source.

[0042] Advantageously, one of the first ion sources is an electron ionisation ion source, in particular a 70 eV electron ionisation ion source. This has the advantage that with the one of the first ion sources being an electron ionisation ion source, a hard ionisation of the respective assay to first sample ions is achieved. Consequently, in

case the first sample comprises molecules as constituent parts, these molecules are likely to become fragmented during their ionisation to first sample ions. Consequently, in the mass spectra assigned to the one of the first ion sources being the electron ionisation ion source comprise information about the mass to charge ratio of the fragments of the molecules. This provides additional information on the constituent parts of the sample.

[0043] One of the first ion sources being a 70 eV electron ionisation ion source has the further advantage that loads of generic libraries of mass spectra of different compounds are available for identifying the constituent parts of the first sample. This is a tremendous advantage when employing the method for non-targeted analysis. In a variant, the one of the first ion sources being an electron ionisation ion source is not a 70 eV electron ionisation ion source.

[0044] Alternatively, none of the first ion sources is an electron ionisation ion source.

[0045] In a preferred variant, one of the first ion sources is a chemical ionisation ion source and one of the first ion sources is an electron ionisation ion source, in particular a 70 eV electron ionisation ion source. This variant has the advantage that from the different mass spectra, information about the entire molecules and about the fragments of the molecules can be obtained. Based from these complementary information, more constituent parts of the first sample can be identified, which is particular advantageous for non-targeted analysis.

[0046] Preferably, before obtaining the two or more assays from the first sample, the first sample is chromatographically separated in a chromatographic column, in particular gas chromatographically separated in a gas chromatographic column or liquid chromatographically separated in a liquid chromatographic column. This has the advantage that due to the chromatographic separation, another separation dimension as compared to the mass spectra is obtained. Thus, more detailed analysis of the first sample is enabled, which is particular advantageous for non-targeted analysis.

[0047] In case the first sample is chromatographically separated in gas chromatographic column, each one of the cycles has preferably a duration in time of 1 second or less, particular preferably 0.1 seconds or less, most preferably of 0.01 seconds or less. Since in gas chromatography, the peaks usually have a full width at half maximum of one to two seconds, this has the advantage that each one of the gas chromatography peaks is mass spectrometrically sampled in multiple cycles, enabling a more detailed analysis of the first sample. In a variant however, at least one of the cycles has a duration of more than 1 seconds.

[0048] Alternatively to these variants, the first sample is not chromatographically separated in a chromatographic column before obtaining the two or more assays from the first sample.

[0049] Advantageously, the mass analyser is a time of flight mass analyser. This has the advantage that a broad

range of mass to charge ratios of the first sample ions can be depicted in the mass spectra.

[0050] Alternatively, the mass analyser is another type of mass analyser like for example an ion trap mass analyser, in particular an orbitrap mass analyser.

[0051] Advantageously, the first sample ions ionised by one of the first ion sources are separated according to their mobility in a drifting region before being mass analysed by the mass analyser.

[0052] Thereby, the drifting region is arranged between the respective one of the first ion sources and the mass analyser and the respective first sample ions are guided through the drifting region for separating the respective first sample ions according to their ion mobility.

Thereby, a gas pressure of a gas, preferably an inert gas, is maintained in the drifting region, the gas pressure being preferably reduced as compared to atmospheric pressure, wherein the first sample ions are preferably pulled by a static electric field through the drifting region or transported through the drifting region by an electromagnetic wave or potential wells moving along the drifting region.

[0053] In a preferred variant, the first sample ions ionised by all said first ion sources are separated according to their mobility in the drifting region before being mass analysed by the mass analyser.

[0054] In this case, the apparatus according to the invention preferably includes this drifting region.

[0055] Alternatively, the apparatus may go without the drifting region and in the method, the first sample ions are not separated according to their mobility in a drifting region before being mass analysed by the mass analyser.

[0056] Advantageously, in parallel to the mass analysis of the first sample by ionising the first sample to first sample ions and obtaining mass spectra from the first sample ions with the mass analyser, a second sample is mass analysed by ionising the second sample to second sample ions and obtaining mass spectra from the second sample ions with the mass analyser. This has the advantage that two samples can be analysed simultaneously. In one example one of the first and the second sample is the sample of interest while the other one of the first and the second sample is a reference sample in order to be able to compare the analysis of the sample of interest with the analysis of the reference sample.

[0057] In a first variant, the second sample ions are ionised in pulses, in particular in the pulses in which the second sample ions are transferred to the mass analyser. In a second variant, the second sample ions are ionised continuously and are transferred in pulses to the mass analyser. In this second variant, the second sample ions are advantageously accumulated in an ion trap from where they are transferred in pulses to the mass analyser or are transferred in a continuous beam of second sample ions which is repeatedly directed into the entrance of the mass analyser and subsequently away to miss the entrance of the mass analyser for transferring the second sample ions to the mass analyser in a pulsed manner.

This can for example be achieved by switching the ion optics in the path of the second sample ions from the ion source with which the second sample has been ionised to second sample ions to the mass analyser.

[0058] In a first preferred variant, for ionising the second sample to the second sample ions, the second sample is transferred to a second ion source and ionised by the second ion source to the second sample ions, wherein the second ion source is separate from the first ion sources with which the assays are ionised to the first sample ions. This has the advantage that an ion source well dedicated to the second sample is used for ionising the second sample to second sample ions. On the one hand, the type of ion source used as second ion source can be chosen to optimally suit the purpose of ionising the second sample to second sample ions. On the other hand, the second ion source can easily be kept physically separated from the first sample, while at the same time, the first ion sources can be kept physically separated from the second sample. Thus, there is no contamination of the first sample ions with second sample ions and vice versa no contamination of the second sample ions with first sample ions.

[0059] In this variant, the apparatus preferably includes the second ion source.

[0060] In a second preferred variant, for ionising the second sample to the second sample ions, the second sample is transferred to one of the first ion sources being a dually used first ion source and ionised to the second sample ions by the dually used first ion source. This means that the dually used first ion source is used on the one hand for ionising one of the assays to the first sample ions and on the other hand for ionising the second sample to the second sample ions. Thereby, the assay and second sample can be ionised to the first and second sample ions, respectively, simultaneously or consecutively. Independent of whether the assay and the second sample are ionised to the first and second ions simultaneously or consecutively, the dually used first ion source has the advantage that the apparatus can be constructed simpler and thus cheaper while the method can be employed with the apparatus with less maintenance of the apparatus.

[0061] In a first preferred variant, the assay which is ionised to the first sample ions by the dually used first ion source is transferred to the dually used first ion source modulated according to a first modulation function, in particular the first modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to the first sample ions, wherein when detecting with the mass analyser the first and second sample ions which have been ionised by the dually used first ion source, a signal from the mass analyser is obtained and a correlation of the signal with the first modulation function is calculated in order to obtain the at least one mass spectrum of the respective first sample ions, the respective mass spectrum being assigned to the dually used first

ion source and the respective one of the assays which is ionised to the first sample ions by the dually used first ion source. This has the advantage that a mass spectrum of the first sample ions ionised with the dually used first ionisation source can be obtained despite the presence of second sample ions since any signal from the second sample ions in the respective mass spectrum is either not present or smeared out to become background noise.

[0062] In a second preferred variant, the second sample is transferred to the dually used first ion source modulated according to a second modulation function, in particular the second modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to the second sample ions, wherein when detecting with the mass analyser the first and second sample ions which have been ionised by the dually used first ion source, a signal from the mass analyser is obtained and a correlation of the signal with the second modulation function is calculated in order to obtain the at least one mass spectrum of the second sample ions, the respective mass spectrum being assigned to the second sample. This has the advantage that a mass spectrum of the second sample ions ionised with the dually used first ionisation source can be obtained despite the presence of the first sample ions ionised with the dually used first ionisation source since any signal from the first sample ions ionised with the dually used first ionisation source in the respective mass spectrum is either not present or smeared out to become background noise.

[0063] In case the assay which is ionised to the first sample ions by the dually used first ion source is transferred modulated according to a first modulation function, in particular the first modulation function being a first pseudorandom sequence having an autocorrelation being a two valued function with one single peak, to the dually used first ion source for being ionised, and the second sample is transferred modulated according to a second modulation function, in particular the second modulation function being a second pseudorandom sequence having an autocorrelation being a two valued function with one single peak, to the dually used first ion source for being ionised, the first modulation function is preferably different from the second modulation function.

[0064] In case the assay which is ionised to the first sample ions by the dually used first ion source is transferred modulated according to a first modulation function, in particular the first modulation function being a first pseudorandom sequence having an autocorrelation being a two valued function with one single peak, to the dually used first ion source for being ionised, and the second sample is transferred modulated according to a second modulation function, in particular the second modulation function being a second pseudorandom sequence having an autocorrelation being a two valued function with one single peak, to the dually used first ion source for being ionised, advantageously a correlation between the first and the second modulation function is

zero. This has the advantage that for both the first sample ions ionised with the dually used first ionisation source and the second sample ions separate mass spectra can be obtained.

[0065] In a further variant, either only the assay which is ionised to the first sample ions by the dually used first ion source is transferred modulated according to the first modulation function to the dually used first ion source for being ionised or only the second sample is transferred modulated according to the second modulation function to the dually used first ion source for being ionised, while the other one of the assay which is ionised to the first sample ions by the dually used first ion source and the second sample is transferred continuously to the dually used first ion source at the same time.

[0066] Alternatively, neither the assay which is ionised to the first sample ions by the dually used first ion source nor the second sample is transferred modulated according to a modulation function to the dually used first ion source.

[0067] In a first advantageous variant, in each one of the cycles, when for a particular one of the first ion sources, the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser and the at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the particular one of the first ion sources, the second sample ions are transferred to the mass analyser for mass analysis, too. This has the advantage that the cycle is as short as if only first sample ions would be mass analysed by the mass analyser. Thus, a better resolution in time of the time evolution of the first sample and/or the second sample is achieved.

[0068] In a first preferred variation of this first advantageous variant, in each one of the cycles, when for the particular one of the first ion sources, the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser and the second sample ions are transferred to the mass analyser, too, the at least one mass spectrum is obtained with the mass analyser from the second sample ions and the first sample ions ionised by and transferred from the particular one of the first ion sources together, the at least one mass spectrum being assigned to the respective one of the first ion sources and to the second sample. This has the advantage that a better resolution in time of the time evolution of the first sample and/or the second sample is achieved in a simple and efficient way.

[0069] In a second preferred variation of this first advantageous variant, in each one of the cycles, when for the particular one of the first ion sources, the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser and the at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the particular one of the first ion sources, the first sample ions ionised by the particular one of said first ion sources are transferred to the mass analyser modulated accord-

ing to a third modulation function, in particular the third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with the mass analyser the first and second sample ions, a signal from the mass analyser is obtained and a correlation of the signal with the third modulation function is calculated in order to obtain the at least one mass spectrum of the respective the first sample ions, the respective at least one mass spectrum being assigned to the particular one of the first ion sources and the respective one of the assays which is ionised to the first sample ions by the particular one of the first ion sources. This has the advantage that a mass spectrum of the respective assay can be obtained despite the presence of second sample ions since any signal from the second sample ions in the respective mass spectrum is either not present or smeared out to become background noise.

[0070] In a third preferred variation of this first advantageous variant, in each one of the cycles, when for the particular one of the first ion sources, the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser and the at least one mass spectrum is obtained with the mass analyser from the first sample ions ionised by and transferred from the particular one of the first ion sources, the second sample ions are transferred to the mass analyser modulated according to a fourth modulation function, in particular the fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with the mass analyser the first and second sample ions, a signal from the mass analyser is obtained and a correlation of the signal with the fourth modulation function is calculated in order to obtain the at least one mass spectrum of the second sample ions, the respective at least one mass spectrum being assigned to the second sample. This has the advantage that a mass spectrum of the second sample ions can be obtained despite the presence of the first sample ions since any signal from the first sample ions in the respective mass spectrum is either not present or smeared out to become background noise.

[0071] In case the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser modulated according to the third modulation function, in particular the third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, and the second sample ions are transferred to the mass analyser modulated according to the fourth modulation function, in particular the fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, the third modulation function is preferably different from the fourth modulation function.

[0072] In case the first sample ions ionised by the particular one of the first ion sources are transferred to the

mass analyser modulated according to the third modulation function, in particular the third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, and the second sample ions are transferred to the mass analyser modulated according to the fourth modulation function, in particular the fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, advantageously a correlation between the third and the fourth modulation function is zero.

[0073] This has the advantage that for both the first sample ions ionised with the particular one of the first ionisation sources and the second sample ions separate mass spectra can be obtained.

[0074] In a further variation, either only the first sample ions ionised by the particular one of the first ion sources are transferred to the mass analyser modulated according to the third modulation function, in particular the third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, or only the second sample ions are transferred to the mass analyser modulated according to the fourth modulation function, in particular the fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, while the other one of the first sample ions ionised by the particular one of the first ion sources and the second sample ions are at the same time transferred continuously to the mass analyser for being mass analysed.

[0075] Alternatively to these variations, neither the first sample ions ionised by the particular one of the first ion sources nor the second sample ions are transferred modulated according to a modulation function to the mass analyser.

[0076] In a second preferred variant, during each one of the cycles, a sequence is performed wherein each element of the sequence is linked to one of the first ion sources in that the respective element begins with starting transferring the first sample ions ionised by the corresponding one of the first ion sources to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the first sample ions ionised by and transferred from the corresponding one of the first ion sources and in that the respective element ends with stopping transferring the first sample ions ionised by the corresponding one of the first ion sources to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the first sample ions ionised by and transferred from the corresponding one of the first ion sources, wherein in each one of the cycles, as a further element to the sequence, the second sample ions are transferred to the mass analyser and at least one mass spectrum is obtained with the mass analyser from the second sample ions, the at least one mass spectrum being assigned to the second sample and the ion source with which the second sample ions have been ionised,

wherein the further element begins with starting transferring the second sample ions to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the second sample ions and ends with stopping transferring the second sample ions to the mass analyser and obtaining the at least one mass spectrum with the mass analyser from the second sample ions. Thereby, the ion source with which the second sample ions have been ionised can be one of the first ion sources or can be the before mentioned second ion source which is separate from the first ion sources. In either case, the advantage is that the mass spectra of the first sample ions ionised with the different first ion sources and as well as the mass spectra of the second sample ions are obtained in a straight forward way, thus, simplifying the data interpretation.

[0077] In a first preferred variant, the mass analyser comprises one detector for detection ions. This has the advantage that the mass analyser can be constructed simpler and thus cheaper. In a second preferred variant, the mass analyser comprises two spatially separated detectors for detecting ions, wherein a first one of the two spatially separated detectors is dedicated to detect the first sample ions ionised by a first one of the first ion sources, while a second one of the two spatially separated detectors is dedicated to detect the first sample ions ionised by a second one of the first ion sources or to detect the second sample ions. This has the advantage that the mass analyser can be optimised for the different ion sources employed and/or for analysing a first sample being very different from the second sample.

[0078] Other advantageous embodiments and combinations of features come out from the detailed description below and the entirety of the claims.

Brief description of the drawings

[0079] The drawings used to explain the embodiments show:

- Fig. 1 a simplified schematic view of an apparatus according to the invention,
- Fig. 2 a simplified schematic view of another apparatus according to the invention,
- Fig. 3 a simplified schematic view of another apparatus according to the invention, and
- Fig. 4 a simplified schematic view of yet another apparatus according to the invention.

[0080] In the figures, the same components are given the same reference symbols.

Preferred embodiments

[0081] Figure 1 shows a simplified schematic view of

an apparatus 1 according to the invention. This figure is used to explain the apparatus 1 according to the invention as well as to explain the method according to the invention when being executed with the apparatus 1.

[0082] The apparatus 1 includes a liquid chromatograph 2 comprising a liquid chromatography column 21 for separating a first sample chromatographically. Furthermore, the apparatus 1 includes an assay obtaining device 3 for obtaining two assays from the first sample, the assay obtaining device 3 being arranged at the end of the liquid chromatograph 2. The apparatus 1 further includes two first ion sources 5.1, 5.2 for ionising the assays to first sample ions. These two first ion sources 5.1, 5.2 are switched in parallel with respect to each other. Furthermore, the apparatus 1 includes a mass analyser 7 for mass analysing the first sample ions. In the present case, this mass analyser 2 is a time of flight mass analyser. In another variant, the mass analyser 2 can be any other mass analyser like for example an ion trap mass analyser like for example an orbitrap mass analyser. In yet another variant, the mass analyser 2 comprises two mass analyser after each other. In either one of these variants, the length of the mass spectra obtained with the mass analyser 2 is 10'000 data points. In variations, the mass spectra can be longer or shorter. In case of shorter mass spectra, the mass spectra provide for example a length of 8'000 data points or 5'000 data points.

[0083] The apparatus 1 additionally includes an assay guiding arrangement 4 for transferring each one of the two assays from the assay obtaining device 3 to the respective one of the first ion sources 5.1, 5.2. This assay guiding arrangement 4 includes two tubes for transferring the assays. Furthermore, the apparatus 1 comprises an ion guiding arrangement 6 for transferring from each one of the first ion sources 5.1, 5.2 the first sample ions ionised by the respective one of the first ion sources 5.1, 5.2 to the mass analyser 7 for obtaining with the mass analyser 7 at least one mass spectrum from the first sample ions ionised by and transferred from the respective one of the first ion sources 5.1, 5.2, the at least one mass spectrum being assigned to the respective one of the first ion sources 5.1, 5.2. Furthermore, the apparatus 1 comprises a control unit 8 for controlling the apparatus 1 for executing the method according to the invention.

[0084] When executing the method according to the invention with the apparatus 1 and thus mass analysing the first sample by ionising the first sample to first sample ions and obtaining mass spectra from the first sample ions with the mass analyser 7, the first sample is inserted into the liquid chromatography column 21 and separated chromatographically. The output of the liquid chromatography column 21 is then divided by the assay obtaining device 3 into two assays which are each transferred with assay guiding arrangement 4 from the assay obtaining device 3 to the respective one of the first ion sources 5.1, 5.2.

[0085] Both first ion sources 5.1, 5.2 are continuous ion sources and thus continuously ionise the assay which

arrives at the respective first ion source 5.1, 5.2 to first sample ions. More precisely, one of the first ion sources 5.1 is an atmospheric pressure chemical ion source (AP-CI). Thus, this one of the first ion sources 5.1 uses a soft ionisation method and therefore maintains molecules in the assay transferred to this first ion source 5.1 intact when ionising the molecules to first sample ions. Thus, in operation of the apparatus 1, the first sample ions ionised by this one of the first ion sources 5.1 comprise such maintained but ionised molecules.

[0086] The other one of the first ion source 5.2 however is a 70 eV electron ion source. I.e., this first ion source 5.2 is an electron ion source (EI) ionising the assay transferred to this first ion source 5.2 at 70 eV. Since this one of the first ion sources 5.2 uses a hard ionisation method, the molecules in the assay to this first ion source 5.2 are fragmented when being ionised to first sample ions. Consequently, in operation of the apparatus 1, the first sample ions ionised by this one of the first ion sources 5.2 comprise ionised fragments of molecules from the first sample.

[0087] Both first ion sources 5.1, 5.2 are connected via the ion guiding arrangement 6 to the mass analyser 7. Thereby, the ion guiding arrangement 6 includes two ion benders 61.1, 61.2 which enable a switching of a direction of the ion beam passing the respective ion bender 61.1, 61.2. Thus, when executing the method according to the invention, the ion benders 61.1, 61.2 are switched such that during a first time interval of 0.004 seconds, the first sample ions from the first ion source 5.1 being the atmospheric pressure chemical ion source are transferred to the mass analyser 7. Subsequently, the ion benders 61.1, 61.2 are switched such that during a second time interval 0.004 seconds, the first sample ions from the other first ion source 5.2 being the 70 eV electron ion source are transferred to the mass analyser 7. During both time intervals, mass spectra are recorded with the mass analyser 7. During the first time interval, ten mass spectra are recorded and assigned to the first ion source 5.1 being the atmospheric pressure chemical ion source. During the second time interval, ten mass spectra are recorded and assigned to the first ion source 5.2 being the 70 eV electron ion source.

[0088] Thus a sequence is performed wherein each element of the sequence is linked to one of the first ion sources 5.1, 5.2 in that the respective element begins with starting transferring the first sample ions ionised by the corresponding one of the first ion sources 5.1, 5.2 to the mass analyser 7 and obtaining the at least one mass spectrum with the mass analyser 7 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 5.1, 5.2 and in that the respective element ends with stopping transferring the first sample ions ionised by the corresponding one of the first ion sources 5.1, 5.2 to the mass analyser 7 and obtaining the at least one mass spectrum with the mass analyser 7 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 5.1,

5.2. Thus, in this picture of a sequence with elements, each element is linked to one of the first ion sources 5.1, 5.2.

[0089] When executing the method according to the invention with the apparatus 1, the sequence with the first time interval and the second time interval is repeated in cycles. Thereby, in each cycle, the mass spectra obtained during the respective cycle are assigned to the respective cycle in order to be able to analyse a time evolution of the first sample during the mass analysis. Since the time interval for each element of the sequence is 0.004 seconds and since the sequence has two elements, the repetition rate of the cycles is a little more than 100 Hz since the duration of one cycle is 0.008 seconds. In a variant, the time intervals can be longer like for example 0.04 seconds. In such a variant, the repetition rate of the cycles is little more than 10 Hz because the duration of one cycle is 0.08 seconds. In another variant, the time intervals can be even longer like for example 0.4 seconds. In such a variant, the repetition rate is little more than 1 Hz because the duration of one cycle is 0.8 seconds.

[0090] In either variant, in each cycle, consecutively for each one of the first ion sources 5.1, 5.2, the first sample ions ionised by the respective one of the first ion sources 5.1, 5.2 are transferred to the mass analyser 7 and ten mass spectra are obtained with the mass analyser 7 from the first sample ions ionised by and transferred from the respective one of the first ion sources 5.1, 5.2, the then mass spectra being assigned to the respective one of the first ion sources 5.1, 5.2. Of course, instead of recording each time ten mass spectra, more mass spectra or less mass spectra can be recorded. For example, each time, five mass spectra can be recorded. Or, in another example, each time, on mass spectrum is recorded. In case more than one mass spectrum is recorded each time, these mass spectra can be added up in order to provide a statistically more significant mass spectrum or they can be maintained individually in order to obtain a better time resolution in case the first sample changes with time.

[0091] In either variant, the duration of one cycle is considerably shorter than a full width at half maximum of the peaks of the chromatogram obtained with the liquid chromatograph 2 from the first sample. Thus, for both first ion sources 5.1, 5.2, a time-dependent, quasi-simultaneous mass analysis of the chromatogram is obtained.

[0092] Figure 2 shows a simplified schematic view of another apparatus 101 according to the invention. This figure is used to explain the apparatus 101 according to the invention as well as to explain the method according to the invention when being executed with the apparatus 101.

[0093] The apparatus 101 shown in Figure 2 is similar to the apparatus 1 shown in Figure 1. In contrast to the apparatus 1 shown in Figure 1, the apparatus 101 shown in Figure 2 includes two ion detectors 162.1, 162.2 in the ion guiding arrangement 106. These ion detectors 162.1,

162.2 are Faraday Cups. In a variant, they are electron multipliers. In yet another variant, they are micro-channel plate (MCP) detectors. In operation of the apparatus 101, during one element of the sequence, the beam of first sample ions originating from one of the first ion sources 105.1 is directed by one of the ion benders 161.1 to the mass analyser 107 for mass analysis, while the beam of the first sample ions originating from the other one of the first ion sources 105.2 is directed by the other one of the ion benders 161.2 to one of the ion detectors 162.2. During the other element of the sequence, the beam of the first sample ions originating from the one of the first ion sources 105.1 is directed by the one of the ion benders 161.1 to the other one of the ion detectors 162.1, while the beam of the first sample ions originating from the other one of the first ion sources 105.2 is directed by the ion benders 161.1, 161.2 to the mass analyser 107 for mass analysis. Thus, each time the beam of first sample ions from one of the ion sources 105.1, 105.2 is not directed to the mass analyser 107 for mass analysis, it is directed to one of the ion detectors 162.1, 162.2 for detecting a number of the first sample ions in the beam during the time the beam is directed away to miss the entrance of the mass analyser.

[0094] As shown in Figure 2, the apparatus 101 further includes a drifting region 109 which is arranged in the ion guiding arrangement 106. This drifting region 109 is for separating the first sample ions passing the drifting region 109 according to their mobility before being mass analysed by the mass analyser 107. Thereby, a gas pressure of an inert gas is maintained in the drifting region 109, the gas pressure being reduced as compared to atmospheric pressure, wherein the first sample ions are pulled by a static electric field through the drifting region 109 for being separated according to their mobility before they are mass analysed.

[0095] Figure 3 shows a simplified schematic view of another apparatus 201 according to the invention. This figure is used to explain the apparatus 201 according to the invention as well as to explain the method according to the invention when being executed with the apparatus 201.

[0096] The apparatus 201 shown in Figure 3 is similar to the apparatus 1 shown in Figure 1. In contrast to the apparatus 1 shown in Figure 1 however, the apparatus 201 shown in Figure 3 includes a gas chromatograph 202 instead of a liquid chromatograph. This gas chromatograph 202 comprises a gas chromatographic column 221. Thus, in operation of the apparatus 201, the first sample is inserted into the gas chromatographic column 221 for chromatographic separation before being divided into the two assays by the assay obtaining device 203. In a variant, the apparatus 201 further comprises a liquid chromatograph arranged in front of the gas chromatograph such that the first sample is chromatographically separated in the liquid chromatograph and subsequently chromatographically separated in the gas chromatograph 202 before being divided into the assays.

[0097] The apparatus 201 shown in Figure 3 furthermore comprises a second ion source 210 for ionising a second sample to second sample ions. This second ion source 210 is connected via the ion guiding arrangement 206 to the mass analyser 207 such that the second sample ions can be transferred from the second ion source 210 to the mass analyser 207 for mass analysis. In a variant not shown in Figure 3, the apparatus further includes a gas chromatograph arranged in front of the second ion source 210 such that the second sample can be chromatographically separated before being ionised and mass analysed.

[0098] The second sample is different from the first sample. In an example, the first sample is polluted air from a factory, while the second sample is fresh air. In this example, a broad non-targeted analysis of the first sample is obtained by the apparatus 201. In order to be able to identify compounds being present in the polluted air as being pollution originating from the factory, the analysis of the first sample can be compared to the analysis of the second sample, the fresh air.

[0099] The control unit 208 of the apparatus 201 shown in Figure 3 enables different modes of operation of the apparatus 201:

In a first mode of operation, in each one of the cycles, when for a particular one of the first ion sources 205.2, the first sample ions ionised by the particular one of the first ion sources 205.2 are transferred to the mass analyser 207 and the at least one mass spectrum is obtained with the mass analyser 207 from the first sample ions ionised by and transferred from the particular one of the first ion sources 205.2, the second sample ions are transferred to the mass analyser 207 for mass analysis, too. Thereby, in each one of the cycles, when for the particular one of the first ion sources 205.2, the first sample ions ionised by the particular one of the first ion sources 205.2 are transferred to the mass analyser 207 and the second sample ions are transferred to the mass analyser 207, too, the at least one mass spectrum is obtained with the mass analyser 207 from the second sample ions and the first sample ions ionised by and transferred from the particular one of the first ion sources 205.2 together, the at least one mass spectrum being assigned to the respective one of the first ion sources 205.2 and to the second sample.

[0100] Similarly, in a second mode of operation, in each one of the cycles, when for a particular one of the first ion sources 205.2, the first sample ions ionised by the particular one of the first ion sources 205.2 are transferred to the mass analyser 207 and the at least one mass spectrum is obtained with the mass analyser 207 from the first sample ions ionised by and transferred from the particular one of the first ion sources 205.2, the second sample ions are transferred to the mass analyser 207 for mass analysis, too. In this second mode of operation, however, in each one of the cycles, when for the particular one of the first ion sources 205.2, the first sample ions ionised by the particular one of the first ion sources

205.2 are transferred to the mass analyser 207 and the at least one mass spectrum is obtained with the mass analyser 207 from the first sample ions ionised by and transferred from the particular one of the first ion sources 205.2, the first sample ions ionised by the particular one of the first ion sources 205.2 are transferred to the mass analyser 207 modulated according to a third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, and the second sample ions are transferred to the mass analyser 207 modulated according to a fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak. Thereby, a correlation between the third and the fourth modulation function is zero. When detecting with the mass analyser 207 the first and second sample ions, a signal from the mass analyser 207 is obtained and a correlation of the signal with the third modulation function is calculated in order to obtain the at least one mass spectrum of the respective the first sample ions, the respective at least one mass spectrum being assigned to the particular one of the first ion sources 205.2 and the respective one of the assays which is ionised to the first sample ions by the particular one of the first ion sources 205.2. Furthermore, a correlation of the signal with the fourth modulation function is calculated in order to obtain the at least one mass spectrum of the second sample ions, the respective at least one mass spectrum being assigned to the second sample. Thus, the stream of the first sample ions ionised by the particular one of the first ion sources 205.2 and the second sample ions is multiplexed when being mass analysed.

[0101] In a third mode of operation, during each one of the cycles, a sequence is performed wherein each element of the sequence is linked to one of the first ion sources 205.1, 205.2 in that the respective element begins with starting transferring the first sample ions ionised by the corresponding one of the first ion sources 205.1, 205.2 to the mass analyser 207 and obtaining the at least one mass spectrum with the mass analyser 207 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 205.1, 205.2 and in that the respective element ends with stopping transferring the first sample ions ionised by the corresponding one of the first ion sources 205.1, 205.2 to the mass analyser 207 and obtaining the at least one mass spectrum with the mass analyser 207 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 205.1, 205.2, wherein in each one of the cycles, as a further element to the sequence, the second sample ions are transferred to the mass analyser 207 and at least one mass spectrum is obtained with the mass analyser 207 from the second sample ions, the at least one mass spectrum being assigned to the second sample and the second ion source 210, wherein the further element begins with starting transferring the second sample ions to the mass analyser 207 and obtaining the

at least one mass spectrum with the mass analyser 207 from the second sample ions and ends with stopping transferring the second sample ions to the mass analyser 207 and obtaining the at least one mass spectrum with the mass analyser 207 from the second sample ions.

[0102] Figure 4 shows a simplified schematic view of yet another apparatus 301 according to the invention. This figure is used to explain the apparatus 301 according to the invention as well as to explain the method according to the invention when being executed with the apparatus 301.

[0103] The apparatus 301 shown in Figure 4 is constructed similar to the apparatus 201 shown in Figure 3. In contrast to the apparatus 201 shown in Figure 3 however, the apparatus 301 shown in Figure 4 does not include a second ion source, but includes three first ion sources 305.1, 305.2, 305.3 for ionising assays to first sample ions. Thereby, two of the first ion sources 305.1, 305.2 are atmospheric pressure chemical ion sources (APCI), while one of the first ion sources 305.3 is a 70 eV electron ion source.

[0104] In correspondence with this number of first ion sources 305.1, 305.2, 305.3, the assay obtaining device 303 of the apparatus 301 is for dividing the first sample into three assays and the assay guiding arrangement 304 is for transferring each one of the three assays from the assay obtaining device 303 to the respective one of the first ion sources 305.1, 305.2, 305.3. Thereby, the assay guiding arrangement 304 includes in its branch from the assay obtaining arrangement 303 to a first one of the first ion sources 305.1 a first nozzle 341 for controlling passage of the assay through the respective branch. This first nozzle 341 is controlled by the control unit 308 such that the assay passing the respective branch is transferred continuously or pulsed in pulses to the first one of the first ion sources 305.1 for being ionised to the first sample ions.

[0105] In order to transfer the first sample ions from the respective one of the three first ion sources 305.1, 305.2, 305.3 to the mass analyser 307, the ion guiding arrangement 306 is extended as compared to the previously described apparatuses 1, 101, 201. This extended ion guiding arrangement 306 comprises three ion benders 361.1, 361.2, 361.3.

[0106] The apparatus 301 shown in Figure 4 furthermore includes a second nozzle 342 for controlling a transfer of the second sample from a sample inlet to the first one of the first ion sources 305.1. This second nozzle 342 is as well controlled by the control unit 308 such that the second sample is transferred continuously or pulsed in pulses to the first one of the first ion sources 305.1 for being ionised to the second sample ions. Thus the first one of the first ion sources 305.1 is a dually used first ion source.

[0107] The control unit 308 enables different modes for operating the apparatus 301.

[0108] In a first mode, the first nozzle 341 and the second nozzle 342 are both operated to continuously trans-

fer the assay and the second sample, respectively, to the first one of the first ion sources 305.1. In this operation mode, the first sample ions and the second sample ions are mass analysed together. This means, in each one of the cycles, in the element of the sequence where the first sample ions ionised by the first one of the first ion sources 305.1 are transferred to the mass analyser 307 and the at least one mass spectrum is obtained with the mass analyser 307 from the first sample ions ionised by and transferred from the first one of the first ion sources 305.1, the second sample ions are transferred to the mass analyser 307 for mass analysis, too, such that the at least one mass spectrum is in fact obtained with the mass analyser 307 from the second sample ions and the first sample ions ionised by and transferred from the first one of the first ion sources 305.1 together, the at least one mass spectrum being assigned to the first one of the first ion sources 305.1 and to the second sample.

[0109] In a second mode, during each cycle, the first and second nozzle 341, 342 are closed during the elements of the sequence which do not require ions from the first one of the first ion source 305.1. Only when the sequences element linked to the first one of the first ion sources 305.1 is executed, the first and the second nozzle 341, 342 are opened. During this particular element of the sequence, the first nozzle 341 is operated pulsed according to a first modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, such that the respective assay is modulated according to the first modulation function when being transferred to the first one of the first ion sources 305.1 for being ionised to the first sample ions. At the same time, during the particular element of the sequence, the second nozzle 342 is operated pulsed according to a second modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, such that the second sample is modulated according to the second modulation function when being transferred to the first one of the first ion sources 305.1 for being ionised to the second sample ions. Thereby, the first modulation function and the second modulation function are chosen such that a correlation between the first and the second modulation function is zero. Furthermore, the first modulation function and the second are chosen to have a length such that they can be run for an integer number of times during the time the particular element of the sequence is executed.

[0110] In this second mode, when detecting with the mass analyser 307 the first and second sample ions which have been ionised by the first one of the first ion sources 305.1, a signal from the mass analyser 307 is obtained and a correlation of the signal with the first modulation function is calculated in order to obtain the at least one mass spectrum of the respective first sample ions, the respective mass spectrum being assigned to the first one of the first ion sources 305.1 and the respective one of the assays which is ionised to the first sample ions by

the first one of the first ion sources 305.1. Similarly, a correlation of the signal with the second modulation function is calculated in order to obtain the at least one mass spectrum of the second sample ions, the respective mass spectrum being assigned to the second sample. Thus, the assay transferred to the first one of the first ion sources 305.1 and the second sample are multiplexed when being ionised and mass analysed.

[0111] In a third mode, during each one of said cycles, a sequence is performed wherein each element of the sequence is linked to one of the first ion sources 305.1, 305.2, 305.3 in that the respective element begins with starting transferring the first sample ions ionised by the corresponding one of the first ion sources 305.1, 305.2, 305.3 to the mass analyser 307 and obtaining said at least one mass spectrum with the mass analyser 307 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 305.1, 305.2, 305.3 and in that the respective element ends with stopping transferring the first sample ions ionised by the corresponding one of the first ion sources 305.1, 305.2, 305.3 to the mass analyser 307 and obtaining the at least one mass spectrum with the mass analyser 307 from the first sample ions ionised by and transferred from the corresponding one of the first ion sources 305.1, 305.2, 305.3. Thereby the first nozzle 341 is only open during the element where the first sample ions ionised by the first one of the first ion sources 305.1 is transferred to the mass analyser 307 such that only during this element, the assay transferred via the first nozzle 341 is transferred to the first one of the first ion sources 305.1.

[0112] Furthermore, in the third mode, in each one of the cycles, as a further element to the sequence, the second nozzle 342 is opened during this further element and closed again at the end of the further element such that the second sample is transferred to and ionised to second sample ions by the first one of the first ion sources 305.1 during this further element. Additionally, during this further element, the second sample ions are transferred to the mass analyser 307 and at least one mass spectrum is obtained with the mass analyser 307 from the second sample ions, the at least one mass spectrum being assigned to the second sample and thus to the first one of the first ion sources 305.1. This further element begins with starting transferring the second sample ions to the mass analyser 307 and obtaining the at least one mass spectrum with the mass analyser 307 from the second sample ions and ends with stopping transferring the second sample ions to the mass analyser 307 and obtaining the at least one mass spectrum with the mass analyser 307 from the second sample ions.

[0113] The invention is not limited to the embodiments described herein. Rather, various variations and amendments to these described embodiments are readily available to the person skilled in the art.

[0114] In summary, it is to be noted that a method and an apparatus pertaining to the technical field initially mentioned are provided, that enable an improved non-target-

ed analysis of a first sample.

Claims

1. A method for mass analysing a first sample by ionising said first sample to first sample ions and obtaining mass spectra from said first sample ions with a mass analyser (7, 207, 307), wherein two or more assays are obtained from said first sample and each one of said assays is transferred to another first ion source (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) and ionised by the respective first ion source (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) to first sample ions, wherein said first sample is mass analysed in cycles, wherein in each cycle, consecutively for each one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3), said first sample ions ionised by the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) are transferred to said mass analyser (7, 207, 307) and at least one mass spectrum is obtained with said mass analyser (7, 207, 307) from the first sample ions ionised by and transferred from the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3), said at least one mass spectrum being assigned to the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3).
2. The method according to claim 1, **characterised in that** each one of said cycles has a duration in time of 1 second or less, preferably 0.1 seconds or less, particular preferably 0.01 seconds or less.
3. The method according to claim 1 or 2, **characterised in that** at least one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) is a continuous ion source.
4. The method according to one of claims 1 to 3, **characterised in that** one of said first ion sources (5.1, 105.1, 205.1, 305.1, 305.2) is a chemical ionisation ion source.
5. The method according to one of claims 1 to 4, **characterised in that** one of said first ion sources (5.2, 105.2, 205.2, 305.3) is an electron ionisation ion source, in particular a 70 eV electron ionisation ion source.
6. The method according to one of claims 1 to 5, **characterised in that** before obtaining said two or more assays from said first sample, said first sample is chromatographically separated in a chromatographic column, in particular gas chromatographically sep-

arated in a gas chromatographic column (221) or liquid chromatographically separated in a liquid chromatographic column (21).

7. The method according to one of claims 1 to 6, **characterised in that** said mass analyser (7, 207, 307) is a time of flight mass analyser.
8. The method according to one of claims 1 to 7, **characterised in that** said first sample ions ionised by one of said first ion sources (105.1, 105.2) are separated according to their mobility in a drifting region (109) before being mass analysed by said mass analyser.
9. The method according to one of claims 1 to 8, **characterised in that** in parallel to the mass analysis of said first sample by ionising said first sample to first sample ions and obtaining mass spectra from said first sample ions with said mass analyser (207, 307), a second sample is mass analysed by ionising said second sample to second sample ions and obtaining mass spectra from said second sample ions with said mass analyser (207, 307).
10. The method according to claim 9, **characterised in that** for ionising said second sample to said second sample ions, said second sample is transferred to a second ion source (210) and ionised by said second ion source (210) to said second sample ions, wherein said second ion source (210) is separate from said first ion sources (205.1, 205.2) with which said assays are ionised to said first sample ions.
11. The method according to claim 9, **characterised in that** for ionising said second sample to said second sample ions, said second sample is transferred to one of said first ion sources (305.1) being a dually used first ion source and ionised to said second sample ions by said dually used first ion source.
12. The method according to claim 11, **characterised in that** the assay which is ionised to said first sample ions by said dually used first ion source is transferred to said dually used first ion source modulated according to a first modulation function, in particular said first modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to said first sample ions, wherein when detecting with said mass analyser (307) the first and second sample ions which have been ionised by said dually used first ion source, a signal from the mass analyser (307) is obtained and a correlation of said signal with said first modulation function is calculated in order to obtain the at least one mass spectrum of the respective said first sample ions, the respective mass spectrum being assigned to said dually used

first ion source and the respective one of said assays which is ionised to the first sample ions by said dually used first ion source.

13. The method according to claim 11 or 12, **characterised in that** said second sample is transferred to said dually used first ion source modulated according to a second modulation function, in particular said second modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to said second sample ions, wherein when detecting with said mass analyser (307) the first and second sample ions which have been ionised by said dually used first ion source, a signal from said mass analyser (307) is obtained and a correlation of said signal with said second modulation function is calculated in order to obtain said at least one mass spectrum of said second sample ions, the respective mass spectrum being assigned to said second sample.
14. The method according to one of claim 9 to 13, **characterised in that** in each one of said cycles, when for a particular one of said first ion sources (205.2, 305.1), said first sample ions ionised by said particular one of said first ion sources (205.2, 305.1) are transferred to said mass analyser (207, 307) and said at least one mass spectrum is obtained with said mass analyser (207, 307) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2, 305.1), said second sample ions are transferred to said mass analyser (207, 307) for mass analysis, too.
15. The method according to claim 14, **characterised in that** in each one of said cycles, when for said particular one of said first ion sources (205.2, 305.1), said first sample ions ionised by said particular one of said first ion sources (205.2, 305.1) are transferred to said mass analyser (207, 307) and said second sample ions are transferred to said mass analyser (207, 307), too, said at least one mass spectrum is obtained with said mass analyser (207, 307) from said second sample ions and said first sample ions ionised by and transferred from the particular one of said first ion sources (205.2, 305.1) together, said at least one mass spectrum being assigned to the respective one of said first ion sources (205.2, 305.1) and to said second sample.
16. The method according to claim 14, **characterised in that** in each one of said cycles, when for said particular one of said first ion sources (205.2), said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) and said at least one mass spectrum is obtained with said mass an-

alyser (207) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2),

said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) modulated according to a third modulation function, in particular said third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with said mass analyser (207) the first and second sample ions, a signal from said mass analyser (207) is obtained and a correlation of said signal with said third modulation function is calculated in order to obtain the at least one mass spectrum of the respective said first sample ions, the respective at least one mass spectrum being assigned to said particular one of said first ion sources (205.2) and the respective one of said assays which is ionised to the first sample ions by said particular one of said first ion sources (205.2).

17. The method according to claim 14 or 16, **characterised in that** in each one of said cycles,

when for said particular one of said first ion sources (205.2), said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) and said at least one mass spectrum is obtained with said mass analyser (207) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2),

said second sample ions are transferred to said mass analyser (207) modulated according to a fourth modulation function, in particular said fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with said mass analyser (207) the first and second sample ions, a signal from said mass analyser (207) is obtained and a correlation of said signal with said fourth modulation function is calculated in order to obtain the at least one mass spectrum of said second sample ions, the respective at least one mass spectrum being assigned to said second sample.

18. The method according to one of claims 9 to 11, **characterised in that** during each one of said cycles, a sequence is performed wherein each element of said sequence is linked to one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) **in that** the respective element begins with starting transferring said first sample ions ionised by the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said first sample ions

ionised by and transferred from the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) and **in that** the respective element ends with stopping transferring said first sample ions ionised by the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said first sample ions ionised by and transferred from the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3), wherein in each one of said cycles, as a further element to said sequence, said second sample ions are transferred to said mass analyser (207, 307) and at least one mass spectrum is obtained with said mass analyser (207, 307) from said second sample ions, said at least one mass spectrum being assigned to said second sample and the ion source with which said second sample ions have been ionised, wherein said further element begins with starting transferring said second sample ions to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said second sample ions and ends with stopping transferring said second sample ions to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said second sample ions.

19. An apparatus (1, 101, 201, 301) for mass analysing a first sample by executing the method according to one of claims 1 to 18, **characterised in that** said apparatus (1, 101, 201, 301) includes:

- a) an assay obtaining device (3, 203, 303) for obtaining two or more assays from said first sample,
- b) first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) for ionising said assays to first sample ions,
- c) an assay guiding arrangement for transferring each one of said assays from the assay obtaining device to the corresponding one of said first ion sources for ionising the respective one of said assays to said first sample ions,
- d) a mass analyser (7, 207, 307) for mass analysing said first sample ions, and
- e) an ion guiding arrangement (6, 106, 206, 306) for transferring from each one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) said first sample ions ionised by the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) to said mass analyser (7, 207, 307) for obtaining with said mass analyser (7, 207, 307) at least one mass spectrum from the first sample ions ionised by and transferred from the respective one of said first ion sources (5.1,

5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3), said at least one mass spectrum being assigned to the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3).

Amended claims in accordance with Rule 137(2) EPC.

1. A method for mass analysing a first sample by ionising said first sample to first sample ions and obtaining mass spectra from said first sample ions with a mass analyser (7, 207, 307), wherein two or more assays are obtained from said first sample and each one of said assays is transferred to another first ion source (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) and ionised by the respective first ion source (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) to first sample ions, wherein said first sample is mass analysed in cycles, wherein in each cycle, consecutively for each one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3), said first sample ions ionised by the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) are transferred to said mass analyser (7, 207, 307) and at least one mass spectrum is obtained with said mass analyser (7, 207, 307) from the first sample ions ionised by and transferred from the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3), said at least one mass spectrum being assigned to the respective one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) and to the cycle in which the respective mass spectrum has been recorded.
2. The method according to claim 1, **characterised in that** each one of said cycles has a duration in time of 1 second or less, preferably 0.1 seconds or less, particular preferably 0.01 seconds or less.
3. The method according to claim 1 or 2, **characterised in that** at least one of said first ion sources (5.1, 5.2, 105.1, 105.2, 205.1, 205.2, 305.1, 305.2, 305.3) is a continuous ion source.
4. The method according to one of claims 1 to 3, **characterised in that** one of said first ion sources (5.1, 105.1, 205.1, 305.1, 305.2) is a chemical ionisation ion source.
5. The method according to one of claims 1 to 4, **characterised in that** one of said first ion sources (5.2, 105.2, 205.2, 305.3) is an electron ionisation ion source, in particular a 70 eV electron ionisation ion

source.

6. The method according to one of claims 1 to 5, **characterised in that** before obtaining said two or more assays from said first sample, said first sample is chromatographically separated in a chromatographic column, in particular gas chromatographically separated in a gas chromatographic column (221) or liquid chromatographically separated in a liquid chromatographic column (21).
7. The method according to one of claims 1 to 6, **characterised in that** said mass analyser (7, 207, 307) is a time of flight mass analyser.
8. The method according to one of claims 1 to 7, **characterised in that** said first sample ions ionised by one of said first ion sources (105.1, 105.2) are separated according to their mobility in a drifting region (109) before being mass analysed by said mass analyser.
9. The method according to one of claims 1 to 8, **characterised in that** in parallel to the mass analysis of said first sample by ionising said first sample to first sample ions and obtaining mass spectra from said first sample ions with said mass analyser (207, 307), a second sample is mass analysed by ionising said second sample to second sample ions and obtaining mass spectra from said second sample ions with said mass analyser (207, 307).
10. The method according to claim 9, **characterised in that** for ionising said second sample to said second sample ions, said second sample is transferred to a second ion source (210) and ionised by said second ion source (210) to said second sample ions, wherein said second ion source (210) is separate from said first ion sources (205.1, 205.2) with which said assays are ionised to said first sample ions.
11. The method according to claim 9, **characterised in that** for ionising said second sample to said second sample ions, said second sample is transferred to one of said first ion sources (305.1) being a dually used first ion source and ionised to said second sample ions by said dually used first ion source.
12. The method according to claim 11, **characterised in that** the assay which is ionised to said first sample ions by said dually used first ion source is transferred to said dually used first ion source modulated according to a first modulation function, in particular said first modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to said first sample ions, wherein when detecting with said mass analyser (307) the first and

second sample ions which have been ionised by said dually used first ion source, a signal from the mass analyser (307) is obtained and a correlation of said signal with said first modulation function is calculated in order to obtain the at least one mass spectrum of the respective said first sample ions, the respective mass spectrum being assigned to said dually used first ion source and the respective one of said assays which is ionised to the first sample ions by said dually used first ion source.

13. The method according to claim 11 or 12, **characterised in that** said second sample is transferred to said dually used first ion source modulated according to a second modulation function, in particular said second modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, for being ionised to said second sample ions, wherein when detecting with said mass analyser (307) the first and second sample ions which have been ionised by said dually used first ion source, a signal from said mass analyser (307) is obtained and a correlation of said signal with said second modulation function is calculated in order to obtain said at least one mass spectrum of said second sample ions, the respective mass spectrum being assigned to said second sample.

14. The method according to one of claim 9 to 13, **characterised in that** in each one of said cycles, when for a particular one of said first ion sources (205.2, 305.1), said first sample ions ionised by said particular one of said first ion sources (205.2, 305.1) are transferred to said mass analyser (207, 307) and said at least one mass spectrum is obtained with said mass analyser (207, 307) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2, 305.1), said second sample ions are transferred to said mass analyser (207, 307) for mass analysis, too.

15. The method according to claim 14, **characterised in that** in each one of said cycles, when for said particular one of said first ion sources (205.2, 305.1), said first sample ions ionised by said particular one of said first ion sources (205.2, 305.1) are transferred to said mass analyser (207, 307) and said second sample ions are transferred to said mass analyser (207, 307), too, said at least one mass spectrum is obtained with said mass analyser (207, 307) from said second sample ions and said first sample ions ionised by and transferred from the particular one of said first ion sources (205.2, 305.1) together, said at least one mass spectrum being assigned to the respective one of said first ion sources (205.2, 305.1) and to said second sample.

16. The method according to claim 14, **characterised in that** in each one of said cycles, when for said particular one of said first ion sources (205.2), said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) and said at least one mass spectrum is obtained with said mass analyser (207) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2), said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) modulated according to a third modulation function, in particular said third modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with said mass analyser (207) the first and second sample ions, a signal from said mass analyser (207) is obtained and a correlation of said signal with said third modulation function is calculated in order to obtain the at least one mass spectrum of the respective said first sample ions, the respective at least one mass spectrum being assigned to said particular one of said first ion sources (205.2) and the respective one of said assays which is ionised to the first sample ions by said particular one of said first ion sources (205.2).

17. The method according to claim 14 or 16, **characterised in that** in each one of said cycles, when for said particular one of said first ion sources (205.2), said first sample ions ionised by said particular one of said first ion sources (205.2) are transferred to said mass analyser (207) and said at least one mass spectrum is obtained with said mass analyser (207) from said first sample ions ionised by and transferred from said particular one of said first ion sources (205.2), said second sample ions are transferred to said mass analyser (207) modulated according to a fourth modulation function, in particular said fourth modulation function being a pseudorandom sequence having an autocorrelation being a two valued function with only one singular peak, wherein when detecting with said mass analyser (207) the first and second sample ions, a signal from said mass analyser (207) is obtained and a correlation of said signal with said fourth modulation function is calculated in order to obtain the at least one mass spectrum of said second sample ions, the respective at least one mass spectrum being assigned to said second sample.

18. The method according to one of claims 9 to 11, **characterised in that** during each one of said cycles, a sequence is performed wherein each element of said sequence is linked to one of said first ion sources

(205.1, 205.2, 305.1, 305.2, 305.3) **in that** the respective element begins with starting transferring said first sample ions ionised by the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said first sample ions ionised by and transferred from the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) and **in that** the respective element ends with stopping transferring said first sample ions ionised by the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3) to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said first sample ions ionised by and transferred from the corresponding one of said first ion sources (205.1, 205.2, 305.1, 305.2, 305.3), wherein in each one of said cycles, as a further element to said sequence, said second sample ions are transferred to said mass analyser (207, 307) and at least one mass spectrum is obtained with said mass analyser (207, 307) from said second sample ions, said at least one mass spectrum being assigned to said second sample and the ion source with which said second sample ions have been ionised, wherein said further element begins with starting transferring said second sample ions to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said second sample ions and ends with stopping transferring said second sample ions to said mass analyser (207, 307) and obtaining said at least one mass spectrum with said mass analyser (207, 307) from said second sample ions.

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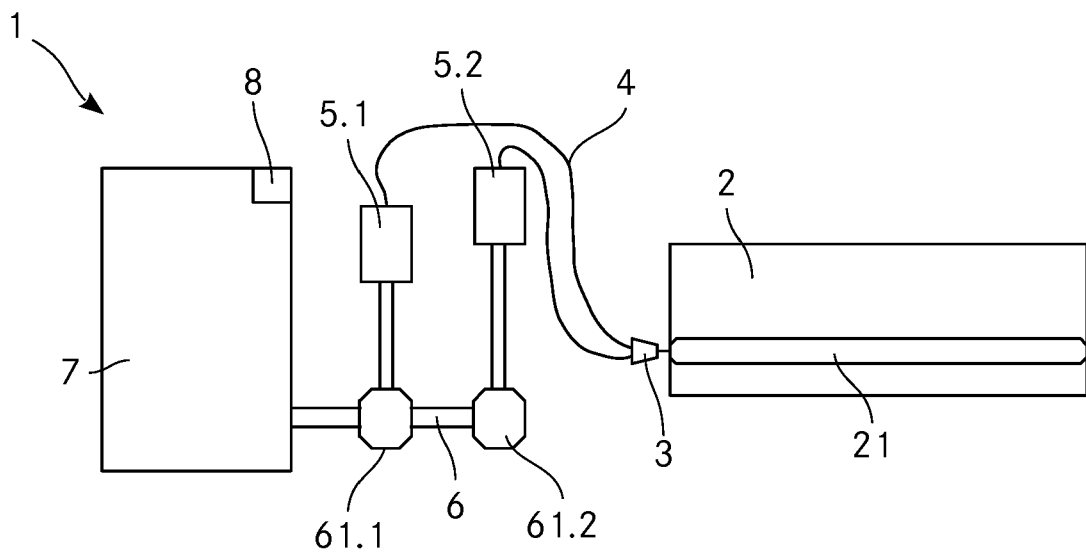


Fig. 1

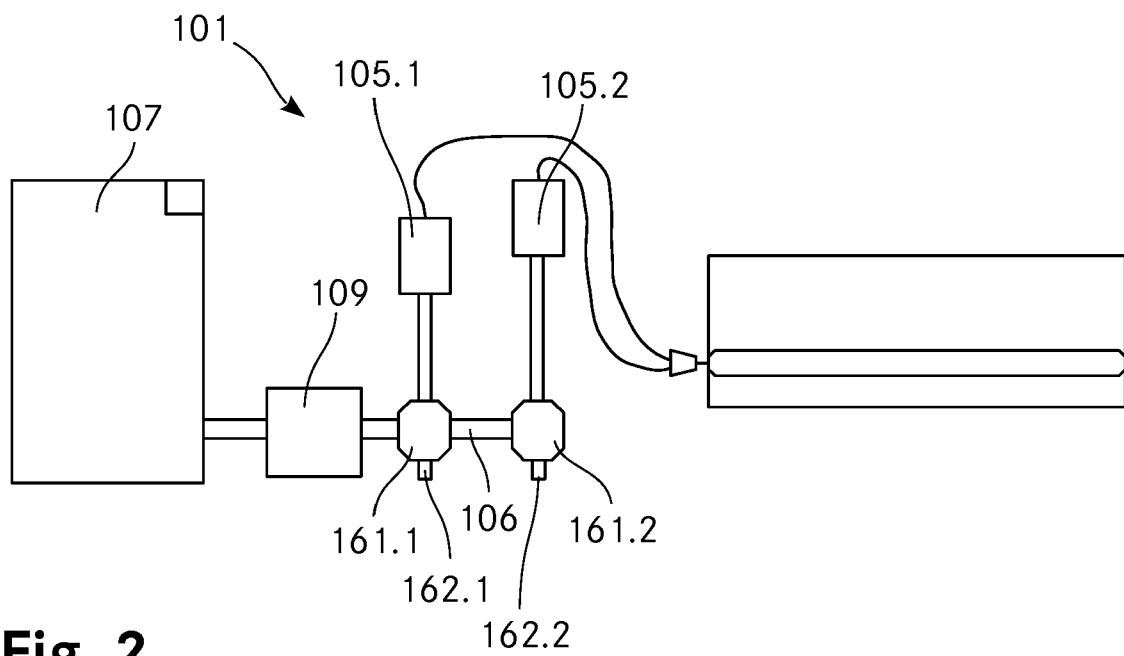


Fig. 2

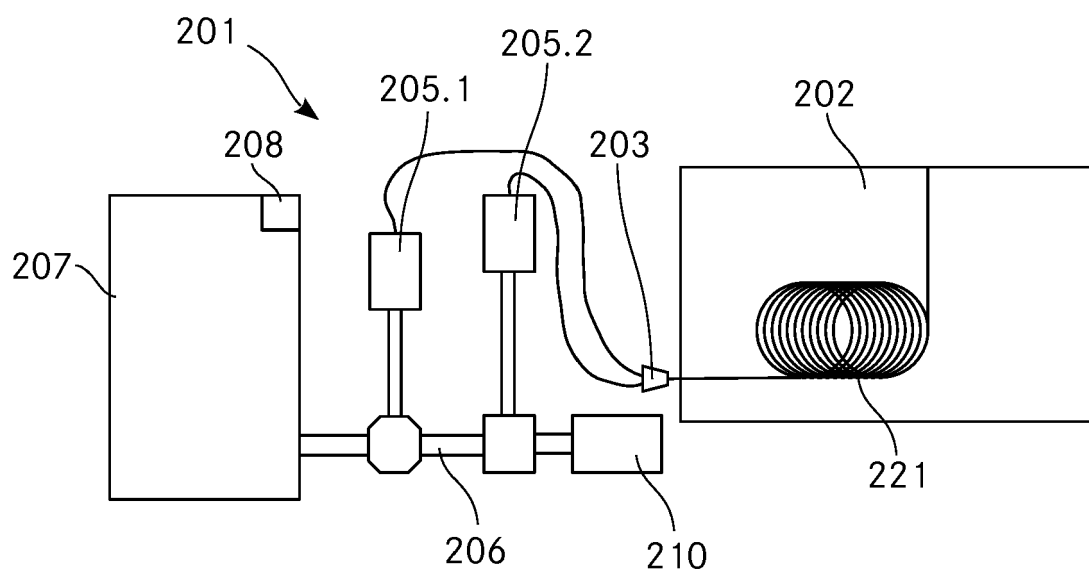


Fig. 3

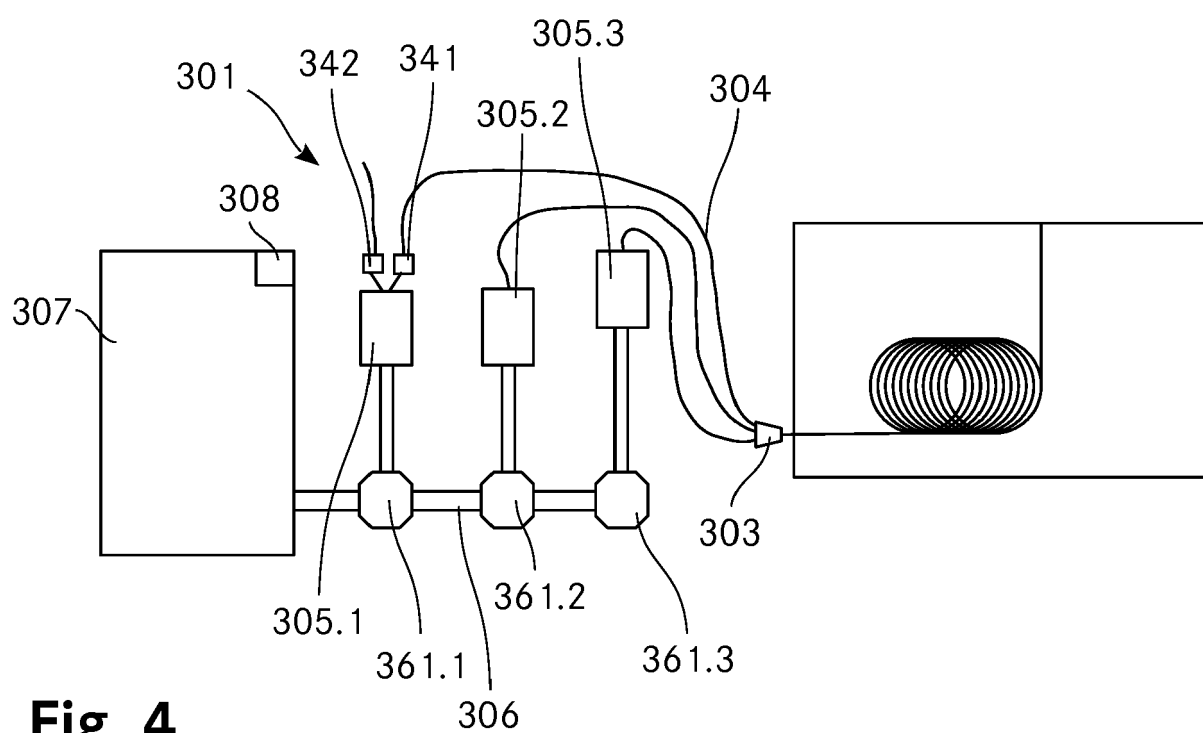


Fig. 4



EUROPEAN SEARCH REPORT

Application Number
EP 19 20 6239

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	EP 2 363 877 A1 (TOFWERK AG [CH]) 7 September 2011 (2011-09-07) * paragraph [0059] - paragraph [0062] * * paragraph [0143] - paragraph [0148] * * paragraph [0180] - paragraph [0184] * * figures 2B, 10 *	1-19	INV. H01J49/00 H01J49/10
X	US 2019/237316 A1 (LOPEZ-HILFIKER FELIPE [CH] ET AL) 1 August 2019 (2019-08-01) * paragraph [0036] * * paragraph [0077] - paragraph [0083] * * paragraphs [0091], [0095] * * figure 1 *	1-19	
A	US 2004/188605 A1 (TANG KEQI [US] ET AL) 30 September 2004 (2004-09-30) * paragraph [0003] - paragraph [0004] * * paragraph [0006] * * paragraph [0019] *	10,12-17	
A	US 2008/073502 A1 (SCHNEIDER BRADLEY B [CA] ET AL) 27 March 2008 (2008-03-27) * paragraph [0058] - paragraph [0060] * * paragraph [0076] - paragraph [0077] * * claims 11-13, 18,19 *	10,12-17	TECHNICAL FIELDS SEARCHED (IPC) H01J
A	US 2017/069478 A1 (BROWN JEFFERY MARK [GB] ET AL) 9 March 2017 (2017-03-09) * paragraph [0151] * * paragraph [0155] *	10,12-17	
A	JP 2004 108917 A (HORIBA LTD) 8 April 2004 (2004-04-08) * paragraph [0006] - paragraph [0007] *	10,12, 13,16,17	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 6 April 2020	Examiner Cornelussen, Ronald
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 19 20 6239

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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06-04-2020

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 2363877 A1	07-09-2011	NONE	
US 2019237316 A1	01-08-2019	CA 3036058 A1 CN 109923637 A EP 3510630 A1 JP 2019529948 A US 2019237316 A1 WO 2018046083 A1 WO 2018046619 A1	15-03-2018 21-06-2019 17-07-2019 17-10-2019 01-08-2019 15-03-2018 15-03-2018
US 2004188605 A1	30-09-2004	NONE	
US 2008073502 A1	27-03-2008	CA 2663698 A1 EP 2070102 A1 JP 2010504504 A US 2008073502 A1 WO 2008037073 A1	03-04-2008 17-06-2009 12-02-2010 27-03-2008 03-04-2008
US 2017069478 A1	09-03-2017	CA 2730559 A1 EP 2308076 A2 EP 2667401 A1 GB 2462190 A JP 5166606 B2 JP 2011529260 A US 2011189788 A1 US 2014051181 A1 US 2017069478 A1 WO 2010012987 A2	04-02-2010 13-04-2011 27-11-2013 03-02-2010 21-03-2013 01-12-2011 04-08-2011 20-02-2014 09-03-2017 04-02-2010
JP 2004108917 A	08-04-2004	JP 4078166 B2 JP 2004108917 A	23-04-2008 08-04-2004

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82