

which is fed with MALDI ions according to this invention. A UV pulsed laser (1) with 60 kilohertz repetition rate delivers finely focused pulses of laser light (2) via a movable mirror (3) onto samples located on a movably mounted sample plate (4) and thus generates expanding plasma clouds (5) containing the analyte ions. These ions can be drawn into an ion funnel and fed in the form of a narrow beam (12) via ion guides (8) and (10) to a time-of-flight mass analyzer, whose pulser (13) accelerates sections of the ion beam via a reflector (15) to an ion detector (16), which measures the ions arriving in sequence according to their mass, in the form of a time profile.

[0021] FIG. 2 provides a schematic representation of an ion source with a slightly different design. The sample plate (21) contains samples (22, 23), which can be irradiated by the pulsed UV laser (24) with a rapid succession of laser light pulses (25) by means of a movable mirror (26). The analyte ions (27) contained in the plasma clouds are transmitted by the ion funnel, which consists of individual apertured diaphragms (28), into the ion guides (29) and (31).

[0022] FIG. 3 shows a time-of-flight mass spectrometer in which the ions generated from the sample (47) on the sample carrier (41) are accelerated axially through the acceleration diaphragms (48) and into the flight path (49). The laser light pulse from the picosecond UV laser (43) is divided in a divider disk (44) consisting, for example, of an array of Einzel lenses; a large number of very small spots, each less than 20 micrometers in diameter, are irradiated on the sample (47) via lens (45) and movable mirror (46).

DETAILED DESCRIPTION

[0023] While the invention has been shown and described with reference to a number of embodiments thereof, it will be recognized by those skilled in the art that various changes in form and detail may be made herein without departing from the spirit and scope of the invention as defined by the appended claims.

[0024] Scarcely any investigations with a reasonable degree of precision relating to the ion yield of the MALDI process are to be found in the literature. This is understandable in view of how difficult it is to perform such investigations: one has to measure a very precisely prepared and weighed sample with constant MALDI parameters until the usually inhomogeneous sample is completely used up. One then has to estimate the often not very precisely known ion transmissions in the individual sections of the mass spectrometer used, calibrate the detector sensitivity, and compute the ion yield from the results of the measurement. This can hardly be achieved satisfactorily for the existing preparation method with dried droplets because the sample is very inhomogeneous.

[0025] If one investigates the ion yield of the MALDI process per analyte molecule on thin-layer preparations as a function of spot diameter, laser shot energy and laser light pulse duration relative to each other—which is much simpler to do—then one finds that, surprisingly and contrary to what is widely stated in the literature, the yield is greatly increased by using very short pulses of laser light of much less than one nanosecond and by vaporizing only a minute amount of sample material of less than one picogram in a very small sample area. High yields of analyte ions are thus achieved: it is quite possible that around ten to one hundred times more analyte ions can be generated from the sample than by using conventional parameters. The absolute numbers of analyte

ions per laser shot are, however, very low; they amount to only around a few hundred analyte ions for the analyte substance of highest concentration in the sample. In mixtures containing many analyte substances in one sample, all of which are to be analyzed, an analyte ion for those analyte substances which are contained in significantly lower concentrations than the main analyte substances in the sample will only be found in every tenth or hundredth pulse of laser light.

[0026] However, without additional measures, this highly efficient type of MALDI is not optimal for the usual MALDI time-of-flight mass spectrometry with axial ion acceleration because the latter technique needs preferably between approx. 2,000 and 10,000 analyte ions per laser shot for satisfactory operation. This MALDI time-of-flight mass spectrometry records the ions of every single laser shot in a separate mass spectrum. Since components of the analyte substances which are present at only one ten thousandth of the concentration of the main component are also to be measured, application of the new technique would mean adding together far more than ten thousand mass spectra to achieve this goal with only one spot per laser light pulse. That would take a long time in mass spectrometric terms, even if it is possible to use a mass spectrometer with a measuring frequency of two kilohertz.

[0027] A first favorable embodiment of a mass spectrometer using this invention is therefore to generate not just a single small laser spot from the light beam of a short UV laser light pulse with a duration of far less than one nanosecond, but several laser spots, each with a diameter of less than twenty micrometers, preferably less than ten micrometers, and to accelerate the thus generated larger number of ions axially into the flight path. With five to twenty laser spots, several thousand analyte ions are generated in each laser light pulse in a form that is favorable for axial MALDI time-of-flight mass spectrometry. The generation of several laser spots from one laser light beam is described in detail in the above-cited publication of the patent application DE 10 2004 044 196 A1 (A. Haase et al.).

[0028] In FIG. 3 such a time-of-flight mass spectrometer is shown schematically. The beam of the light pulse from the UV laser (43) is multiply divided in a divider disk (44). The divider disk (44) can consist of, for example, a field of small Einzel lenses, which generate a large number of small focal points, which are then focused onto the sample (47) by the lens (45) and the moving mirror (46). In this way a large number of small spots are generated on the sample according to the invention. The sample (47) is located on a sample support plate (41), which can be moved by a movement device (42) in order to bring the various samples on the sample support plate into the light beam, and also to move the spots across the sample between laser light pulses, in addition to the guidance by the moving mirror (46). The ions are formed into an ion beam (49) by the acceleration diaphragms (48), and this beam is focused to the detector (51) via the energy-focusing reflector (50).

[0029] In contrast, for a time-of-flight mass spectrometer that operates with orthogonal ion injection, a constant ion current and a normal scanning rate of 5,000 to 10,000 mass spectra per second, the conditions of the method according to the invention are virtually ideal, even with only a single spot per laser light pulse, if a sufficiently high frequency of the laser light pulses is selected. It is therefore a further favorable embodiment to use a laser pulse rate of at least twenty kilohertz, preferably at least fifty kilohertz for this purpose. There