

a counter-flow of the gas in the drift region, resulting in a shortening of the drift region. In this case, arbitrarily high mobility resolutions can, in theory, be achieved for ions of a selected mobility, which are held over a long period in equilibrium between the electric force of attraction and the viscous drag in the gas; but unfortunately only in theory. For practical applications there are fundamental limits which make the method unusable because the diffusion of the ion cloud, which is in equilibrium between the electric force of attraction and the viscous drag in the gas, does not stop either radially or axially at any time. Therefore, the ion cloud drifting apart by diffusion quickly exceeds all instrument dimensions.

[0009] Compared to the numerical values for mass resolutions in mass spectrometry, the mobility resolutions which can be achieved in practice are generally very low. The first commercial ion mobility spectrometer for bioorganic ions, which is very successful on the market, has a mobility resolution of only $R_{mob}=10$ to 15. With a mobility resolution of $R_{mob}=10$, two ion species whose collision cross-sections differ by only 20 percent can be readily separated.

[0010] Only highly specialized academic working groups have, as yet, been able to achieve significantly higher mobility resolutions of between $R_{mob}=60$ and 100, in rare individual cases up to $R_{mob}=150$, with drift lengths roughly between two and six meters and field strengths between 2,000 and 4,000 volts per meter, making it possible to differentiate between ion species whose mobilities differ by only one to three percent. Ion mobility spectrometers with a resolution above $R_{mob}=60$ shall be called "high resolution" here.

[0011] Since long mobility drift regions also entail strong transverse diffusion, longer drift regions must have a large diameter in order that the ions do not arrive at the wall electrodes. A well-tried method is therefore to guide the ions back to the axis of the drift region once they have passed through part of the drift region, after about two meters, for example. This is done using so-called "ion funnels". These consist of a large number of stacked ring electrodes, closely spaced by only a few millimeters apart, whose aperture diameters taper continuously from the diameter of the drift region, between 30 and 40 centimeters, for example, to around two to five millimeters and thus form a funnel-shaped enclosed volume. The two phases of an RF voltage, usually of several megahertz and between a few tens of volts and one hundred volts, are applied alternately to the apertured diaphragms, thus generating a pseudopotential which keeps the ions away from the funnel wall. A DC electric field is superimposed on the RF voltage by a DC voltage gradient, and this electric field pushes the ions slowly to the narrow exit of the funnel and through it. It has been found that such ion funnels do not measurably reduce the mobility resolution of a long drift region.

[0012] Ion funnels are not only used to guide the ions back to the axis of the drift region in ion mobility spectrometers; they are also used in mass spectrometers in general to capture larger ion clouds and thread them into narrow ion guides. As can be seen in the example shown in FIG. 2, such ion funnels are often found in mass spectrometers with an electrospray ion source, in which ions generated outside the vacuum system are transferred, together with a curtain gas, through inlet capillaries into the vacuum, where they are captured by ion funnels and freed of most of the curtain gas. As shown schematically in FIG. 2, some mass spectrometers even contain two such ion funnels, placed in series, in order to quickly

move from a region with higher pressure of a few hectopascals at the end of the inlet capillary to a region with lower pressure of between about 10^{-4} and 10^{-2} pascal. Inside these ion funnels exists a focused flow of the curtain gas, which under circumstances can even have all the characteristics of a jet flying at the speed of sound, due to the adiabatic cooling.

[0013] It should be briefly mentioned here that such gas flows are also often found in other types of ion guide, particularly if they are close to ion sources, such as the ion guide (11) of FIG. 2. Such ion guides can simply have the form of hexapole or quadrupole rod systems, which are operated with RF voltages, for example. A series of ion-optical lenses can also form an ion guide. Ion guides can be constructed with axial electric fields to actively push the ions through, although such ion guides are rare, as yet, except for ion funnels.

[0014] It is known that the conditions for conformational changes which occur by changes of the gas temperature can also be studied in ion mobility spectrometers. If, for example, the gas temperature is continuously increased in a region where the prevailing gas density and the dwell time of the ions allow that they can largely attain the temperature of the gas, and if the mobilities are measured as a function of the temperature, it is then possible to investigate transitions from one type of folding to another. It is particularly possible to determine the energy thresholds which have to be exceeded for conformational changes. Very fast cooling of the ions from a very hot state allows the most probable conformational states to be frozen and thus measured. Slow cooling of previously hot ions can often be used to find the conformational isomer with the lowest energy level.

[0015] For many biochemical applications, particularly protein chemistry applications for determining conformational states, a mass-accurate mass spectrometer, for example a time-of-flight mass spectrometer with an integrated mobility measuring station having a mobility resolution of $R_{mob}=30-50$ would already be eminently suitable. This could separate ions with mobilities differing only by some three to six percent. Conformational changes are often accompanied by mobility changes of at least this order of magnitude. This range of $R_{mob}=30-50$ shall therefore be called "medium-resolution" in the following, while the region below $R_{mob}=20$ shall be considered to be "low-resolution". The region with $R_{mob}>60$ has already been defined above as "high-resolution".

[0016] It should be noted here, that mobility resolution is essential for many applications, but mobility precision might be even more essential. Mobility precision is the precision for the determination of the mobility K_0 . The precision characterizes how well the mobility constant for a single ion species can be reproduced. With a good mobility spectrometer of $R_{mob}=50$, the mobility constant K_0 may be determined with a precision of 0.2 percent or even better.

[0017] Several arrangements of mobility spectrometers are known where the ions are mass-analyzed in a high-resolution time-of-flight mass spectrometer, in addition to the measurement of their mobility, the aim being to obtain mass spectra and mobility spectra of the ion mixtures at the same time. It is of particular interest if daughter ion spectra of ions of a selected mobility can also be acquired in order to obtain additional information on the structure of the ions.

[0018] For such combinations, current types of high-resolution ion mobility spectrometer have the disadvantage of being several meters long. Such a solution is unfavorable for commercial instruments. Even medium-resolution ion mobil-