

## HIGH-RESOLUTION ION MOBILITY SPECTROMETRY

### PRIORITY INFORMATION

**[0001]** This patent application claims priority from German Patent Application No. 10 2009 050 041.3 filed on Sep. 17, 2009, which is hereby incorporated by reference.

### FIELD OF INVENTION

**[0002]** The present invention relates generally to measuring ion mobilities in gas that moves against a field barrier.

### BACKGROUND OF THE INVENTION

**[0003]** A typical mass spectrometer is used for determining mass-to-charge ratios of sample ions. The term “mass-to-charge ratio” refers to the ratio of a mass  $m$  of the ion to a dimensionless number of elementary charges  $z$  of the ion. This charge-related mass  $m/z$  therefore has a physical dimension of a mass. In the following disclosure, the term “mass-to-charge ratio” may also be referred to using the terms “mass of an ion” or an “ion mass”.

**[0004]** The term “ion species” refers to ions having substantially identical elemental compositions, charges and three-dimensional structures. An ion species generally includes all the ions of an isotope group. While ions in the isotope group may have slightly different masses, they typically have substantially equal mobilities.

**[0005]** Isomers of a primary structure of bioorganic molecules (i.e., structural isomers) and isomers of a secondary or tertiary structure (i.e., conformational isomers) typically have substantially equal masses, but different geometrical forms. It is therefore practically impossible to differentiate structural and conformational isomers as a function of their mass. Some information regarding an isomeric structure can be obtained using fragment ion mass spectra. A more efficient and certain method to identify and distinguish isomers, however, is to separate the isomers according to their different ion mobilities.

**[0006]** Today, ion mobilities are predominantly obtained by measuring ion drift velocities in long drift regions under influence of an electric field. A typical drift region for measuring ion mobility includes an inert gas (e.g., helium or nitrogen) disposed therein. Sample ions (i.e., ions of the substance under investigation) are pulled through the gas by the electric field. The electric field is generated, for example, by DC potentials on ring electrodes that line the drift region. A large number of collisions with gas molecules provide each ion species with a relatively constant drift velocity  $v_d$  that is more or less proportional to the electric field strength  $E$ :

$$v_d = K_0 \times E.$$

**[0007]** The proportionality factor  $K_0$  may be referred to as the “ion mobility” of an ion species. The ion mobility is a function of temperature, gas pressure, type of gas, ionic charge and the collision cross-section of the ions.

**[0008]** Isomeric ions with the same charge-related masses  $m/z$  and different collision cross-section typically have different ion mobilities at the same temperature, pressure and type of gas. Isomers with the smallest geometric dimensions typically have the greatest mobility and therefore the highest drift velocity through the gas. Unfolded protein ions, for example, undergo more collisions than tightly folded protein ions. Protein ions which are unfolded or partially folded

therefore arrive at the end of the cell later than strongly folded ions of equal mass. Structural isomers (e.g., proteins with glycosyl, lipid or phosphoryl groups at different sites), however, also have different collision cross-sections, which allow them to be distinguished by measuring their ion mobility.

**[0009]** Under conditions when the electric fields  $E$  are relatively strong, the electric field strength equation is provided as follows:

$$v_d = K_0 \times E + K_1 \times E^2.$$

The factor  $K_1$  indicates how the collision cross-section changes under the influence of the electric field. The constant  $K_1$ , however, is typically so small that it can be ignored. Precision measurements of the mobility  $K_0$  should account for this dependence. It is typically advantageous therefore to carry out precision measurements at low field strengths.

**[0010]** The folding structures of ions, which can be identified via their mobility, have become increasingly important during chemical and biological research. Devices for measuring the mobility of ions therefore have been incorporated into mass spectrometers in order to combine the measurements of the charge-related mass of ions with measurements of collision cross-sections. The folding structures determine the mechanism of action and thus the function of the molecules in the living organism. Different folding, for example, can signify normal or abnormal functioning of biopolymers in bio-systems, and hence health or disease of tissue parts or even whole organisms.

**[0011]** Several academic research groups have coupled ion mobility spectrometers with mass spectrometers. In such systems, the mobility drift region typically has a pressure range of several hectopascals, a length of four or more meters for higher mobility resolutions, and electric field strength of 2,000 or more volts per meter. In this pressure range, the drifting ions do not form many complexes with other substances. The mobilities of the ion species therefore can be measured without interferences, unlike mobility measurements at atmospheric pressure. Long drift regions, however, typically have relatively large diameters because the ions diffuse radially over long distances.

**[0012]** The ions are typically introduced into the drift region by temporally short ion pulses. The ions initially take the shape of spatially small ion clouds, which are pulled through the drift region by the electric field. In the gas of the drift region, the ion clouds are diffused into the surrounding space by collisions statistically distributed by spatial directions and kinetic energies due to the molecular Brownian motion. The diffusion takes place in both a forward and backward direction, and also at right angles to the drift direction. The gas in the drift region is maintained, for example, at a temperature between approximately 150 and 300 degrees Celsius. Alternatively, the gas in the drift region may be cooled for special experiments.

**[0013]** The mobility resolving power (hereinafter “mobility resolution”) is defined as:

$$R_{mob} = K_0 / \Delta K_0,$$

where  $\Delta K_0$  is the width of the ion signal of the mobility  $K_0$  at half height, measured in units of the mobility. The mobility resolution  $R_{mob}$  is influenced predominantly by the diffusion broadening of the ion clouds, especially for long drift regions and high electric field strengths. Other influences, such as the space charge, tend to be negligibly small. The part of the mobility resolution determined by the diffusion broadening is defined as: