Ion Mobility Spectrometry in the Netherlands

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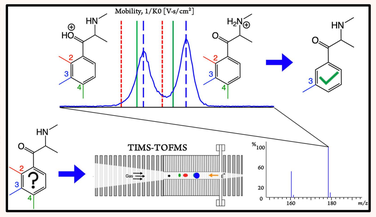
Amsterdam

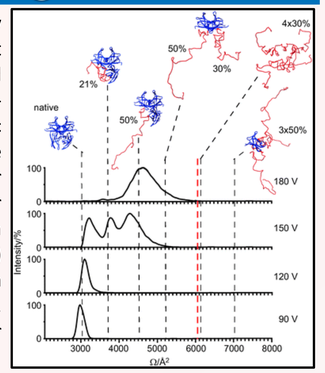
As the legal status of new psychoactive substances (NPS) depends on their chemical structure, newly synthesized isomeric derivatives of NPSs must be clearly identified, especially in the field of forensics. The presented study, see graphical abstract, uses TIMS-TOF-MS to discriminate between methylmethcathinone (MMC) and bicyclic rings.



With the presented workflow it was possible to identify cathinone isomers in confiscated street samples, powder and liquid, with only solvation or dilution as the sample preparation. The bimodal distribution of the two protomers (*O*- or *N*-protonated) with its increased mobility ($1/K_0$) separation helped to identify the substances more confidently at concentrations between 20 and 200 ng/mL. As a prospect, isomeric mixtures will be evaluated in the same system. [1]

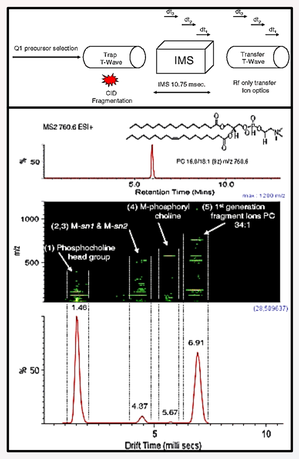
Utrecht

This article reviews the ion mobility developments in protein research. It introduces the working principles and applications of and drift-tube (DT), travelling-wave (TW) and high-field asymmetric waveform (FA) forms of IMS as well as the differential mobility analyzer (DMA or GEMMA) that is used for macromolecular complexes. In the presented figure it is shown how ion mobility mass spectrometry (IMMS) can be used to collisionally activate a protein in the gas-phase to induce unfolding of it. Different voltages in the collision chamber lead to a shift in collision cross section and to a split into a multimodal population. The degree of unfolding (red) is calculated from the crystal structure of the native protein (blue). The stages of unfolding indicate that complete unfolding is reached at 180 V of activation voltage. [2]



Leiden

In this study mouse plasma was screened for fatty acyls moieties. Here, the fatty acyl substituents could be located as well as the position of their double bonds. This was done by using time-aligned parallel fragmentation (TAP), see top panel. A quadrupole-selected precursor is trapped and fragmented in a travelling-wave (TW) collision cell before getting separated in TW-IM cell. Hereafter, a second fragmentation occurs in the TW-transfer cell before the ions were released into the mass spectrometer. This yielded various axes of separation, see bottom panel, and thus allowed for a detailed investigation of mechanisms on how fatty acyl moieties can react. These include but are not limited to the choline formation from fatty acyls and condensation reactions of acylium structures. [3]



IMS metrics of the Netherlands

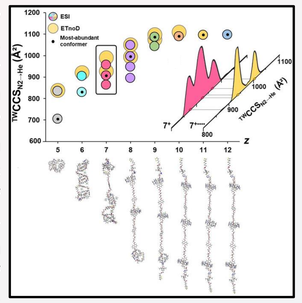
The research with and focussed on ion mobility spectrometry within various Dutch academic and indus-trial R&D groups goes back some 15 years. With the proteomics institute at the UU* (Heck), the three dimensional structure of native proteins, and protein complexes was investigated. In 2012, and in collaboration with Bruker Daltonics a prototype of the TIMS technology was implemented at DSM Research. Among all research groups there has been a particular interest in “strategies” to increase the resolution of IMS by adduct formation for small molecules (Somsen VU*, Honing UM*, Oomens RU*), synthetic polymers (Honing and Jordens DSM*), derivatisation (Kohler VU*), assessment of double positions in complex lipids (Hankemeier LU*) and the conformation of native proteins (Heck UU*). The development of hyphenated GC-IMS to support “metabolism research” has a history at the RU* (Buydens). [4]

*DSM – Dutch State Mines (Geleen), LU – Leiden University, RU – Radboud Universiteit (Nijmegen), UM – University Maastricht, UU – University Utrecht, VU – Free University (Amsterdam)

The size of each circle represents the number of publications of the respective location with the edge color-coded for the first-time publication ranging from 1998 to 2023. The top half of the fill represents the primary research field and the bottom half of the fill the second field of research. The color encodes for structural molecular research (●), for (bio)-medical research (●) of body fluids and foodstuff, and technological (●) such as computational, theoretical and engineering contributions as well as all review articles.

Nijmegen

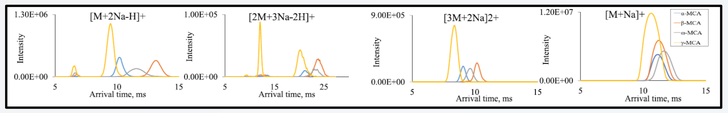
This study focusses in foldamers, mechanically entangled moieties with secondary structures, as are promising candidates for molecular switches. A non-dissociative electron transfer in the gas phase was used to reduce the moiety and induce a co-conformational transition of a donor-acceptor oligorotaxne* foldamer. This was achieved by quadrupole-selecting a precursor of up to z = 12^+, that is consecutively charge-reduced by using non-dissociative electron transfer (ETnoDP). The low-charged products of this are then analyzed by ion mobility mass spectrometry (IMMS). In parallel to that, the structures are also measured using infrared ion spectroscopy (IRIS). The figure shows the experimental results of the collision cross section determination with z = 7^+ in detail. The equilibrium geometries at the bottom panel show the most abundant closed-shell confirmation as obtained by a PM6 level of theory. [5]



* A rotaxane is a mechanically interlocked dumbbell-shaped molecule which is threaded through a macrocycle [wiki/en]

Maastricht

The presented study uses tandem mass spectrometry travelling-wave ion mobility to investigate mixtures of isomeric forms of bile acid steroids in the gas phase, as these molecule have a potential as diagnostic biomarkers. As shown in the figure below, the multiply charged, non-conjugated muricholic acids (α-, β-, ω-, γ-MCA) were well separated if two or more sodium ions are present. The different MCAs thus have a stronger tendency to either favour a curled or planar confirmation around the sodium ion, increasing the difference in collision cross section (CCS) between them. The singly charged mono-sodium adducts however, are much closer in CCS. They are thought to be lee well separated because a single sodium ion causes all the MCAs to curl around the sodium ion, effectively removing most of the variation in collision cross section between them. [6]



References

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