

## HOOKED DIFFERENTIAL MOBILITY SPECTROMETRY APPARATUS AND METHOD THEREFORE

**[0001]** This invention was made with Government support under Contract DE-AC06-76RLO1830 awarded by the U.S. Department of Energy. The Government has certain rights in the invention.

### FIELD OF THE INVENTION

**[0002]** The invention is in the field of ion mobility spectrometry (IMS) and mass spectrometry. More specifically, it is an apparatus and method for improved interfacing between differential mobility spectrometry (DMS) or field asymmetric waveform ion mobility spectrometry (FAIMS) analyzers and various stages of analytical instrumentation.

### BACKGROUND OF THE INVENTION

**[0003]** Mass spectrometry (MS) is the core technology of state-of-the-art biological analyses, including proteomics, metabolomics, and other "omic" fields of the post-genomic era. However, even with the formidable power of modern MS, nearly all real-world samples require prior separations. Those separations had traditionally been performed in the condensed phase (liquid or solid), e.g., liquid chromatography (LC), capillary electrophoresis (CE), capillary isoelectric focusing (CIEF), and gel electrophoresis in one or two dimensions such as sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and 2-D gel. A major attraction of separations based on ion transport, including differential mobility spectrometry (DMS), is a huge throughput gain over condensed-phase methods allowed by high speed of ion motion in gases compared to that in liquids.

**[0004]** DMS, also termed field asymmetric waveform ion mobility spectrometry (FAIMS), or ion mobility increment spectrometry, has emerged as a powerful analytical tool of broad utility for separation of ionic mixtures and characterization of ions in the gas phase, especially in conjunction with mass spectrometry (MS). DMS analyses are based on the difference between ion mobilities at high and low electric fields. Ions are filtered while pulled through a gap between two electrodes carrying an asymmetric waveform by gas flow or, longitudinal electric field. The spatial form of electric field inside the gap that controls DMS performance depends on the gap shape, and several geometries including planar, cylindrical, and spherical have been considered. Recent work has established that the highest resolution and best resolution-sensitivity trade-off are provided by homogeneous electric field found in planar DMS devices.

**[0005]** Instruments that combine DMS with MS offer exceptional sensitivity, specificity, and dynamic range. The applications of DMS/MS span the fields such as pharma R&D, toxicology, proteomics, metabolomics, health care, natural resource management, product quality assurance, and environmental monitoring. The advent of LC/DMS/MS and DMS/IMS/MS platforms has made DMS particularly attractive for analyses of extremely complex samples ubiquitous in proteomics and metabolomics.

**[0006]** Despite significant advantages of planar DMS over curved geometries in terms of resolution, duty cycle, and quantification accuracy/dynamic range, all commercial DMS/MS systems to date have employed cylindrical DMS

designs comprising two coaxial electrodes, where ions are focused to the annular gap median by inhomogeneous electric field. One reason for this has been that cylindrical DMS (in the configuration with gas flow along the axis, implemented, e.g., in the Ionalytics Selectra®) is particularly easy to couple to MS using a hemispherical terminus. In the homogeneous electric field of planar DMS, ions are free to spread both across and laterally to the gap under the influence of diffusion and mutual Coulomb repulsion. This eventually produces ribbon-shaped ion beams with the cross-section approximately defined by the DMS gap. Such wide beams cannot be transmitted through standard MS inlets (of either the capillary or orifice/curtain plate type) without great ion losses.

**[0007]** Slit apertures known in the art provide a greater overlap with ribbon-shaped ion beams emitted by planar DMS than circular apertures, reducing ion losses at the interfaces of planar DMS with MS, IMS, or other subsequent stages and thus improving analytical sensitivity. Ions captured by such apertures may be effectively focused using electrodynamic ion funnels taught, e.g., in U.S. Pat. Nos. 6,979,816, 6,818,890, and 6,967,325, incorporated herein. High-pressure ion funnels allow expanding the area of slit apertures, which further increases the utilization of ions delivered by DMS. Nonetheless, the slit is still much smaller than the opening of DMS gap at any reasonable pressure and pumping capacity in the front MS region, and substantial ion losses remain.

**[0008]** Hence one would desire to focus thick ribbon-like ion beams generated by planar DMS prior to the conductance limit to following instrument stages, including, e.g., MS, IMS, and like stages operated at lower gas pressure. Achieving that objective requires new devices and methods.

**[0009]** In another aspect, ions may initially be injected into DMS at various points across the gap, including some close to electrodes. In cylindrical DMS, those ions are rapidly bunched near the gap median by focusing due to inhomogeneous electric field, which minimizes non-selective ion loss to the electrodes immediately upon injection. In contrast, in planar DMS ions injected proximately to electrodes are commonly lost because of diffusion and Coulomb repulsion, which may contribute to a lower sensitivity of prior planar DMS systems compared to cylindrical DMS. Hence it may be advantageous to bunch ions injected into planar DMS to the gap median prior to their separation.

### SUMMARY OF THE INVENTION

**[0010]** Disclosed herein is an apparatus and method for focusing rectangular ion beams output by planar DMS analyzers into thinner beams that could be more effectively transmitted to subsequent instrument stages through constrained apertures. Those stages include, but are not limited to, mass spectrometry (MS), ion mobility spectrometry (IMS), and combinations, including, e.g., IMS/MS. Examples of integrated systems thus include, e.g., DMS/MS, DMS/IMS, LC/DMS/MS, LC/DMS/IMS, DMS/IMS/MS, and LC/DMS/IMS/MS.

**[0011]** According to the invention, a substantially planar DMS analyzer is interfaced to a subsequent or preceding stage using a curved DMS element, where a thick ion beam emitted by said analyzer or injected into it for ion filtering is compressed to the gap median by a DMS ion focusing effect in a spatially inhomogeneous electric field. To minimize ion losses in the curved element, the range of DMS separation parameters selected by the periodic asymmetric waveform