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Mass and Structural Selective Ion Soft_Landing for Separation, Collection and Characterization of Amyloid-Beta Peptide Structures and their Role in Alzheimer Disease

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Abstract

Advancements in ion mobility technology, particularly Structures for Lossless Ion Manipulations (SLIM), have enabled the detailed characterization of heterogeneity of biomolecular structures in a sample. SLIM enables the resolution of subtle variations of molecular structures (e.g. separation of conformations, isotopes, double bond positions, stereoisomers, isotopologues, isotopomers, etc.) which could be markers for diseases. SLIM also enables IMS separations with high resolution, high throughput, high ion utilization efficiency. In this work, we will present SLIM technology and its game-changing ability to perform analytical separations with unprecedented utility and precision. Particularly we will present the development of IMS technology that utilizes the sample nearly 100% of the time (as against traditional IMS which uses sample about 1% of the time owing to the pulsed nature of IMS). Further, we will present the ability to use such high ion utilization IMS separator in conjunction with high structural resolution and mass spectrometry to perform structure and mass selective soft-landing of biomolecular species.

The ability to collect material with structural and mass selectivity using SLIM enables in building materials of biomolecules to test hypotheses about their functionality in disease inception and progression. One potential model system we intend to study is the effect of conformations of amyloid-beta peptides in the kinetics of aggregation of beta-sheets, which are considered the leading cause for neuro-degenerative Alzheimer's disease. We propose to collect individual structures of Aβ peptides using our mass and size selection capability while maintaining their functionality, reintroduce the selective structures into the solution phase and study how the kinetics of aggregation occurs in-vitro. This will potentially provide an understanding of the specific Aβ structures' role in aggregation and thus providing opportunities for early disease detection and interventions. A similar approach can be extended to other disease models where molecular structures play a role in disease prognosis.