

The Study of Protein Folding Pathways: Advances in Mass Spectrometry

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DESCRIPTION

Protein folding is a fundamental process that governs the three-dimensional structure and function of proteins. Understanding how proteins adopt their native conformations has been a longstanding challenge in the field of biochemistry. In recent years, mass spectrometry has emerged as a powerful tool for investigating protein folding dynamics and gaining insights into the intricate folding pathways.

Proteins are linear chains of amino acids that must fold into specific three-dimensional structures to carry out their biological functions effectively. However, unraveling the complex process of protein folding has proven to be a formidable task. Misfolding and aggregation of proteins are associated with numerous diseases, such as Alzheimer's and Parkinson's, emphasizing the importance of studying protein folding in both healthy and pathological contexts. Mass spectrometry techniques have revolutionized the field by providing unique capabilities for analyzing protein folding dynamics at the molecular level. Mass spectrometry is a versatile analytical technique that enables the determination of a protein's mass and its fragment ions. In the context of protein folding studies, two main MS-based approaches have gained prominence: hydrogen/deuterium exchange and ion mobility spectrometry.

Hydrogen/deuterium exchange mass spectrometry allows the characterization of protein folding intermediates and the detection of transient structural changes by measuring the exchange rate of backbone amide hydrogens. Ion mobility spectrometry-mass spectrometry provides insights into the conformational landscape of proteins by measuring their collision cross-sections, revealing information about their shape and size.

Hydrogen/deuterium exchange mass spectrometry: Probing protein dynamics

Hydrogen/deuterium exchange mass spectrometry is a widely used technique for investigating protein folding and dynamics. It involves subjecting a protein or protein complex to a controlled

exchange of labile hydrogens with deuterium in a solvent. By monitoring the time-dependent uptake of deuterium, researchers can determine the accessibility and stability of various regions within the protein. Hydrogen/deuterium exchange mass spectrometry provides information about protein folding intermediates, folding kinetics, conformational changes, and the effects of ligand binding on protein dynamics. Combining hydrogen/deuterium exchange mass spectrometry with high-resolution mass spectrometry allows for the identification and localization of deuterium incorporation at the peptide level, enabling detailed mapping of folding events.

Ion mobility spectrometry and mass spectrometry are used to study of protein structure

Ion mobility spectrometry coupled with mass spectrometry offers complementary insights into protein folding. Ion mobility spectrometry separates ions based on their size, shape, and charge in the gas phase, providing information about the protein's conformational properties. By measuring the drift times of protein ions, researchers can determine the collision cross-sections, which reflect the overall shape and compactness of the protein. Ion mobility spectrometry-mass spectrometry allows the characterization of conformational ensembles, identification of folding intermediates, and investigation of protein-protein and protein-ligand interactions.

Furthermore, recent advances in data analysis algorithms have enabled the reconstruction of 3D models of proteins based on their collision cross-sections, providing a valuable link between solution-phase protein folding and gas-phase structure.

Mass spectrometry has emerged as a analytical technique for investigating protein folding and gaining insights into the conformational dynamics of proteins. The combination of hydrogen/deuterium exchange mass spectrometry and Ion mobility spectrometry-mass spectrometry provides a complete understanding of protein folding processes, helping scientists unravel the mysteries of molecular conformation and paving the way for new therapeutic strategies targeting protein misfolding diseases.

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