

International Summit on Current Trends in Mass Snd

Current Trends in Mass Spectrometry July 13-15, 2015 New Orleans, USA



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Approach to structures of difficult protein targets by means of monitoring hydrogen-deuterium exchange with mass spectrometry – New clothes for the old emperor

It is estimated that a stunning 25–30% of eukaryotic proteins are mostly disordered, while more than half of eukaryotic proteins and more than 70% of signaling proteins have long regions of disorder – IDRs. Due to a variety of reasons access by classic methods (crystallography or NMR) to this vast part of structural proteome including IDRs and other difficult protein targets, is severely limited. A major breakthrough in the methodologies available to study the structures of this class of proteins is a must. In this respect recent developments of mass spectrometry-based approaches to protein structure analysis are the most promising path. Both, new approaches, like ion mobility separation (IM), electron transfer dissociation (ETD) or technical improvements in the methods already known (like measurements of the hydrogen-deuterium exchange kinetics - HDex) or combination of both (solution/gas phase HDex combined with IM and/or ETD) represent such a major breakthrough, providing new types of experimental constraints and unique access to structural properties of difficult protein assemblies which in combination with classic methods speed up their structural characterization. Using HDex-based multipole approaches we have successfully characterized several protein assemblies (vimentin oligomers, kinetochore proteins, histone pre-mRNA processing assembly, perfringolysin toxin membrane pores and alike). These results will be presented to illustrate recent breakthrough developments in approach to structural characterization of difficult protein targets.

Biography

Michał Dadlez has completed his PhD in 1992 from the Institute of Biochemistry and Biophysics, Pol. Acad. Sci. and postdoctoral studies from Whitehead Institute, MIT, Cambridge, MA, supervised by Prof. Peter S. Kim. He organized Mass Spectrometry Lab, IBB PAS in 2001, being its head since then. In 2006 he became a Professor of Biophysics. He has published more than 90 papers in peer-reviewed journals. His major field of interest are protein structure studies with use of MSbased methods (HDex, X-linking, Ion Mobility separation, etc.)

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