High resolution IMS-MS for artifact-free structural analysis of proteins

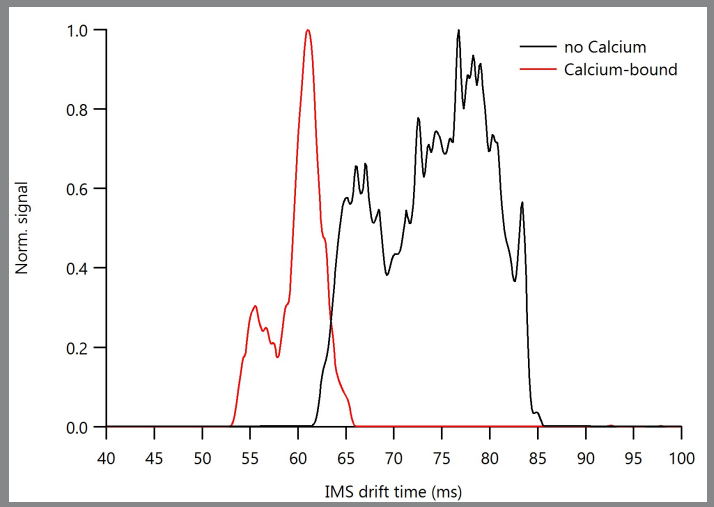
Michael Groessl
TOFWERK, Switzerland
ims-tof@tofwerk.com

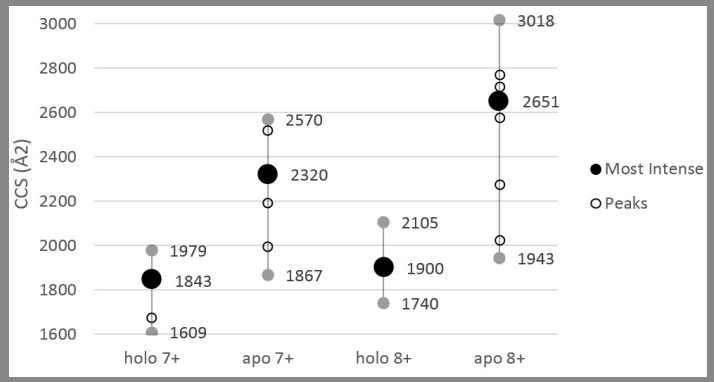
IMS-TOF

Over the last decade, numerous papers have reported IMS-MS investigations of biomolecules, especially proteins. In these studies, IMS-MS is used to probe the three-dimensional shape of biomolecules as well as the composition, stoichiometry, and arrangement of units in biomolecular complexes. Yet, the majority of these studies were conducted either on drift-tube IMS instruments that do not operate under low-field conditions or on travelling wave IMS (TWAVE or TWIMS) instruments. Use of such instruments can lead to artifacts due to collisionally-induced heating and imprecise measurements of collision cross sections.

The TOFWERK IMS-TOF is a drift-tube based IMS-MS instrument that operates under low-field conditions with a high pressure- and temperature-controlled IMS cell. This ensures that native conditions are preserved during the ion mobility separation. Additionally, the IMS-TOF exhibits superior ion mobility resolution, thus allowing deeper insight into the conformational diversity of biomolecules. This is demonstrated here for the calcium-binding protein calmodulin, an essential and ubiquitousmessenger protein. Calmodulin is activated by binding Ca^{2+} ions which substantially changes the structure of the protein and therefore its interactions within signalling pathways.

High-resolution IMS-MS under low-field conditions in a pressure- and temperature-controlled IMS drift cell allows separation of multiple protein conformers.





TOFWERK IMS-TOF reveals the conformational complexity of calmodulin. An IMS trace of calmodulin for the 7+ charge state is shown (top) as well as a plot with the collision cross sections for detected peaks in the IMS traces of the 7+ and 8+ charge states (bottom). Data were obtained either under denaturating conditions (apo; "no Calcium") or under native ESI conditions (holo; "Calcium-bound"). Nitrogen was used as the buffer gas and the drift-tube was operated at 1000 mbar, 30°C and a reduced field-strength of 2 Td.

TOFWERK