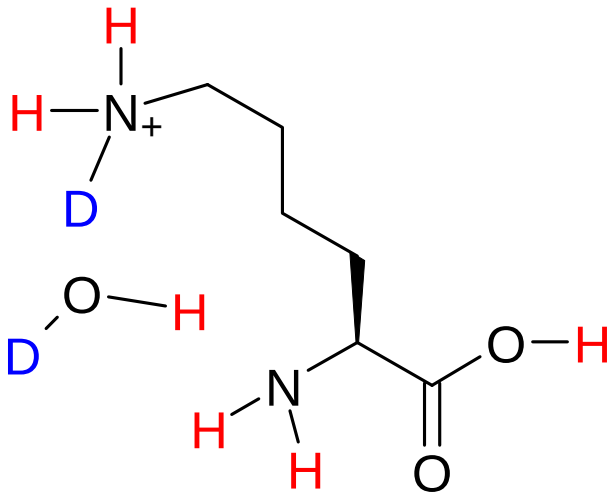
Conformational determination of peptides in the gas phase by hydrogen deuterium exchange

Tandem mass spectrometry is widely used in proteomics applications to sequence peptides in order to identify proteins. The gas-phase structure of these peptides, including different conformations and sites of proton location, can influence the fragmentation patterns, making correct identification difficult using protein sequencing algorithms. Sequencing might be improved by incorporating these different factors into the algorithm.

We use a technique called hydrogen/deuterium exchange (HX) to probe the structure of peptides in the gas-phase in order to shed light on factors that affect the conformation and protonation motifs. CD_3OD or D_2O is allowed to interact with the molecule of interest for varying lengths of time within the cell of a high-resolution mass spectrometer. By studying how the hydrogens are exchanged with the deuteriums from the reagent, we can learn about the conformation/protonation motifs that may affect fragmentation. A secondary aim of the research is to better understand the gas-phase HX mechanism itself—a general mechanism has been developed, but many of the factors that affect exchange behavior are unclear. Molecular modeling and other gas-phase techniques are currently used to aid in data interpretation.

Campbell, S.; Rodgers, M. T.; Marzluff, E. M.; Beauchamp, J. L.; *J. Am. Chem. Soc.*, **1995,** *117,* 12840



Exchange between lysine and D_2O (exchangeable hydrogens in red, deuteriums in blue)