Stability and (un)folding of a peptide helix in the gas phase from first-principles: Ac-Ala$_{15}$LysH$^+$

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Peptides in vacuo offer a unique, well-defined test bed to match experiments directly against first-principles approaches that predict the intramolecular interactions governing peptide and protein folding. In this respect, the polyalanine-based peptide Ac-Ala$_{15}$-LysH$^+$ is particularly interesting, as it is experimentally known to form helices in vacuo, with stable secondary structure up to ∼750K [1]. Room-temperature folding and unfolding timescales are usually not accessible by direct first-principles simulations, but this high T scale allows a rare *ab initio* view. We here use van der Waals (vdW) corrected [2] density functional theory in the PBE generalized gradient approximation as implemented in the all-electron code FHI-aims [3]. We show by long Born-Oppenheimer *ab initio* molecular dynamics that Ac-Ala$_{15}$-LysH$^+$ indeed unfolds rapidly (within a few ps) at T=800K and 1000K, but not at 500K. Most importantly, the observed stability depends critically not just on a correct inclusion of H-bonds and the designed termination effects, but also on vdW interactions. If these are *not* properly included, the helix unfolds already at 700K and the strcutural stability at 500K is mostly 3_{10}-helical, in disagreement with experiments; when vdW is included, the temperature stability is raised and the α-helical structure is stabilized at lower temperatures.

[1] M. Kohtani *et al.*, JACS 126, 7420 (2004).

[2] A. Tkatchenko, M. Scheffler, PRL 102, 073005 (2009).

[3] V. Blum *et al.*, Comp. Phys. Comm. 180, 2175 (2009).

[4] Alex Tkatchenko, Mariana Rossi, Volker Blum, Joel Ireta, and Matthias Scheffler, *to be published.*