Modulation of the Peptide M Absorption Spectrum with the pH

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The recently synthesized Peptide M,[1] a β-hairpin 18-mer containing a tyrosine-tryptophan dyad, features a pH-dependent absorption spectrum, offering the possibility to combine Constant pH Molecular Dynamics (CpHMD) techniques with Quantum Chemistry methods.
CpHMD aims at sampling efficiently both the phase space and the protonation state space of titrable residues. Its implementation in Amber[2] follows a sequential MD-then-Monte Carlo approach in which 1) standard MD is run in explicit solvent for a given distribution of protonation microstates and 2) protonation state change probability is evaluated for each ionizable residue interacting with the rest of the biomolecule in implicit solvent, after that the solvent and all nonstructural ions have been stripped. If the protonation state is changed, the restored solvent is relaxed before going on with the remaining MD steps.
In this work, we applied the CpHMD method to the Peptide M in order to obtain informations on the protonation states population; 40000 snapshots were taken from the trajectories at pH 5 and 11, coupled with the protonation microstate information and used to calculate the Time-Dependent B3LYP absorption spectrum at pH 5 and 11 of the tyrosine fragment embedded in the system environment.

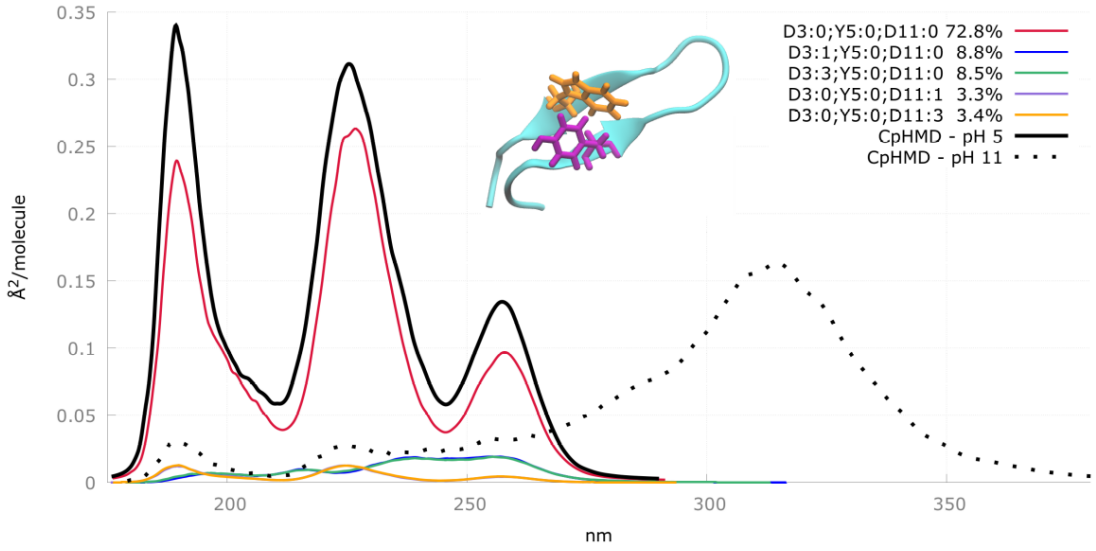

Figure 1: Calculated absorption spectrum of peptide M (tyrosine fragment, in purple) at different pH values (in black) and for the five dominant microstates at pH 5 (in colors, with the respective population percentage).

The results (Fig. 1) show a good agreement with the experimental data, highlighting a redshift at the higher pH value; moreover, all microstates contributions can be taken into account. Thus, this approach can presumably safely be implemented on bigger systems (e.g. proteins).

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