Modelling spectroscopic signatures of turns in short peptides

MENANT Sébastien;[A] **TOGNETTI Vincent**;[A] **OULYADI Hassan**; [A] **SEGALAS-MILAZZO Isabelle**;[A] **GUILHAUDIS Laure**;[A]

A) Univ Rouen Normandie, INSA Rouen Normandie, CNRS, Normandie Univ, COBRA UMR 6014, INC3M FR 3038, 1 rue Tesnière, 76821 Mont St Aignan, Cedex, France

sebastien.menant@univ-rouen.fr

Electronic Circular Dichroism (ECD) and Nuclear Magnetic Resonance (NMR) are experimental methods of paramount importance for the elucidation of polypeptide secondary structures. Among these structures, turns are essential patterns in bioactive peptides, but they are also much more difficult to characterize than helices or sheets due to the size of such motifs.

Starting with short peptides, in which turn conformations predominate, our goal is to predict the ECD and NMR signatures of turns[1]. Our work follows a previous theoretical study combining classical molecular dynamics and quantum chemistry calculations[2]. The latter are performed within a state-of-the-art hybrid QM/MM framework in which the environment effects are described using an advanced polarizable embedding scheme, and excited states are computed by Time Dependent-Density Functional Theory (TD-DFT)[3].

In this joint theoretical and experimental work, ECD and NMR spectra were first recorded on realistic peptides of biological interest, namely the Piv-Pro-D-Ser-NHMe and Ala-Phe-Ala (AFA) ones. From the computational side, ECD spectra and NMR indirect spin-spin coupling constant were simulated using the previously mentioned advanced theoretical methodology. The choice of the various parameters (force field, exchange-correlation functional, basis sets…) has been carefully assessed, as well as the convolution and fitting procedure following the spectra simulations. Our results showed that the designed protocol allows for a quantitative agreement between experimental and theoretical results, paving the way towards a better understanding of turn structures in solution.

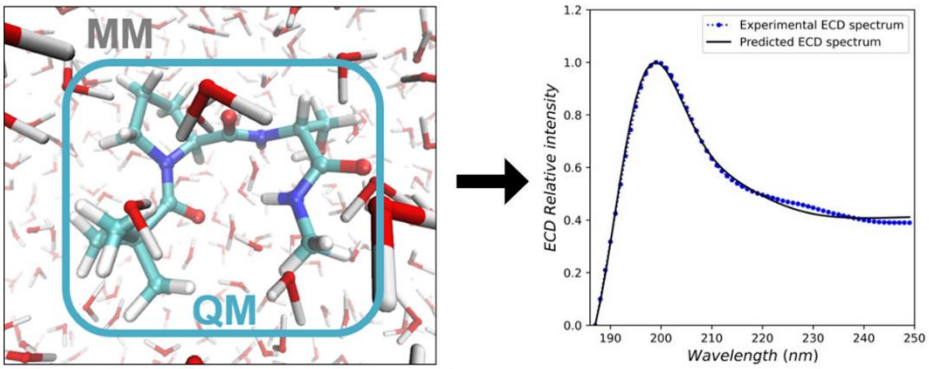

Figure 1. Solvated peptide (on the left) and its corresponding ECD spectra (on the right)

Keywords: turn conformation, electronic circular dichroism, nuclear magnetic resonance, time-dependent density functional theory, polarizable embedding, molecular dynamics.

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