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IR/UV laser spectroscopy of secondary structures in isolated peptide chains: an original insight onto the non-covalent interactions that shape proteins

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Protein shape and flexibility is governed by non-covalent interactions that need to be accurately described by molecular structure simulations. However, the computational methods adapted for large molecules like proteins have difficulties to reproduce precisely these non-covalent interactions and cannot reach the level of structural details required to address many biological relevant issues. Special efforts are currently done to document these interactions by carrying out experiments on simple model systems[1] in order to help the development of reliable DFT-D calculations[2] and polarisable force fields explorations.[3] The selectivity of the IR/UV double resonance spectroscopy of gas phase isolated peptides (less than 10 residues) laser desorbed and cooled in a molecular beam enables us to discriminate the spectral signature of the several H-bonds shaping the molecular conformation. This can be carried out for each conformation detected in the molecular beam, providing a precise IR fingerprint of the intramolecular **hydrogen bond network** of these molecules[4] and references therein These IR frequencies are directly compared to the calculated frequencies of selected conformations of the isolated molecule for assignment purpose. Once the experimentally observed conformations are known, the accuracy and the predictability of several computational methods can then be assessed through their ability to provide structures for each conformation that are both geometrically and energetically in accordance with the experimental results. In addition to H-bonds, other weaker non-covalent interactions such as NH-π, $\pi - \pi$ or π-CH_3 are also at play in these systems. They can indeed impact the H-bond network in a measurable way, which makes the investigation of these computationally challenging weak forces also accessible to this powerful experimental technique.

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