Séminaire du laboratoire de Chimie Physique

"Modeling the structure of phosphorylated Amino acids "

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Phosphorylation of proteins by kinase enzyme on the specific amino acid residues i.e. Serine, Theronine and Tyrosine regulates various cellular mechanisms like signal transduction, gene regulation, cell survival and transport of metabolites through membrane. Therefore, necessity to determine optimized geometries and bonds mobility of these phosphorylated amino acid residues which may impart more insight for understanding the structural changes post phosphorylation. We used computational chemistry method to produce infrared spectra for the monohydrated phosphotyrosine system ($pTyrH^+$-H_2O) and protonated di-peptide $[Gly\text{-}pTyr+H]^+$.[1-2] Further, we presented molecular dynamics simulations associated to a polarizable force field (AMOEBA) as a means to produce infrared spectra including temperature and anharmonic coupling effects that are necessary for a full comparison with experiment. We discussed the relevance of the Dipole moment Auto-Correlation Function (DACF) / AMOEBA combination to model infrared spectra for protonated phosphorylated amino acid ($pSerH^+$) in comparison with recent IRMPD experiments.[3] After obtaining the signature spectra for these phosphorylated amino acids, the study is further extended to determine the structure and characteristics of charged (R^+-K^+-pS-H-E) pentapeptide using polarizable AMOEBA force field. We performed extensive conformational sampling of pentapeptide structures via Replica Exchange Molecular Dynamics (REMD) method using TINKER program. Further, the sampled low energy structure of pentapeptide is evaluated with quantum chemistry calculations for optimization and IR vibrational spectra generation. Therefore our strategy, in particular, long simulations allow for significant sampling and statistical averaging for higher flexible system, leading to meaningful comparison to experiments.

Reference:

1. Structure of singly hydrated, protonated phospho-tyrosine . D. Scuderi, J. M. Bakker, S. Durand, P. Maitre, A. Sharma, J. K. Martens, E. Nicol, C. Clavaguéra, G. Ohanessian (*International Journal of Mass Spectrometry*, 308(2-3),338-347(2011)).
2. Assessment of density functionals for describing geometries and IR spectra of phosphorylated compounds. Ashwani Sharma, Gilles Ohanessian, Carine Clavaguéra (*Journal of Molecular Modeling,* 20:2426, (2014)).
3. Finite temperature infrared spectra from polarizable molecular dynamics simulations. David Semrouni, Ashwani Sharma, Jean-Pierre Dognon, Gilles Ohanessian, Carine Clavaguéra (*Journal of Chemical Theory and Computation*, 10(8) 3190-3199 (2014)).

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