High pressure effects on spectroscopic and thermodynamic properties of small biomolecules

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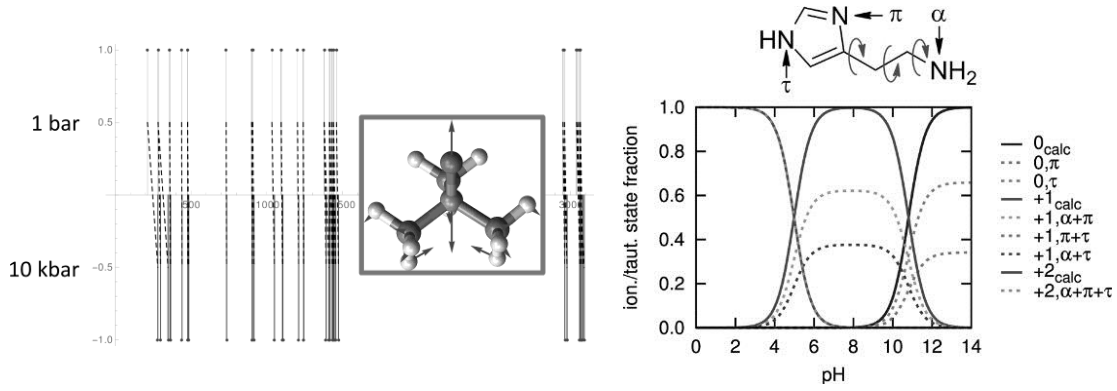
Biochemical processes of a vast number of lifeforms are accommodated to extreme conditions such as deep oceanic water. High pressure has substantial impact on the molecular basis of biological function. This poses a challenge to computational modelling approaches since the applicability of conventional empirical molecular force fields is questionable especially if chemical reactions are involved. As a step toward clarifying the situation, we need to account for high pressure in quantum-chemical (QC) calculations. A suitable methodology is provided by the "embedded cluster reference interaction site model" (EC-RISM) [1-3] that combines statistical-mechanical 3D RISM integral equation theory and QC calculations. In this context the impact of pressure is introduced by using solvent susceptibility functions containing all pressure dependent solvent properties. Besides a suitable technique for modelling the solvation features, we need to couple the method with an adequate sampling approach for molecules with acidic and basic sites or substantial conformational freedom, which can all be functions of applied pressure. Pressure therefore influences the intramolecular free energy surface which is also reflected in vibrational properties.

We investigated several of this processes for model systems such as the protein fold stabilizer trimethylamine-*N*-oxide (TMAO) [4,5] and the important neurotransmitter histamine. We illustrate the methodology in a pressure range of 1 bar up to 10 kbar to demonstrate the relevance of electronic polarization under extreme pressure conditions. The modulation of infrared bands of TMAO can be captured by pressure-dependent EC-RISM calculations [6], indicating the appropriate computational framework. Based on these benchmark data, the methodology is applied to histamine, revealing tremendous high pressure effects on partial molar volumes, populations, and pK_a, resulting in pressure and pH-dependent tautomer equilibria with potential impact on life-sustaining processes under extreme conditions.



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