

Natural Orbital Functional Theory Applied to Biologically relevant systems: Oxydative Stress in Amino Acid Side Chains

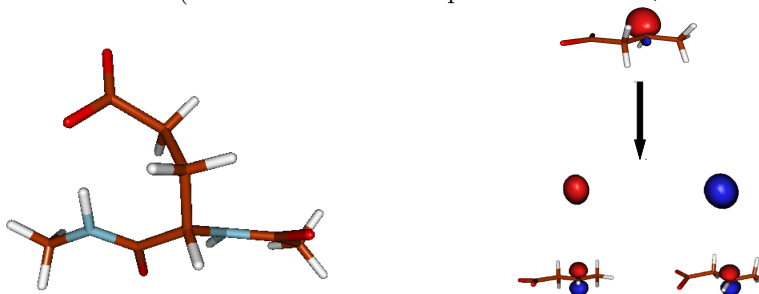
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The Natural Orbital Functional Theory (NOFT) is a new computational method that unlike DFT can deal with the static correlation problem at much cheaper cost than most wavefunction based methods. However, none has ever attempted such a calculation on medium-size molecules. The aim of this project is two-fold: on the one hand, we will show that calculations on such medium-size molecules (see the left side of Figure 1) are nowadays possible, and, on the other hand, we will test the performance of PNOF5 [1] functional in biologically relevant reactions, such as oxydative stress in amino acid side chains by the attack of hydroxyl radical.

In order to study such reaction, we have used a symplified model. Only the amino acid side chains have been considered, closed by a methyl group to simulate the C_{α} . The reaction thermodynamics of the reaction under study, $RXH + \cdot OH \rightarrow \cdot RX + H_2O$, can be calculated as a sum of two simple dissociation processes, $RXH \rightarrow \cdot RX + \cdot H$ and $\cdot H + \cdot OH \rightarrow H_2O$. Note that all possible X-H dissociations have been considered (being X: C, N, O, S) from all amino acid side chains. In the right part of Figure 1, the calculated natural orbitals for such dissociation for a C-H bond in glutamic acid are depicted. Note that the bond is localized at the minimum, while delocalized between these two atoms at the infinite (two orbitals with occupation number 1). Therefore, as CASPT2, PNOF5 describes correctly the homolytic dissociation of these bonds. It should be mentioned that both PNOF5 and CASPT2 methods predict the S-H bond of cysteine as the most likely to be attacked. Then, C-H bonds are the preferred target of hydroxyl radicals, followed by O-H bonds and finally, the N-H bonds. PNOF5 predicts results that are in between CASSCF and CASPT2, with a mean deviation from the latter of around 5 kcal/mol.

Figure 1: On the left, tripeptide model for glutamic acid. On the right, Natural Orbitals for the C-H bond at the minimum, and at the dissociation limit (two orbitals with occupation numbers 1)



[1] M. Piris, X. Lopez, F. Ruiperez, J. M. Matxain, J. M. Ugalde, "A natural orbital functional for multiconfigurational states", The Journal of Chemical Physics 134, 164102 (2011).