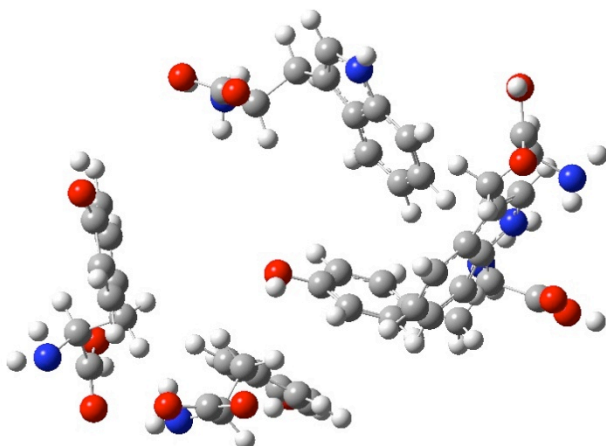


Ligand Binding and Charge Migration in AChBP's Aromatic Box

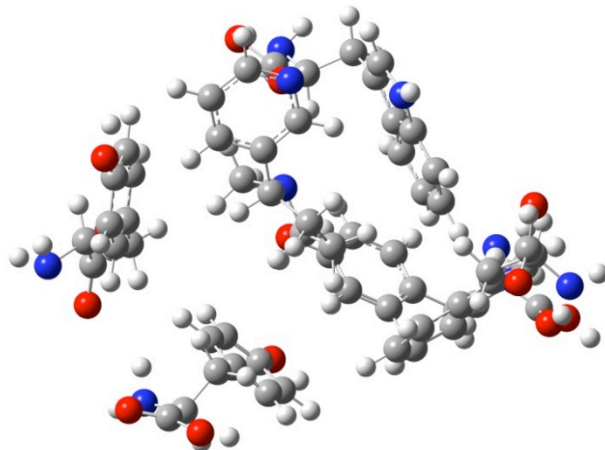
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The active site of the Acetylcholine Binding Protein, called the *aromatic box* for its five aromatic amino acid components, is a receptor for nicotine in the brain. To try to better understand how charge interactions are involved in nicotine binding, we calculated Mulliken atomic charges. The structures that we studied include isolated amino acids, isolated nicotine, the aromatic box without nicotine, and nicotine bound to the aromatic box from the protein's crystal structure. The Mulliken atomic charges of the various structures were calculated using both correlated WFT and select DFT methods. In addition, we examined charge convergence over a range of basis sets from 3-21g to 6-311+g*. We found that the charge migration in the aromatic box was relatively minor compared to nicotine's considerable charge migration. We also experimented with adding both implicit and explicit solvents to the aromatic box and observed the resulting charge migration. Finally, we docked additional ligands—morphine, cocaine, and galantamine—and calculated interaction energies (using the 6-311++g** basis set) to further map the electronic structure of the aromatic box.



Aromatic Box: No Nicotine



Aromatic Box: With

Figure 1: Aromatic box binding site from AChBP (TRP 143, TYR 89, TYR 185, TYR 192, TRP 261) with and without nicotine.