Local Properties at Protein-Ligand Interfaces

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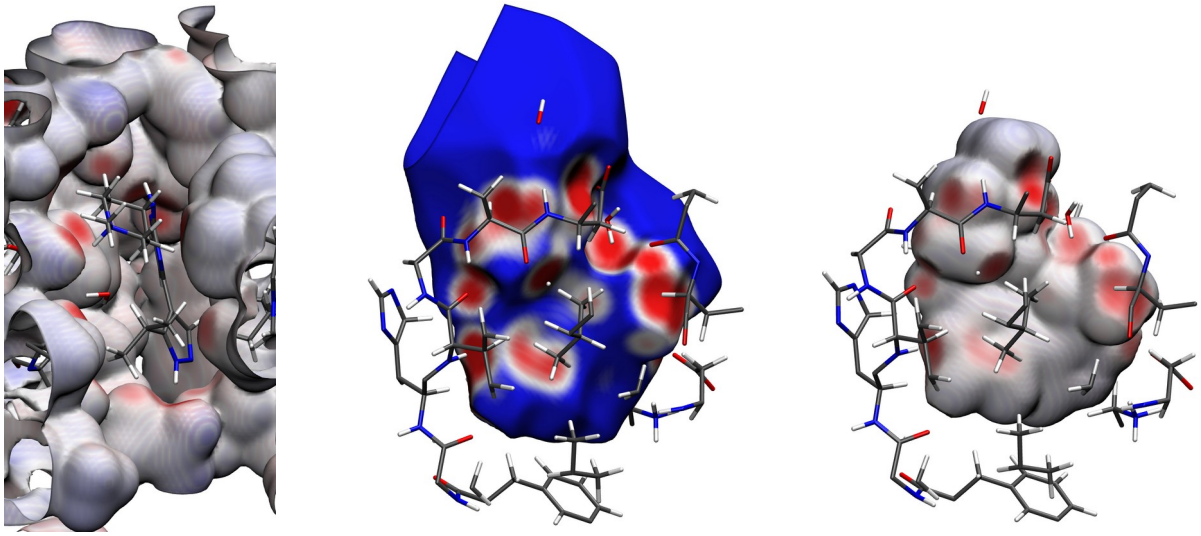
The ability to calculate the variational NDDO-based wavefunction [1] for a complete protein-ligand complex makes new approaches to analyzing protein-ligand interactions possible. Using EH5Cube or ParaSurf [2] to calculate local properties on molecular surfaces starting from the HDF5 wavefunction file generated by EMPIRE [3,4,5,6] we can evaluate properties such as the molecular electrostatic potentials and field, local ionization energy and electron affinity, and local hardness and electronegativity at the protein-ligand interface.

We will describe the calculations involved and present trends in ligand-protein binding, in particular the changes induced in the surface properties of the ligand by the protein (and vice versa).



[1] Self-Consistent Field Convergence for Proteins: A Comparison of Full and Localized-Molecular-Orbital Schemes C. R. Wick, M. Hennemann, J. J. P. Stewart, T. Clark, *J. Mol. Model.*, **2014**, *20*, 2159. https://doi.org/10.1007/s00894-014-2159-y

[2] https://www.ceposinsilico.de/products/parasurf.htm

[3] EMPIRE: A highly parallel semiempirical molecular orbital program: 1: Self-Consistent Field Calculations, M. Hennemann and T. Clark, J. Mol. Model. **2014**, *20*, 2331. https://doi.org/10.1007/s00894-014-2331-4

[4] EMPIRE: A highly parallel semiempirical molecular orbital program: 2: Periodic boundary conditions, J. T. Margraf, M. Hennemann, B. Meyer, T. Clark, *J. Mol. Model.*, **2015**, *21*, 144. https://doi.org/10.1007/s00894-015-2692-3

[5] EMPIRE: A highly parallel semiempirical molecular orbital program: 3: Born-Oppenheimer molecular dynamics, J. T. Margraf, M. Hennemann, T. Clark, *J. Mol. Model.*, **2020**, *26*, 43. https://doi.org/10.1007/s00894-020-4293-z

[6] https://www.ceposinsilico.de/products/empire.htm