MS19-2-6 A rush to explore protein–ligand electrostatic interaction energy with Charger #MS19-2-6

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Abstract
The mutual penetration of electron densities between two interacting molecules complicates the computation of an accurate electrostatic interaction energy based on a pseudo-atom representation of electron densities. The numerical exact potential and multipole moment (nEP/MM) method is time-consuming since it performs a 3D integration to obtain the electrostatic energy at short interaction distances. Nguyen et al. (2018) recently reported a fully analytical computation of the electrostatic interaction energy (aEP/MM). This method performs much faster than nEP/MM (up to two orders of magnitude) and remains highly accurate. A new program library, Charger, contains an implementation of the aEP/MM method. Charger (Vukovic et al., 2021) has been incorporated into the MoProViewer software (Guillot et al., 2014). Benchmark tests on a series of small molecules containing only C, H, N and O atoms show the efficiency of Charger in terms of execution time and accuracy. Charger is also powerful in a study of electrostatic symbiosis between a protein and a ligand. It determines reliable protein–ligand interaction energies even when both contain S atoms. It easily estimates the individual contribution of every residue to the total protein–ligand electrostatic binding energy. Glutathione transferase (GST) in complex with a benzophenone ligand was studied due to the availability of both structural and thermodynamic data (Schwarz et al., 2018). The resulting analysis highlights not only the residues that stabilize the ligand but also those that hinder ligand binding from an electrostatic point of view. This offers new perspectives in the search for mutations to improve the interaction between protein and ligand partners.

References

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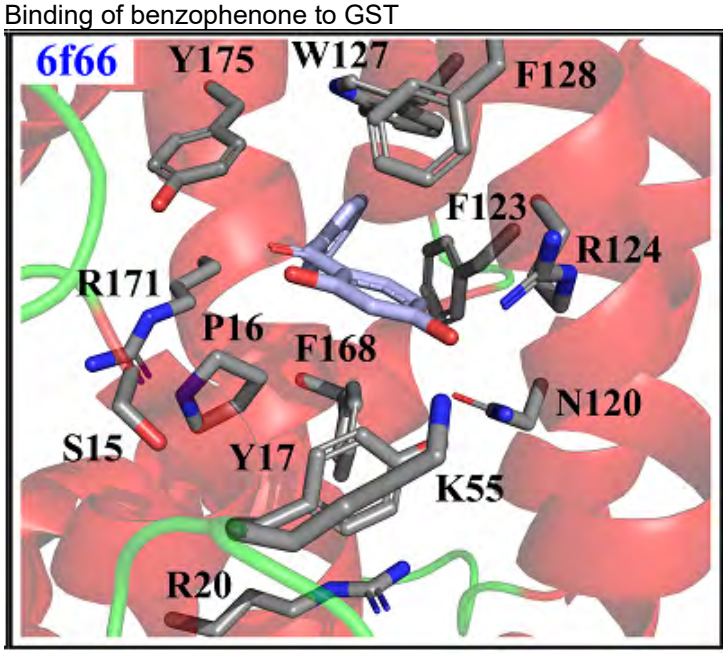
Binding of benzophenone to GST



Energy contribution of residues to binding