EDIA – A New Estimate of Electron Density of Individual Atoms for Validating Water Molecules

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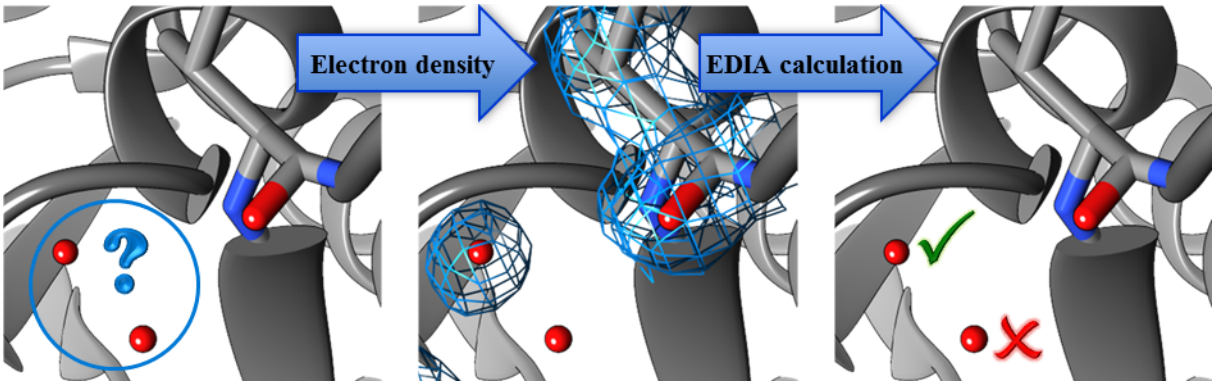

Water plays a key role in all biological systems. It forms part of the environment for biological macromolecules, mediates between protein-ligand as well as protein-protein interactions, and is indispensable for thermodynamic properties such as the hydrophobic effect.

Lately, more attention was put on water molecules being predicted and classified by a broad range of methods, such as WaterMap [1], SZMAP [2], or WaterScore [3]. Rarely those methods have been correlated in an extensive statistical analysis with water molecules from PDB structures. The only experimental evidence available for water molecules is the electron density, which has so far been completely neglected. Existing measurements concerning electron density quality like RSR and RSCC show drawbacks especially on single water molecules. [4],[5]

Therefore, we have developed a new estimate of electron density around individual atoms, called EDIA. It is an intuitive value, taking into account the experimental data from electron density within the van-der-Waals radius of an atom. A high-resolution subset from the PDB [6] with resolution better than 1.5 Å was compiled, consisting of 5,485 PDB structures containing more than 2.3 million water molecules. EDIA values were calculated for all water molecules. According to existing electron density a further characterization was performed into resolved and unresolved water molecules. In a subsequent analysis diverse structural criteria such as number of hydrogen bonds, the hydrogen bonding partners, as well as preferred environments, were evaluated.

About 9% of water molecules of the whole data set were not characterized as well resolved. This highlights the importance of taking electron density into account in order to avoid incorporating noise into any analysis concerning water molecules. Our data set will be made freely available, including EDIA values and our analysis concerning structural characteristics. This data set can help improving and validating computational methods for placing water molecules.

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