Beyond multipolar pseudoatom transferability: accounting for intermolecular polarization effects in protein-ligand complexes.

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It is of interest to build realistic charge distribution models of biological macromolecules. For this purpose, there are computationally efficient approaches based on transferable building blocks. Transferable quantities can be electron density parameters of atoms or of functional groups, or localized orbitals giving access to molecular charge distributions [1]. The first case is at the basis of libraries of transferable multipolar pseudoatoms built either from X-ray diffraction experiment [2], or from single point quantum calculations [3,4]. Electron density parameters transferred to molecular structures from these libraries are however either averaged, or issued from gas-phase quantum calculations. They are therefore practically devoid of any intermolecular effects due to the non-covalently bonded environment. These effects should be accounted for, especially in protein-ligand complexes.

To compensate this drawback, we implemented in the MoProViewer software methods designed to account for intermolecular dipolar induction in a transferred multipolar electron distribution [5]. For this purpose, atomic anisotropic polarizabilities have been added to the definition of transferable multipolar pseudoatoms, as defined in the ELMAM2 library.

The construction of this database of polarizabilities associated to ELMAM2 transferable pseudoatoms will be described, and comparisons of the resulting polarization energies against a theoretical reference will be presented. Finally, application examples on protein ligand complexes will be discussed.

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