Computation of electrostatic interaction energies in biomacromolecules from a pseudoatom databank - strengths and weaknesses

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Fast but accurate computation of electrostatic interactions in macromolecular systems is a continuous challenge. Various efforts have been put in developing new generation force fields which treat electrostatics in more sophisticated way than atomic point charge approximation. Application of higher-order electric multipole moments seems to be natural way of improvement [1]. But the point multipole expansion has also its limits. It is not accurate enough to properly describe interactions at “short distances” due to penetration effects.

Pseudoatom databanks were primary developed to improve scattering model used in analysis of X-ray diffraction data [2-4]. They allow to go beyond neutral and spherical representation of atoms while modelling crystal electron density. The methodology rely on the concept that aspherical charge densities of atoms having similar chemical environment are transferable enough to build a databank. The Hansen-Coppens pseudoatom model [5] based on a finite spherical harmonic expansion of the electron density around each atomic center is used in this approach.

The University at Buffalo Databank (UBDB) of pseudoatoms is developed not only to provide better interpretation of diffraction data but also as a more general tool to reconstruct electron density of any (macro-) molecule and to compute electrostatic properties from it, electrostatic interaction energies (Ees) in particular. Having access to charge density, instead of point multipole moments, direct integration over density distributions can be used for short distances within the Exact Potential / Multipole Moments (EPMM) scheme of Ees computation [6]. Thus penetration of charge density can be properly accounted for.

Since its first version, UBDB has been largely extended and applied in analysis of many biological systems [7]. More elaborate studies on the strengths and weakness of UBDB become possible. Are we really better than point charges? How can we be faster in Ees computation? Do we really need heksadecapole level of Hansen-Coppens model expansion to estimate Ees in biomacromolecular complexes? How short “short distances” are for typical intermolecular interactions in biological systems? How big charge penetration effect on Ees is? Does it really depend on asphericity of electron density distribution? These, and many others, are the questions we are asking ourselves and I will present the answers we have at moment [8].

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