

Charge Density Studies of Biological Macromolecules : beyond the Spherical Atom Model, Benoît Guillot,*
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At subatomic resolution, electron density reveals fine details related to charge transfer and deformation of the valence electron density due to chemical bonding and intermolecular interactions. A spherical atom model of electron density (IAM model) does not allow to take into account these features in the refinement. However, in small molecules charge density studies, the Hansen & Coppens [1] multipolar model is commonly used. It allows the asphericity of the atomic electron density to be parameterized and quantified against experimental data. With increasing number of biological macromolecules structures solved at subatomic resolution, it becomes necessary to extend charge density studies methods from small molecules to larger systems. Here we present the software MoPro [2] which is dedicated to structural and charge density refinement of such structures. MoPro implements spherical and multipolar atomic models, and combines methods usually applied both in biological macromolecules and in small compounds crystallography fields. We will also present some applications of these methods to several macromolecular systems, including 0.66 Å resolution Human Aldose Reductase [3,4] and 0.62 Å resolution RD1 Antifreeze protein [5].

[1] Hansen N.K. & Coppens P. (1978) *Acta Cryst.*, **A34**, 909-921.

[2] Guillot B., Viry L., Guillot R., Lecomte C. & Jelsch C. (2001) *J. Appl. Cryst.*, **34**, 214-223.

[3] Howard E., Cachau R. E., Mitschler A., Chevrier B., Barth P., Lamour V., Joachimiak A., Sanishvili R., Van Zandt M., Sibley E., Moras D. & Podjarny A. (2003) *Prot. struct., funct. and gen.* To be published.

[4] Muzet N., Guillot B., Jelsch C., Howard E. and Lecomte C. (2003) *Proc. Natl. Acad. Sci. USA* **100**, 8742–8747.

[5] Ko T.P., Robinson H., Gao Y.G., Cheng C.H.C., DeVries A.L. & Wang A.H.J. (2003) *Biophys J.* **84**, 1228-1237.