s3.m2.p5 **Refinement of proteins at subatomic resolution.** C. Jelsch, B. Guillot, R. Guillot & C. Lecomte. *LCM3B-CNRS-UHP BP-239 54506 Vandoeuvre-les-Nancy Cedex. France*. L. Viry - *Centre Charles Hermite, Batiment LORIA, 54506 Vandoeuvre-les-Nancy. France.*
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At very high resolution (d<0.9 Å), the approximation of the free spherical atom, even with the use of anisotropic temperature factors, is insufficient to model the molecular electron density[1]. An accurate modeling has to take into account the formation of chemical bonds between the atoms, which deforms the electronic cloud around the atoms. In the Hansen & Coppens formalism[2], the electron density is described in terms of multipoles combination and atomic charges. This formalism is implemented in the program MOLLY for the charge density refinement of small molecules, which usually diffract at subatomic resolution as their atomic thermal motion is moderate.

With the increasing number of protein structures coming out at atomic[3] or even subatomic resolution[4], the software MOPRO has been developed for the charge density refinement of macromolecules. In this modified version of the original MOLLY, the structure factors and normal matrix calculations have been parallelized. The least-squares minimization with matrix inversion, which is inappropriate with regard to the large number of variables, has been replaced by an optimized conjugate gradients procedure. Several other necessary modifications and optimizations have also been applied to the original program in order to adapt it to macromolecular systems refinement. The normal matrix turns out to be extremely sparse under certain conditions.

As first applications, the crystallographic refinement of the protein crambin (46 amino acids) at 0.54 Å resolution[4], and aldose reductase (315 amino acids) at 0.65 Å resolution[5] will be presented.

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