ATOMIC RESOLUTION MACROMOLECULAR CRYSTALLOGRAPHY WITH SYNCHROTRON RADIATION

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The recent developments at modern third-generation synchrotron radiation facilities with highly sensitive, fast and reliable detectors have a huge impact on macromolecular X-ray crystallography. High-brilliance synchrotron sources allow to determine macromolecule structures with atomic and subatomic resolution. In connection with a number of methodological improvements and new crystallographic software ranging from data processing to refinement [1], all it gave the opportunity to determination of the macromolecular structures with unprecedented extremely high resolution and quality, at a level traditionally reserved for small molecules.

At this resolution, individual atoms are clearly resolved and fine details of the structures become visible direct in the electron density maps.

The main importance of such structures is the possibility of having broader insights into macromolecule function. At very high resolution, hydrogen atoms can be seen in electron density maps and the detailed information about the protonation states of catalytically important residues can be studied, what often is critical for full understanding of molecular mechanisms.

The high data to parameter ratio permits the refinement of individual anisotropic atomic displacement parameters and the information on the mobility of a macromolecule and dynamic processes can be read from the crystal structure.

Atomic resolution gives the opportunity for clear definition of multiple conformations, although the proportion of disordered residues is higher at higher resolution, and the disorder is seen as distinct alternative conformations.

Water in macromolecule crystal occupies 30 – 70 % of the unit cell and plays an important role in macromolecule's function and stabilization. Ultrahigh resolution data allows to refine water molecules with anisotropic displacement parameters and refine them with fractional occupancies. In this situation analysing the subtle hydrogen bond network, involving precisely located water molecules, is possible.

Atomic resolution structures can be refined without or with only weak stereochemical restraints. Macromolecular models refined at ultrahigh resolutions, for well ordered structures, can be used for validation and improvement of stereochemical restraint libraries [1, 2], commonly used during refinement of lower resolution structures.

References

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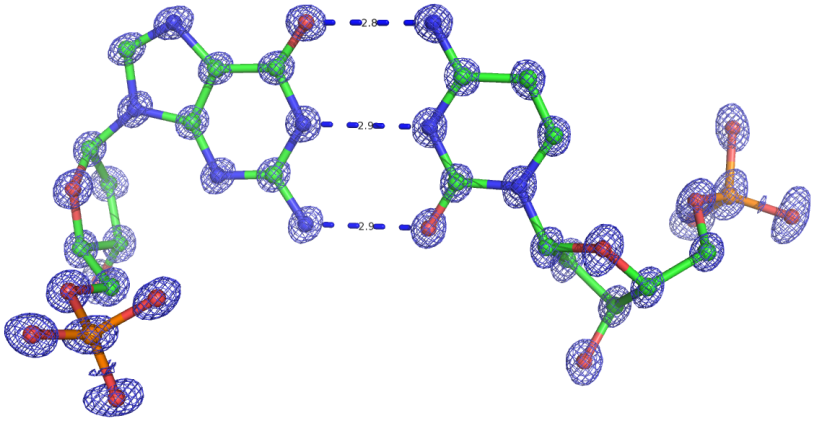

Figure 1: Fragment of electron density map of extremely high resolution structure of Z-DNA hexamer duplex d(CGCGCG) [4]. Cyt3-Gua10 base pair with the corresponding F_{obs} map at 1.5σ contour level, resolution 0.53 Å.