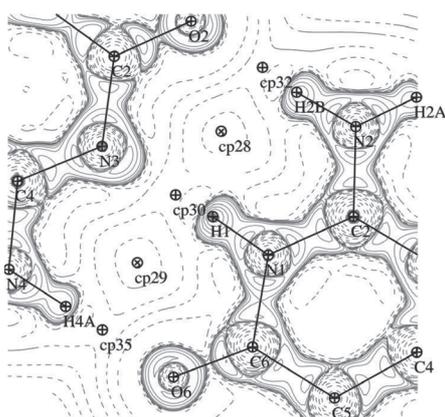


**MS18-02** Charge density analysis of macromolecules: case studies of small protein and DNA fragment. Maciej Kubicki, Mariusz Jaskólski, Szymon Krzywda. *Faculty of Chemistry, Adam Mickiewicz University, Poznań, Poland.* E-mail: [mkubicki@amu.edu.pl](mailto:mkubicki@amu.edu.pl)

X-ray diffraction provides an insight into the electron density distribution in crystals. Standard methods are based on independent atom model (IAM) approximation, which assume the spherically-averaged, neutral atoms. This model is the basis of unprecedented success of X-ray crystallography as a tool for “looking at the molecules”. However, the details of electron density distribution (bonding density, lone pairs etc.) are outside the possibilities of standard model.

The expansion of IAM into the non-spherical ‘pseudoatom’ model allows to analyze the fine details of the electron density distribution. This procedure is highly demanding experimentally, but it offers – often together with Atoms-in-Molecules approach – the possibility of deeper understanding of the nature of bonds and other interactions.

The “frontier” application of the method is in the field of macromolecules; however the very subject makes the biggest obstacle: the number of the protein and DNA crystal structures determined at subatomic resolution ( $<0.8\text{\AA}$ ) is very small and even for these handful of structures disorder, solvent, ligands etc. make the additional problems. We will present our results for two proteins (BPTI [1] and cytochrome  $c_6$ [2]) and for Z-DNA hexamer [3].



Laplacian map of one of the base pairs in the DNA hexamer.

These results are far from perfect but will probably be a good starting point for the discussion of the limits of the method.

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**Keywords:** charge density; macromolecules; topological analysis

**MS18-03** Experimental Charge Density Analysis of the Nature of C-Br $\cdots$ N $\equiv$ C Interactions in Biologically Active Compound. Maura Malinska,<sup>a</sup> Waldemar Pribe<sup>b</sup>, Krzysztof Wozniak<sup>a</sup> <sup>a</sup>University of Warsaw, Faculty of Chemistry, Poland <sup>b</sup>The University of Texas, USA E-mail: [mmalinska@chem.uw.edu.pl](mailto:mmalinska@chem.uw.edu.pl)

(E)-3(6-bromopyridin-2-yl)-2-cyano-N-(S0-1-phenylethyl)acrylamide, **WP1066**, is a novel type STAT3 inhibitor developed to inhibit its activation. Experimental charge density distribution in **WP1066** has been established using high resolution X-ray diffraction data collected at 90K to evaluate quantitatively the nature of the C-Br $\cdots$ N $\equiv$ C halogen bond in the molecular crystal. Moreover, the occurrence of the halogen bond and hydrogen bond in this structure gives the opportunity for comparison of the interaction energy and details of charge density distribution. The topological analysis of the total charge density was performed for the C(1)-Br(1) $\cdots$ N(5) $\equiv$ C(25) halogen bond and N(1)-H(1N) $\cdots$ O(2) hydrogen bond. The  $\rho(r)$  values at the critical points of these interactions are:  $0.059(1) \text{ eA}^{-3}$ ,  $0.77(2) \text{ eA}^{-5}$  and  $0.19(4) \text{ eA}^{-3}$  and  $1.45(6) \text{ eA}^{-5}$ , respectively. Charge transfer (0.33 e) occurs between molecules connected by the halogen bond. Electron density is anisotropically distributed around the bromine atoms in the crystal studied. The bromine atoms exhibit electrophilic character along the axis of C-X bond and nucleophilic character perpendicular to this axis. Interaction energy of the H(1N) $\cdots$ O(2) hydrogen bond is ten times stronger than the energy of halogen bonding.

**Keywords:** halogen bond, hydrogen bond, charge density