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Vitamin D analogous – structure and charge density analysis. Maura Malinska[a], Andrzej Kutner[b], Krzysztof Wozniak[a], [a]*Faculty of Chemistry, University of Warsaw, Poland,* [b]*Pharmaceutical Research Institute, Warsaw, Poland*
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The biological actions of the hormonally active form of vitamin D3, 1,25-dihydroxyvitamin or calcitriol and its synthetic analogs are mediated by the nuclear vitamin receptor VDR [1], which is also involved in cell proliferation, differentiation, and immunomodulation. For example, activated T and B lymphocytes, prostate, breast, and colon cancer cells exhibit increased level of VDR protein when compared with their normal counterparts. This activation or disease-specific up-regulation of VDR protein provides an opportunity to treat these conditions with VDR ligands. Calcipotriol, Calcitriol and Alfacalcidol are examples of vitamin D analogs that have undergone clinical trials with positive outcome [2,3].Conformational analysis and multipole model based on Hansen-Coppens formalism [4] obtained from theoretical structure factors. This approach revealed differences between the above analogous. The conformation of the cyclohexane A-ring is especially important as it does participate in protein binding. This ring exist in the two chair conformations, called α-form and ß-form, in which hydroxyl at C3 is in equatorial and axial positions, respectively. Studies of the vitamin D receptor (VDR) ligand binding domain, indicated strong hydrogen bonds between C1-OH and C3-OH hydroxyls and aminoacid residues Thr415 and Tyr401, respectively [5]. The charge density analysis shows that the change in side chain exert an influence on the whole molecule. Study of hydrated and anhydrous crystal structures and obtained multipole model demonstrate conformational and charge density distribution differences in molecules with α and ß-forms of A-ring.

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Charge Density of Lysozyme by the Maximum Entropy Method. Jeanette Netzel, Sander van Smaalen
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The Maximum Entropy Method (MEM) is applied to high-resolution X-ray diffraction data of hen egg-white lysozyme [1] (PDB reference: 2vb1, d_{min} = 0.65 Å) to reconstruct model-independently its charge density. Disorder in main- and side-chain residues and atomic sites can be revealed and described by the MEM without introducing constraints on the parameters to be refined. The electron density at bond critical points, their principal curvatures and their Laplacians are determined according to Bader's Atoms in Molecules Theory [2]. Energy densities at bond critical points are calculated according to Abramov [3]. Geometrical, topological and energetic properties of chemical bonds and non-bonded interactions are characterized to allow a structural and thus a functional study of this enzyme.

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Keywords: charge density, maximum entropy method, protein structure interactions

FA4-MS37-P19

Topological properties of gridded charge densities. Prathapa Siriyara Jagannatha[a], Sander van Smaalen[a], Lukas Palatinus[b, a] [a]*Laboratory of Crystallography, University of Bayreuth, Germany,* [b]*Institute of Physics, Na Slovance 2, Prague, Czech Republic*
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The electron density of α–Glycine has been studied in order to determine the effect of the grid size on the distribution of charge densities and their topological properties. The electron densities of α–Glycine with different grid sizes have been determined according to: (1) The independent atom model, (2) The maximum entropy method and (3) The multipole model. These densities have been analyzed according to Bader's quantum theory of atoms in molecules (QTAIM) [1], using the computer program EDMA [2]. The diffraction data of α–Glycine have been taken from Destro et al [3]. Three different grid sizes (0.08Å, 0.04Å and 0.02Å) have been used for analysis. It has been found that the grid size has no influence on the values of the interpolated electron density at bond critical points, but it does influence the values of the Laplacian of covalent bonds and hydrogen bonds as well as integrated properties, like atomic charges. The Laplacian values for different grid sizes of covalent bonds differ by up to 0.32% for C-H bonds and by 76% for C-O bonds.

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FA4-MS37-P20

The transferability of atomic multipoles for amino acids and peptides Magdalena Woińska[a], Paulina M. Dominiak[a], [a]*Chemistry Department, University of Warsaw, Poland*
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Popular force fields usually employ point charges. Supplementing atomic charges with higher electrostatic moments leads to more accurate charge distribution models. New generation force fields based on multipole models require high level of transferability of atomic multipole moments. The aim of this work was to analyze the level of