Late and Special Abstracts

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DIFFRACTION STUDIES OF INTERACTIONS BETWEEN POLY(ETHYLENEGLYCOL) AND PROTEINS

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X-ray structure determination of synthetic polydisperse polymer material in atomic resolution is difficult problem because of virtual impossibility to prepare crystals suitable for diffraction experiment [1]. Quite different situation is when one is interested in the interaction of individual polymer molecules with biological material. About 40-70 % of volume of protein crystals form large cavities filled by solvent. In principle, any water soluble molecule with specific adhesion to the protein surface can be observed in the maps of electron density. The crystals of large proteins have large cavities which can incorporate even high molecular weight water soluble polymers.

Interactions of poly(ethyleneglycol), the topic of our interest, is used in many medical applications (targeted transport of drugs in body, support scaffold for cell growth, etc.). Adhesion of poly(ethyleneglycol) to proteins has already been used and observed long time ago. Poly(ethyleneglycol) with molecular weight 400 up to 20 000 is often used as precipitant for protein crystallization.

Poly(ethyleneglycol) is very polymorph ligand for proteins and forms a large scale of interactions – from coordination bonds to cations, hydrogen bonds and also hydrophilic interactions. The most tight binding of the end of poly(ethyleneglycol) chain at the protein surface is winding the polymer chain around the positively charged side chains of lysine, arginine and histidine. Figure 1

shows the example of poly(ethyleneglycol) anchored at the basic residue rich region of the protein surface (PDB code 1O57 [2]). Review of all ligand specific binding types is available from author.

[1] J. Hašek, J. Labský, Index of Polymer Structures 95, ISBN 80-901748-3-3, CSCA, Prague 1995.

[2] H.M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T.N. Bhat, H. Weissig, I.N. Shindyalov, P.E. Bourne, *Nucleic Acids Research,* 2000, 28, 235-242.
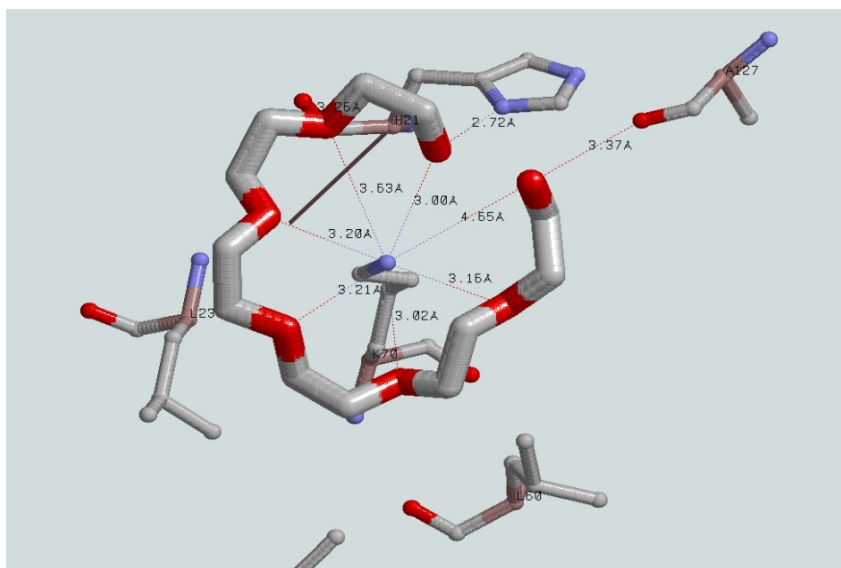
T1 - P18

LCDP – A NEW METHOD FOR STRUCTURE ANALYSIS AND QUALITATIVE AND/OR QUANTITATIVE PHASE ANALYSIS.

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A new method is proposed which provides excellent results in the field of structure analysis and refinements from powders and also of Q/Q phase analysis. The method was originally developed for the latter and the original idea was based on the fact, that the number of unique powder patterns is not infinite. If such a statement is true, it is easy to prove algebraically that any "new" pattern can be approximated by a Linear Combination of (already known) Diffraction Patterns. Analogy with LCAO method used in quantum chemistry is evident and in fact the LCDP does not use standard LS method, but SCF, either standard or perturbed. Inasmuch as it would be computationally difficult to use *all* diffraction patterns to approximate a new one, for a daily practice some subsets have been tested starting from a very simple (a mixture of SiO_2, Al_2O_3, Y_2O_3 and TiO_2) to rather complicated ($PbSO_4$, ZSM-5 and C_3S), etc. The user's database "Harpagon" containing more than 10 000 calculated standards was created employing so called Biegler's coding, which is, in contrast to the existing methods less disk space demanding and computationally very fast. A Round Robin was organized to test the method and the success rate obtained in several independent laboratories was ~87.568%. Although the method was originally designed for phase analysis, its power in structure refinement and later also in structure solution was soon recognized, when theoretical diffraction patterns were generated using the data collected in various databases. Again, *per analogiam*, it was proposed that a new structure is just and only *i*) to a certain degree perturbed known one, or, *ii*) is in fact a linear combination of some already solved crystal structures (for example structures built from inorganic polyhedra or organic rings). In the first case the value of so-called perturbation operator is sought in the iteration process (SCF). If such a value drops below a pre-defined Bayesian limit , the structure is solved and, as a side effect, also refined. In the more complicated cases, the limit is iterated along with other parameters until self-consistence is achieved. In the second case a matrix of the values is sought and the process is therefore much more time consuming. The variances of structural parameters are weighted linear combinations of the known ones. Required machine time is well-comparable to the that typical for some non-deterministic procedures. The procedure can also work in a "reverse" mode, i.e. can step-by-step suggest new crystal structures (and their powder patterns), whose combination can give the unknown one. This mode proved to be very useful for beginners and also for those, who deal with disoredered or OD strucures. Needless to say that some not very amorphous structures can be also solved, provided higher orders of the operator are included. However, in such a case the user must be aware of rather large matrices and a 64 bit processor is recommended. Otherwise the accuracy is lost and multiple solutions may occur. The program LCDP was written in the Liszp language and will be distributed under the GNÜ license for an affordable price. The conditions and more details will be given in *Neues Jahrbuch fűr Kristallographie (Monathshefte)*, **784** (2004). It is expected that when the "reverse" mode is improved, the need for other databases but by user generated and maintained will be soon very low.