P.03.10.4
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Specificities of Binding of Different Inhibitors of Cahepsins
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Thiol protease Cathepsins play a significant role in proteolysis especially in certain desease states in humans.Mode of inhibition by different protein inhibitors in not clear yet.Keeping this in mind modeling studies were initiated with previously known and rcently identified inhibitors of stefin family with intact and truncated n-terminal inhibitor.We find that role of N- terminal wedge as well as the second hairpin loop is very important. Inhibition mechanism also differs for endo and exo peptidase.
Keywords: thiol protease, cathepsins, stefins

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Multi-component Analysis of Raw Diffraction Data
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Computational methods in macromolecular crystallography are pursued to enable structure solution of the most challenging molecular targets, where crystals inherently have low scattering power.

For such molecules, an optimal modeling of measured intensity is essential to extract and describe phasing signals. However, this analysis is not straightforward in the experiments pushing the limits, where phasing signal is correlated with non-isomorphism or radiation induced changes. Alternative solutions, like correcting for radiation damage with high-redundancy data that reduce the correlation, are not possible with heavy exposures limiting the crystal lifetime. Without the high-redundancy data, the current approaches to deal with radiation-induced changes are numerically unstable.
A statistical description was developed and implemented to solve this problem, making it possible to both correct for and/or recover the phasing signal from radiation damage changes, even from data of limited redundancy. This approach creates a new framework for an analysis of signal-to-noise ratio in many areas of macromolecular crystallography. The results and their potential consequences will be presented.
Keywords: macromolecular crystallography, diffraction, radiation damage

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Sizes of Molecules in Organic Crystals: the Voronoi-Dirichlet Approach
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Crystallographic data on 69011 molecular compounds were selected from the CSD by means of the program package TOPOS [1]. All the compounds are completely refined structures without metal atoms. The sizes of molecules have been calculated as the volumes of molecular Voronoi-Dirichlet polyhedra (VDPs) [2]. To construct molecular VDPs, the method by Peresypkina & Blatov [2] implemented in the ADS program (part of the TOPOS package) was used. After calculation 100632 molecules have been detected and volume distributions were constructed for the most frequent molecules.

The conclusions from the data obtained are that the volume of a molecule is rather constant and that variations follow a normal distribution and the mean volume value is almost coincident with the volume of a molecule in a homomolecular crystal. The last conclusion follows from the fact that almost all molecular volumes in the homomolecular crystals lie within the 95% confidence intervals, whose half-width is *ca* 10% of the mean value. This means that the influence of a crystal field on the size of a molecule is found to be slight and nearly equal in homo- and heteromolecular crystals. This trend can be violated if a molecule is surrounded by a good deal of highly polarized atoms or if a molecule is disordered or surrounded by disordered molecules.

The results obtained show that molecular VDPs can be used to model molecular domains and to reveal factors causing variations in domain sizes. These results can be useful, *e.g.*, for predicting organic substrates that can occupy the receptor cavity [3].

[1] Blatov V.A., Shevchenko A.P., Serezhkin V.N., *J. Appl. Cryst.*, 2000, **33**, 1193. [2] Peresypkina E.V., Blatov V.A., *J. Mol. Struct. (Theochem)*, 1999, **489**, 245-236. [3] Virovets A.V., Blatov V.A., Shevchenko A.P., *Acta Cryst.*, 2004, **B60**, 350-357.
Keywords: molecular compounds, Dirichlet domain, computational analysis of crystallographic data

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The Rational Design of Molecules for Use as Friction Modifiers
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Car engines require protection from corrosion and wear. To this end it is possible to attach small molecules to the metal surfaces which can form a layer and reduce friction and corrosion. Previous work has shown that carboxylates are good head groups for attachment of molecules to metallic surfaces containing iron [1].

We have been looking at the binding of carboxylate molecules to lightly oxidised Fe(III) systems through statistical trends in similar systems present in the CSD. We are interested in the geometry of these systems to enable us to understand what makes the carboxylate group a good surface active group for such systems. From this we hope to be able to design molecules which can attach to iron surfaces in a controlled, predictable way in order to function as friction modifiers.

Thus far we have shown that of all the common binding modes, the binding of each oxygen atom in the carboxylate to two different iron centres is the most prevalent form. On closer inspection there appears to be little strain in the bond angles of the carboxylate and only minor distortion of the iron centres from regular octahedral geometry. This suggests that there is good orbital line-up between the two moieties and is thus it is a good template for the design of an attachment group.

[1] Harris S.G., *University of Edinburgh*, 1999.
Keywords: surface chemistry, molecular modeling, database mining

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Identifying NCS in Electron Density Maps: A Pattern Recognition Approach
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The determination of the NCS operators between multiple copies of a protein in an asymmetric unit is essential to the process of density modification and phase improvement by NCS averaging. This process improves the quality of the electron density and aids structure determination. The real-space method presented here determines the NCS operators between related copies of a protein by recognizing structurally similar regions. The algorithm uses rotation invariant features (based on a preliminary backbone trace) to perform feature based matching between density patterns. These matches are then extended by fragment superposition. This algorithm allows for the NCS operators to be determined early on in the structure determination process and requires neither the location of heavy atoms nor any other sequence information.

The results of testing this algorithm on 20 representative proteins