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Ribitol and Xylitol: Explaining the Differences in Physical Chemical Properties
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The diastereomeric pentoses xylitol [1] and ribitol [2] show some remarkable differences in their physical properties in the solid state. Though xylitol has the lowest melting point (T = 93° C) it has a higher density (ρ = 1.540 g/cm³) than ribitol (T = 102° C, ρ = 1.488 g/cm³).

Based on accurate X-ray diffraction data we have performed experimental electron density studies and rigid-body TLS analyses, in order to analyse the interplay between entropy and enthalpy contributions to the free energy, and thereby explain the observed differences in physical properties.

Topological analyses of the electron densities show that the chemical bonds of the two pentoses are identical. Though the compounds have different hydrogen bond patterns, they most likely have very similar crystal packing energy. A result in accordance with calorimetric measurements and interaction energies derived from periodic DFT calculations.

Assuming that the translational and librational molecular normal modes are harmonic and uncoupled from the motion of neighbouring molecules we find the difference in vibrational entropy in the solid state to be 6 J mol^{-1} K^{-1}, a result that accounts quantitatively for the difference in melting point.

[1] Kim H. S., Jeffrey G. A., *Acta Cryst*., 1969, B**25**, 2607-2613. [2] Kim H.S., Jeffrey G. A., Rosensten R. D., *Acta Cryst*., 1969, B**25**, 2223-2230.
Keywords: charge density, chemical physical properties, rigid-body analysis

MS64 DIFFICULT PHASING AND DIFFICULT STRUCTURES IN STRUCTURAL BIOLOGY

Chairpersons: Bi-Cheng Wang, Alexandre Urzhumtsev

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How to deal with Pathological Crystals of Macromolecules
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Although macromolecular crystallography is rapidly becoming largely routine due to advances in the methods of data collection, structure solution and refinement, difficult cases are still common. We have recently completed a number of structure determinations that utilized less than perfect crystals and these cases exemplify various difficulties faced by protein crystallographers. The structure of the proteolytic domain of *Archaeoglobus fulgidus* Lon was solved with crystals that contained superimposed orthorhombic and monoclinic lattices in a seemingly single crystal. Another, hexagonal crystal form exhibited unusually large degree of non-isomorphism that was not apparent in the analysis of the unit cell parameters. Crystals of the *A. fulgidus* Rio1 kinase exhibited both pseudosymmetry and twinning that masked the problems during analysis of intensity distribution. We will discuss the ways of identifying the observed phenomena and the approaches to solving and refining macromolecular stuctures if only less than perfect crystals are available.
Keywords: pseudosymmetry, twinning, non-isomorphism

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Phasing at Resolution higher than the Experimental one
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We have developed a novel procedure which, combined with classical electron density modification (EDM) techniques, is able to:
a) extrapolate moduli and phases of non-measured reflections with resolution lower or higher than the experimental one;
b) actively use such moduli and phases in typical situations met in macromolecular crystallography:
1) *ab initio* phasing: data resolution (RES_{obs}) in the interval 1.5-1.0Å, an approximated electron density available (e.g., after the application of *EDM* procedures) with mean phase error (MPE_{obs}) in the range (25°, 60°);
2) *SAD-MAD*, *SIR-MIR*, *SIRAS-MIRAS* phases: RES_{obs} in the interval 2.8-1.5Å, an approximated electron density available with MPE_{obs} in the range (40°, 65°);
3) *ab initio* phasing, RES_{obs} in the interval 1.5-1.0Å, no phase information available.

Our results [1,2] indicate that in case 3 extrapolation can make difference between success and failure. In cases 1 and 2 the extrapolation procedure is able to reduce the mean phase error of the measured reflections, provides sensible estimates (in modulus and phase) for additional reflections behind and beyond RES_{obs}, and increases the interpretability of the final electron density map.

[1] Caliandro R., Carrozzini B., Cascarano G.L., De Caro L., Giacovazzo C., *Acta Cryst.*, 2005, D, *in press*. [2] Caliandro R., Carrozzini B., Cascarano G.L., De Caro L., Giacovazzo C., *Acta Cryst.*, 2005, D, *submitted*.
Keywords: macromolecular crystallography, extrapolated reflections, resolution

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A Challenging 90 Residue Problem for X-ray Crystallography: the ^{2}F1-^{3}F1 Module Pair of Human Fibronectin
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Human fibronectin (Fn) is a large multidomain protein found in the extracellular matrix and plasma. It is involved in many cellular processes. The ability to bind Fn is a characteristic that has been demonstrated for a number of pathogens. Although the structures of two F1 module pairs have been determined by NMR, no X-ray structures have been reported so far.

Fibronectin crystals of the ^{2}F1-^{3}F1 module pair diffracting to 1.7 Å were obtained but they exhibited symptoms of possible twinning (1). Initially, we attempted to solve the structure by MR using different ensembles of the NMR models, but after many different strategies failed, we moved on to MIR methods. A number of different derivative datasets were collected, and all showed partially occupied sites but did not give interpretable maps. In-house data were collected for the sulphur SAD method, but this also failed. RIP was tried next, and although a large signal from the breakage of the 4 disulphide bonds was obtained, the maps were again uninterpretable.

We then collected highly redundant S-SAD data to a highest resolution of 2.15 Å. A sulphur signal was measured, but yet again the maps were uninterpretable. Eventually, the structure was solved when the phase information from the S-SAD and RIP data were combined.

Data were collected at the ESRF, beamlines ID 14-4 and BM 14, and at the SRS, station 9.6.

[1] Rudiño-Piñera E., Schwarz-Linek U., Potts J. R., Garman E. F., *Acta Cryst.*, 2004, D**60**, 1341-1345.
Keywords: fibronectin, RIP, sulphur SAD

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NCS and Normal Modes Ensembles Solve Difficult MR Problem
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We describe a strategy that has been used to push further the molecular replacement limits by taking advantage of the