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Membrane sorting between secretory and endocytic organelles is predominantly controlled by small carrier vesicles or tubules that are layered on their cytoplasmic faces by specific protein coats. Recently we have begun studies of a novel putative membrane coat complex termed retromer. Retromer contains five subunits, Vps35, Vps26, Vps29, Snx1 and Snx2 and is responsible for tubule-based retrieval of proteins from the endosomal system to the Golgi, for example recycling mannose-6-phosphate receptors that traffic lysosomal hydrolases from the TGN to endosomes. We have determined the crystal structure of the mammalian retromer subunit Vps29, showing that it has structural similarity to divalent metal-containing phosphoesterases. However, although Vps29 can coordinate metals in a similar manner it has no detectable phosphatase activity *in vitro*, suggesting a novel specificity or function. We show that Vps29 and Vps26 bind directly to distinct regions of Vps35 and together form a high affinity heterotrimeric sub-complex. Mutagenesis reveals the structural basis for interaction of Vps29 with Vps35 and subsequent membrane association of Vps29 *in vivo*. Furthermore, we demonstrate that a conserved hydrophobic surface distinct from the primary Vps35 binding site can mediate assembly of the Vps29p-Vps26p-Vps35p sub-complex with sorting nexins in yeast, and mutation of either site results in a defect in retromer-dependant membrane trafficking.

Keywords: membrane trafficking, protein phosphatases, X-ray structure

MS37.26.5

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Crystallization of Molybdate-Binding Protein of Xanthomonas citri

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We report the crystallization and prelliminary data of the periplasmic molybdate-binding protein (ModA) of the plant pathogen *Xanthomonas citri*, responsible for the cancer disease affecting citrus plants. Structures of molybdate transporters have been solved in other species including *Escherichia coli* and *Azotobacter vinelandii* [1, 2], however, no ortholog derived from plant-associated bacteria have been reported so far. The 26 kDa protein has been overproduced in *E. coli*, purified, and crystallized in complex with Na_2MoO_4. The crystallization of ModA using the sitting-drop vapour-diffusion method with PEG 4000 as precipitant is described. Crystals belong to the orthorhombic space group $P222_1$, with unit-cell parameters a = 68,16, b = 172,21, c = 112,05. A X-ray diffraction data were collected to a maximum resolution of 1,7 Å using a synchrotron-radiation source. Structure refinement is in progress. The ongoing biochemical characterization in combination with the structural analysis, will assist the elucidation of the structure-activity relationship in regulating the uptake of molybdate in *Xanthomonas*.

[1] Hu Y., Rech S., Gunsalus R.P., Rees D.C., *.Nat.Struct.Biol.*, 1997, **4**, 703-7. [2] Lawson D.M., Williams C.E., Mitchenall L.A., Pau R.N., *Structure.* 1998, **6**, 1529-39.

Keywords: ModA protein, Xanthomonas citri, crystallization

MS38 CONTROLLED BUILDING OF CRYSTALS FROM NON-COVALENT INTERACTIONS

Chairpersons: Christer Aakeroy, Alessia Bacchi

MS38.26.1

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Understanding and Using Solution Chemistry to Direct Crystal Nucleation

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Our understanding of non-covalent interactions which determine crystal packing in the solid state has progressed enormously over the last years due largely to the explosion in numbers of crystal structure determinations and their availability via the Cambridge Structural Database. In the context of *controlled* building of crystals however, this information is not enough, we also have to consider the interactions which exist in the solution phase at the time of nucleation. Such information can be gleaned from a number of sources: thermodynamic and colligative data (eg solubility, freezing point depression); UV/vis spectroscopy; vibrational spectroscopies; NMR; and neutron scattering.

This paper reports on the use of these techniques in understanding the key interactions in highly concentrated solutions of urea, benzoic acid, tetrolic acid, sulfamerazine and 2,6dihydroxybenzoic acid. In many cases there is a clear link between solvent mediated self assembly and the resulting crystal structures.

Keywords: nucleation, solutions, chemistry

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Molecular Tectonics : from Tectons to Networks

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Molecular crystals are compact and periodic entities. They are defined by the nature of their molecular components and interactions between them in the solid state. Although a crystal is described by translation of the unit cell into three directions of space, one may describe it as a network by considering intermolecular interactions as specific recognition patterns. The approach dealing with such an analysis is called molecular tectonics [1]. The latter is based on tectons which are construction units bearing within their backbone assembling programmes. The design and formation of molecular networks with predefined dimensionality and connectivity may be ensured by the nature and localisation of recognition sites within the structure of tectons.

The strength of molecular tectonics is related to the fact that not only it allows to describe a given crystal in terms of networks but, also and more interestingly, this approach allows to conceive molecular networks through the specific design of tectons [2].

A variety of tecons and molecular networks based on diverse intermolecular interactions will be presented.

[1] Hosseini M. W., *Acc. Chem. Res*.,2005, **38**, *in press*. [2] Hosseini M. W., *Cryst. Eng. Comm*, 2004, **6**, 318.

Keywords: tectons, networks, chemistry

MS38.26.3

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Testing the Reliability of the Self-complementary Noncovalent Interactions: Supramolecular Implications and Supramolecular Design

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Noncovalent interactions play a special role in supramolecular chemistry, which has been defined by Lehn [1] as “chemistry beyond the molecule”. Noncovalently assisted synthetic procedures are used to assemble various types of supramolecular species. These syntheses rely on the stabilization provided by noncovalent interactions between recognition sites incorporated within precursors. As a recognition motif utilized to guide the synthesis, various types of noncovalent interactions can be used. These are, specifically, hydrogen bonds (H-bonds), stacking interactions, electrostatic interactions, hydrophobic interactions, charge-transfer interactions, and metal coordination [2]. Unconventional polymers composed of covalent and noncovalent bonds differ dramatically from standard, conventional polymers with just covalent bonds. They posses novel physical, optical, electrochemical, photochemical, biological, and catalytic properties. Targeted synthesis of macro- and supramolecular structures of various sizes, shapes, and functionality has now become possible. Supramolecular chemitry offers incredible applications in various

fields such as medical chemistry (drug delivery systems), host-guest chemistry, catalysis and molecular electronics.

[1] Lehn J.-M., *Angew. Chem.,Int. Ed. Engl*., 1988, **27**, 89, *ibid*. 1990, **29**, 1304. [2] Lehn J.-M., Atwood J. L., Davies J. E. D., MacNicol D. D., Vögtle F., *Comprehensive Supramolecular Chemistry*, Eds. Pergamon, Oxford, 1996.
Keywords: supramolecular, noncovalent interactions, coordination compounds

MS38.26.4
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Recognition of Weak Interactions at the Gas-crystal Interface
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Molecular self-assembled materials are promising in several fields such as gas storage, selective recognition, separation and modulation of the functions of active molecules. The application of the principles of self-assembly and crystal engineering permit the shaping of specific nanoscale environments where guest molecules, through new weak interactions, are entrapped. We could obtain an empty-pore hexagonal structure (solved by single-crystal analysis) held together by a network of weak interactions and fabricate supramolecular architectures that cooperatively stabilize gases that diffuse in. The molecular crystal can store large amounts of carbon dioxide and methane selectively over nitrogen, oxygen and hydrogen [1]. NMR spectroscopy could measure intermolecular distances and recognize the specific interactions that contribute to the overall stabilization. The impressive upfield shifts caused by the aromatic ring currents on gas molecules at the van der Waals contacts provide a tool for understanding the preferred topology of the gases interacting with the inner surface of the porous crystal. A variety of conjugated molecules can be encapsulated in the infinite nanochannels of 0.5 nm of the host matrix. Weak host-guest CH···π and π···π interactions form collectively a stable architecture with all the active molecules aligned along the crystallographic *c* axis in thermally stable single crystals.

[1] Sozzani P., Bracco S., Comotti A., Ferretti L., Simonutti R., *Angew. Chem. Int. Ed.*, 2005, **44**, 2. [2] Sozzani P., Comotti A., Bracco S., Simonutti R., *Angew. Chem. Int. Ed.*, 2004, **43**, 2811.
Keywords: molecular crystals, intermolecular interactions, NMR spectroscopy

MS38.26.5
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Peptide-Based Organic Microporous Materials
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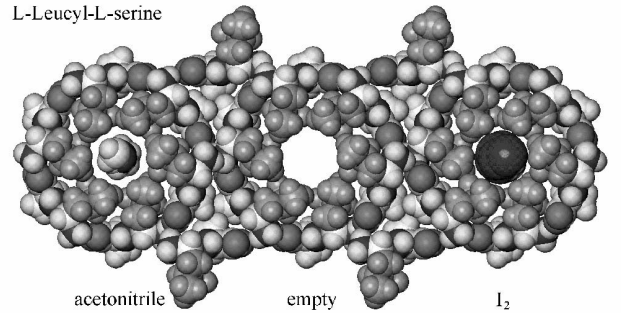
In the last few years, small peptides have emerged as an unexpected source of microporous materials. Uniquely among organic molecules, these compounds may not only form crystal structures with nanotubes with der Waals' diameter from 3.2 to 10 Å, but cocrystallized solvent molecules located in the channels can often be removed with full retention of the peptide scaffold. Subsequently, absorption of other organic or inorganic molecules can take place.



This presentation gives an overview of the known microporous peptide structures, with special emphasis on recent experimental results, as for the dipeptide L-leucyl-L-serine (see illustration).
Keywords: nanotubes, peptides, supramolecular structures

MS39 POWDER DIFFRACTION OF PROTEINS
Chairpersons: Robert H. Blessing, Jeremy Cockcroft

MS39.26.1
Acta Cryst. (2005). A**61**, C53
Recent Developments in Protein Structure Analysis from Powder Diffraction Data
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The central problem in using powder diffraction data for the solution of crystal structures is that the structure factor information is severely limited relative to that obtained from a single crystal covering the same region of reciprocal space. The scattering from a single crystal is represented in reciprocal space by an array of slightly broadened delta functions; their intensity measurement is a simple integration of the peak intensity above background. For a powder diffraction experiment, the reciprocal space picture is of a nested series of spherical shells broadened by sample and instrumental effects; the density of these shells increases cubically with distance from the reciprocal space origin. Their intensity corresponds to that of the structure factor responsible for the shell and its multiplicity. Extraction of the individual structure factor intensities that form the powder pattern is then compromised by the increasing overlap of these shells. This is particularly acute for proteins as the diffraction patterns are made from a very large number of structure factors. However, the unprecedented sharpness of protein powder pattern peaks and their position sensitivity to sample environment provides a means of overcoming the loss of information. This talk will present some recent results on the problem of extracting structure factors and the improvement possible from using combinations of protein powder patterns.
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Keywords: powder diffraction, proteins, structure determination

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Molecular Replacement with Powder Diffraction Data
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As more and more protein folds become known, the molecular replacement (MR) method[1] becomes a more attractive method for structure solution. We will demonstrate that synchrotron powder data are sufficient to solve the simple MR problem of finding the position and orientation of the origin of the unit cell with respect to a single protein molecule. A series of examples of small proteins (including lysozyme, trypsin, myoglobin, thaumatin and apoferritin) that cover symmetries from cubic down to monoclinic will be described.

The challenges encountered in more complex molecular replacement problems depend on both the quality of the search model and experimental data. For single-crystal experiments, the data are effectively error free and this essentially reduces to a question of model quality. The peak overlap problem can be so severe for powder experiments that significant gains are possible when peak overlaps are accounted for. The effects of both counting statistics and instrumental resolution on the likely success of a molecular replacement approach with powder data will also be discussed. While the finding that powder data are sufficient for simple molecular replacement problems is not surprising in view of the complexity of small molecule structures that are now be solved from such data, the routine applicability to macromolecular structures remains to be established.

[1] Rossman M. G., *Acta.,Cryst.*, 1990, **A46**, 73-82.
Keywords: powders, proteins, molecular replacement