signals of the snRNPs. As an import adaptor snurportin1 bridges the interaction between the m_3G-cap bearing snRNPs and the nuclear import receptor importin-β, which mediates the interaction with and translocation through the nuclear pore complex. Snurportin1 contains a N-terminal importin-β-binding (IBB) domain and a m_3G-cap-binding region, which shows no similarity to other known nuclear import factors. We have solved the crystal structure of the m_3G-cap binding domain of snurportin1 by means of MIRAS, and the structure was refined at 2.4 Å resolution. The crystal structure reveals an unexpected binding mode for the m_3G-cap, that significantly differs from other cap-binding proteins such as eIF4E and CBP20. The structural basis for the discrimination of m^7G-cap bearing RNAs by snurportin1 will be discussed.

Keywords: RNA-protein interactions, nuclear transport, MIRAS

MS44.27.5

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Structural Basis for Antigene and Antisense Duplexes with Modified Nucleotides

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Oligonucleotides containing polyamines are currently being evaluated as potential antigene and antisense compounds. Those with 5-(*N*-aminohexyl)carbamoyl-2'-deoxyuridine (^{N}U) and its 2'-*O*-methyl derivative (^{N}U$_m$) exhibit improved nuclease resistance. Furthermore, these nucleotides stabilize duplex formation of the modified DNA and its target DNA or RNA strand. X-ray structures of these duplexes have shown good correlation between the conformational changes and the observed chemotherapeutic properties.

The amide groups of the modified uracil bases form six-membered rings through the intramolecular NH---O4 hydrogen bonds, so that the aminohexyl chains protrude into the major grooves. Some of the terminal ammonium groups are involved in intra-duplex interactions with phosphate oxygen anions, whereas the others interact with those of the adjacent duplex. Such interactions contribute to the stability of duplex formation. The 2'-*O*-methyl modification in ^{N}U$_m$ shifts the ribose ring toward the C3'-*endo* conformation and influences duplex stability. Observed changes in the dimensions of the minor grooves and in the hydration structures are well correlated to nuclease resistance.

Keywords: antigene, antisense, crystal structure

MS45 PACKING OF ORGANIC MOLECULAR COMPOUNDS

Chairpersons: Jonathan W. Steed, Carolyn Brock

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Porosity in Molecular Crystals

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Crystals composed of purely organic compounds have largely been ignored as gas sorption substrates since such molecules usually pack with efficiencies in the narrow range of 60 to 67%. Consequently, void spaces larger than 25Å^3 are seldom encountered in organic solids. The host lattices of solvated inclusion compounds are often described as possessing zero-, one-, two- or three-dimensional solvent-accessible voids if the guest molecules are located in isolated cavities, channels, layers or networks of channels, respectively. It is therefore attractive to envision facile removal of the solvent molecules from these materials to yield highly porous host lattices analogous to those of zeolites. In reality, the process of desolvation is almost always accompanied by reassembly of the host molecules in the solid state to form one or more so-called apohost phases, where the pure compound is once again efficiently packed. However, a few exceptions to this phenomenon are known to exist.

We are interested in using the principles of crystal engineering to design and construct new solids for applications such as gas sorption. Although the availability of vacant lattice voids is essential, these solids are apparently not required to be "porous" in the classical sense when considering the van der Waals surfaces of the constituent host molecules. This contribution will focus very generally on the concept of porosity in molecular crystals, and on the phenomenon of guest transport within a solid host framework.

Keywords: porous materials, self assembly supramolecular chemistry, crystal engineering

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Exploring Structures and Structural Phenomena: The Derived Crystal Packing Model

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Improvements in the prediction and the design of molecular crystals have been dramatically enhanced the last decades. However, several problems during crystallization such as polymorphism or two-dimensional defects can lead to difficulties in interpreting the success of a theoretical study.

In this context, we developed the Derived Crystal Packing (DCP) model [1]. This two-step procedure allows to generate crystal structures (daughter phases) starting from periodic fragments retrieved from a known mother phase. The study of many examples has shown that concomitant polymorphism, twinning and epitaxies can be a direct consequence of the structural and energetical similarities between the mother and the daughter phases.

Theses issues will be illustrated by the case of (±) Modafinil, a pharmaceutical compound known to crystallize in several polymorphic forms and solvates [2].

[1] Gervais C., Coquerel G., *Acta Cryst. B*, 2002, **58**, 662. [2] Pauchet M., Gervais C., Courvoisier L., Coquerel G., *Cryst. Growth. Des.*, 2004, **4**, 1143-1151.

Keywords: crystal structure prediction, twinning, polymorphism

MS45.27.3

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Crystal Structure Analysis and Solid Form Selection in the Pharmaceutical Industry

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The selection of the solid form is an important milestone in the development of new drug product. The aim of the process is to select the solid form with the most desirable properties including aqueous solubility, chemical and physical stability and suitable drug product processing attributes for formulation e.g. mechanical properties. The selected form may be either the free base or acid of the active pharmaceutical ingredient (API) or a salt.

It is vital to ensure the most thermodynamically stable polymorphic form has been selected. Different polymorphs have unique physical properties resulting in different solubilities, chemical and physical stabilities and different bioavailabilities. Metastable polymorphs may convert to more stable forms on processing and examples of this have been reported [1]. The characterization of all solid forms is important and can provide many intellectual property opportunities [2].

Crystal structure analysis, taking a molecular perspective of the crystalline state, can be combined with both manual analytical techniques (e.g. PXRD, thermal analysis, microscopy) and automated high throughput solid form screening techniques to ensure the optimum solid form is selected.

[1] Bauer J.F., Spanton S., Henry R., Quick J., Dziki W., Porter W., Morris J.,