Our method employs *ab initio* polyalanine models (or 'decoys'), produced in large numbers then clustered based on the presence of similar core structures. The largest of these clusters is likely to be closest to the native structure [2]. Such *ab initio* modelling may result in an accurate prediction of the structural core of the target, but with inaccurate loops and termini. We have been developing an automated pipeline for the processing of *ab initio* models for use in Molecular Replacement. We show that truncation and clustering of models into ensembles can give a successful result where a single search model would fail. We find that the addition of a selection of side chains can also be used to improve the success rate.

Importantly, the likely success or failure of the modelling can be predicted based on characteristics of the protein such as length and secondary structure, and by the convergence of the modelling program to produce a large cluster of models with a similar core structure. Predictions of success can be given at each stage of the pipeline as data are accumulated to give feedback to the user, and to prioritise models for use in Molecular Replacement.

The pipeline has been tested on 241 proteins between 40-120 residues long, using Rosetta to produce 1000 decoys for each target. Ensembles were produced from these decoys, and Molecular Replacement carried out using MrBUMP. For 40 proteins, at least one search model was placed within 3Å of the deposited structure by MrBUMP, and in a further 42 cases, one or more search model was positioned to within 3-6Å. In 137 cases, ARP/wARP rebuilds resulted in mapping of traced residues to sequence. Of these, 71 proteins show a 50% or greater sequence coverage ratio with 20% or more of the backbone traced.

We have thus shown that *ab initio* modelling can be a viable route to structure solution for many small proteins. Initial results with other *ab initio* programs show success where Rosetta models failed. Similarly, we are extending this work to other rebuilding programs such as buccaneer which may well improve performance further.

This pipeline will be made freely available, and may ultimately require only the input of the protein sequence along with the experimental data. Unlike other computationally intensive methods [3], this method is suitable for modest hardware, allowing for broader adoption.

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Keywords: modelling, molecular_replacement, automated_ structure_solution

MS.58.5

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Release 7.2 of ARP/wARP software suite

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ARP/wARP is a software project for automated model building and refinement in macromolecular crystallography. The software is the result of years of development in the areas of X-ray crystallography, informatics and statistical pattern recognition. ARP/wARP is an iterative procedure based on the use of hybrid macromolecular models that is integrated with model refinement and reconstruction to provide a unified approach. The software protocols are computationally efficient and provide an easy-to-use pipeline for the building of models of proteins, poly-nucleotides, bound ligands and solvent.

Version 7.2 of ARP/wARP was recently released and contains new techniques and approaches for the building models of large, low-resolution structures using non-crystallographic symmetry (NCS) and motif searching. NCS-related parts of a structure are rarely built in the same way during model building. A beneficial side effect of this is that each copy provides information that is not present in another copy. By combining this intrinsic information the model building process is improved and the overall completeness of built structures at low resolution is increased. Coupled with novel implementations for enhanced protein chain tracing, the use of NCS provides improvements of up to 18% in model completeness (from 55% to 73% at 3.2Å, for example).

Further developments include automation in modelling of bound ligands that are partially ordered. The electron density map can be automatically screened for density corresponding to any of a cocktail of potential ligands and those that fit best are automatically built. Furthermore, in instances where the density is insufficient to allow accurate identification of atomic coordinates of particular ligands, 'partial' ligands, comprised only of the fragments whose atoms are in unequivocal density, can be modelled.

The graphical front-end *Arpnavigator* allows users to view models in real time while they are automatically built and refined. With the 7.2 release the functionality of the front-end has been considerably extended, and new file formats and display styles of molecules are supported. Publication quality images in standard colours are now easier to produce.

Keywords: model_building, refinement, crystallographic_ Software

MS.59.1

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Halogen vs. Hydrogen bonding in the design of anion receptors

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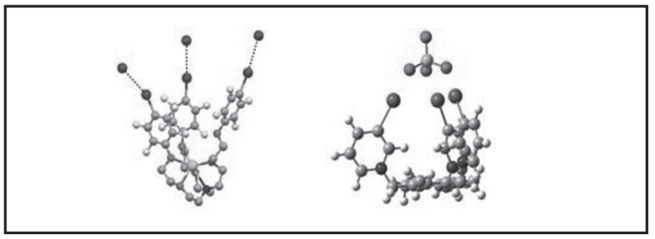
Halogen bonding (XB), namely any noncovalent interactions involving the positive region of the electrostatic potential surface of halogen atoms [1], has proven its efficiency and reliability in supramolecular chemistry, crystal engineering, and materials science [2]. Its potential and use in anion coordination and anion-templated assembly has been discovered and investigated only recently [3].

In this contribution, we report some examples of anion binding driven by halogen bonding where halides anions act as halogen bonding acceptors.

We will also present how XB directs the self-assembly of oxyanions, by far the most numerous class of anions in organic chemistry, forming discrete adducts and 1D, 2D, or 3D supramolecular networks with halocarbons. Some specific examples will be discussed in order to identify new supramolecular synthons based on halogen bonding and to outline some general principles for the design of effective and selective receptors based on this interaction [4].

It will be demonstrated that the replacement of hydrogen with halogen atoms into anion receptor scaffolds may develop as a convenient strategy to improve binding and selectivity.



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Keywords: halogen bonding, anions, supramolecular chemistry

MS.59.2

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Ionic, hydrogen or halogen bonds? Relevance for predicting crystal structures

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Describing a solid as a salt or a cocrystal and identifying the hydrogen or halogen bonds is central to crystallographic discussions, but there are borderline cases with proton disorder or long intermolecular distances. Is making these distinctions essential for predicting the crystal structures? This is investigated by modelling crystal structures using quantum mechanical calculations on the isolated neutral molecules or ions, and then modelling crystals as bound by the intermolecular electrostatic, repulsion and dispersion forces, with no explicit hydrogen or halogen bonding terms [1].Crystal energy landscapes are calculated for three pyridinium carboxylate salts and the corresponding pyridine carboxylic acid cocrystals. The most stable crystal structures of the salt and cocrystal are compared with each other and the experimental crystal structures [2]. Despite the steric similarity of the neutral, COOH···N(arom), and ionic, COO-···H-N+(arom), forms of the carboxylic acid pyridine heterosynthon, the relative energies of various crystal structures are sensitive to whether the solid is modelled as a salt or cocrystal. The hydrogen bonding appears to be sufficiently well described to predict the observed structures, although periodic electronic structures calculations are needed to confirm the proton disorder observed in one system. In contrast, many halogenated crystal structures have been correctly predicted by simply modelling the intermolecular interactions as the sum of electrostatic, repulsion and dispersion interactions, although modelling the anisotropy in the repulsive wall can be important [3], [4], [5].

The crystal energy landscapes show the variety of alternative crystal structures that are competitive with the observed structures in thermodynamic stability [6].The range of compromises between all the intermolecular interactions within the crystal structures that are calculated to be thermodynamically favourable can be seen as a stringent test of whether the initial assumptions about the intermolecular forces are physically reasonable

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Keywords: computation, intermolecular, prediction

MS.59.3

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Halogen bonding involving metallate ions and anionic ligands

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The predominantly electrostatic nature of halogen bonds [1], [2] makes anions excellent halogen bond acceptors. Over the past 10 years we have studied the formation of halogen bonds in metal complexes, including metallate anions and related neutral complexes in which formally anionic ligands serve as the halogen bond acceptor.

The talk will provide a survey of halogen bonding across different anionic ligand types (and their corresponding metallate anions), focussing on halide ligands (X), which permit tunability of the acceptor group as well as the halogen bond donor [3], cyanide [4], [5] and thiocyanate ligands [5].

The relative strength of halogen bonds in the solid state has been established [1], [2], [3] and the determined quantitatively in solution [6]. The response of C–X···X–M halogen bonds to changes in pressure and temperature have been studied in the solid state [7] as has the guiding role of such interactions (alongside hydrogen bonds) in solid state reactions [8].

A brief perspective on the scope of halogen bonding across a wide range of other ligands will also be provided [9].

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Keywords: halogen bond, hydrogen bond, metallate ion

MS.59.4

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Electronic factors affecting the I-I bonds in the simplest polyiodides

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