

merohedral (twin law matching a symmetry operation in the crystal system, but not crystal point group) and pseudo-merohedral (where the twin law belongs to a higher symmetry lattice than the structure obeys). The most common type of merohedral twinning is hemihedral involving two twin domains. We have also observed two cases with four twin domains (tetartohedral; PDBids 2PRX and 3NUZ). Improvements in software have simplified the detection and treatment of twinned data. When the project was started, twin refinement was limited to SHELXL and CNS or using detwinned data in cases of low twin fractions. The addition of twin refinement to phenix.refine and remlac has expanded the options for refining twinned data. A review of the twinning cases at the JCSG provides a guide for the characterization, solution and refinement of twinned structures.

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**Keywords:** twinning, structural genomics, macromolecular crystallography

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### Advances in the CRANK software suite for automated crystal structure solution

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CRANK is a suite for automated macromolecular crystal structure solution that enables different crystallographic programs to seamlessly communicate. The current release can build structures automatically from single- and multiple-wavelength anomalous diffraction data and single isomorphous replacement with anomalous scattering data [1]. The latest release of CRANK includes several new algorithms which both increase robustness and speed up the automatic structure solution process.

Several improvements were made in substructure determination. While most programs use the absolute value of Bijvoet differences,  $\Delta F = |F^+| - |F^-|$ , as an estimate of  $|F_A|$ , a multivariate joint probability distribution, implemented in the AFRO program, is used in CRANK to obtain more accurate values for  $|F_A|$ . The substructure determination process was sped up substantially by allowing substructure detection to be terminated early without running all trials and by quickly evaluating whether a correct solution for the substructure was located.

In density modification it is often assumed that the initial and density-modified map are independent. We have developed a multivariate function for phase combination that rectifies this assumption by considering the observed Friedel pairs directly from a SAD experiment, accounting for the correlation between the initial and density-modified maps and refining the errors that can occur in a single-wavelength anomalous diffraction experiment. The maps produced by this multivariate phase combination program lead to many more structures being built automatically [2]. We also recently implemented a new cross-validated scheme for accurate error-parameter estimation in likelihood-based phase combination that results in improved phase probability and figure of merit estimates [3].

The use of experimental phase information in refinement is known to improve automated model building results. For SAD and SIRAS [4] experiments CRANK uses a multivariate likelihood function implemented in the program REFMAC [5], that takes as input the diffraction data, heavy atom coordinates and the calculated structure factors and accounts for the correlation between them. By using all

experimental information directly, the multivariate functions overcome limitations of the function that uses Hendrickson–Lattman coefficients to incorporate experimental phase information in refinement.

CRANK can be run either via a command line program GCX or through a *ccp4i* graphical user interface: both require only minimal input to run. Users however may also set-up a custom-made pipeline using any program at each step, customize variables for the individual steps and define the start and end step for a pipeline.

CRANK is licensed under GPL v2 and available from the CCP4 suite ([www.ccp4.ac.uk](http://www.ccp4.ac.uk)) or [www.bfsc.leidenuniv.nl/software/crank](http://www.bfsc.leidenuniv.nl/software/crank)

[1] N.S. Pannu et al., *Acta Cryst.*, **2011**, *D67*, 331–337. [2] W.-J. Waterreus, P. Skubák et al., *Acta Cryst.*, **2010**, *D66*, 783–788. [3] P. Skubák, N.S. Pannu, *Acta Cryst.*, **2011**, *D67*, 345–354. [4] P. Skubák, G.N. Murshudov, N.S. Pannu, *Acta Cryst.*, **2009**, *D65*, 1051–1061. [5] Murshudov et al., *Acta Cryst.*, **2011**, *D67*, 355–367.

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### Novel Approach to Automatic Scoring of Protein Drop Images Using UV Fluorescence

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Analyzing vast numbers of images is a time consuming bottleneck that affects most protein crystallization experiments. So far, software based image analysis tools for automatic scoring and ranking these images have generally failed because of various image artifacts caused by plates, lighting, and drop geometry. The recent commercial introduction of UV fluorescence imaging for protein crystallization has brought new opportunities for simpler and more reliable approaches to image analysis. Most existing analysis tools rank images using methods such as edge, shape, intensity, and frequency analysis.

With the new UV technologies it is now possible to rank based on protein fluorescence which also has the advantage of differentiating protein versus salt. We have developed a new analysis tool that when integrated with the CrystalTrak software provides the user with a fluorescence score which can be used to filter images from the image viewer those images with little to no fluorescence. This greatly reduces the number of images needing review. Due to the fact that the UV fluorescence images are free of many of the artifacts found in visible images the algorithm has been shown to be very reliable at eliminating clear drops with no false negatives. The methods used produce a score that is fundamentally a ratio of fluorescence signal versus background noise. The user then has the ability to set their own threshold based on this score determining how sensitive they want the algorithm to be and filter as many images as desired. Due to the fact that the Rigaku Minstrel HT UV uses the same optics for the visible and UV images the analysis tool also provides the ability to overlay the detected fluorescence signal over top of the visible images to highlight the items of interest in the visible image.

**Keywords:** biomacromolecule, crystallization, microscopy

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### Fully Automated Cryogenic Crystal Screening System

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