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A distributed web-based system for the management of high-throughput crystallization trials at the Oxford Protein Production Facility

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The discovery of crystallization conditions for proteins and other macromolecules remains an essentially trial-and-error process. Several hundred trials may be required in order to identify conditions which produce diffraction-quality crystals, and even then not all proteins can be persuaded to crystallize. The use of sparse-matrix screening kits has made this process increasingly routine, but the need to set up many thousands of trials and to inspect them regularly makes this vital stage of structure determination particularly suitable for the high-throughput approaches of miniaturization, parallelization and automation. The Oxford Protein Production Facility (OPPF) was one of the first laboratories in Europe to explore the potential for nanolitre-scale sitting-drop crystallization and has developed robust and automated protocols which yield measurably greater success and repeatability than manual procedures [1]. Since December 2002, some 1.2 million crystallization trials have been created and more than 34 million images of these crystallizations have been acquired using the automated storage vault and imaging system at the OPPF. The management of this number of crystallization trials poses large data management problems, and in the absence of alternative software the OPPF has developed a web-based crystallization trial management system appropriate to the scale of the OPPF operation [2]. This system is available securely over the internet (for example, a fully featured demonstration of the software is available at http://www.oppf.ox.ac.uk/vault). We describe the operation and management of the OPPF crystallization facility, focusing on the features of the web interface that make it suitable for the remote management of many thousands of crystallization trials. This platform is freely available and is now being developed into a generic system compatible with several types of imaging and storage hardware. The development work is being done in collaboration with other laboratories as part of the PiMS project (http://www.pims-lims.org) and BioXHIT projects (http://www.bioxhit.org) as a module compatible with the rest of the PiMS laboratory information management system (LIMS) project.

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New Developments for Automated Protein Crystallization in Microplates

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Protein structures play an important role in structural genomics initiatives as well as part of drug discovery efforts. High-throughput protein crystallization techniques become therefore increasingly important. The demand for sophisticated and diversified platforms, especially with regard to optical properties, surface properties, and suitability for small sample volumes, has resulted in the creation of highly specialized platforms. An interesting aspect for protein crystallization is the usage of plastic microfluidic structures for liquid-liquid diffusion crystallography. Plastic micro-structured devices allow the analysis of a large number of crystallization conditions within a limited timeframe according to the liquid - liquid diffusion method. When combined with the benefits of low protein / reagent consumption, ease of handling and time conservation, such microfluidic devices offer enhanced opportunities to achieve protein crystallizations in a high throughput manner. One of the major challenges in structural biology is the resolution of membrane protein structures. For the crystallization of membrane proteins the usage of detergents is mandatory. Crystallization drops that contain detergents tend to spread on flat surfaces. A hydrophobic plate surface effectively prevents drop deformation on flat surfaces and allows the combination of excellent optical properties of flat bottom plates with superior surface features, thereby enabling the use of flat-well plates for membrane protein crystallography.