Center for Eukaryotic Structural Genomics

Technology Dissemination Report

CESG Tech Report No.	019
Title	CrystalFarm Pro Software Package
Research Unit	Crystallography
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Figure 1: Startup Screen. Figure 1 shows the startup screen for the program. The user supplies simple credentials to access the database. Although the program itself does not modify the database, we have separately created a user "readonly" with restricted access privileges to the crystalfarm database tables.

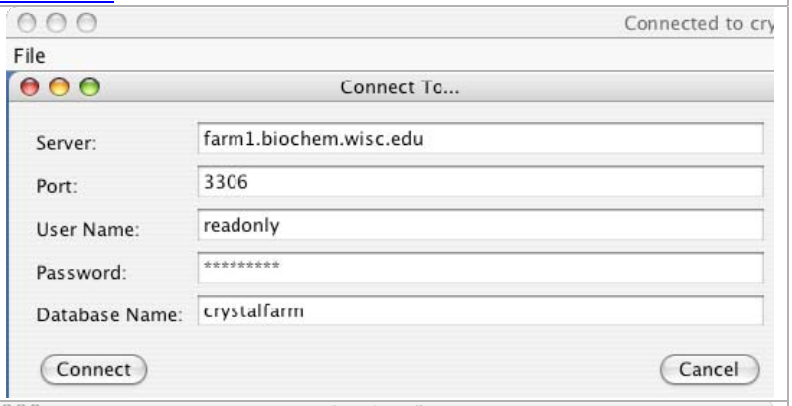


Figure 2: View Images by Score Theshold shows the results of selecting a specific screen, and viewing images associated with it. The ability to frame images above a user specified score threshold allows quick access to the most relevant results. If the screen is laid out in a "rational" fashion, an experienced user will learn a great deal about the pH and reagent preferences of a given target by simply adjusting the sliding threshold scale. Otherwise, selecting a specific image will show the crystallization constituents below the thumbnail display. In this case, we have decided to optimize the lead condition highlighted in green in Figure 2.

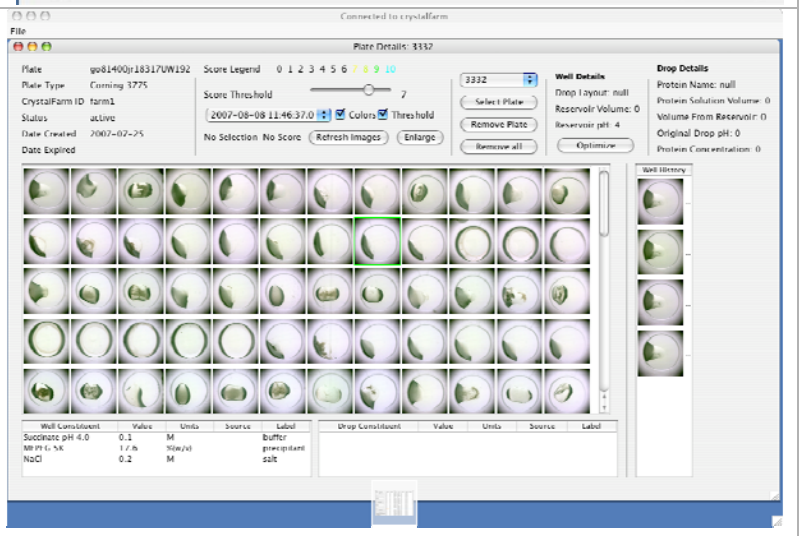
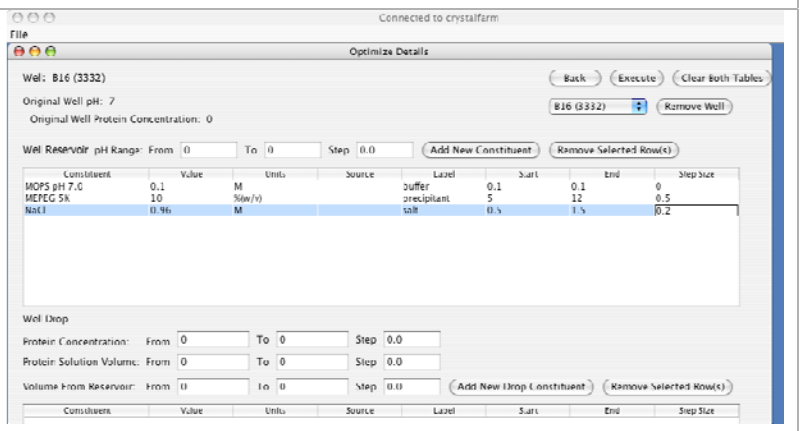
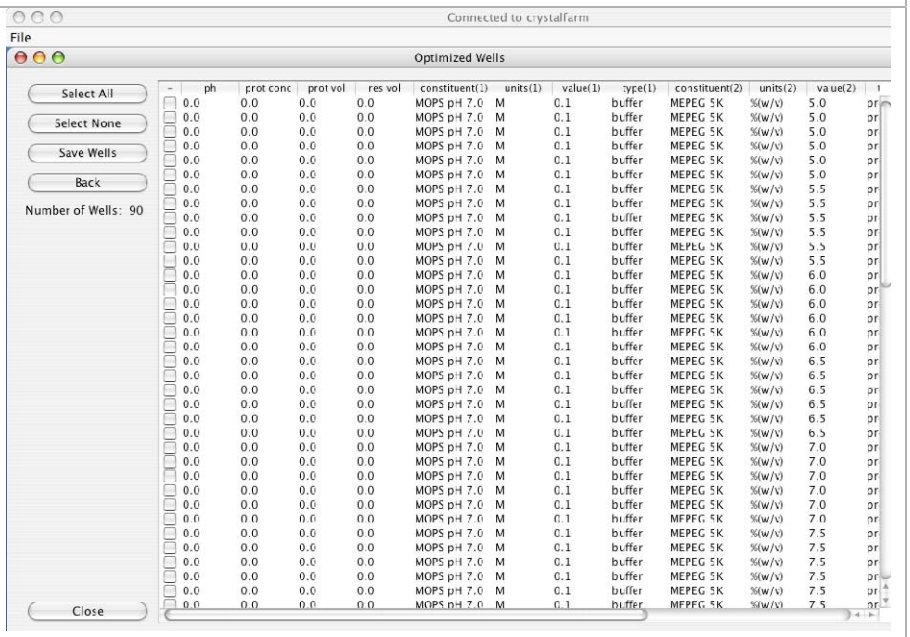


Figure 3: Initiate Optimization shows the optimization window, where a multidimensional grid screen around a given lead can be developed. **Figure 4** shows the results. Other important features: automatically generated optimization conditions stored in a buffer, where they can be edited before committing to a given optimization, results of more than one parameter set can be easily merged in the interface, and additional constituents not present in the first hit can be added to the optimization strategy,



communicates the strategy to the CrystalFarm via an XML interchange file.

Figure 4: Optimization Results shows an alternative, non-image-centric way of looking at crystallization results. In this case, all reagents involved in experiments giving a response above 6 (in our scoring scheme, all promising crystalline material). This target seems to be crystallizing best at or slightly below neutral pH, and a wide number of constituents are associated with lead conditions. The ability to summon this type of information with a few mouse clicks is a great aid to optimization experiments. It is also possible to focus on a specific reagent in a group of plates, and show all reagents associated with it, and the resulting scores for that group of plates. Again, this is valuable information for directing optimization experiments.



Summary

In parallel with, and partially fueled by the needs of the Protein Structure Initiative, several vendors have developed fully automated plate storage and imaging systems to support high-throughput crystallography. These fully automated systems were once the exclusive province of large pharmaceutical companies and PSI centers. Perhaps partially facilitated by the PSI, they are now increasingly commonly found in the largest research groups, and as departmental or shared facilities.

The Center for Eukaryotic Structural Genomics, in conjunction with Bruker AXS, has developed a software platform that interacts with the CrystalFarm automated imaging systems, and considerably augments the functionality of the standard commercial software distributed with these systems. The software is distributed as CrystalFarm Pro by Bruker AXS, and is therefore immediately relevant not only to our Center, but the wider biomedical research community.

CrystalFarm Pro interacts directly with the DBMax (MySQL) database on the CrystalFarm imaging system. It does not replace the standard software, but rather provides several additional functionalities. First, it provides a different viewing framework for the images with scores. Perhaps more importantly, it provides customizable data harvest and other important reporting capabilities absent from the default system. One on the most powerful features of the CrystalFarm software, the ability to gather comprehensive performance data on a particular screen, integrated over all instances of that screen in a CrystalFarm system, integrated over all time. This is invaluable for identifying “dead” conditions in general screens that fail to produce viable leads. It would be almost impossible to gather these results from lab notebooks, without a centralized repository of information. CrystalFarm Pro is able to go through a database with a terabyte of scored image information, and distill it to a

report in a few minutes.

We are presently very close to releasing a version of CrystalFarm Pro that can write worklist files for Tecan liquid handling systems. The abstractions used for this are very similar to those used in Sesame. We believe that this capability will be of great utility to departmental and non-PSI CrystalFarm installations that lack the resources to develop custom robot control interfaces. The program also generates reports that are of great utility for "housekeeping" purposes. For example, a standard report returns a list of plates that have unscored images that need attention. This is certainly very useful for the serial possession model (pipeline) that characterizes structural genomics work, and would also be useful for shared departmental installations.

In summary, CrystalFarm Pro software extends "structural genomics" strength data-mining and optimization support to any lab with a CrystalFarm imaging system. The software is under active development and is expected to have impact outside the Protein Structure Initiative.

Acquiring the Technology	dan.frankel@bruker-axs.com
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