Help Conquer Cancer June 2012 Update

Since our last update, we have launched a GPU version of HCC, and started processing two important new types of protein crystallization data.

HCC on the GPU

Paper publication

As announced in March in the forums, our HPCS 2011 conference paper describing the design, testing, and performance of our GPU implementation of HCC was finally published:

> Kotseruba, Y., Cumbaa, C.A. and Jurisica, I. (2012) High-throughput protein crystallization on the World Community Grid and the GPU. *Journal of Physics: Conference Series* **341** 012027 doi:10.1088/1742-6596/341/1/012027

Launch of the GPU Beta

Beta testing for HCC/GPU began on March 13, 2012. We are delighted by the enthusiastic response to GPU computing from World Community Grid members. We know you are eager to crunch more units, and are working to release the next round as soon as possible.

GPU processing represents an entirely different computational platform than any CPU platform supported by *HCC* or other World Community Grid projects. The methods to efficiently compute results differ greatly. The code implementing HCC on the GPU is consequently very different from our CPU code, and must be written to perform well on the wide range of graphics cards supported by the project. We are currently examining results from the latest round of beta testing, and are busy tweaking our GPU algorithms to improve the consistency and reliability of the calculations.

We anticipate a large increase in the processing rate of Help Conquer Cancer work units once HCC/GPU switches from beta to production. In preparation for the increased processing rate of the project, we have upgraded our storage hardware, and are busy preparing new work units. We look forward to the successful completion of GPU beta testing.

New experiments being processed by HCC

The bulk of the data processed by the Help Conquer Cancer project has come from high-throughput screens of globular proteins from the Hauptman-Woodward Institute's High-Throughput Screening lab. In December 2011, we expanded the scope of the *HCC* project to

cover two new categories of experiment: optimized crystallization trials, and membrane protein crystallization screens.

From crystallization screening to optimization

A crystallization screen tests the target protein against a wide array of chemical conditions for a cocktail (mixture of salts, buffers, and precipitants) that will cause protein crystals to grow out of the mixture. The crystals detected in these screens are not always directly usable in X-ray crystallography. In general, the cocktail in a crystallization screen that produces a hit is not optimal for that protein. The crystal may be too small or fragile, or may diffract X-rays poorly. Small changes in the protein or cocktail concentrations, or slight changes to the pH of the solution may result in a better-quality crystal. Once initial crystallizing conditions for a protein have been detected by a crystallographer (possibly assisted by *HCC* results), the optimization phase of protein crystallization follows.

Our collaborators at the Hauptman-Woodward Institute have devised a method for high-throughput crystal optimization using the same cocktails, and the same robotic liquid-handling and imaging equipment as used in the high-throughput screens. By varying the ratios of protein solution to cocktail solution added to each experiment, HWI crystallographers can vary the concentrations of cocktail and protein in new crystallization experiments, and thereby determine the optimal ratio. By repeating the same set of experiments at multiple temperatures, crystallization can be optimized across two dimensions. Figure 1 shows some initial results of this process.

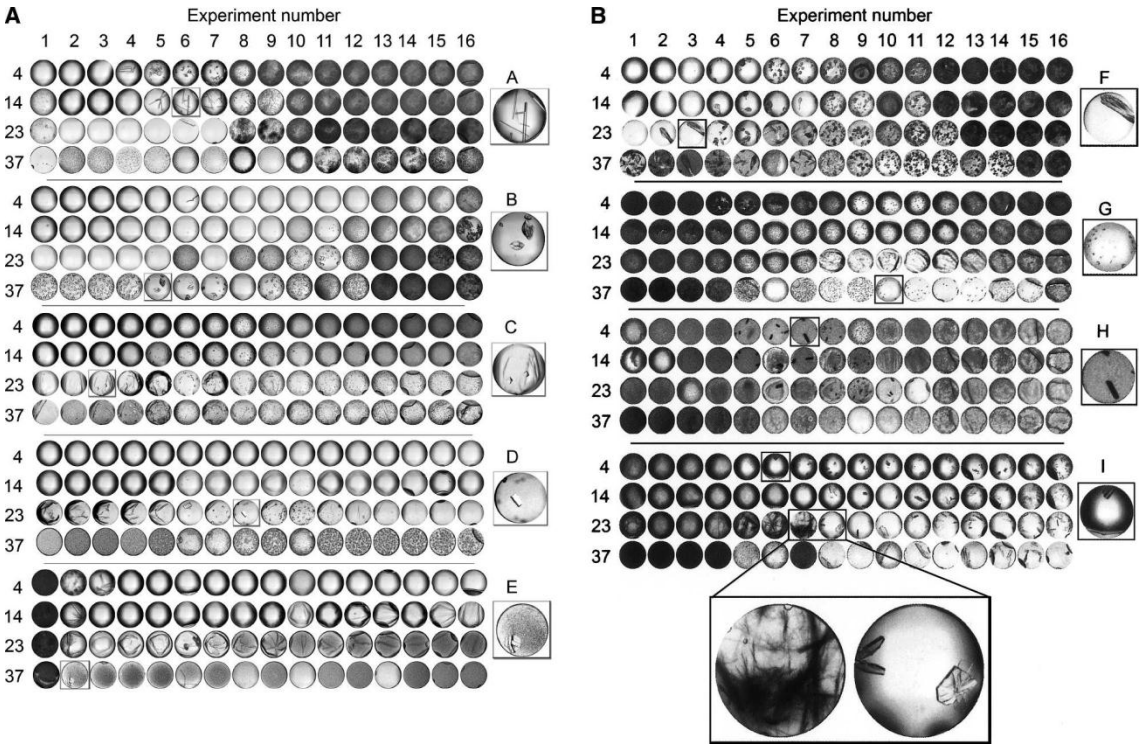

Figure 1: Protein crystal optimization using Hauptman-Woodward's Drop-Volume Ratio/Temperature method. Nine different optimization matrices are shown. The protein/cocktail ratios are highest for column 1 and lowest for column 16. Temperatures in centigrade are marked in the rows. Source: Luft, J. R., Wolfley, J. R., Said, M. I., Nagel, R. M.,

Lauricella, A. M., Smith, J. L., Thayer, M. H., Veatch, C. K., Snell, E. H., Malkowski, M. G. and DeTitta, G. T. (2007), Efficient optimization of crystallization conditions by manipulation of drop volume ratio and temperature. *Protein Science*, **16**: 715–722. doi: 10.1110/ps.062699707

Screening membrane proteins

There are three major classes of proteins: globular, membrane, and fibrous. Globular proteins are water-soluble, reside entirely within or without the cell, and are most easily studied by X-ray crystallography and other protein-structure-determination methods. Membrane proteins are not completely water-soluble, and contain oily regions that keep them embedded in the cell wall or other cellular membranes. Membrane proteins are vastly important to cell function and therefore biology and medicine, but their insolubility makes them difficult to study, and very difficult to crystallize. In the last decade, crystallographers have made progress in the field of membrane protein crystallization by adding detergents to their cocktails. In particular, crystallographers at the Hauptman-Woodward Institute have developed a high-throughput screen of 1536 different cocktails for membrane proteins and demonstrated its ability to produce X-ray diffraction-quality crystals. Figure 2 shows some crystals of membrane proteins produced by this process.

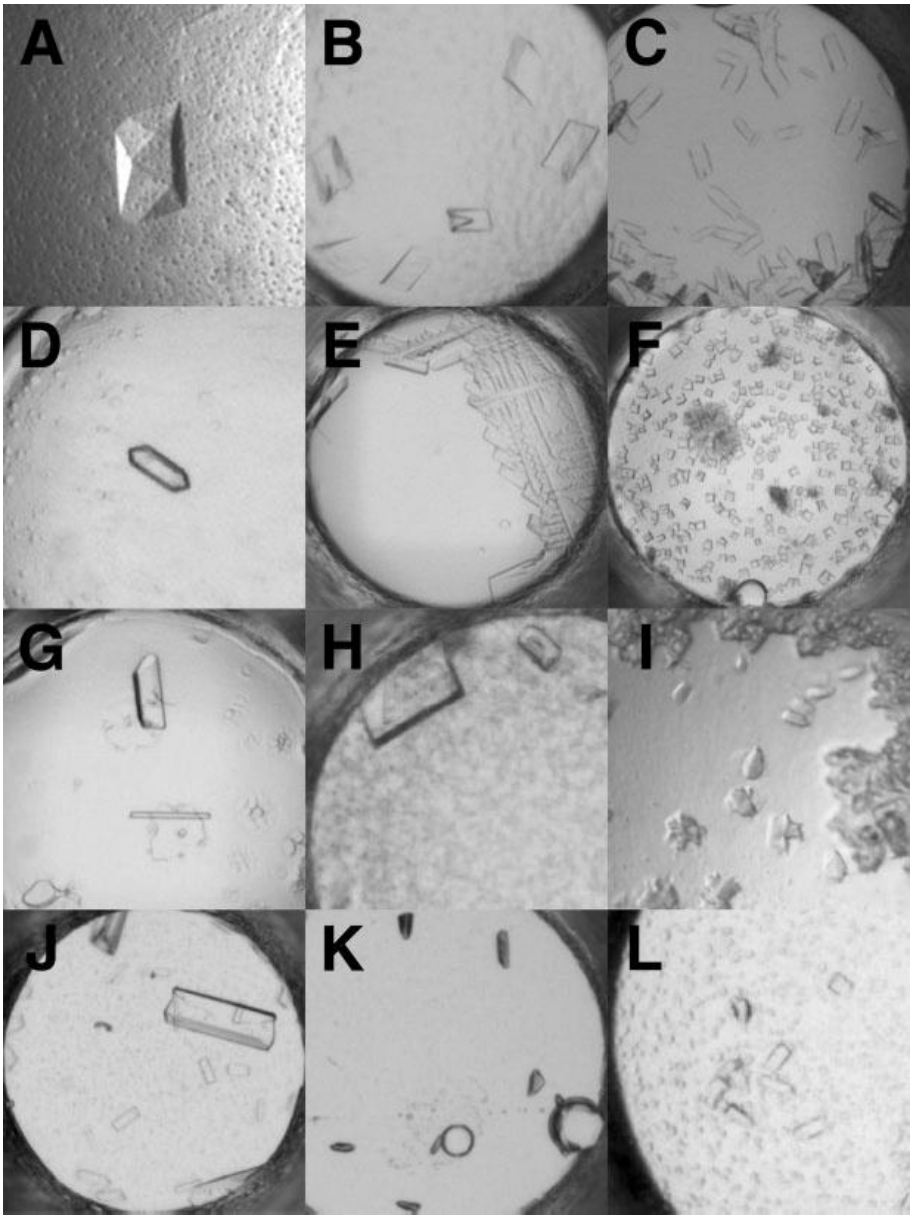

Figure 2: Crystals of membrane proteins identified using the HWI 1536 screen. Source: Koszelak-Rosenblum, M., Krol, A., Mozumdar, N., Wunsch, K., Ferin, A., Cook, E., Veatch, C.K., Nagel, R., Luft, J.R., Detitta, G.T. and Malkowski, M.G. (2009) Determination and application of empirically derived detergent phase boundaries to effectively crystallize membrane proteins. *Protein Science*. **18**(9):1828-39.