CRYSTAL BRAIN DOCUMENTATION

Phase IV

July, 2001

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OVERVIEW

Purpose

This document describes the functional specifications of the sophisticated management and tasking system involved in the screening, crystal growth, image analysis and harvesting processes at Syrrx, Inc. Together, the components comprising this automated system – the computer hardware and software, network, database, robots and underlying automation engine(s) – are referred to as "Crystal Brain" or CB. The Crystal Brain system represents a collaborative effort between Syrrx and the Systems Technology Division of Titan Corporation. This document describes the current and future (not yet implemented) features of the Crystal Brain system.

Definitions

Agencourt: The screening machines, robots, Cartesian liquid handling equipment, and Crystal Brain automation components involved with crystal plate preparation.

ASRS: Automated Storage and Retrieval System. The rule-based system within the Forts providing storage of crystal plates and retrieving plates for scheduled image events, harvesting, transfer to long-term storage, or disposal.

Client Software: This refers to the Windows-based applications through which users (scientists, technicians, etc.) can access and store Crystal Brain-related information. Examples of client software applications are: Batch Editor, Protein Plate Editor, Screen WorkBench, and Schedule Editor.

Crystal Brain: (also referred to as "CB") The sophisticated management and tasking system for automation of protein screening and crystallization processes. Processes controlled by Crystal Brain include: machine level automation, protein plate and crystal plate preparation, tracking plate history, tracking of image results, exception management, report generation, and system metrics monitoring.

Crystal Brain Database: The database management system comprised of Oracle 8i and associated utilities, used for data storage and retrieval for Crystal Brain processes. This database is the heart of the Crystal Brain system, and is used by all processes and sub-systems.

Crystal Brain Engine: The behind-the-scenes intelligent software (rules-based system) that drives the Crystal Brain system. The Crystal Brain Engine uses data from the Crystal Brain Database and the Directors in each room to schedule workflow, handle errors, and display system notifications.

Director: The portion of Crystal Brain that talks to the automation equipment (machines and robots) and to the Crystal Brain database. There is one Director in each room: Agencourt, Fort Knox,

Fort Bliss. The Crystal Brain Directors are responsible for scheduling, workflow management, machine control, data collection control, and updating the Crystal Brain database.

Fort Knox: The crystallization imaging and storage facility, kept at a temperature of 4 degrees Celsius. It contains the Optimag Image equipment, robots, and Director.

Fort Bliss: The crystallization imaging and storage facility, kept at a temperature of 20 degrees Celsius. It contains the Optimag Image equipment, robots, and Director.

GUI: Graphical User Interface. The computer-based interactive tool with which users interact with Crystal Brain applications. Crystal Brain applications use a Windows 2000 GUI.

Hozine: A contraction of the words "hotel" and "magazine." A hozine is a crystal plate storage rack, capable of holding up to 88 individual 96-well plates. There are multiple hozines in each of the Forts.

Marquee: A display, located in the Agencourt Room, used by technicians to monitor processes. Notifications/alerts are posted to the Marquee by Crystal Brain Engine.

Mozine: A mobile hozine (see Hozine). A mozine is a mobile crystal plate rack, used for transporting batches of crystal plates from Agencourt (plate preparation room) to the Forts (imaging rooms).

OASIS: Optimag Automated Optical Slider Inspection System. This is the crystal image processing system, comprised of an imager, an image analyzer and MS-SQL database. There are two OASIS systems in each of the Forts (Fort Knox and Fort Bliss), one on each side of the room.

Protein Brain: A companion automation application to Crystal Brain.[future] Protein Brain supports and automates the protein creation (expression) and production processes at Syrrx. These proteins are later used in the screening and imaging process, controlled by Crystal Brain.

Resilient Link: Refers to a dual connection or path, whereby when one connection goes down the other path continues operating.

Robot: The machine responsible for accessing and handling individual crystal plates. There is a robot and robot controller in each room (Agencourt, Fort Knox and Fort Bliss). Robots respond to commands from the Director.

Screen: A process that exposes a protein to a defined combination of solutions (mother liquors) to test for crystal growth. Screens are generally referred to as Coarse Screens or Fine Screens (see Coarse vs. Fine Screens).

VPN: A virtual private network is a private data network that makes use of the public telecommunication infrastructure allowing the creation of a secure link between a corporate LAN and remote user's PC.

Web Server: The computer system responsible for servicing user requests and displaying Crystal Brain-related information as web pages. This system allows users to view Crystal Brain data from remote sites, over the Internet. It uses Cold Fusion as the interface to the Crystal Brain database, and MS Internet Explorer (version 5 or higher) as the user interface.

System Architecture

The Crystal Brain system is built on a Windows 2000 server backbone utilizing TCP/IP via 100BaseT and gigabit Ethernet, and a combination of copper and fiber media. The Crystal Brain system is separate and isolated from other Syrrx and Novartis computer systems, LANs and informatics. The main computer and network equipment housed in the Computer Room at Syrrx, shown in Figure 1, is connected to each of the Crystal Brain rooms – Agencourt, Fort Knox, Fort Bliss – via fiber (gigabit Ethernet). Table 1 lists the automation control equipment and the Crystal Brain network components by physical location. The Crystal Brain system was designed to be easily modifiable, configurable and expandable.

The Crystal Brain computer systems contain various levels of hardware and software redundancy for maximum data protection. The goal was to construct a system that maximizes data integrity and protection, optimizes throughput, and allows for future growth. There are two servers, configured as an Oracle Cluster (Cluster Node 1 and Cluster Node 2 in Figure 1), utilizing Oracle FailSafe for Windows Clustered Servers. Each of these servers is a Pentium III Xeon 866/256 Cache machine equipped with 256 Mbytes of SDRAM, and three hard drives with sufficient capacity for the Oracle and the Windows2000 Enterprise Operating System. The two servers (Cluster Node 1 and Cluster Node 2 in Figure 1) are connected via Fibre Channel to Network Attached Storage (NAS) (i.e., a Disk Array) with 500GB capacity. The Disk Array uses RAID-5 technology and contains hot-swappable disk drives, with a RAID-1 Supervisor. Maintenance and management may be performed via the administration console, accessible via a KVM switch as shown in Figure 1.   A backup tape system, having 1TB native/ 2TB compressed storage capacity, is maintained locally.

Network components are Extreme Networks Resilient Links (Black Diamond and Summit switches in Figure 1). Where possible, Fast Ethernet (100Mbps) and fibre (Gbps) is used to maximize throughput. There is currently no network management software supplied with the Crystal Brain LAN.

The Crystal Brain Database utilizes Oracle8i Server and relies on Window2000 Clustering Technology. Oracle's FailSafe is used to monitor and configure the database for fail-over capabilities. The Crystal Brain database is setup to auto-archive to the local hard drive with transaction logging where appropriate. The principal programming language for Crystal Brain's Windows-based user interface is Microsoft's Visual C++. Microsoft foundation classes are used as required.

THE SYRRX VPN
Remote access to the Crystal Brain system is available via a virtual private network (VPN), using Syrrx's existing firewall and T1 connection to the Internet. This provides users access to Crystal Brain's Web Server, via the Internet, using Microsoft Internet Explorer as the

primary user interface (see Web Server). The VPN maintains privacy through the use of a point-to-point tunneling protocol (PPTP) and security procedures (encryption) while connecting users or sites over a public network. The VPN is also used by the remote software engineers for debugging and system monitoring.

Figure 1: COMPUTER ROOM – Crystal Brain Equipment Racks
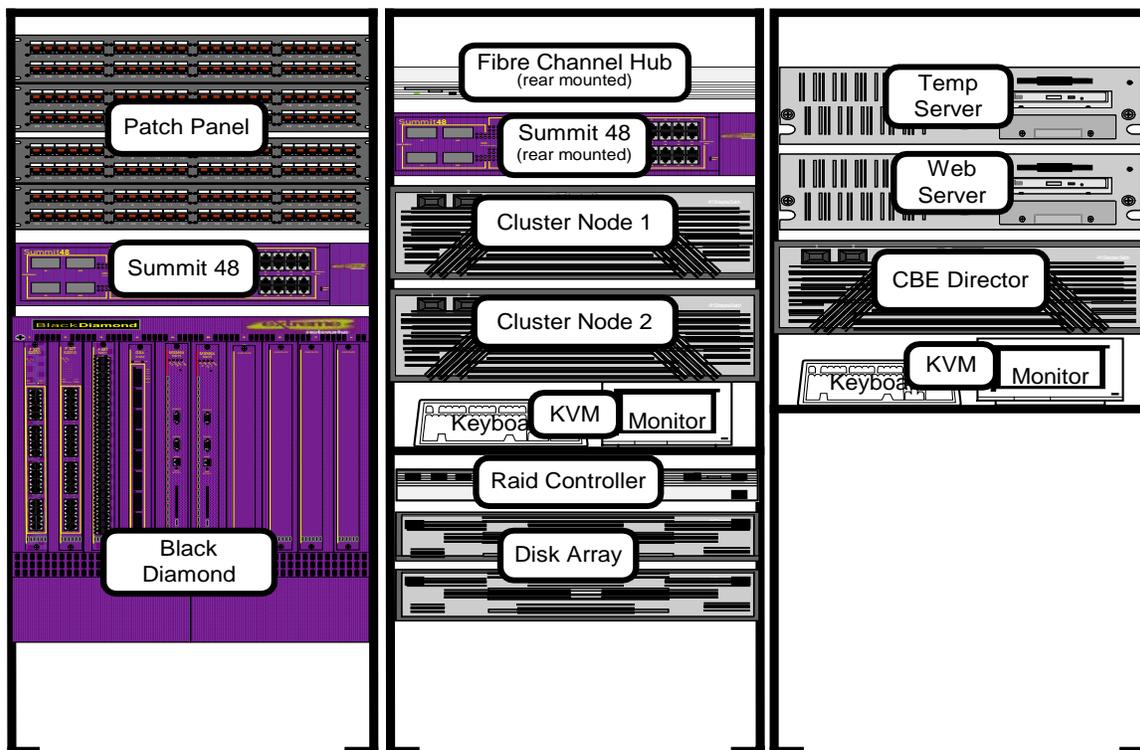
TABLE 1. Components of the Crystal Brain System by Physical Location

ITEM	FUNCTION
COMPUTER ROOM	
Patch Panel	Provides Ethernet connectivity to user workstations
Summit 48	100Mbps Ethernet switch. Provides connectivity between various Crystal Brain computer components.
Black Diamond	Multifunction enclosure with various connectivity modules, functioning as a router. Provides fiber and copper connectivity between various components at Gbps/100Mbps speeds.
Fibre Channel Hub	Provides fiber media connectivity for connectivity from the Cluster Nodes to the Disk Array.
Cluster Node 1	Oracle server upon which the Crystal Brain Database resides. Mirrored with Cluster Node 2.
Cluster Node 2	Oracle server upon which the Crystal Brain Database resides. Mirrored with Cluster Node 1.

Raid Controller	Provides control for the disk array using a RAID-5 configuration.
KVM	Keyboard, monitor and mouse configured through a switch that allows them to control and communicate to any of the Cluster Node servers.
Disk Array	Multiple disk drives configured so that the data on them is written in a redundant matter, controlled by the Raid Controller.
Temp Server	A non-production server, used for development and testing.
Web Server	Provides access to Crystal Brain information as remotely accessible web pages.
CBE Director	Crystal Brain Engine Director, the server that provides intelligent automation control among the various Crystal Brain components

AGENCOURT	
Robot ("Big Yellow")	Moves crystal plate from station to station within Agencourt
Automated Screen System	Dispenses stock solutions from bottles in mezzanine to selected wells on 96-well crystal plates
Shaker	Shakes plate to mix solutions
Protein Dispense Machine	Dispenses desired protein from a 96-well source plate to wells on a crystal plate
96-Head Aspirate/Dispense Machine	Aspirates solutions (screen contents) from wells in the crystal plate, and dispenses them onto the protein drops in wells of the same crystal plate
Marker	Puts a marking (drop of ink) on hazardous crystal plates
Tape Machine	Seals (covers) each crystal plate with tape to prevent evaporation
Quad Stacker	Stacks crystal plates into mozines. Four mozines fit on top of the stacker and the plates are stacked from the bottom up.
Audit Box	Destination for rejected and audit crystal plates
Agencourt Director	Automation control system that directs operations in the Agencourt Room
Marquee	A display used by technicians to monitor processes. Notifications/alerts will be posted to the Marquee by Crystal Brain Engine.

FORT KNOX – 4°C	
Optimag Imager 1 (side A)	Vision system that takes digital images of the wells on the crystal plates. There are two per fort, one on each side.
Optimag Imager 2 (side B)	Vision system that takes digital images of the wells on the crystal plates. There are two per fort, one on each side.
Image Analyzer	Stores and analyzes the images from the Optimag Imagers
Fort Knox Director	Automation control system that directs operations in the Fort Knox Room
Robot	Moves the crystal plates from the mozines and hozines to the imaging stations and back again

FORT BLISS – 20°C	
Optimag Imager 1 (side A)	Vision system that takes digital images of the wells on the crystal plates. There are two per fort, one on each side.
Optimag Imager 2 (side B)	Vision system that takes digital images of the wells on the crystal plates. There are two per fort, one on each side.
Image Analyzer	Stores and analyzes the images from the Optimag Imagers
Fort Bliss Director	Automation control system that directs operations in the Fort Bliss Room
Robot	Moves the crystal plates from the mozines and hozines to the imaging stations and back again

| **LABORATORY OFFICE AREA** | |
| Crystal Brain Workstations | PCs connected to the Crystal Brain system that allow users (scientists and technicians) to interact with the system |

Scientific Underpinning

The success of the Human Genome Project (HGP) and the progress made in genetic and protein research have sparked the development of new drug discovery techniques. Each of the 30,000-40,000 human genes represents a code for a specific protein. Medical research has determined that certain proteins are either the cause of disease or are actively involved in the disease process. The goal of modern drug research is to develop compounds to bind these proteins, and thus block their interaction. There are a huge number of variables associated with finding the optimal mixture of reagents that will bind the protein, thus creating a crystal that may become the basis for a drug. This process is largely a repetitive testing endeavor, involving thousands of individual experiments. The computational power and robotic automation provided by Crystal Brain is what makes these thousands of experiments able to be performed quickly, accurately, and with minimal labor. Solving the 3-dimensional structure of these proteins and protein-ligand compounds is performed using X-ray crystallography techniques, a very computationally-intensive endeavor. Figure 2 shows the scientific workflow of this drug discovery process.

Figure 2: SCIENTIFIC WORKFLOW
**A Simplified View of Drug Discovery**
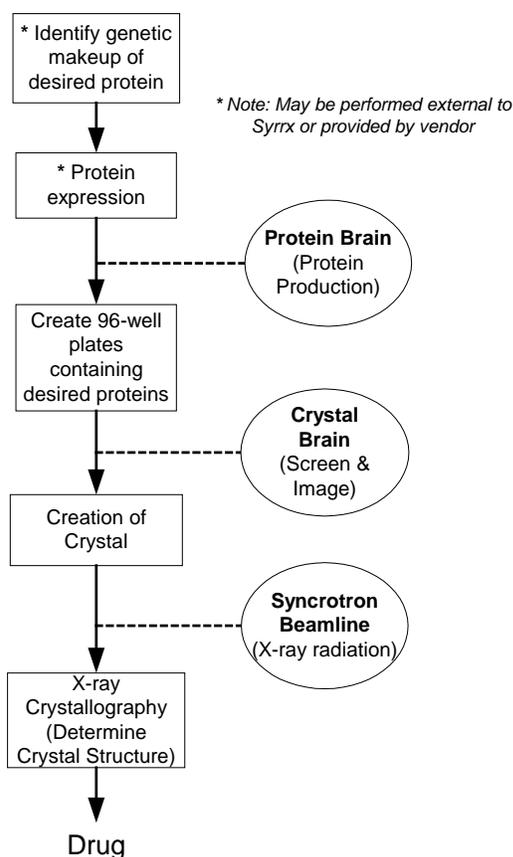
CRYSTAL BRAIN PROCESS FLOW

Crystal Brain Process Summary

Figure 3 depicts the workflow processes that Crystal Brain manages. Scientists at Syrrx design various laboratory experiments to look for compounds that will lead to crystallization of certain proteins. This process is called screening.

In the Experiment Definition process, scientists define the screening experiment parameters to Crystal Brain. The Crystal Plate Preparation process then begins in Agencourt. 96-well plates are prepared with various accommodations of proteins and stock solutions, per the screening experiment definition. The Crystal Brain Database, in concert with the Crystal Brain Engine, manages and controls these activities. When completed, the crystal plates enter the Forts (currently a manual process of carrying the mozine(s) from Agencourt to the appropriate Fort(s)) to begin the Crystallization and Imaging process. While in the Forts, the plates are imaged periodically, in accordance with the schedule previously defined by the scientist during experiment definition. Scientists may decide, based on image results, to harvest a particular plate. Crystal Brain and/or the scientist may determine that a refinement in the screening (e.g., a secondary or fine screen) is warranted. At the conclusion of the scheduled imaging events, the crystal plates may be taken to long-term storage or may be disposed.

The following sections describe each of these processes in further detail.

Figure 3: CRYSTAL BRAIN PROCESS FLOW
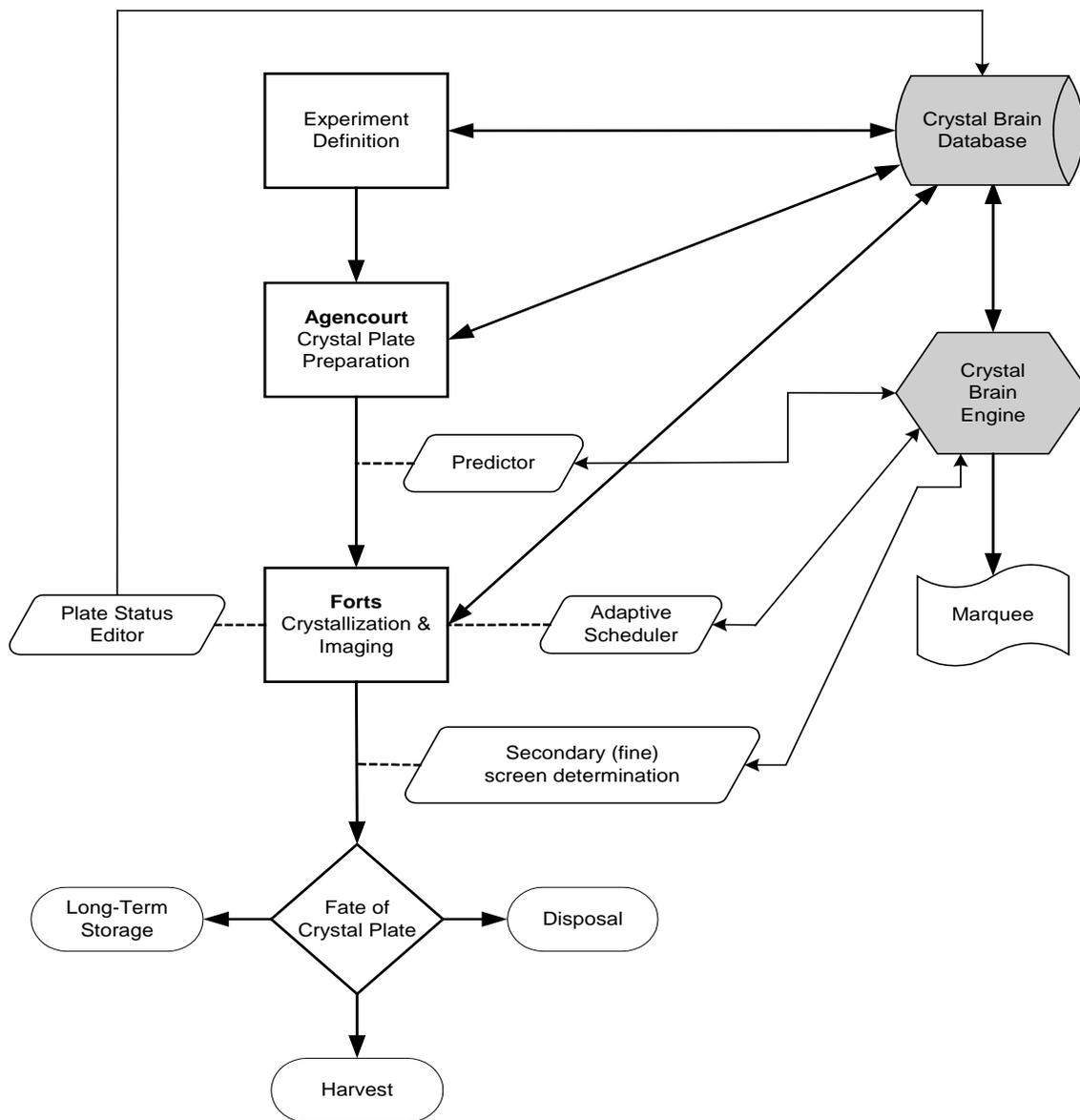
Experiment Definition Process

In the Experiment Definition process, scientists define the screening experiment parameters to Crystal Brain. Four main tools (application programs) are used in the experiment definition process, as shown in Figure 4. These are explained below. Each one writes user-entered data (user = scientist) to the Crystal Brain database for use later in the Agencourt and Fort processes.

Figure 4: EXPERIMENT DEFINITION PROCESS
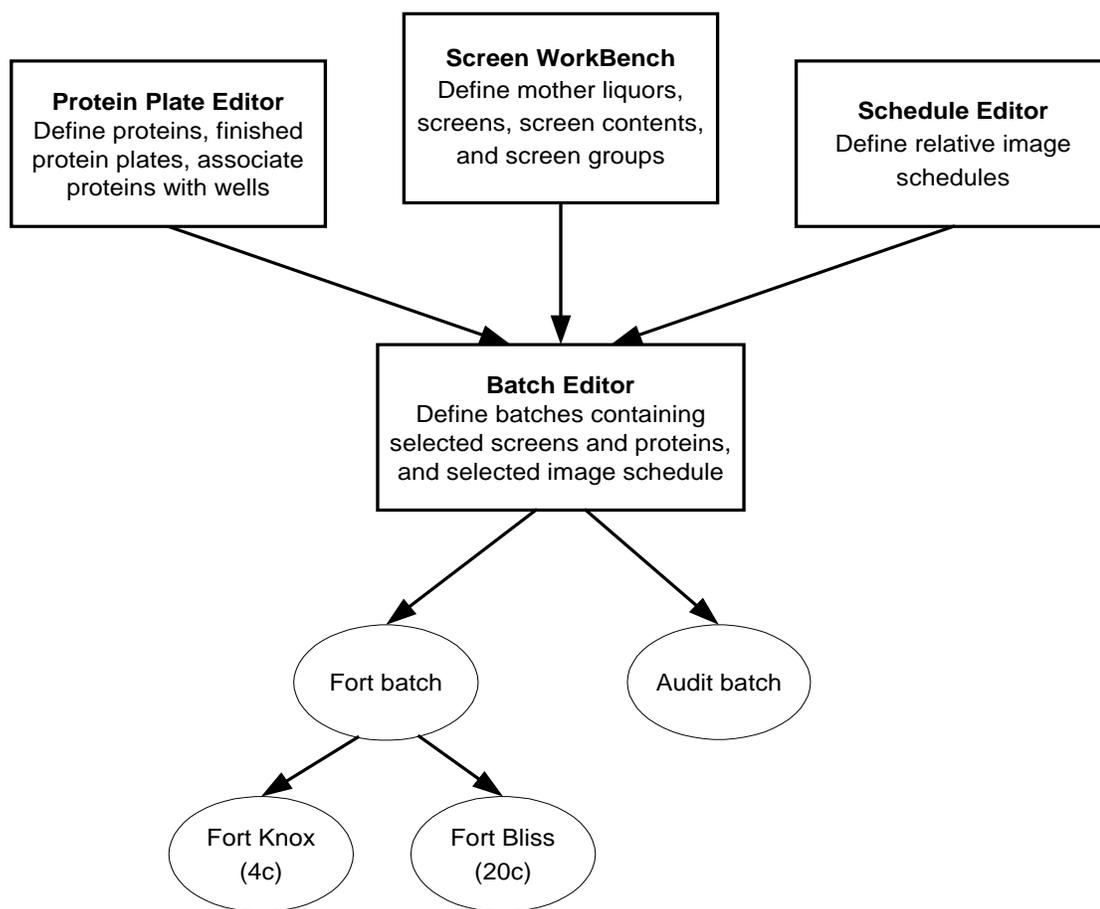
SCREEN WORKBENCH

Using a tool called Screen Workbench, the mother liquors (source reagents), screens, screen contents and screen groups are defined. Individual stock solutions are purchased or prepared, and are loaded into bottles in the mezzanine. Each bottle is barcoded to indicate its contents. Currently, there is no Stock Solutions Editor application. Stock solutions data is input manually into the following tables in Crystal Brain: Stock_Solution, Bottle_Stock, Stock_Barcode. The Fine Screen Machine will dispense these solutions into the wells on 96-well crystal plates (see Agencourt Processes).

The Screen WorkBench tool allows a user to define how the individual stock solutions are combined, in various proportions, concentrations, pHs, etc., for a particular experiment. Each unique combination of stock solutions is referred to as the screen content (stored in the Screen_Content table). Up to 96 screen contents can be run on a single 96-well crystal plate, one in each well. The 96-well plate can be broken down into various areas (groups of wells) called grids. The user can specify a combination of stock solutions, at particular concentration and pH intervals for example, to cover each grid. The user may also reserve an area of a plate (grid) for a special purpose. The Screen WorkBench application calculates solution volumes and percentages and/or concentrations for each well, totaling 100 microliters. A screen group refers to all the grids that comprise a single 96-well plate (named in the Screen_Group table).

A screen is an instance of a screen group with a specified volume of protein (protein_drop_volume) and specified dispense volume (ml_drop_volume) of screen content. These are stored in the Screen table and are used by the 96-Head Machine and the Protein Dispensing Machine during crystal plate preparation in Agencourt.

COARSE SCREENS VS. FINE SCREENS

The screening process consists of different combinations of stock solutions associated with a protein. Whether a screen is "coarse" or "fine" is a matter of semantics. Typically, a coarse screen refers to the initial screening process, where a variety of stock solutions are tested. A fine screen refers to a secondary screen or a refinement of the initial screen. Results gathered from the coarse/initial screen are used to refine the selection of stock solutions for the subsequent/fine screen. For example, suppose a coarse screen tested solutions with pH 5.0, 6.0, 7.0, and 8.0. Imaging results showed crystallization at pH 5.0 and 6.0 but none at pH 7.0 or 8.0. A refinement of this screen might be to test solutions with pHs 4.5, 5.0, 5.5, 6.0 and 6.5. The coarse and fine screen recipes (combinations of stock solutions and proteins) may be generated by the user (scientist). A future enhancement will allow Crystal Brain to automatically generate fine screen recipes based on coarse screen image results and a Fine Screen Mix Algorithm provided by Syrrx. The fine screen mix algorithm can be edited further by the user [future].

Using a tool called ProteinPlate Editor, individual 96-well plates containing source proteins can be defined. Each protein plate is barcoded so it can be easily identified by the Protein Dispensing Machine. The barcode is the same as the protein plate name, up to 8 characters in length (finished_protein_plate table).

Each plate may be assigned an expiration date by the user. After expression, a protein has a defined shelf life, typically 7-14 days. At the time of coarse screen, the protein should typically be no more than 2 days after expression. Doing this will allow up to 7 days of results-gathering from the coarse screen, before determining whether a fine screen (a refinement of the coarse screen) should be performed (see Fort Processes). This means at the time the fine screen is performed on the same protein, there would still be up to 5 days of viability before that protein "expires." See Protein Tracking.

Each well of the 96-well protein plate – identified as A01, A02,... H11, H12 – is given a unique ID# (Finished_Protein_Well table). The desired content of each well is defined by the user: the protein name, its concentration (in mg/ml), the buffer, and target. Together, these parameters are referred to as the finished protein (Finished_Protein table). There can be up to 96 finished proteins on a finished protein plate, one in each well. There may be up to four protein plates loaded into the protein dispensing machine in Agencourt at any one time. The finished protein plates defined using the Protein Plate Editor (Finished_Protein_Plate table) are later used in Batch Editor, where the user may select particular finished proteins to be merged (combined) with various screen contents on crystal plates.

Protein Tracking [future]
A protein storage area is reserved for new and in-process expressions prior to screening. Crystal Brain performs the following types of tracking of proteins throughout their life cycle:

▪ *Date Tracking:* Crystal Brain will track the proteins in refrigerated storage by utilizing a time-based methodology as follows. The "birth date" is the defined as the creation of a new protein expression. When a protein is associated with a particular well on a protein plate – using the Protein Plate Editor tool – an expiration date is given to the protein plate by the user. The "clock" keeps ticking throughout the coarse and fine screen processes. Crystal Brain will mark proteins as expired when they reach their expiration date. A user may also manually mark a protein as expired. If a protein expires before a fine screen can be run, Crystal Brain will automatically send a message to the protein expression room [future]. A user may then reinitialize the protein expression request; e.g. the protein will need to be re-expressed, but not re-cloned. Alternatively, the user may manually alter the protein's expiration date to allow more time for the fine screen. Once a protein fine screen has begun, the protein expiration clock is ignored.

- *Location Tracking* [future]: The actual physical location of a protein can be tracked throughout its life cycle. While in refrigerated storage, a user may enter the storage location in the protein-tracking database. Once the protein is in a barcoded protein plate (see Protein Plate Editor), the user may scan the barcode to enter a new storage location into Crystal Brain. Plate location is tracked through the Crystal Brain database. Each time a plate is entered or removed from storage, a barcode reader must be used to log the event. After a plate has completed the protein expression process and the plate is subsequently scanned, the operator is queried as to which operation they desire: Plate/protein validation or Plate storage location update.

- *Inventory/Utilization Tracking* [future]: A future application within Crystal Brain will keep an inventory of what is currently in the refrigerated storage. Protein utilization within Agencourt (during the crystal plate preparation process) will also be tracked. Crystal Brain will post alerts when screens are defined using proteins whose volume is insufficient to complete the task.

SCHEDULE EDITOR

The ScheduleEditor tool allows the user to define relative image schedules (actually, time intervals) – in terms of days, hours, and minutes – for the periodic imaging done in the Forts. For example, one schedule might have images taken immediately (at time 0 days, 0 hours, 0 minutes), then again every 12 hours for the next 2 days, then again every 2 days for the next 2 weeks, and so forth. A typical relative image schedule spans a time period of 28 days. Each relative image schedule is defined by one or more relative times (expressed as days, hours, minutes) and associated time tolerances. The tolerance is the "window" during which the image may be taken. For example, even though it may desirous for one image to be taken 24 hours after a previous one, it may be acceptable for the actual image taking to occur anywhere from 22 hours to 26 hours after the previous one, i.e., a two-hour (120 minute) tolerance, making it a four-hour image taking time window. These windows (tolerances) are used to help schedule events for the Fort robots. Relative image schedules built using the Schedule Editor tool are later used in Batch Editor, where the user may select one of the relative image schedules for each batch of crystal plates they define.

RELATIVE VS. ABSOLUTE IMAGE SCHEDULE

The imaging times in Schedule Editor are referred to as relative image schedules. They represent time intervals desired between successive images. These are stored in the Relative_Image_Schedule table. The relative image schedules may be thought of as "generic" and are re-used and associated with individual batches as needed. This is in contrast to absolute image schedules, which refer to a specific date and time on which the image is taken (for example, Wednesday, June 13, 2001 at 5:23pm). The absolute image start times are stored in the Absolute_Image_Schedule table.

BATCH EDITOR

Using the Batch Editor tool, batches of crystal plates containing selected screen and protein combinations, may be defined and associated with a particular image schedule. A batch may contain up to 88 individual 96-well crystal plates – the capacity of a [mozine](). The number of crystal plates in a batch is called the batch fort size (maximum = 88). The Batch Editor allows the user to view a list of screens (previously defined by the user in [Screen WorkBench]()), and a list of protein plates (previously defined by the user in [Protein Plate Editor]()). The user selects individual finished proteins to be merged (combined) with the various selected screens, to create the crystal plates in a batch (Batch_Content table).

ONE PLATE, ONE PROTEIN

When creating batches of crystal plates for analysis, it is important to note that although the individual wells on the crystal plate may have varying different stock solutions to be tested, each will have the same finished protein; i.e., only one protein per crystal plate. Recall that a finished protein plate may contain up to 96 wells with a different finished protein in each well (see [Protein Plate Editor]()). This means that the finished protein from a single well on a finished protein plate will be used in *all* wells of a single crystal plate (see [Protein Dispensing Machine]()). However, within a batch, each crystal plate may have a different finished protein.

AUDIT BATCHES VS. FORT BATCHES

There are two types of batches: Fort batches and Audit batches. Fort batches refer to a grouping of crystal plates destined to go to the cold room (Fort Knox) or warm room (Fort Bliss) for imaging analysis. Audit batches refer to a grouping of crystal plates that will be analyzed "manually." Within BatchEditor, the user may add, edit, or delete fort batches or audit batches. At the end of the crystal plate assembly process in Agencourt, fort batches are placed in output mozines to be taken to the appropriate fort, while audit batches are placed in the [Audit Box]().

For each fort batch, a relative image schedule is selected (see [Schedule Editor]()). All crystal plates within a batch will have the same relative image schedule (stored as relative_schedule_number in the Batch table).

The user will be able to set a scheduled start time for each batch. If left blank, the Agencourt process will not start. Once a scheduled start date is given (scheduled_start field in the Batch_Fort table), the robots will begin to execute the [Agencourt processes]() at that given date. It is important that the user not enter a scheduled start date until it is confirmed that the selected mother liquors and finished protein plates are available on the [Agencourt process]() floor. All batch forts within a batch will have the same scheduled start date.

<u>CRYSTAL PLATE BARCODES</u>

Individual crystal plates must be uniquely identified in order for the <u>Agencourt Director</u> to track each crystal plate through the crystal plate preparation process, and to uniquely identify which combinations of screens and proteins are to be dispensed into each well on each crystal plate (see <u>Agencourt Process</u>). Because of this, the crystal plates come pre-barcoded from the manufacturer. Within Batch Editor, individual unique barcodes may be assigned to a crystal plate. However, if an automated screen is being performed, the user does not need to enter a barcode via Batch Editor. The barcode is automatically associated with the crystal plate as it is run through the <u>Fine Screen Machine</u>. Crystal Brain stores this barcode in the Crystal_Plate table. However, if a manual screen is being run, the user would need to manually enter the barcode of the crystal plate via Batch Editor (see <u>Automated Screen</u> vs. <u>Manual Screens</u>).

Note: Once a batch has started its <u>*Agencourt process*</u> *(has a Start_Agencourt date in the Crystal_Plate table), it becomes "read-only" and may no longer be edited by the user in Batch Editor.*

Agencourt Process Flow

Agencourt is comprised of a series of stations where the preparation of the crystal plates containing various combinations of screens and proteins takes place. Figure 5 diagrams the process flow within the Agencourt room. The movement of the crystal plates, controlled by the Staubli robot ("Big Yellow"), is shown with the open arrows. Prior to beginning any of the Agencourt processes, the user must have defined the relevant crystal plate parameters in the Experiment Definition Process. The tools used in the experiment definition process (Protein Plate Editor, Screen Workbench, and Batch Editor) populate the Crystal Brain database with information that is used by Crystal Brain throughout the Agencourt processes. As the crystal plates are moved from station to station within Agencourt, data is written to the Crystal Brain database (station_ID is updated in the Crystal_Plate table), so that each plate can be tracked throughout the Agencourt Process.

Figure 5: AGENCOURT PROCESS FLOW

Note: Open arrows indicate movement controlled by Robot

Determine Screen Type

Manual Screen

Automated Screen

Create Source Plate(s)

Shaker

Protein Dispensing Machine

Fine Screen Machine
Dispenses Stock Solutions

Diving Board

96-Head Machine

Aspirates Screen Contents

Dispenses Screen Contents onto Protein Drop

Rejected Plates

Audit Box
Manual Offload Station for Audit and Rejected Plates

Taping Machine

Non-hazardous Audit Plates

Hazardous Audit Plates

Hazardous Plate Marking

QuadStacker

End Agencourt Process

Begin Crystal Brain Engine Process

Predictor

Route mozine to appropriate Fort

DETERMINE SCREEN TYPE

The first step of the Agencourt process is to determine the type of screen – either automated or manual. In an automated screen, the Fine Screen Machine is used to dispense the desired solutions (i.e., mother liquors) comprising the screen contents into the crystal plates. Using the data stored in the Crystal Brain database, the Fine Screen Machine knows how much of each solution to dispense into each well. Keep in mind, that although this is referred to as the "Fine Screen Machine," it can be used for the automated dispensing of solutions (mother liquors) for either fine or coarse screens. [See definition of Coarse vs. Fine Screen.]

In a manual screen, the various solutions comprising the screen contents are dispensed into each well of the crystal plate manually. This is done offline by a laboratory technician. However, the crystal plate is still defined in the Crystal Brain database (see Experiment Definition), just as would be done with an automated screen. However, the screen contents are coded as "No dispense" so that within Agencourt, the Fine Screen Machine would know not to dispense any solutions onto that plate. After the technician has finished manually dispensing the screen contents into the appropriate wells, the crystal plate is manually placed on the diving board. The diving board is the area at the end of the Fine Screen Machine from which the robot grasps the plate to move it to the next station in the process.

SCREEN TIMELINE

Within Batch Editor, the user sets the desired scheduled start time (date and time) for a batch. This is stored in the Batch_Fort table, as the scheduled_start. Using this date and time, the Agencourt Director knows to start the crystal plate preparation process. Once begun, the Agencourt Director populates the start_Agencourt field in the Crystal_Plate table. Once this field is populated, the batch of which that plate is a member becomes "read-only" in Batch Editor, i.e., no further editing of the screens and proteins by the user is permitted in Batch Editor. Later, during the Fort Processes, Crystal Brain checks to see if seven days (a configurable variable amount of time) have elapsed since the start_Agencourt time (see Fort Processes).   If so, and there are positive image results during those first seven days, Crystal Brain will prompt the user for a refinement of this initial screen (see Fine Screen Determination) [future].

A screen must be started on a recently expressed protein within two days of creation of the protein. In the Protein Plate Editor, a user will set the expiration date of the protein plate. Although this should be the same as the shelf life of the proteins contained on the plate, the user may edit this as appropriate. If an initial (coarse) screen is not begun within two days of protein expression, then by the time a fine screen may be started on these same protein(s) – approximately seven days later – the proteins may already be expired. In Batch Editor, the user is notified when defining a screen using an expired protein plate.

FINE SCREEN MACHINE

Bottles containing stock solutions (Stock_Solution table) are housed on the mezzanine. Individual bottles are barcoded (Stock_Barcode table). Nozzles from each bottle are hooked up to the Fine Screen Machine (Bottle_Stock table). The system can accommodate up to two Fine Screen Machines. Currently, only one Fine Screen Machine is in use. All bottle stock solutions are mapped to the nozzle_2 field of the Bottle_Stock table. There are 96 nozzles, hooked up to 96 different stock solutions, active at a time for the Fine Screen Machine. [Keep in mind, that although this is referred to as the "Fine Screen Machine," it can be used for the automated dispensing of solutions for either fine or coarse screens.]

When a plate begins processing in Agencourt, the AgenCourt Director will notify Crystal Brain that the scheduled screen run has begun. The date and time are recorded in start_Agencourt in the Crystal_Plate table (see Screen Timeline). Since crystal plates come pre-barcoded from the manufacturer, the barcode of the crystal plate is automatically associated with each plate as it is run through the Fine Screen Machine (stored in barcode field of the Crystal_Plate table). It may take several minutes for a crystal plate to move through the Fine Screen Machine. When complete, the crystal plate is moved via a conveyor belt to the diving board. Any plates that had their contents manually dispensed, rather than being dispensed by the Fine Screen Machine, will be placed on the diving board as well (see Automated Screen vs. Manual Screen). Manual screen plates must have their barcodes manually entered via Batch Editor prior to being placed on the diving board; otherwise they will be rejected.

SHAKER

From the diving board, the Agencourt robot picks up each plate and places it on the shaker. The shaker is an orbital mixer, which allows the solutions just dispensed by the Fine Screen Machine to be mixed without "spillover" into neighboring wells. The shaking process takes approximately 30 seconds per plate. Two plates may be on the shaker at one time.

REJECTED PLATES

As a crystal plate is moved from station to station within Agencourt, it might be rejected for a number of reasons. For example, if its barcode becomes illegible, there is no barcode, or the barcode is not present in the database, the plate will be rejected. Although Figure 5 shows rejected crystal plates moving from the Shaker to the Audit box, a crystal plate may be rejected at any time, at any station, throughout the Agencourt process. When a plate is rejected, the Agencourt robot moves it to the Audit Box. The Audit Box can house up to 10 plates, and the Agencourt robot monitors this. When an attempt is made to place the 11th plate in the Audit Box, a message is displayed on the Agencourt Director, telling the user that the Audit Box requires attention. Besides storing rejected plates, the Audit Box houses all audit plates at the completion of their assembly in Agencourt (see Audit Batch).

96-HEAD MACHINE

The 96-Head Machine is so called because there are 96 nozzles, one for each well on a 96-well plate. The 96-Head Machine is also called the Aspirate and Dispense Machine because of its two main functions: it aspirates screen contents and dispenses screen contents onto the protein drops of the 96-well plate. Here is the typical sequence of events:

1. The 96-Head Machine aspirates (sucks up) a defined volume of the well contents from each well of the 96-well plate. [Recall this volume is defined by the user in Screen WorkBench during the experiment definition process, and is stored in the Screen table as ml_drop_volume].

2. Then, the Agencourt robot moves the crystal plate to the Protein Dispensing station.

3. While the plate is at the protein dispensing station, the 96-Head Machine goes through a "cleaning" process. The nozzles, now full with the aspirated screen contents, are cleaned and prepped so that they are ready to deliver a precise nanoliter volume.

4. When the crystal plate is returned to the 96-Head Machine, after having the desired protein applied to each well (see Protein Dispensing Machine), the desired precise volume of screen contents is dispensed onto the protein drop in the shelf area of the crystal plate. [Recall the dispensed volume is defined by the user in Screen WorkBench during the experiment definition process, and is stored in the Screen table as ml_disp_volume].

5. Finally, the robot moves the crystal plate to the Taping station, while the 96-Head Machine goes through a washing process to wash out the nozzles, before the next plate is aspirated.

PROTEIN DISPENSING MACHINE

During the experiment definition process, the user associated particular proteins with particular wells on a protein plate, using Protein Plate Editor. These protein plates are then manually prepared by a technician. A unique barcode is associated with each protein plate, and the definition of the contents of each well is stored in the Crystal Brain database. In a similar manner, the user, using Batch Editor, has previously associated a particular protein (a well from a protein plate) with a particular screen recipe for each crystal plate.

The Agencourt technician will be prompted by the Agencourt Director to load certain protein plates into the Protein Dispensing Machine. A maximum of four protein plates maybe loaded into the unit at one time. If a screen recipe calls for a particular plate and the plate is not present in the Protein Dispensing Machine or if a crystal plate (well) has an invalid association to a protein, the Marquee will notify the technician an invalid condition exists with the offending plate and will reference the offending plate's barcode. The condition will be defined (i.e., no recipe associated with plate or required plate not loaded in Agencourt's Protein Aspirate and Dispense Unit).

Note: To optimize throughput of the Agencourt system, all proteins on a protein plate should be associated to a recipe prior to downloading a recipe to Agencourt. This prevents the system from calling for different protein plates frequently.

Continuing on with the process flow, the Protein Dispensing Machine aspirates the desired protein from a 96-well protein plate and dispenses a controlled amount into the shelf area on all wells of a single crystal plate. The size of the protein drop dispensed is defined by the user in Screen WorkBench during the experiment definition process, and is stored in the Screen table as protein_drop_volume. Recall a single crystal plate must have the same protein dispensed into all its wells (see One Plate, One Protein).

STATION-TO-STATION WORKFLOW
Not all crystal plates will visit every station in Agencourt. For example, it may be desirous to define an experiment for calibration or machine testing purposes, and thus define a crystal plate with no protein associated with it: the protein_drop_volume, ml_disp_volume and ml_drop_volume in the Screen table all equal zero. In this case, the crystal plate would be moved directly from the Shaker to the Taping Machine, bypassing the 96-Head Machine and Protein Dispensing Machine. The Agencourt Director checks the experiment definition (i.e., the data stored in the Crystal Brain database) for each barcoded crystal plate, and instructs the Agencourt robot where to place each crystal plate next in the workflow process, accordingly.

TAPING MACHINE

After the dispensing phase on the 96-Head Machine, the crystal plate is moved to the Taping Machine. A clear piece of cellophane tape is placed over the entire crystal plate. This prevents the solutions in the wells from evaporating. The tape also adheres to the dividers between each well, preventing neighboring wells from mixing with each other. The shelf area, where the protein drop is dispensed, has a lower divider, and does not contact the tape. Therefore, the solutions in the wells are free to mix with the protein on the adjoining shelf.

HAZARDOUS PLATE MARKING

After taping, the crystal plate may be moved to one of two stations: the Hazardous Plate Marking station or the QuadStacker. If there are hazardous materials contained on the plate (radiolabeled or hazardous chemicals, for example) that cannot be disposed of in the regular trash at the conclusion of the experiment, the crystal plate will be moved to the Hazardous Plate Marking station. Here, a robot places a drop of ink as a marking near the barcode on the barcode label on the crystal plate. This is used later to know how to dispose of the crystal plate (see Plate Disposition). After marking, if the crystal plate is in an Audit Batch, the robot will move it to the Audit Box. Otherwise, if the crystal plate is in a Fort Batch, the crystal plate will continue on to the QuadStacker.

QUADSTACKER

After the crystal plate is assembled and marked as hazardous, if appropriate, the Agencourt robot moves the plate into a mozine for eventual transport to the Forts. Only plates that are part of Fort Batches (destined for Fort Knox or Fort Bliss) will be loaded into mozines. Plates that are part of an Audit Batch will have been moved to the Audit Box prior to this step.

Four mozines fit on top of the QuadStacker. As plates are completed, they are stacked into the mozine from the bottom up. When a batch is completed, the Marquee will display a message telling the technician that the mozine is ready for transport, and to which Fort (Fort Knox or Fort Bliss) it should be taken. The technician must manually carry the completed mozine to the desired fort destination. When the technician removes the mozine from Agencourt, the Agencourt Director senses the removal of the mozine, and clears the attention_req flag in the Station table.

MARQUEE

In the Agencourt room, there is a display unit – called the Marquee – that is used by technicians to monitor Crystal Brain processes. Notifications and alerts are posted to the Marquee by Crystal Brain Engine. These notifications/alerts include:

- Notifying the AgenCourt technican that the Protein Dispensing station needs attention. The Agencourt Director will post additional information, such as which protein plates need to be loaded in the Protein Dispensing Machine.
- Notifying the Agencourt technician of the destination (Fort Knox or Fort Bliss) of the output mozines.
- Notifying the Agencourt technician that a failure occurred at the Fine Screen Machine. The Agencourt Director will post additional information about the associated failure.
- Notifying the Agencourt technician that one of the Forts needs attention or is down. The Fort Director will post additional details, such as what specifically within the Fort needs attention (harvest mozine, etc.).

The Marquee is a scrolling LED computer-driven output device similar to a DataLiner. It is connected directly to the Crystal Brain LAN via Agencourt's Summit 10/100 switch. The text displayed on the Marquee is preprogrammed in Crystal Brain and sent to the display based on certain event triggers. Once an event has been responded to (e.g., removal of output mozine, loading of appropriate protein plates, etc), the display is cleared. If multiple events are in the queue, the display will scroll through all active event messages.

MALFUNCTIONS

If a malfunction occurs at a station in Agencourt that prevents that station's process from being completed, the plate involved will be rejected. For example, if during the dispensing of the protein drop, a malfunction with the Protein Dispensing Machine occurs and not all wells on the plate

received the required protein drop, that plate will be rejected and the Agencourt robot will place this plate in the Audit Box.

If the Agencourt Director is shutdown, upon restart it will check for the presence of crystal plates in the Fine Screen Machine, and notify the Agencourt technician to remove these plates (since their contents cannot now be trusted). After removing the plates, the technician presses "OK" on the Agencourt Director, and two things will happen. First, the barcode of the removed plate(s) will be erased from the record in the Crystal_Plate table. Next, a new "replacement" crystal plate(s) will be made, starting again at the beginning of the process (at the Fine Screen Machine) with a new barcoded plate. Each time the Agencourt Director is restarted, it checks to see if a rejected plate needs to be re-created and, if so, inserts a new plate into the workflow. The barcode of the new "replacement" plate is now placed into the Crystal_Plate table.

PREDICTOR

The Predictor is a Crystal Brain Engine process that uses a prediction/estimation algorithm for loading the Forts. In Agencourt, batches of crystal plates headed to the forts are loaded in the QuadStacker, into four output mozines. The Predictor determines which fort (Fort Knox or Fort Bliss) the plates are to be taken to, and, via the Marquee and Agencourt Director, the Agencourt technician is notified of the destination of the output mozine. The Agencourt technician then carries the output mozine(s) to the appropriate fort(s). The Predictor also determines which imager within the fort (side 1 or side 2) the incoming plates should be imaged on, based on best availability. Upon arrival in the forts, the crystal plates are imaged immediately (top priority, see Task Prioritization), at the side determined by the Predictor. Thereafter, this side is known as the "root side" for that batch of crystal plates. For all subsequent images throughout their stay in the fort, the batch will have a preference for that "root side." This means, that if at all possible, all subsequent images will be taken on the imager on that same side.

Within the forts, the Adaptive Scheduler is responsible for optimizing the throughput of the imaging in the forts. At the conclusion of each imaging event for each batch, the Adaptive Scheduler re-assesses the image schedule for that batch. Based on the time it took to image that batch and other intervening or possibly conflicting events, the Adaptive Scheduler will update the date and time for the next scheduled image event (see Adjusted Image Schedule). Therefore, the Predictor only operates for a short window of time, while a batch is transitioning between Agencourt and the forts, to determine where the output mozines go; i.e., which fort, imager, and side. Once in the fort, the Adaptive Scheduler and fort robot take over.

Fort Processes

There are two rooms, referred to as forts, where crystal plates are housed during the imaging process. Fort Knox is kept at a constant temperature of 4°C and is referred to as the cold room. Fort Bliss is kept at a constant temperature of 20°C and is referred to as the warm room. Crystal plates that have completed their assembly process in Agencourt are received into the appropriate fort to begin the imaging tasks. Figure 6 diagrams the process flow within the Forts. The movement of the crystal plates from their mozine or hozine storage locations to the imaging stations and back again is controlled by a robot. Plates are moved and scheduled for image events as a batch (recall a batch can contain up to 88 plates).

Earlier, during the Experiment Definition Process, the user will have defined the relative image schedule and desired fort (Fort Knox and/or Fort Bliss) for each batch using the Batch Editor tool. The relative image schedule is used to create the absolute image schedule entries just prior to introduction of the mozine to the fort. The entire absolute image schedule for the complete batch is written at one time to the Crystal Brain database, in the Absolute_Image_Schedule table.   Using the Image Event Viewer tool, the user can graphically view the image events, including conflicts, for each imaging station in each fort. Using the Plate Status Editor tool, the user can select a batch, or even individual crystal plates within a batch, for harvesting, removal to long-term storage, or disposal.

Figure 6: FORT PROCESS FLOW

Fort Knox: 4° C – Fort Bliss: 20° C
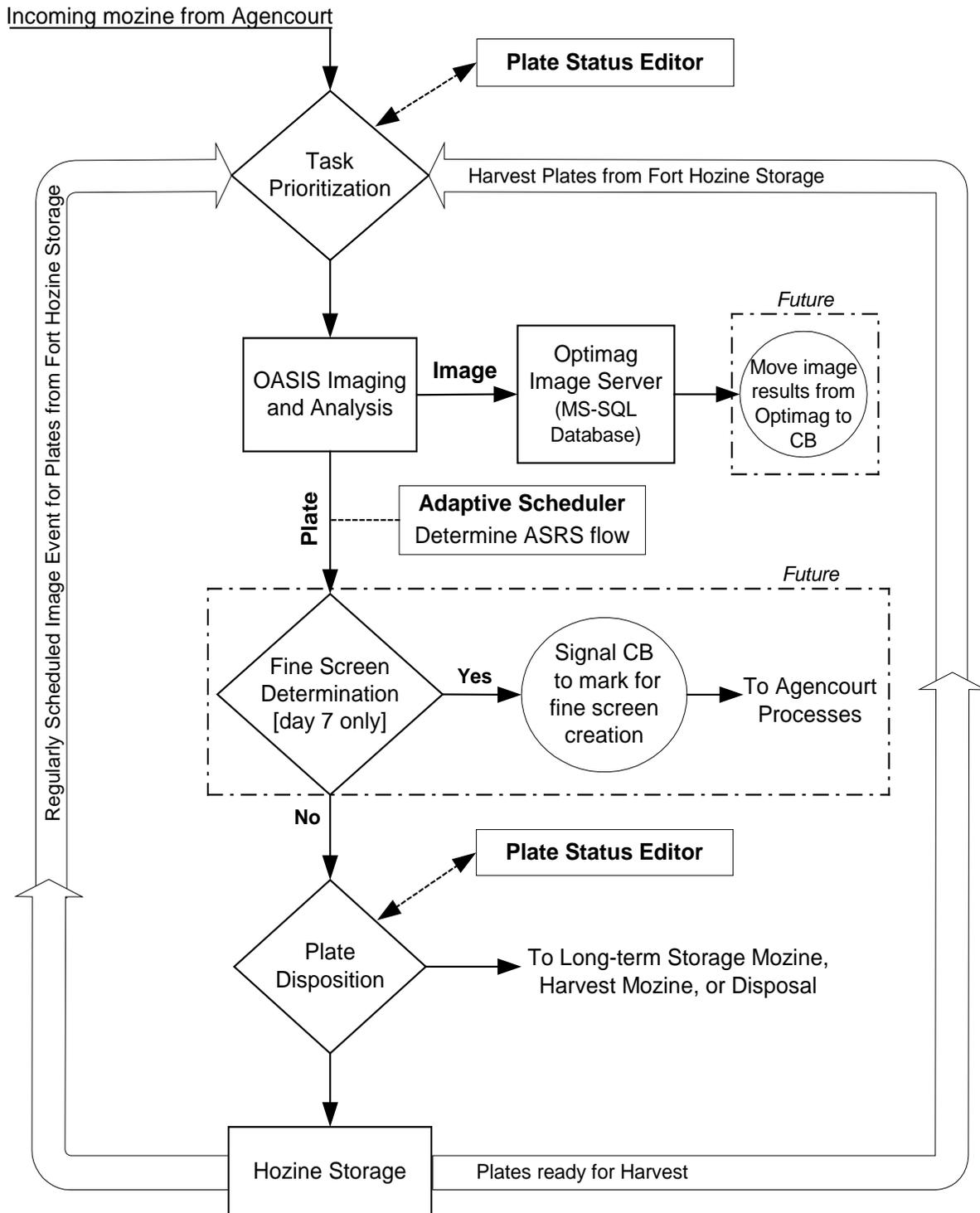
TASK PRIORITIZATION

The Directors in each fort determine which task to do next, based on the following order of prioritization:

1. Incoming mozines from Agencourt are given top priority. The Fort Director will automatically send the incoming batch to the imager as soon as possible. The Predictor in conjunction with the Adaptive Scheduler determines which imager (which side of the fort) is best suited to image the incoming batch as soon as possible. The Fort Director records the actual date and time the imaging began in the absolute_schedule_start field in the Absolute_Image_Schedule table.

2. Second priority is given to harvest plates. Individual plates or entire batches may be marked for harvest using the Plate Status Editor tool. Harvesting involves a final image (not part of a regularly-scheduled image event) and subsequent removal of the plates from the Fort.

3. Third priority is any regularly-scheduled image event for batches housed in the fort hozine storage. These will be imaged according to the adjusted_schedule_start time (calculated by the Adaptive Scheduler) in the Absolute_Image_Schedule table.

4. Last priority is given to plates that have completed all their regularly-scheduled image events, and thus need to be dispositioned (transferred to the Long-term Storage mozine, the Harvest mozine (after completing final image in #2 above), or Disposal).

Each batch (mozine = 1 batch) will have the same image schedule; e.g. all plates within a batch will be imaged consecutively, according to the same schedule, with no intervening plates from other batches. When the image of the last plate in a batch is completed, the Fort Director runs through its task prioritization, as stated above, to determine the next task.

FORT WORKFLOW

Each fort has two input mozines and two output mozines. The input mozines receive crystal plates into the fort from Agencourt (see Task Prioritization, task #1 above). Additionally, a user may insert a manually created crystal plate, or a plate not present in the Crystal Brain database into an incoming mozine, for a "one-time" image. The Fort Director will display a warning acknowledging that the incoming crystal plate is not in the database (no scheduled image events). In this case, after the incoming plate is imaged, it will be placed by the fort robot into the long-term storage output mozine. However, *normally* after imaging an incoming batch (with scheduled image events in the system), the plates are placed in a hozine within the fort to await their next scheduled image event. The batches are tagged back to the image schedule based on their hozine location in the fort, which is tracked by the fort robot.

The two output mozines are where the fort robot stacks crystal plates to be removed from the fort. One output mozine is reserved for harvest plates (see Harvest); this is Mozine #1. The other is reserved for plates headed to long-term storage (see Long-Term Storage); this is Mozine #2. The

Fort Director controls the loading of these mozines by the fort robot and provides any warnings/alerts associated with these output mozines.

THE FORT DIRECTOR

Each fort contains an intelligent automation control system that directs operations in that fort (see Fort Knox Director and Fort Bliss Director). These Fort Directors interact with the Crystal Brain database, provide instructions to the fort robot, and display important warning messages to the user. The Fort Directors of each fort report to Crystal Brain the time the imaging for a batch has begun and concluded. This time is used to build a heuristic record of the batch imaging requirements, which are used in the scheduling optimization and balancing algorithms (see Adaptive Scheduler).   The Fort Director also provides alert messages to the Marquee in Agencourt when an error condition exists in the forts, and provides warnings to the user when output mozines need attention (see Harvest and Long-Term Storage).

IMAGE EVENT SCHEDULES

Each fort room (Fort Knox and Fort Bliss) has two imaging systems, one on each side of the room. The goal is to balance the two imagers in each room so that no one imager is more heavily tasked than another.   The Predictor analyzes current image tasking to find the appropriate fort and imaging side into which to enter the incoming mozine from Agencourt. Once in the fort, the Adaptive Scheduler is responsible for optimizing the throughput of the imaging in the forts. At the conclusion of each imaging event for each batch, the Adaptive Scheduler re-assesses the image schedule for that batch. Based on the time it took to image that batch (image_processing_time in the Absolute_Image_Schedule table) and other intervening or possibly conflicting events, the Adaptive Scheduler will update the date and time for the next scheduled image event (see Adjusted Image Schedule) for that batch.

The relative image schedule defines the interval between image events for a batch, as well as the tolerance (window) for each event (see Schedule Editor). The desired relative image schedule for each batch is selected by the user using the Batch Editor tool during experiment definition. The absolute image schedule refers to a specific date and time on which the images are actually begun. However, due to scheduling conflicts within the Forts, these exact times may need to be juggled to accommodate other image events for other batches. The adjusted image schedule represents the image schedule that results when accommodations are made for conflicts and taking into consideration the tolerances permitted.

ADAPTIVE SCHEDULER

The Adaptive Scheduler, a Crystal Brain Engine process, uses the time_tolerance field in the associated Relative_Image_Schedule table to determine how to juggle the image events, so that an image is taken within the desired window. The new adjusted time is referred to as the adjusted_image_schedule, and is stored in the Absolute_Image_Schedule table. After a

batch has completed an image event, the Adaptive Scheduler runs through its optimization routine and determines the new adjusted date and time for the next image event for this batch, using the time_tolerance specified in the Absolute_Image_Schedule.

Example: Let's say you have an absolute image schedule of June 13, 2001 at 8:45am. However, with a four-hour tolerance, and taking into consideration other image events scheduled near the same time, the adjusted image schedule becomes June 13, 2001 at 12:15pm.

Additionally, the Adaptive Scheduler makes every effort to accommodate the image-taking on the same side each time (i.e., the imager on the same side of the fort, see root side). However, in order to meet the tolerance window, the Adaptive Scheduler will switch to the other imager on the other side of the same fort, if necessary. The side on which the image is actually taken is stored in the adjusted_side field in the Absolute_Image_Schedule table. This time and placement juggling is done automatically by the Adaptive Scheduler, behind the scenes, every time a new batch enters the fort or an existing batch has completed an image event. If an image event cannot be adjusted so that it still occurs within the desired window, the unresolved_image_event field in the Absolute_Image_Schedule table will be set.

Below are listed the rules and constraints that are taken into consideration when scheduling image events:

- If possible, schedule the next image event for a batch on the same imager (same side of the fort) as determined by the Predictor (i.e., the root side). If that imager is down, or if the desired time tolerance cannot be met using that imager, then the batch will be scheduled on the other imager in the same fort.

- Once a batch is introduced to one of the forts, it stays at that fort. If both imagers at the Fort are down, they will need to be repaired as soon as possible. There is no manual transportation of plates from one fort to the other.

- Image events more than 24-hours old (configurable, based on LookBackTime in the Settings table) but did not occur, are marked as "skipped" in the database.

- When an imager is down for a period of time, scheduled image events will likely be missed. When the imager comes back online, only the most recent missed image event will be processed. All previous missed events will be assigned the status of "skipped" (skip_image_event is set to 1 in the Absolute_Image_Schedule table). For example, suppose both imagers in a fort are down for a period of 4 days: Monday through Thursday. A batch was scheduled to be imaged each of those four days, at 1:30pm, but these images could not take place. The imagers come back online again at 8am on Friday morning. The Adaptive Scheduler will mark the Monday, Tuesday and Wednesday events as "skipped" in

the database, and will immediately attempt to run the last skipped event – Thursday. Therefore, at 8am on Friday, the Thursday 1:30pm scheduled image event will be run.

IMAGE EVENT VIEWER

All image events are run through the Adaptive Scheduler optimizer (see above); however conflicts still occur. The Image Event Viewer application shows for each side of each fort, the scheduled image tasks, based on the adjusted image schedule. Using the Image Event Viewer tool, the user can clearly see (depicted graphically on a time grid, and color-coded) where the conflicts are occurring and which batches are the source(s) of the conflict(s). The user can select any date and view a 28-day time window of image events. Image Event Viewer is a "read-only" application – no data is updated or written to the database by the user.

OASIS IMAGING AND ANALYSIS

OASIS is the name of the imaging and analysis system from Optimag. There are two Optimag Imaging systems in each fort – one per side. During an image event, the fort robot takes a batch of crystal plates to one of the imagers (determined by the Adaptive Scheduler), and places each plate in succession onto the imaging stage. The imaging stage moves the plates so that each well can be imaged individually. Each imager can image one plate per minute (96 wells per minute or 1.6 wells per second). After each well is imaged, the images are sent to the Optimag image server for processing. [see sample images in the Appendix]. The image server then performs a series of image processing tasks to quantify crystal development in each well [future]. Each image is given a score to indicate the extent of crystallization [future]. In the future, these scores will be communicated to Crystal Brain and stored within the Crystal Brain database; however, at this time the OASIS and Crystal Brain systems do not share data with one another.

The Optimag servers operate on a Microsoft SQL database. These servers are coupled to the LAN servicing the Forts. Data is maintained on the servers for a period of 29 days, after which they are automatically overwritten.   Prior to overwriting of the image files, all uncompressed images will be archived to tape over a GB Ethernet link on the Fort LAN. No images are transferred over the Crystal Brain LAN.

In the future, when the OASIS image data is stored within Crystal Brain, users of Crystal Brain will be able to view all the image scores (per well) and view the available images associated with each well (future Image Viewer application). This will be used to make decisions on Fine Screen (see Fine Screen Determination) and for analyzing progress of crystallization experiments.

FINE SCREEN DETERMINATION

Proteins have limited viability, typically 7-14 days (see Protein Plate Editor). Because of this, it is essential that image results be reviewed early – during the first 5-7 days in the fort – for all coarse screens. If crystallization is noted during the first 5-7 days, a decision may be made about pursuing

a refinement of the coarse screen (a fine screen), while there is still some protein viability left (see Coarse vs. Fine Screen). In the future, Crystal Brain will have a rule-based system that processes a set of rules and constraints based on scored images (from OASIS) to automatically schedule Fine Screens. Additionally, this rule-based system could also schedule harvesting, disposal or long-term storage of plates based on image results (see Plate Disposition).

[Future]: Ideally, after 7 days (configurable), Crystal Brain will identify the top 16 (configurable) "hits" – positive image results, based on crystallization scores from OASIS – and prompt the user for confirmation [future]. The user could then use the Image Viewer (future application) to preview these images, manually score and/or annotate them, and validate or change the results. Once validated, Crystal Brain will use an algorithm (yet to be defined) to define the combinations of mother liquors for a Fine Screen (i.e., the fine screen recipe). The user may then edit this Fine Screen recipe as appropriate, and indicate whether the batch will be an automatic or manual screen type (see Determine Screen Type). Once the Fine Screen experiment has been defined and confirmed, a new batch will begin the Agencourt processes. The Agencourt technician will be prompted, via the Marquee and Agencourt Director, to load the appropriate protein plates in the Protein Dispensing Machine, if not already present.

PLATE DISPOSITION

After entering the forts, there are three possible fates for the crystal plates: harvest, long-term storage or disposal. Figure 7 diagrams the flow of these plate dispositions. The user may select individual plates, or entire batches, for disposition using the Plate Status Editor tool.

Figure 7: CRYSTAL PLATE DISPOSITION
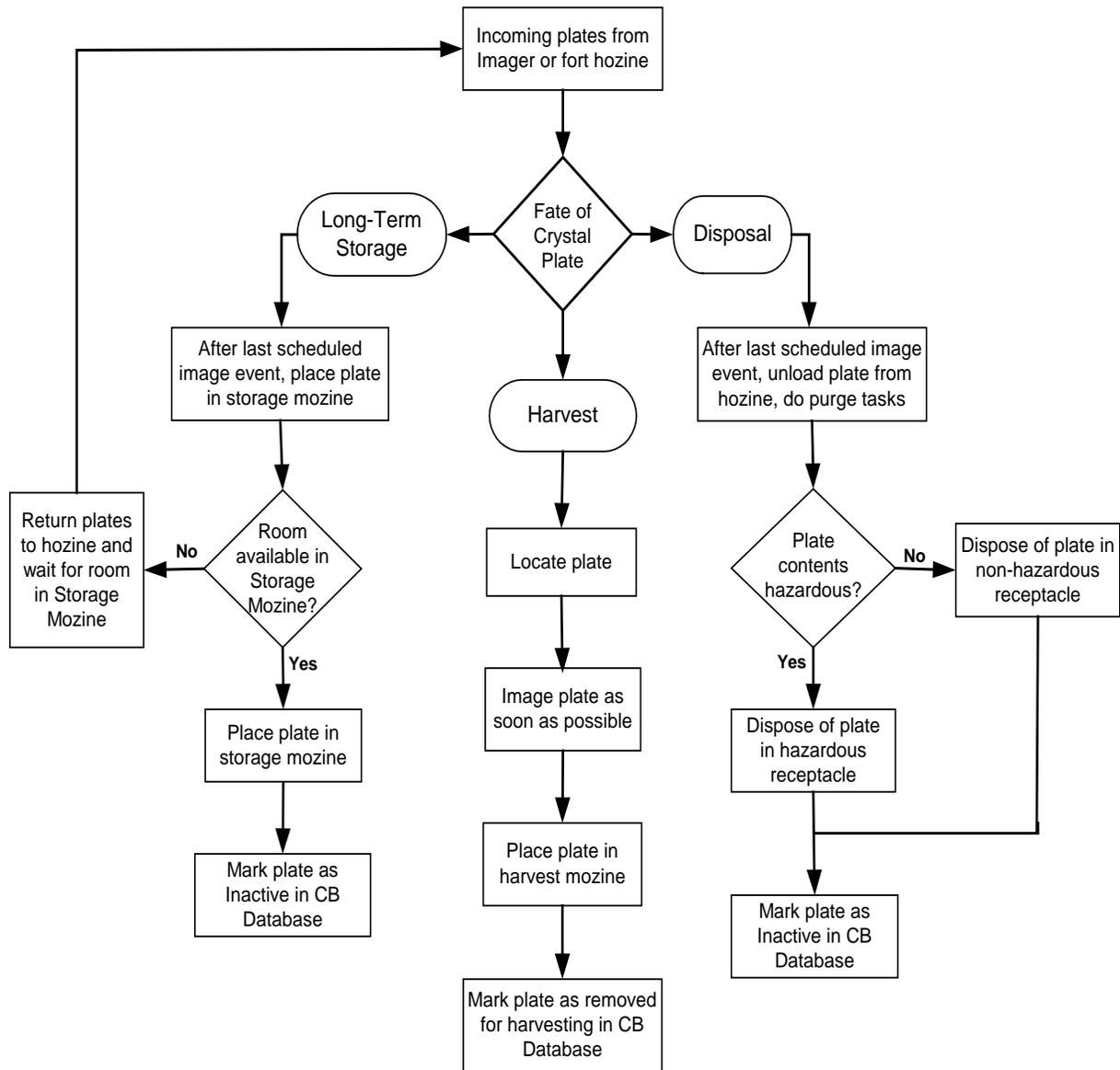
HARVEST

A batch or a single plate may be harvested before it has completed all its scheduled image events. For example, although a crystal plate may have a 28-day image schedule, it may be desirous to harvest the plate after day 7 if there are positive image results and a fine screen will be forthcoming (see Fine Screen Determination) on this same protein. Using Plate Status Editor, the user may select the desired plate(s) or batch(es) for harvest. This updates the Crystal Brain database with the date and time (harvest_date in Crystal_Plate table). Within the forts, the Fort Director will locate the desired plate/batch and begin imaging it as soon as possible. Recall this is its second workflow priority (see Task Prioritization, #2). No matter what the scheduled image events are for a plate targeted for harvest, the plate will immediately be imaged just prior to harvest. Figure 7 diagrams this process.

After a plate targeted for harvest is imaged, the fort robot places the plate in output mozine #1, the harvest output mozine (see Fort WorkFlow). At this point, the plate_status field in the Crystal_Plate table will be set to a value of 5 to indicate that the plate has been dispositioned and is awaiting pickup in the output harvest mozine. The robot will continue loading the harvest output mozine as needed, including plates from different batches, until it is full. When the harvest mozine is full or needs attention, the light over it will begin fast-blinking, and an alert will be sent to the Marquee in Agencourt. The Fort Director will display a descriptive message telling the user that the harvest mozine needs attention. When the harvest mozine is removed and emptied, the light over it goes out. When the mozine is again returned to the fort and is ready to begin receiving more harvest plates, the light over it will be on (but not blinking). At this point, the plate_status field in the Crystal_Plate table is set to 0 or null, to indicate it is inactive (i.e., no longer in the fort), and the end_fort field in the Crystal_Plate table is updated with the date and time the plate exited the fort.

LONG-TERM STORAGE

Long-term storage of a plate or batch may often be desirous. This is currently the default for all manually prepared plates or plates introduced into the forts which are not present in the database (see Fort Workflow). The user may designate a batch or a single plate for long-term storage using the Plate Status Editor tool. However, this action is not acted upon by the Fort Director until *after* all the scheduled image events for that plate/batch have been completed. [Note: This is in sharp contrast to the harvesting process, which can occur *before* a plate/batch has completed all its scheduled image events]. For example, suppose a plate/batch has a 28-day image schedule, and on day 20 the user designates it for long-term storage. The regularly-scheduled image events continue on days 20 through 28. Then, on day 28, after its last image event has been completed, the fort robot will place the plate/batch in the long-term storage output mozine, mozine #2 (see Fort Workflow). Therefore, the entire image cycle is completed before the plate/batch is taken to long-term storage. Figure 7 diagrams this process.

If the After a plate has been moved to long-term storage, a flag is placed in the station_id field of the Crystal_Plate table to indicate that plate is no longer active in the Crystal Brain System.

Unlike the harvesting process which is plate oriented, the long-term storage process is batch oriented. A harvest output mozine may contain plates from different batches. However, the long-term storage output mozine can only contain plates from a single batch before considered "full", even if that means only one plate from the batch was selected for long-term storage. When the long-term storage output mozine is "full" or needs attention, the light over it will begin fast-blinking, and an alert will be sent to the Marquee in Agencourt. The Fort Director will display a descriptive message telling the user that the long-term storage output mozine needs attention. During this time, when the long-term storage mozine is not available to receive additional incoming plates, any plates destined for long-term storage will temporarily be placed back into a fort hozine. When the long-term storage mozine is removed and emptied, the light over it goes out. When the mozine is again returned to the fort and is ready to begin receiving more long-term storage plates, the light over it will be on (but not blinking). Any plates that were temporarily placed back into a fort hozine, can now be placed into the long-term output mozine. Once the long-term storage mozine has been removed, the plate_status field in the Crystal_Plate table will be set to 0 or null, to indicate the plate is no longer active, and the end_fort field in the Crystal_Plate table will be updated with the date and time the plate exited the fort.

DISPOSAL

Crystal plates that show no crystallization activity would typically be targeted for disposal. The user may designate a batch or a single plate for disposal using the Plate Status Editor tool. However, the plate/batch is not actually disposed of until *after* all the scheduled image events for that plate/batch have been completed. Figure 7 diagrams this process. Recall that some plates may contain hazardous chemicals (see Hazardous Plate Marking). For these, the hazardous flag is set in the Crystal_Plate table. When a plate is targeted for disposal, the Fort Director checks the hazardous flag to determine how to dispose of the plate. There are two chutes leading to trash cans – one for hazardous plates, and one for non-hazardous plates – in each fort.   After its last scheduled image event, a plate targeted for disposal will be moved by the fort robot to the appropriate waste chute. Periodically, a technician will need to check the hazardous and non-hazardous trash manually. There are no sensors currently to tell Crystal Brain when these trash cans are full or need attention. After a plate has been disposed, the plate_status field in the Crystal_Plate table is set to 0 or null, to indicate the plate is no longer active, and the end_fort field in the Crystal_Plate table is updated with the date and time the plate exited the fort.

PLATE STATUS EDITOR

Using the Plate Status Editor tool, the user may do the following:
- Select a plate disposition – harvest, long-term storage or dispose – for individual crystal plates, or for entire batches within a fort;

- Add, modify or skip a scheduled image event for an entire batch fort.

When crystal plates come out of Agencourt, destined to the Forts, they automatically have the default disposition of long-term storage. In the Crystal_Plate table, the long_term_storage field is set to "1." During the time the crystal plates are incubated in the forts, it may be desirous to harvest the plate(s) or batch, if they show early crystal growth (for example). When the user changes the status of the plate or batch to "Harvest" using the Plate Status Editor, Crystal Brain enters the harvest_date (the current date and time) into the Crystal_Plate table (see Harvest). Alternatively, it may become desirous to dispose of a plate or batch if there was no growth during its imaging cycle. When the user changes the status of the plate or batch to "Dispose" using the Plate Status Editor, Crystal Brain clears the harvest_date field and sets the long_term_storage field to "0" in the Crystal_Plate table (see Disposal). The user may continue to change the plate dispositions (to harvest, long-term storage or disposal) as necessary, so long as the batch has not yet completed its last image event.

Recall that during the experiment definition process, the user selected a relative image schedule for each batch of crystal plates (see Schedule Editor and Batch Editor).   While in the forts, the Adaptive Scheduler assigns the actual image event times, adjusting the image schedule as necessary to accommodate other events (see Image Event Schedules and Adjusted Image Schedule). Using the Plate Status Editor, the user can see the status of all image events for a batch:
- Done: image event completed,
- Skipped: image event was skipped – not done,
- Blank: image event still scheduled – not yet done.

Note: Unlike the plate disposition, which may be done at either the batch or individual plate level, the image event status can only be manipulated for an entire batch within a particular fort.

Within Batch Editor, the relative image schedule applies to an *entire* batch, where there may be one 4° C batch fort and one 20° C batch fort – i.e., *both batch forts are assigned the same image schedules.* However, within Plate Status Editor, the image schedules in each of the forts may be manipulated *independently.* For example, on the same batch (same batch name, different batch_fort_id), the user may add or skip events for the plates in the 4° C fort but leave the plates from the same batch in the 20° C fort unchanged.

MISSED IMAGE EVENTS
When an imager is down for a period of time, scheduled image events will likely be missed. When the imager comes back online, only the most recent missed image event will be processed. All previous missed events will be assigned the status of "skipped" (skip_image_event is set to 1 in the Absolute_Image_Schedule table) by Crystal Brain Engine. This allows the forts to have one "catch-up" event per batch before getting back on schedule. Alternatively, a user may deliberately set a future image event to be skipped – or

may "unskip" an image event previously set to be skipped which has not yet occurred – using the Plate Status Editor tool. However, the Adaptive Scheduler checks all image events more than 24-hours past due (configurable, based on LookBackTime in the Settings table) and will set all but the most recent image event to a status of "Skip."

Example: Suppose both imagers in a fort are down for a period of 4 days: Monday through Thursday. A batch was scheduled to be imaged each of those four days, at 1:30pm, but these images could not take place. The imagers come back online again at 8am on Friday morning. The Adaptive Scheduler will mark the Monday, Tuesday and Wednesday events as "skipped" in the database (viewable via Plate Status Editor), and will immediately attempt to run the last skipped event – Thursday. Therefore, at 8am on Friday, the Thursday 1:30pm scheduled image event will be run.

Using the Plate Status Editor, the user may add new image events – above and beyond those specified by the relative image schedule – for a batch. For example, suppose a particular image schedule runs for 28 days, taking one image per week. The user may add additional image events – perhaps one image event every other day during the third and forth weeks, or perhaps one image event immediately (now) – as desired. The user may also modify the date and time of previously-scheduled image events if desired. All additions and modifications to image events using Plate Status Editor cause both the absolute_schedule_start and the adjusted_schedule_start fields to be set to the newly-desired event dates and times, and set the time_tolerance to zero in the Absolute_Image_Schedule table. Later, during Crystal Brain Engine's regular process, the Adaptive Scheduler may wind up shifting the desired times (due to other image events and constraints) and will update the adjusted_schedule_start field as necessary. When this happens, since the time tolerance window of zero is violated, the unresolved_image_event field will be set by the Adaptive Scheduler in Crystal Brain Engine.

Note: The Plate Status Editor application does not allow any modifications (changing date and time, or skipping an event) if the event has a status of "Done".

WEB SERVER

ARCHITECTURE OVERVIEW

The Crystal Brain Web Server is a computer running Microsoft IIS that accesses Crystal Brain's Oracle database and displays the information in the form of web pages. Users, even those remote to the Crystal Brain LAN, can access the Web Server over the Internet or VPN (see The Syrrx VPN) and can view the data with only an Internet browser (Microsoft Internet Explorer). The Web Server was written using Cold Fusion, JavaScript, and DreamWeaver Development Tools for html editing. The Web Server provides read-only user access to Crystal Brain – no data input or updating is permitted.

HOME FUNCTIONS

Once the user has accessed the Home Page, the following options are displayed along the left pane: Contact Us, Register, and Login.

CONTACT US
This allows the user to e-mail the Syrrx Web Master.

REGISTER
The user is prompted to enter a name and password. A lookup is done in the Users table of Crystal Brain. A user must be activated by Syrrx after being added to the Users table. All registrants are reviewed daily by Syrrx for addition to the system. Users are assigned a privilege level, which controls their level of access to the system (see Admin).

LOGIN
Once a user's registration has been accepted and they have been added to the system, a user may login with a name and password.

ADMIN
The Admin function will only display for users with a level 4 privilege. The Admin facility allows level 4 users (the system manager) to administer the users: add new users to the User table, and assign a privilege level to a user. Privilege levels can range from 1 to 4, with 1 being a restricted level and 4 being the system manager level. Depending on the level of a user, the user may see different views or have different options within the Web Server application.

APPLICATION FUNCTIONS

After a user logs in, the following options are displayed along the left pane: Stock Solutions, Proteins, Crystal Plates, Statistics, Plate Analysis, and Batch Report. Depending on the privilege level of the user some options may or may not appear (see Admin).

STOCK SOLUTIONS

This option shows the user the various stock solutions extracted from the Stock_Solution table and the Bottle_Stock table. The user may click on a column heading to sort the listing by that column.

PROTEIN

This option shows the user data extracted from the Finished_Protein_Plate table. The user may click on the barcode of interest (i.e., select the desired protein plate), to see the associated data from the Protein_Well table. From here, the user can click on the common name, to see a listing of all protein plates and crystal plates containing that protein. If desired, the user can drill down further by clicking on the batch name. This will display a batch report, similar to that shown when selecting the Batch Report function from the main menu along the left pane (see below).

CRYSTAL PLATES

Using this option, a user may select to view a list of active, or inactive, or all (active and inactive) crystal plates. Inactive crystal plates have a blank station ID. Data from the Crystal_Plate table is displayed.

STATISTICS

Currently there are four types of statistics a user select to may view. These are as follows:

- Active Crystal Plates Undergoing Coarse and Fine Screen: This displays a pie chart showing the portion of total screens that are coarse, fine and other. This is determined by extracting data from the screen_type field in the Screen table.
- Active Crystal Plates by Creation Date: This displays a bar graph with increasing dates scrolled from left to right.
- Hazardous/Non-hazardous: This displays a pie chart showing the proportion of crystal plates marked hazardous or non-hazardous. This is determined by checking the hazardous field from the Crystal_Plate table.
- Inactive Crystal Plates: This displays a pie chart showing the portion of inactive crystal plates (no longer in the system) that were disposed, harvested, and place in long-term storage, as well as whether they were hazardous or non-hazardous.
- Batch Information Screen: This shows the following three statistics: the average number of plates per batch, the maximum number of plates per batch, and the minimum number of plates per batch.

- Screen Frequency for Crystal Plates: The user is prompted to enter a date, and the display shows the number of coarse and number of fine screens processed on that date. [Currently does not work]

PLATE ANALYSIS

This function currently does not work.

BATCH REPORT

The user is prompted to enter a begin and end date. The display shows all batches completed by Agencourt between those dates. This uses the end_Agencourt field in the Crystal_Plate table. Depending on the user's privilege level, the user may also see a list of column names with check boxes. If so, the user can check the particular columns they are interested in seeing in the batch report. When the list of batches is displayed, the user may select individual batches (click on check box beside batch name) to run a detailed batch report. The application also gives the user the option of getting the report in a printable format.

FUTURE

The following tasks are yet to be assimilated into Crystal Brain, but are desired to be incorporated into future application phases.

REPORTS

Reports summarizing data in the Crystal Brain database or providing system metrics and statistics are desired. Here are some examples:

- Expired Proteins Report: text-based report that shows proteins picked to go to Fine Screen, but have expired in the meantime.

- Harvest Report: text-based report that depicts all proteins scheduled for harvesting.

- Fine Screen Report: text-based report that depicts all plates/wells that have been selected for the fine screen.

- Plates in Process Report (Tracking): a graphical report that will allow a user to look at historical data of plates processed at Agencourt and the Forts. Sample shown below.

- Proteins in Storage Report: text-based report that depicts all proteins stored at the particular storage room.

- Consumable Report (Fluid status): text-based report that depicts all the liquors that need to be reordered.

- Fort Capacity/Efficiency Report: graphical report depicting number of plates processed and number of images taken at each of the image servers in the forts.

- System Metrics Report: a graphical report that will allow user to look at historical data of Agencourt and Fort performance parameters. Sample shown below.

Sample – Crystal Brain Machine Performance Parameters Report

Machine Performance Parameters

Plates Processed
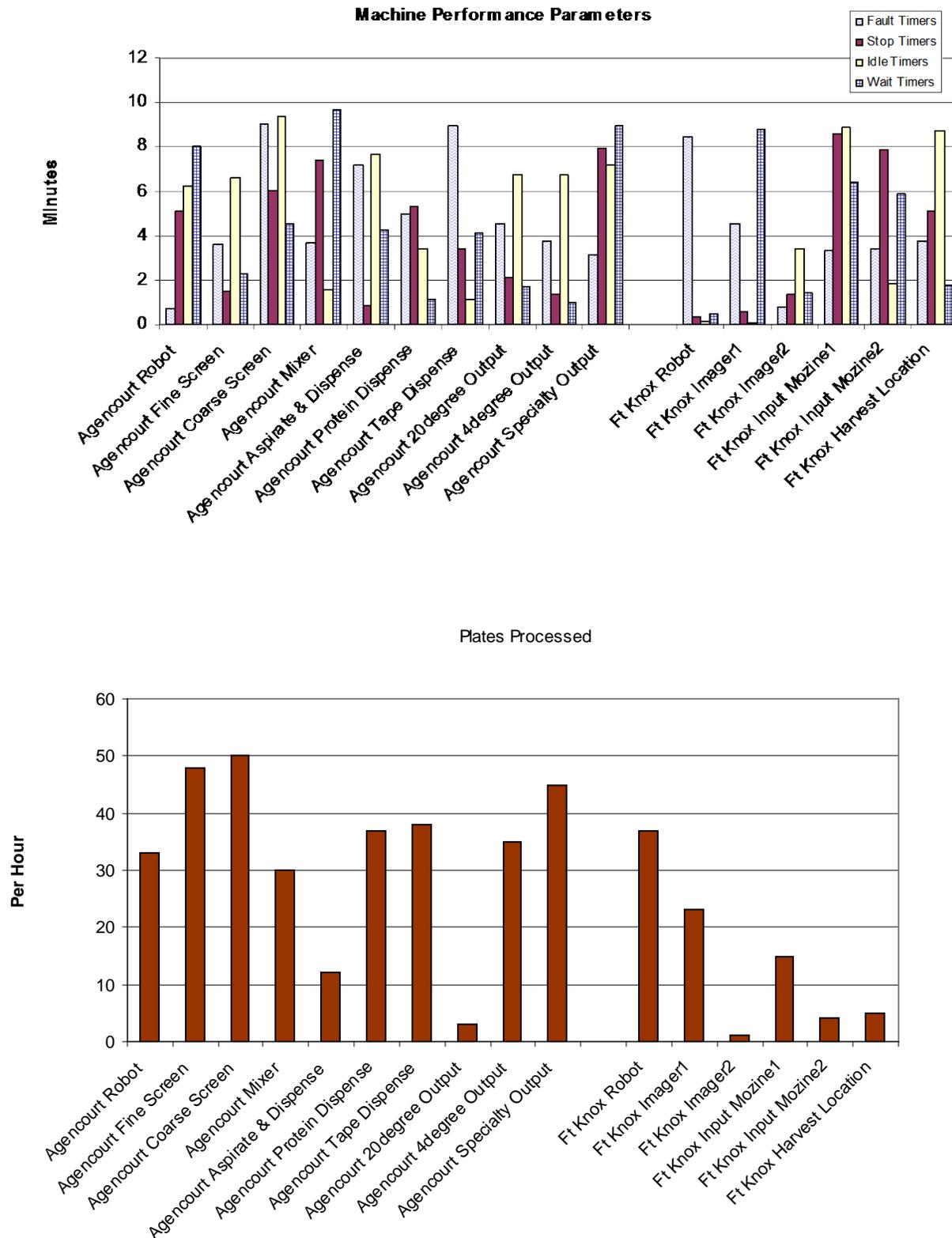
GRAPHICAL REPRESENTATIONS OF EQUIPMENT STATUS

Currently, the robots in Agencourt and the Forts interact with Crystal Brain through the Agencourt and Fort Directors. If a fault is encountered, the Director communicates this to Crystal Brain Engine and Crystal Brain Engine, in turn, can post alerts and notifications to the Marquee for the user. However, there is no mechanism for tracking or looking at these faults, plotting their frequency and type over time (for example), in a graphical or statistical way. Also, there is little or no feedback from some of the laboratory equipment, such as the Cartesian liquid handlers, to Crystal Brain. These are all desired in future versions of the Crystal Brain system.

INTEGRATION OF OPTIMAG IMAGING ANALYSIS DATA INTO CRYSTAL BRAIN DATABASE

Currently, the Optimag OASIS Imaging System analyzes and stores its image data on its own servers, in an MS-SQL database, and no image information is exchanged with Crystal Brain. This prevents the Crystal Brain system from being able to do its Fine Screen Determination and other important analysis and predictive tasks, as well as precludes an Image Viewer capability integrated with the rest of Crystal Brain. It is desirable for certain elements of the image data, such as the scoring information, to be stored in Crystal Brain's Oracle database. An interface, export-import facility or other means of data sharing between these two applications is imperative.

PROTEIN BRAIN

The protein expression processes, as well as the comprehensive tracking of protein creation and usage, is extremely data intensive and integral to rounding out Crystal Brain's functionality. Protein Brain was originally conceived as a companion automation application to Crystal Brain, supporting and automating the protein expression and production processes at Syrrx. These proteins are later used in the screening and imaging process, controlled by Crystal Brain. At this time, the Protein Brain project is being pursued by Syrrx independently of Crystal Brain.

WEB SERVER ENHANCEMENTS

One goal of the Web Server was to allow remote users (perhaps scientists and project leaders at pharmaceutical companies allied with or clients of Syrrx) to be kept informed about the progress of the proteins of particular interest to them, via the Internet. Currently, the functionality of the Web Server is more along the lines of a concept; it is not being used routinely by scientists or project leaders as part of their daily work. The Web Server design needs further study in order to identify the functions and features required by users as well as the most desirable presentation of the data (graphical, tables, pie charts, etc.). In addition, some of the existing Web Server applications are implemented only incompletely or are not fully functional; these need further programming and testing.

ENHANCE SCREEN WORKBENCH TO ACCOMMODATE ADDITIVES

The addition of additives, such as cryo-preservatives and other chemicals, to the screen solution mixtures has been identified as a need in the preparation of crystal plates. This work is being pursued currently as part of Phase 5 of the Crystal Brain project. An additive option will be added to the 96-Head Aspirate/Dispense station in Agencourt. The Screen WorkBench application will be enhanced to allow for incorporating these additives in the experimental definition process. The Agencourt method will be expanded to support additives. The associated Crystal Brain database table additions and modifications will be made.

APPENDIX A.

Network Hardware for Crystal Brain System

Acronyms Used:

        NAS: Network Attached Storage

        FC-AL: Fibre Channel Arbitrated Loop

        DAE: Disk Array Enclosure

        DPE: Disk Processor Enclosure

        DLT: Digital Linear Tape

SERVER   http://www.wsm.com/

Manufacturer – Western Scientific

Existing interface – Fibre Channel, 100BASE-T

The InFusion X3 is a feature-rich, Xeon-based 2-way server that delivers enterprise level system availability and exceptional performance. It has an Intel Pentium III Xeon 700 MHz processor, and 256 MB ECC registered memory, expandable to 2.0GB. The InFusion X3 offers leading edge technology with 33MHz PCI Fibre Channel interface and PCI 1000BASE-SX Gigabit NIC card, and 3COM 100BASE-T network cards. It also has three 18.2 Ultra 160 disk drives.

NETWORK ATTACHED STORAGE   http://www.wsm.com/

Manufacturer – Western Scientific

Existing interface – Fibre Channel, SCSI

This unit is a 510GB Tsunami RAID Active/Active Redundant RAID with Dual Fibre-channel copper/optical host connection. It is a rack mount redundant storage array with two removable active load-balancing controllers and 1GB of mirrored cache. The complete system includes RAID module, data storage and task manager utility. Tsunami RAID active/active module has two removable load sharing controllers each with 233MHz Intel Strong ARM 32-bit RISC CPU, 512MB mirrored cache, 64-bit data path, removable GBIC-based FC host cards and (8) 80MB/sec Ultra2 LVD SCSI disk channels. Data storage consists of (16) 36.4GB 10,00rpm SCA hot-swappable disk drives (15 data/parity drives + 1 global hot-spare).

AIT BACKUP SYSTEM   http://www.wsm.com/

Manufacturer – Western Scientific

Existing interface – Fibre Channel

WSM Superstore AIT backup system has 1.0TB native capacity or 2.0TB with compression. This unit is Ultra 2 LVD SCSI-3 and includes Sony AIT-2, 50/100GB tape drives, 22 removable slots, two fixed. It has an exchange time of 8 seconds and FCO Fibre Channel option with dual multi-mode optical.

SUMMIT SWITCH   http://www.extremenetworks.com/

Manufacturer – Extreme Networks
Existing interface – 100-BASE-T

10/100/1000 Mbps Ethernet Layer 3 Switching the Summit 24 Switch offers affordable leading edge Layer 3 switching technology for 10 times the performance of intranets. It has 24 10/100 Mbps Ethernet/Fast Ethernet auto-sensing ports and one flexible, physically redundant Gigabit port. It supports full line-rate non-blocking routing performance on all ports (over 5.1 million IP packets per second and 8.5 Gbps throughput). It provides support for standards-based routing protocols: RIP/ RIPv2, as well as support for up to 12,000 MAC addresses for handling networks of virtually any size.   The Summit 24 switch can provide dedicated 10/100 Mbps links to desktops and servers or multiple 100 or 1000Mbps links can be aggregated to load-share traffic. It also supports dual-load shared backbone connections.

MARQUEE LED DISPLAY   http://www.ies-1.com/

Manufacturer – Alpha Technologies
Existing interface – Serial Computer Interface

The Alpha 4120R message display is a 2-line indoor LED message center. It has the ability to display two lines of 2.1-inch characters or for maximum impact, one line of 4.8-inch characters. Maximum number of characters displayed in 2-line format is 60 (typical is 40). Display is designed to quickly display large amounts of information in three colors – red, green and amber.

LABEL PRINTER   http://www.dymo.com/

Manufacturer – Dymo
Existing interface – Serial or USB port

LabelWriter turbo for Windows 2000 is one of the fastest and most versatile label printers available for Windows, printing most labels in just 2 seconds. It handles more than 40 different labels up to 2-1/2″ (56mm) wide. The turbo comes with DYMO Label Software, and integrates directly with Microsoft Word, outlook, Goldmine and ACT and works with other software through standard print drives.   This label writer uses direct thermal print technology

eliminates ribbons, toner and ink cartridges.   It prints 30 labels per minute and works on networks with no additional hardware (Windows version.)

FIBRE CHANNEL HUB   **http://www.wsm.com/**

Manufacturer – Western Scientific
Existing interface – Fibre Channel

Western Scientific 10-port Fibre Channel Hub that connects the disk array to the servers and tape backup drive.

CRYSTAL BRAIN DIRECTOR   **http://www.wsm.com/**

Manufacturer – Western Scientific
Existing interface – 100BASE-T

Western Scientific Fusion X3 Dual Processor PIII Workstation with 700 MHz Xeon processor with 1MB, and RAID-5 technology. It has dual 18.2GB Ultra 160 hot-swappable disk drives and a 100BASE-T network card, 19″ color monitor and a Diamond Viper II 2000 Video card.

WEB SERVER   **http://www.wsm.com/**

Manufacturer – Western Scientific
Existing interface – 100BASE-T

Western Scientific PIII 866 MHz workstation, with 256 MB cache and 256 MB ECC registered memory, expandable up to 768 MB. It has a Matrox G4000 graphics card with 32MB, a CD-ROM drive, floppy drive, and 45GB Ultra IDE disk drive. It comes with an Intel 10/100 Ethernet card, 19″ monitor, mouse, keyboard and Windows 2000 Professional installed.

PROTOCOL CONVERTER   **http://www.lantronix.com/**

Manufacturer – Lantronix
Existing interface – RS232 serial connection

MSS-VIA (Variable Interface Architecture) device server provides communication between a serial interface and a 10/100 Ethernet network. It is capable of supporting TCP/IP, IPX and LAT protocols. It has serial speeds of up to 230Kbps.

APPENDIX B.
## SAMPLE CRYSTALLIZATION IMAGES FROM OASIS
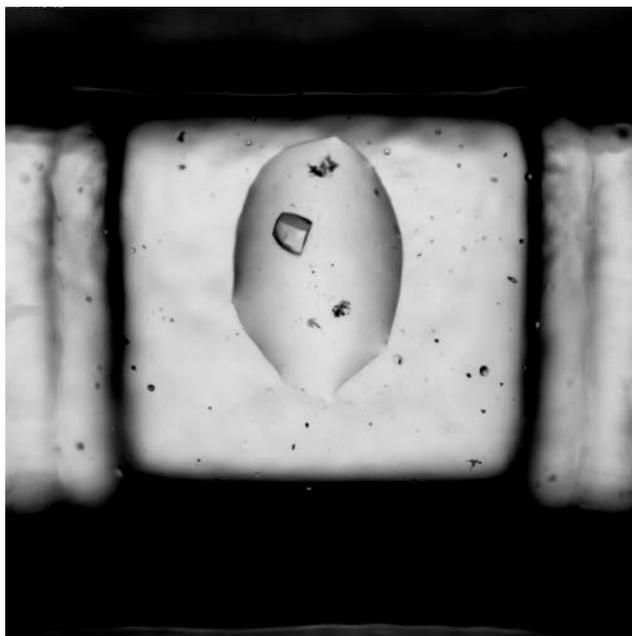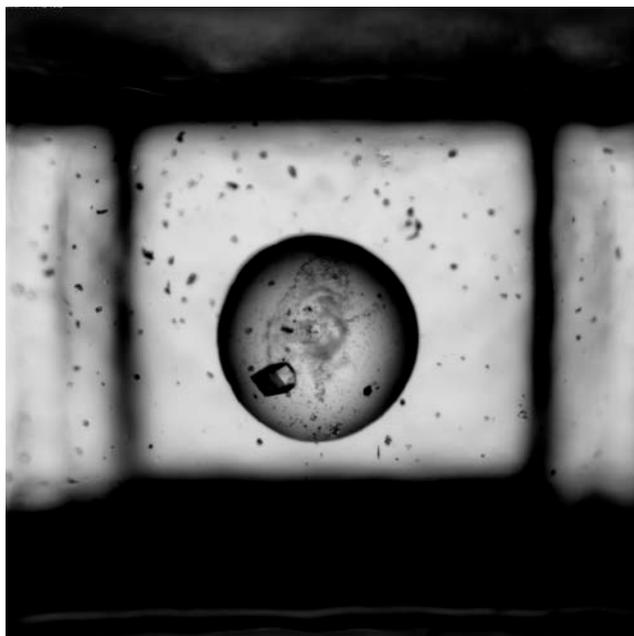
\<path\> File Name Plate ID Score Well#

Schedule Fine Screen	Schedule Harvest

\<path\> File Name Plate ID Score Well#

Schedule Fine Screen	Schedule Harvest
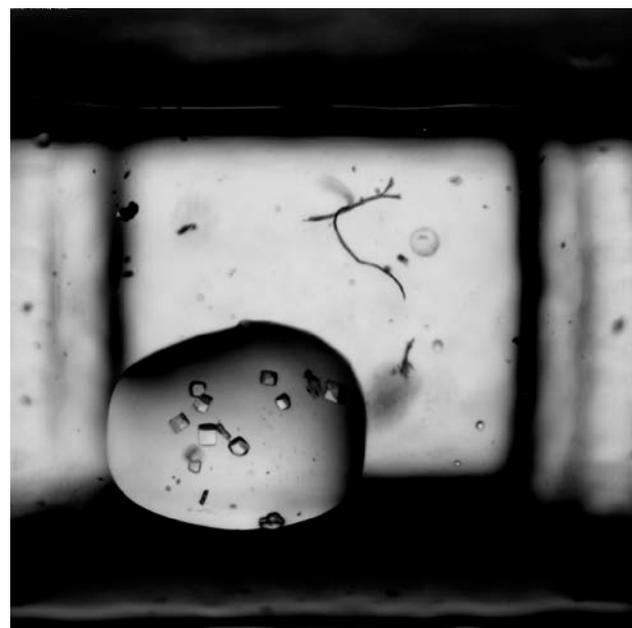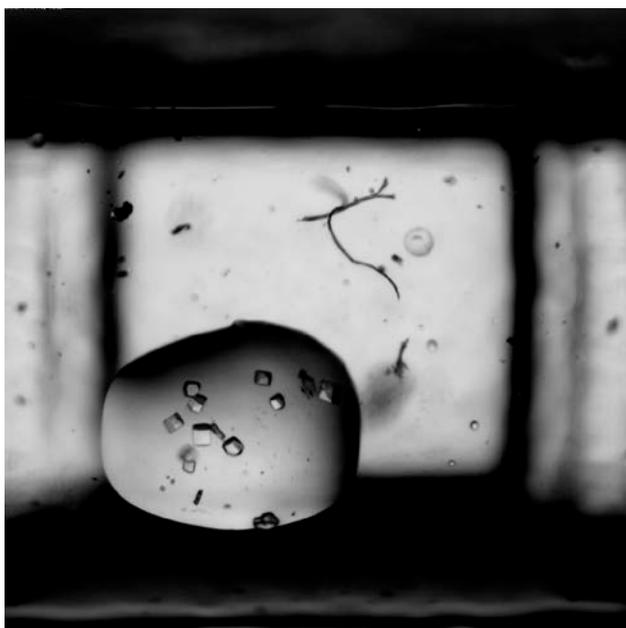
\<path\> File Name Plate ID Score Well#

Schedule Fine Screen	Schedule Harvest

\<path\> File Name Plate ID Score Well#

Schedule Fine Screen	Schedule Harvest

Sample - Crystal Brain Detail Image Viewer

IMAGE ANNOTATION