Overview:

This document presents abstraction hierarchy (AH) models of the processing equipment used in high-throughput screening (HTS) of molecular compounds on a highly-automated robotic line for drug discovery. This modeling work has been completed as part of a larger cognitive work analysis (CWA) on biopharmacologist planning and execution of high-throughput molecular compound screening and analysis of resulting data. The CWA includes a goal-directed task analysis (GDTA) of operator behavior and additional AH modeling of the automated control systems used by operators to manage processing equipment.

AH models are hierarchical, structural models consisting of multiple levels of abstraction. Rasmussen (1985) applied AH models in work domain analysis. At the highest level of abstraction, the models define the purpose of automation in the work domain. The lowest level of an AH model represents the physical components of the system. In between are the generalized functions of the automation. Linkages among the levels represent how the purpose of the automation is implemented through specific devices and they provide an explanation of why certain components are needed to achieve a system purpose (Rasmussen, Pejtersen & Goodstein, 1994).

An AH model is typically presented using a grid of 3 columns and 5 rows (see Figure 1). The columns (from left to right) present decomposition of the system (as a whole) to presentation of component processes and physical devices. The rows (from top to bottom) present functional decomposition of the system from the overall purpose through generalized functions to the physical components supporting the functions. “Means-ends” connections are also presented across the rows.

Equipment Models:

The Appendix presents AH models for HTS line equipment used in a highly automated enzyme-based (Trypsin) assay of organic compounds for the potential to serve as bases for new drug development. The equipment includes a bar code print and apply device for labeling micro-plates (culture plates) used in the screening process and facilitating tracking during screening; an automated pipetting (liquid transfer) system (Biomek2000) for filling plates with enzyme substrates, test compound extracts and other reagents; an incubator for bringing the temperature of reactions on the culture plates to normal human body temperature; an optimized robot for handling and transporting micro-plates to and from various workstations on the line (devices); and an automated plate reader for analyzing the enzyme activity in each well (each culture) on a micro-plate. All this equipment is integrated as part of the HTS line (see Figure 2). Each device can be programmed for operation by using proprietary software applications. The entire line is programmed for operation and controlled by a central process control system.
<table>
<thead>
<tr>
<th>Goal or purpose</th>
<th>“Highest level of abstraction in model”</th>
<th>“Component level” (refer to components in descriptions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General constraints affecting system goals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic functions of system</td>
<td>“Abstract function level”</td>
<td></td>
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<tr>
<td>Components of system required to achieve functions</td>
<td>“Generalized function level” (Includes identification of system components.)</td>
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</tr>
<tr>
<td>Components of system required to achieve functions</td>
<td>“Physical function level” (Includes identification of components. Describes how objects of system relate to achieving higher-level functions.)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. General form of Abstraction Hierarchy model.

Figure 2. High-throughput screening robotic system for enzyme-based testing of compounds.
The first model presented in the Appendix is that of the bar code printer and reader. At the highest level of the model, the purpose of the equipment is identified (upper-left corner of grid); that is, to assign identifications to plates and recognize plate labels during the assay process. Directly below this level, the general constraints affecting the goal or purpose of the device (i.e., any constraining functions) are identified. For the bar code device, the constraints to plate identification include labeling and reading.

The constraining functions are represented at the abstract function level in the model. Below this level, the generic functions for the device are identified, including the process of system initialization, the process of printing, the process of applying bar codes, and the process of reading bar codes. At the same generalized function level in the model, these generic processes are broken down into component processes (see the same row of the model). For example, the component processes for the generic process of reading include the process of activating the scanner, the process of moving the microplate for scanning and the process of positioning the plate holder as part of the bar coding device. The component processes for printing include feeding the labels and printing foil and applying thermal material from the foil to the label. Other component processes are identified in the model.

The next lower level in the model is the physical component and function level. Here the subsystems required to complete the printing, applying and reading functions are identified. They include the label-paper feeder, the foil feeder, the print head, a vacuum gripper, a laser scanner, the microplate holder, and a manual entry keypad and LCD. At the same physical function level in the model, these subsystems are broken down into components (see the same row of the model). The level of detail of the model is limited based on the expert and analysts determination of what component knowledge may be critical for operators to understand how the equipment functions and to be able to diagnose faults, etc.

Beyond the elements of the model, means-end connections are presented among the generic and component processes, the device subsystems and components, the generic processes and subsystems, and the component processes and components of the device. Following the links (lines) from the top of the diagram down to the bottom, an operator can discover how each function is implemented by the equipment. Following the links from the bottom of the diagram to the top, and operator can learn why the various subsystems or components exist as part of the system.

Results:

In general, the AH models developed on the HTS line equipment and automation can be used to support development of future operator training programs, or user manuals. The AH models can serve as a basis for educating operators on connections between system components, automation functions and physical devices in order to promote fault diagnosis under error conditions.

The combination of the AH models with the results of the GDTA on biopharmacologist planning and execution, and analysis of HTS operations is expected to provide a meta-method for understanding of how HTS operator needs are currently addressed (or not) by existing automation and information display technologies. This approach is expected to be superior to using GDTA alone for identification of existing system shortcomings and future design needs. Specifically, the integration of the results of the AH and GDTA methods will allow for relation of a biophramacologists’ goal structure and critical decisions (as part of the assay process) to the
purpose of automated systems on the HTS line and functions and components. The approach is expected to identify which components of existing systems may be unnecessary or inadequate for operator system state/situation awareness and decision making processes. The results of the combined analyses may also serve as bases for formulating future automation design guidelines.

References:

APPENDIX: Abstraction Hierarchy models for HTS line equipment.
States, operational conditions, and settings of bar coding system components

Assign ID to, and recognize, micro-plates

Label and read micro-plates

Process of system initialization

Process of printing bar code

Process of applying bar code

Process of reading bar code

Label paper feeder

Foil feeder

Printer

Vacuum gripper

Apply and read controller

Laser scanner

Plate holder

Manual entry keypad

LCD display

Process of verifying available paper/foil

Process of moving plate holder to home position

Process of paper/foil feed

Process of applying thermal ink to label

Process of removing label from backing paper

Process of locating label position and blowing label on micro-plate

Process of activating reader (scanner)

Process of moving plate for scanning

Process of verifying label

Rotating feed motor

Feed reel for labels

Take-up reel for labels

Feed reel for foil

Take-up reel for foil

Reel position sensors

CPU

Thermal print head

RS-232C connection to PC

Vertical translation motor

Vacuum pump

Rotation motor

Translational motor

Rotational control motor

Translational control motor

CPU

RS232C to printer

RS-232C connection to PC

Laser diode

Rotating (scan) mirror

Receiver (photo diode)

RS-232 C connection
States, operational conditions, and settings of incubator system components

- Heating coils
- Thermometer
- LCD to view current and set temperature
- Gas bottle and line
- Pressure regulator
- CO₂ measuring device
- CO₂ control system
- Water tray (completely passive)
- Plate transfer platform
- Activation switch
- Motor and blades
- Mechanized plate holder
- Optic sensor to detect plates
- Two-axis trans. control unit
- Belt drive
- Position sensor
- Turntable
- Manual/auto switch
- Position switch (10 settings)
- Locking system
- Integrated heating coils
- Trans. control unit
- Tracks to guide door
- Door position sensor
- Rotation motor
- Gas (CO₂) control system
- Plate hotels/racks (completely passive - no components)
- Fan unit
- Water tray
- Incubator lid/backdoor
- Carousel
- Plate shuttle
- Incubator
- Front door and integrated heater
- Heating system
- Control climate conditions in oven
- Process of heating incubator
- Process of controlling CO₂
- Process of verifying plate at transfer station
- Process of opening/closing incubator door
- Process of running fan
- Process of setting and verifying heating system state
- Process of setting and verifying gas system state
- Process of verification plate at transfer station
- Process of moving plate shuttle
- Process of mixing atmosphere and ensuring humidity
- Process of stocking/unstocking
- Process of verifying plate at transfer station
- Process of positioning carousel
- Process of running fan
- Activation switch
- Motor and blades
- Rotation motor
- Belt drive
- Position sensor
- Turntable
- Manual/auto switch
- Position switch (10 settings)
Analyze biological samples for activity

Optical measurement of sample state

- Process of priming device
  - Process of priming temperature
  - Process of priming pump(s)
- Process of sample prep./modification
  - Process of receiving plates from robot position
- Process of loading/unloading plates
  - Process of returning plates to robot position
- Process of measurement
  - Process of sample exposure to light
  - Process of method selection (e.g., absorbance)
- Process of shaking plates
- Process of heating/cooling plates
- Process of positioning plates for measuring wells
- Process of activity detection

Plate shuttle (shaker)

Liquid dispensing and disposal system

Heating system

Optical measurement system

System controller

- Plate holders
  - X, Y axis trans. unit
- Shaker motor
- Position sensors
- Linear track(s)
- Access door
- Mounted/locked dispensers (2)
- Mobile dispensers (1)
- Waste reservoir
- Syringe pumps
- Washing reservoir (1)
- Internal source reservoirs (3)
- Heating coils/plates
- Thermometer
- Light source (lamp)
- Light detector
- Filters
- Filter turntable (revolving wheel)
- Linear track and belt drive

States, operational conditions, and settings of plate reader system components