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NSF Information Technology Research (ITR) Annual Review

“Intelligent Human-Machine Interface & Control for Highly Automated Biological Screening Processes”

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The Cognitive Ergonomics Laboratory
Senior Personnel

- **Kaber (PI)** - Cognitive work analysis (CWA) and user interface design for usability and function.
- **Chow (co-PI)** - High-throughput screening (HTS) process simulation and model of network control of multiple screening lines.
- **St. Amant (co-PI)** - Structured knowledge representation, cognitive model development, and design for human-robot interaction (HRI).
- **R. Stoll (co-PI)** - Liaison to URO and PI on parallel grant from German SMV.
Research Assistants

- Becca Green (IE) - Cognitive task analysis (CTA); abstraction hierarchy (AH) modeling; user interface design (UID) evaluation and recommendations.
- Noa Segall (IE) - CTA; AH modeling; UID evaluation.
- Zheng Li (ECE) - Real-time resource allocation and scheduling for network-based control; Adaptive bandwidth allocation.
- Rangsarit (Jae) Vanijjirattikhan (ECE) - Petri Net and simulation modeling of HTS processes (e.g., sample plate preparation).
- Thomas Horton (CS) - Translation of structured knowledge representation results to computational cognitive model code.
- Lloyd Williams (CS) - Graphical knowledge representation methods as basis for cognitive modeling.
Organizational Partners

**URO (funded by SMV):**

- Complimentary research - “Physio-ergonomic Optimized Human-machine Interfaces for Life Science Automation.”
  2. Develop web-based access and interfaces for remote screening data analysis.

- NCSU to provide HTS UID recommendations to URO for evaluation in “home-grown” control software and for web interface development.

- NCSU to share computational cognitive model of screening supervisor performance with URO to define optimal HRI approach.
Other Collaborators

- Consultation on cognitive modeling work:
  - Enhancement of ACT-R (adaptive control of thought-rational) cognitive architecture.
  - Develop visual processing routines for models for effective application of architectures to HRI.
    - Mike Byrne (Rice University)
    - Mike Fotta (DNAmerican, Inc.)
    - Mark St. John (Pacific Science & Engineering)
    - Frank E. Ritter (Pennsylvania State University)
Activities of IE Subteam

- Review of CWA literature.
- Goal-directed task analysis (GDTA) of supervisory control of HTS lines (structured interviews with expert biopharmacologist).
- AH modeling to describe configuration and function of automated devices on HTS line.
- Comparison of CTA method results for UID recommendation formulation.
No comprehensive method for work-domain analysis (WDA), including problem and constraint ID. 

CTA can be used to support work-centered design but no application to interactive systems. 

CTA useful for identifying conditions for which auto may be used by operators. 

WDA method can also be used to ID auto needs. 

AH modeling has been applied to auto. 

Research supports use of multiple CTA methods: 
  - AH models used to ID limitations of auto to support operator. 
  - ID gaps in operator understanding of systems and training needs. 

Across studies, no systematic approach for translation of CWA results to system/UID guidelines for performance.
Method:

- Conduct procedural task analysis on basic HTS method development using COTS.
  - ID steps of auto enzyme-based assay on HTS line.
- Interview expert biopharmacologist to describe knowledge structures in use of HTS automation.

Goal, subgoal, task, decision, info needs:

1.1. Adapt “bench-top” method to HTS line for rapid identification of useful compounds:
   1.1.3. Establish plate configuration to achieve statistically valid results:
      T1 Ensure no edge effects in assay process (e.g., thermal effects on wells at edges of plates).

Do I need to include empty wells at perimeter of plate?
- Need - Number of sample concentrations to be included on plate.
- Need - Cost of leaving plate wells empty.
Overarching Goal and Major Subgoals

1. Find “hits” among a huge number of compounds as fast as possible and at low cost

1.1. Adapt “bench-top” method to High-throughput Screening (HTS) line
   - Identify steps that need to be performed as part of (automated version of) assay
   - Identify appropriate micro-plate types for assay
   - Establish plate configuration to achieve statistically valid results
   - Identify automated devices to use to perform steps of assay
   - Identify time critical steps as part of assay as basis for sequencing steps
   - Identify feasible sequences of steps in assay that allow for successful execution of experiment (i.e., is there any flexibility in sequence of steps in method?)
   - Adapt manual pipetting steps to automated version of assay
   - Design measurement approach to facilitate analysis of inhibition of enzyme activity by sample compounds
   - Develop program for assay method using HTS line control software (e.g., Beckman Coulter-SAMH)
   - Ensure reproducibility of results from HTS line

1.2. Ensure results of assay meet quality criteria
   - Identify criteria for quality factors
   - Calculate quality statistics based on sample data
   - Compare test statistics with criteria

1.3. Optimize assay method for efficiency
   - Avoid bottlenecks
   - Establish optimal sequence of steps in assay
   - Optimize pipetting steps
   - Identify available work-in-process storage space

1.4. Conduct accurate analysis of data from assay
   - Establish criterion activity level for identifying “hit”
   - Use basic statistical analysis to identify and address outliers in data
   - Determine enzyme activity levels (e.g., Trypsin) (conduct data analysis)
   - Determine variation in enzyme activity levels
   - Decide whether test compound is active

1.5. Generate understandable reports of results for clients
   - Address customer information needs for decisions on test compounds (i.e., to support determination of whether further investigation of compounds is needed)
Content of GDTA to be used as basis for structured knowledge representation method (SHAKEN) and to begin cognitive model development.

Data in lowest block can be used to define information display content for screening process planning software.

- Establish plate configuration to achieve statistically valid results
- Identify whether edge effects are present (e.g., thermal effects on wells at edges of plates)
- Determine where to place control and control blank samples on test plate
- Determine order in which concentrations of test extracts (compounds) should be dispensed to test plates
- Determine whether multiple compounds can be tested on a single plate (determine whether a separate plate needs to be used for each compound)

- Do I need to include empty wells at perimeter of plate?
- What constitutes good plate organization?
- Can serial dilutions be used in preparing sample plates?
- What order of concentrations is logical given the proposed test plate layout?
- How many concentrations are to be tested for each compound?
- How many test replications are to be used for each sample concentration?
- How many controls must be included on plate?
- How many replicates are to be used in the experiment?

- Number of sample concentrations to be included on plate
- Cost of leaving plate wells empty
- Serial dilution must be started with highest sample concentration first
- Plate type being used (i.e., 96 well or 384 well)
- Replicates
AH Modeling

- Abstract representation of physical device (e.g., bar coder, incubator, line robot, plate reader, pipette) and auto to control device.

(Proprietary device software or action/config. dialog in overall method editor (e.g., SAMI).)

- Define purpose of automation, general functions, and ID physical components/interface options.
- Show how purpose is implemented and why components are needed for functions.

- Supports operator learning of auto functions and how to access through interface
AH Model for Bar Coder Software

**Interface Decomposition**

- **Columns** - Decompose software system (as whole) to specific interface features.
- **Rows** - Decompose purpose and general functions to specific functions options.

**Function Decomposition**

- **Label and read micro-plates**
  - Define global operation of device
  - Select (global) action
  - Select type of bar code
  - Store type of bar code
  - Define content of bar code
  - Select among action options (Automation, Read, Manual Use)
  - Select among label format options (Code 128, Code 39, text only)
  - Select among label position on microplate
  - Select plate position for reading
  - Set offsets for label height (relative to top/bottom of plate)
  - Set frequency of bar code verification (or none)
  - Select plate position for reading
  - Print and apply device software
  - Select “Update” option
  - Manual entry of position of code on label (in mm)
  - Manual entry and store number of read periods
  - Manual entry of label prefix and suffix with auto indexing of string
  - Select among “Read” or “No-Read” options
  - Select among reading error handling options (log error, flag error and stop)
  - Select among verification error handling options (i.e., errors during verification of bar code on plate against SILAS ID - Ignore, or log and stop)

- **Print and apply control**
  - Select among label format options (Code 128, Code 39, text only)
  - Select among label position on microplate
  - Select plate position for reading
  - Set offsets for label height (relative to top/bottom of plate)
  - Set frequency of bar code verification (or none)
  - Select plate position for reading
  - Print and apply device software
  - Select “Update” option
  - Manual entry of position of code on label (in mm)
  - Manual entry and store number of read periods
  - Manual entry of label prefix and suffix with auto indexing of string
  - Select among “Read” or “No-Read” options
  - Select among reading error handling options (log error, flag error and stop)
  - Select among verification error handling options (i.e., errors during verification of bar code on plate against SILAS ID - Ignore, or log and stop)

- **Reading control**
  - Select (global) action
  - Select type of bar code
  - Store type of bar code
  - Define content of bar code
  - Select plate position for reading
  - Set parameters for addressing reading errors
  - Set parameters for verification errors (reading previously labeled plates)
  - Select plate position for reading
  - Print and apply device software
  - Select “Update” option
  - Manual entry of position of code on label (in mm)
  - Manual entry and store number of read periods
  - Manual entry of label prefix and suffix with auto indexing of string
  - Select among “Read” or “No-Read” options
  - Select among reading error handling options (log error, flag error and stop)
  - Select among verification error handling options (i.e., errors during verification of bar code on plate against SILAS ID - Ignore, or log and stop)
Comparison of CTA Results

- Review decisions and info needs for goals in GDTA and compare with auto functions and interface content reflected in AH model.
  - ID components of software not supportive of operator goals (reduce unnecessary options).
  - ID components inadequate to meet info needs.
- Make UID recommendations:
  - Interface format suggestions organized based on taxonomy of usability heuristics. \cite{Nielsen1993}
  - Interface content/auto capability recomms. organized based on taxonomy of auto. \cite{Parasuraman2000}
Example UID Recommendations

1.1.9.4 Facilitate test plate incubation

Task 1 steps:
Preparation (heating) of plates:
- Input/select minimum time, Input/select maximum time
  - Input time estimate (manual entry)
Apply micro-environment to test plates:
- Process of setting and verifying heating system state/temperature
  - Use touch-keypad to set temperature
Control of plate incubation processes:
- Setting and activating plate chamber heat
  - Manual start-up or auto activation

Decisions identified by expert. Tasks steps dictated by existing software.

Recommendations:
- Allow temp. and duration setting with one dialog.
- Eliminate redundancy in config. methods - use keypad or software not both.
- Suggest temp. and duration based on LIMS database.
  (Target user control and freedom and error prevention.)

Integrate incubator into method

What is the incubation duration for the plate?

What is the temperature of the incubator microenvironment required by the assay?

Knowledge of “bench top” assay, as documented in literature

The Cognitive Ergonomics Laboratory
Activities of ECE Subteam

- Model IP-based remote real-time system supervisory control of multiple HTS lines.
- Develop MATLAB/SIMULINK based simulator of robots on HTS lines.
- Investigate adaptive bandwidth allocation algorithm for control of multiple HTS lines.
- Plan for integration of simulation with the computational cognitive model and prototype process control interface.
Petri Net Modeling of HTS Lines

- High-level Petri Nets, including timed and colored, appropriate for HTS line modeling.
  - Can incorporate process time data on “healthy” and faulty conditions and resource attributes.

- Nets can capture process synchronization, asynchronous events, parallel operations and resource conflicts (unlike queuing networks).

Chen et al., 2005  Zuberek, 2004

Zurawski & Zhou, 1994

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Overall Supervisory Control Model

Model includes four HTS lines under control of single supervisor. Central server relays user control commands and system state feedback. Each line monitored for device errors and real-time process quality assurance.
Subsystem Model

Each line includes multiple stations equipped with multiple sensors and can accept multiple control commands. Process quality parameters are monitored in real-time at each step in method.
Target Subsystem Process: Sample Plate Preparation

Sample Plate Preparation

Stock solution, deep well plates.

Biomek2000 work surface consider to be storage buffer.

Each plate in process is considered token or entity in Petri Net model.

Gross process time estimates from Entzian and Junginger.

Create sample plates with different concentrations of compound.
Petri Net and Simulation Models

- $p_n$ - Places on process line.
- $t_n$ - Transitions among nodes (define robot actions on token from $p_i$ to $p_{i+1}$).
- Tokens are manipulated by robots ($R_n$) (e.g., ORCA ($R_1$), Biomek2000 ($R_2$)).

Focus on sample plate preparation process.
Network-Based Control of Multiple HTS Line

- Relevant scheduling methods for addressing adaptive bandwidth allocation problem exist:
  - Real-rate scheduling models. e.g., Goel et al., 2004
  - Feedback elastic scheduling models. e.g., Chen & Dai, 2003

- Current work focused on mathematical formulation of multiple line control problem.
  - Definitions of structure of physical subsystems on HTS line at CELISCA are critical.
  - Using sampling rate scheduling approach to model bandwidth allocation in network control.
• Complexity of subsystem signals \( (u_i) \) indicator of potential process errors (i.e., process device or quality parameter errors).
• Sampling frequency \( (f_i) \) for specific subsystem adapted by server based on system signal state.
• Greater bandwidth \( (B_i) \) allocation to subsystems exhibiting faulty states for increased sampling.

Adaptive bandwidth allocation algorithm automatically adjusts frequency of sampling for subsystem with error condition.
Activities of CS Subteam

- Survey tools for automated translation among cognitive modeling formalisms (e.g., SHAKEN).
- Formalize translation between AI planning language (PDDL - Planning Domain Defn. Language) and code of cognitive modeling architecture (ACT-R).
- Extend capabilities of ACT-R architecture in area of visual processing to support HRI design.
- Survey interaction mechanisms/presentation techniques of existing approaches to HRI.
- Plan integration of tools with interface design activity and process simulation work.
Building Tools for Modeling HRI in HTS Processes:

- Translate between natural language of CTA (GDTA) and structured/programming language for cognitive modeling (e.g., ACT-R).
  - GDTA to PDDL (via SHAKEN) - CTA result translated to AI formalisms (planning language) including:
    - Conditionals on environmental states for action.
    - Outcomes of action on environment.
    - Representation of knowledge about UI feature dependencies.
  - PDDL to ACT-R (via G2A extension):
    - Translate from AI planning formalisms to ACT-R (cognitive model) primitives (using Lisp code).

Ghallab et al., 1998
St. Amant et al., 2004
Step 1: Develop SHAKEN Model for Translation of CTA Result to PDDL

- SHAKEN - Web-based interactive tool based on mixture ("Martini") of knowledge representation methods.

Hierarchy of tasks for ensuring assay quality. Links represent precedence and composition relationships.

Node are combined or linked to represent tasks.
Step 2: Encode CTA model and Output in PDDL Form

GDTA hierarchical outline

SHAKEN knowledge formulation

Output Lisp-based code

Translation to PDDL syntax

CTA result as planning representation

;;; THIS SAVE FROM CMAP OF: _Ensure-assay-quality5223
;;; KM REPRESENTATION OF THIS "PROTOTYPE"

(disable-classification)

(Ensure-assay-quality has (superclasses (Event)))

(Ensure-assay-quality now-has (prototypes (_Ensure-assay-quality5290)))

(_Ensure-assay-quality5290 has
  (prototype-of (Ensure-assay-quality))
  (prototype-scope (Ensure-assay-quality))
  (prototype-participants (_Ensure-assay-quality5290
    _ID-quality-criteria5291
    _Assess-run-quality5292
    _Calculate-quality-stats5293
    _Compare-test-stats5294 _Time-Interval5295
    _Establish-CV5296
    _Establish-IC50-criterion5297
    _Establish-Z-factor-criterion5298 _Place5299
    _Time-Interval5301 _Determine-Z-factor5302
    _Generate-avg-IC50s5303
    _Determine-sample-CV5304 _Place5305
    _Time-Interval5306
    _Compare-assay-Z-to-criterion5307
    _Compare-avg-IC50s-to-data-for-compound5308
    _Compare-sample-CVs-to-criterion5309
    _Place5310 _Time-Interval5311 _Place5312
    _Establish-CV-limit5313
    _Establish-CV-out-of-limit-allowed5314
    _CV-criterion5315 _Sample-CV5316))}
Extending Scope of Models for HRI Domains

- Development of extensions to ACT-R architecture to enhance visual routines:
  - Include component for focus of visual attention to model task requiring real-time monitoring.
  - Allows for cognitive model to interact with same interfaces (process screen images) actual user sees and promotes validity of evaluation.

- Combine modeling extensions with high-level assessment of impact of human-robot interface content and format on behavior.
  - Critique of conventional HCI metaphors for HRI design.
Year 2 Planning

**Major tasks:**

- Prototype usable interface alternatives for interactive screening process control tasks (Summer/Fall 2005).
- Develop computational cognitive model of supervisory controller behavior in HTS process control and data analysis (“ensure quality assay”) (Fall 2005/Spring 2006).
- Prototype of MATLAB/SIMULINK-based simulator of HTS line in plate preparation (Fall 2005/Spring 2006).
- Apply cognitive model to control HTS line simulation through interface prototypes (Summer/Fall 2006).

**Follow integrated approach to research tasks to increase pace of knowledge discovery.**
Project Planning

- Conceptual diagram of project analyses and models, and information flows:

  Cognitive modeling to focus on goals ensuring assay results meet quality criteria (See 1.2 in GDTA).
  - No custom software for task.
  - Task can be performed iteratively to refine process.
Training Opportunities

- **IE subteam activities:**
  - Graduate student learning of CTA methods.
  - URO biochemist/process engineer familiarization with CTA methods.
  - URO use of GDTA/AH models from developing training materials.
  - Training of students to use CTA results as basis for UID.

- **ECE subteam activities:**
  - MATLAB/SIMULINK simulation can be used by process engineers in developing/testing new automation ideas for HTS lines.
  - Integration of simulation with control interface prototypes supports student training on iterative UID process.
  - Presentation of research results in grad. courses (ECE 556; ECE 716).

- **CS subteam activities:**
  - Grad. student learning of knowledge acquisition and planning tech.
  - Training of graduate student in basic cognitive model construction.
Publications and Website

♦ Journal Manuscripts:

♦ Conference Proceedings Papers:

http://people.engr.ncsu.edu/dbkaber/NSF_ITR/
Contributions

- Across disciplines - Highly specialized student training in research methods and life sciences auto leading to rare base of technical professionals for industry.

- CS subteam:
  - Novel integration of CTA and AI research methods to support cognitive modeling.
  - Bridge between AI planning area and cognitive modeling not explored - approach to translations between planning and cognitive model languages is novel.

- ECE subteam:
  - Novel HTS process simulation supporting human-centered design of interfaces and adaptive network control technology.
  - Novel quality of control concept for human interaction with life sciences automation.
  - Novel IP-based time-sensitive system monitoring and fault detection control.

- IE subteam:
  - No prior research has applied CTA methods to life science processes.
  - Novel combination of GDTA and AH modeling to ID shortcomings of existing auto and to support UID recommendations.