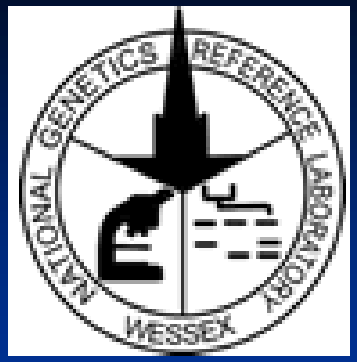


Robotics and System Integration

Chris Mattocks

Intended use

- What assays are going to be automated?

		No of tests per patient	
		Few	Many
Sample throughput	Low	✗	✓
	High	✓	✓✓

- If many different assays, are they compatible? – i.e. can they be arrayed on the same plate?
- How many different compatible assays will be automated
- **Need for standardised primer design**

Batching

Assumptions:
Fragments per test = 35
Patients per year = 500
Controls per batch = 3

batches (exons)/ plate	*batch size*	*total controls required*	*1x full screen (plates)*	*efficiency loss %*	*Batch collection [days]*	*Batch type*
1	93	3	0.38	0	68	Full plate per exon/batch
2	45	6	0.39	3	33	
3	29	9	0.40	7	21	
4	21	12	0.42	11	15	
6	13	18	0.45	19	9	
8	9	24	0.49	29	7	Row per exon/batch
12	5	36	0.58	55	4	Column per exon/batch
24	1	72	1.46	288	1	1x Patient per batch

Intended use

- What processes are going to be automated?
  - DNA quantification
  - PCR setup
  - PCR cleanup
  - Check gels
  - Sequencing setup
  - Dye terminator removal
  - Preparation for gel/capillary loading

Intended use

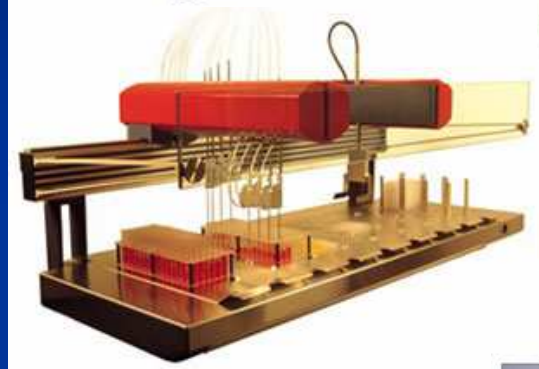
- What level of automation is required?
  1) Pre-aliquoting primers for a standard PCR assay Manual addition of DNA
  2) Complete setup of known number of PCRs in standard layout
  3) Complete setup of variable number of PCRs dependent on current work load

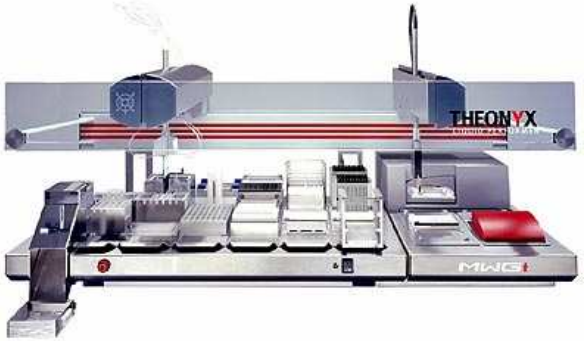
Assay design

- Standardise assays where possible
- Simplify assays where possible
- Consider the implication of methodologies used.

PCR cleanup	Advantages	Disadvantages
EXO/SAP	Simple, robust	Viscosity of reagents, integrated PCR block or manual intervention, requires incubation.
Size exclusion plate	Simple, robust fast	Cost, integrated vacuum manifold or manual intervention, pipetting involved in recovery can be difficult.
Paramagnetic beads	Simple, robust fast, no integrated equipment required	Re-suspending beads can be problematic, requires plate handling capability, carryover.

Which robot?





Deck layout

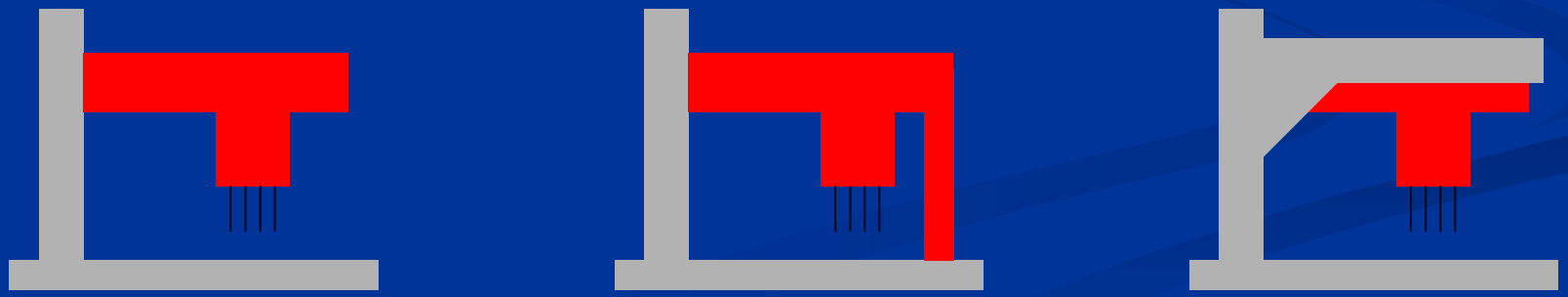
- Good positive location of labware / equipment at each deck position
- Solid enough to deal with forces required for tip loading
- On deck or off deck access to integrated equipment needed for the process – dead space
- Suitable wash station and waste disposal arrangements
- Try to use one deck setup for all programmes
- Safety STOP – eg light curtain, access door.

Deck layout

- Ensure the deck has enough positions for the processes you want to automate. Allow space for:
  - Input plate
  - Output plate
  - Reagents
  - Processing position(s) if required
  - Disposable tips if required
- Can increase capacity of instrument by adding storage stacks or hotels (on or off deck) for input plate, output plate and/or disposable tips

Travelling Arm

- One or two
- Carries pipetting head and/or manipulator
- X, Y movement ususally cable or belt
- Z movement often rack and screw
- Cantilever or ‘bridge’ may have implications for tip loading.



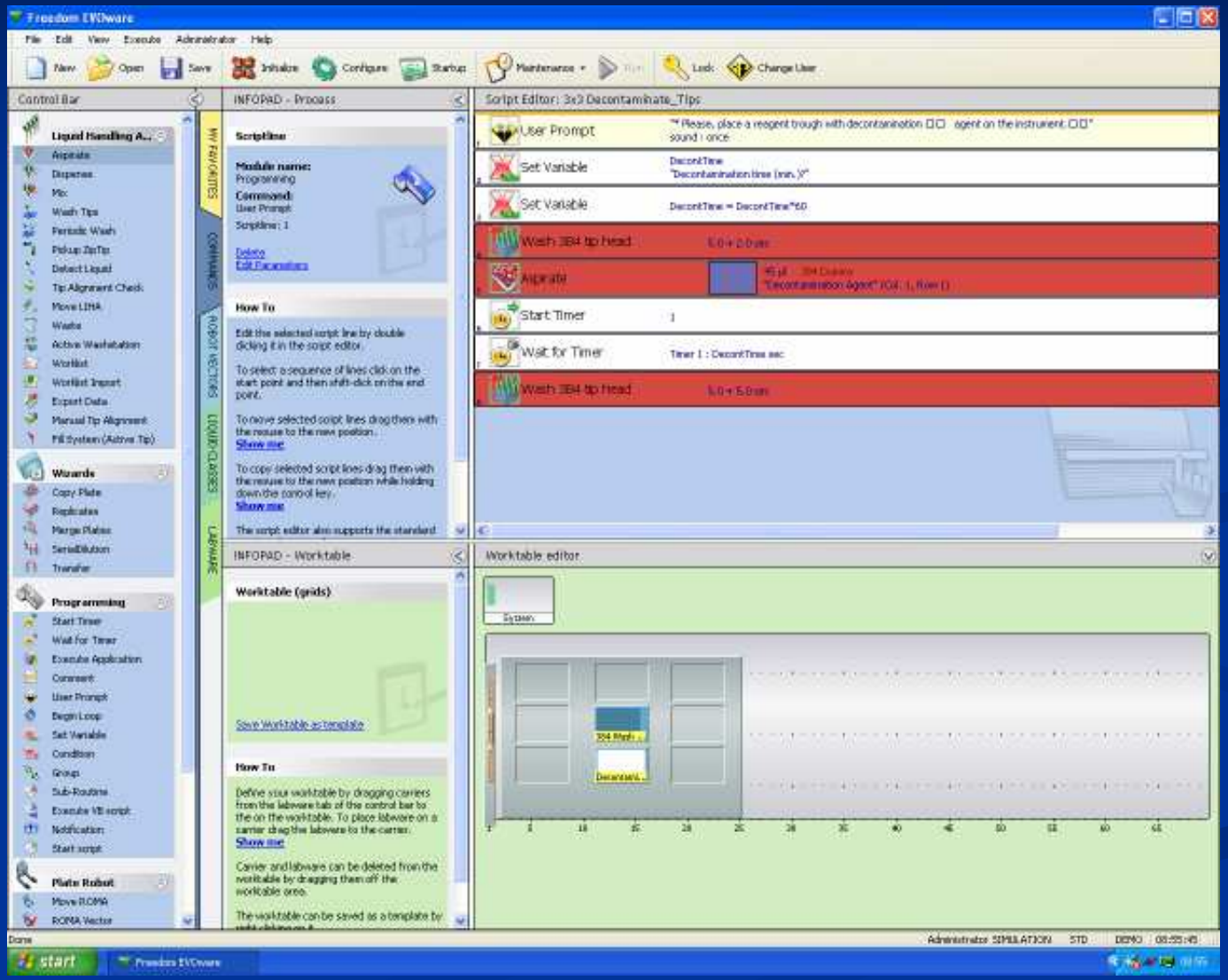
Heads

- Pipetting
  - Exchangeable heads (different volume pipettes, manipulator)
  - No of tips: 1, 4, 8, 96, 384
  - Fixed tips, disposable tips, combination
  - Varispan, Flexispan (?)
  - System liquid
  - Direct displacement
  - Liquid level sensing: capacitance based, pressure based
  - Tube capping systems
  - Safety STOP

Heads

- Pipetting performance
  - Pipetting accuracy is usually defined for an 'into liquid dispense'
  - In general diagnostic tests will not push the pipetting performance (consider ↓ concentration ↑ volume)
- Manipulator
  - Exchangeable head, second arm, composite.
  - Landscape, portrait
  - Off deck access

Software

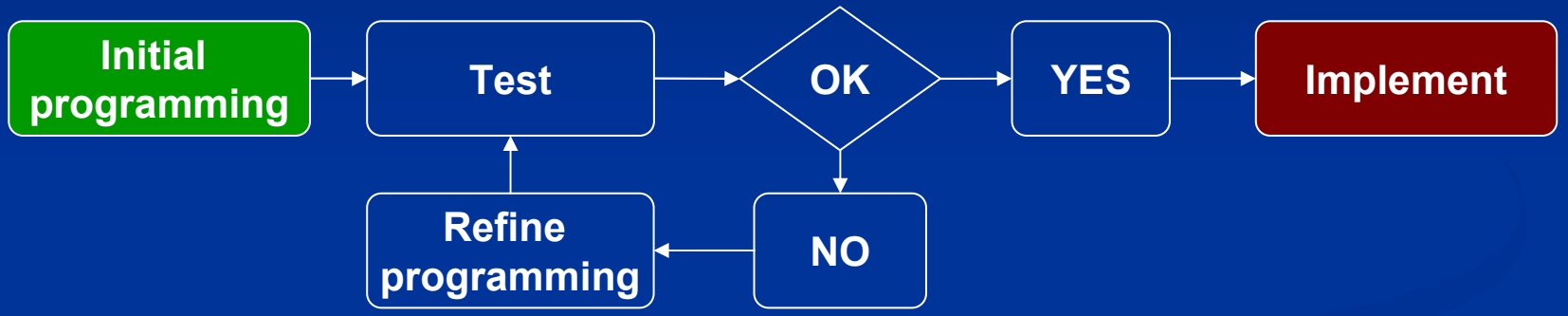

Freedom EVOware
File Edit View Execute Administrator Help
New Open Save Initialize Configure Startup Maintenance Lock Change User
Control Bar
Liquid Handling A...
Aspirate
Dispense
Mix
Wash Tips
Periodic Wash
Pick up ZipTip
Detect Liquid
Tip Alignment Check
Move LIHA
Washs
Active Washstation
Worklist
Worklist Import
Export Data
Manual Tip Alignment
Fill System (Active Tip)
Wizards
Copy Plate
Replicates
Merge Plates
SerialDilution
Transfer
Programming
Start Timer
Wait for Timer
Execute Application
Comment
User Prompt
Begin Loop
Set Variable
Condition
Group
Sub-Routine
Execute VB script
Notification
Start script
Plate Robot
Move ROMA
ROMA Vector
INFOPAD - Process
Scriptline
Module name:
Programming
Command:
User Prompt
Scriptline: 1
Delete
Edit Parameters
How To
Edit the selected script line by double clicking it in the script editor.
To select a sequence of lines click on the start point and then shift-click on the end point.
To move selected script lines drag them with the mouse to the new position.
Show me
To copy selected script lines drag them with the mouse to the new position while holding down the control key.
Show me
The script editor also supports the standard
INFOPAD - Worktable
Worktable (grids)
Save Worktable as template
How To
Define your worktable by dragging carriers from the labware tab of the control bar to the on the worktable. To place labware on a carrier drag the labware to the carrier.
Show me
Carrier and labware can be deleted from the worktable by dragging them off the worktable area.
The worktable can be saved as a template by
Script Editor: 3x3 Decontaminate_Tips
User Prompt
"Please, place a reagent trough with decontamination DD agent on the instrument DD"
sound once
Set Variable
DecontTime
"Decontamination time (min.)"
Set Variable
DecontTime = DecontTime*60
Wash 384 tip head
Aspirate
"Decontamination Agent" (Col: 1, Row 1)
Start Timer
1
Wait for Timer
Timer 1 : DecontTime sec
Wash 384 tip head
Worktable editor
Done
Administrator SIMULATION STD DEMO
start
Freedom EVOware

Software

- Generally icon driven, drag and drop
- Labware definitions (predefined, custom)
- Pipetting methods (predefined custom)
- Liquid classes (predefined custom)
- Hierarchical structure:
  - Basic commands (transfer liquid, move plate)
  - Command breakdown (eg aspirate)
  - Detailed parameters (eg air gaps, pipetting speed)
- Advanced commands
  - Loops
  - Variables
  - Custom scripts
  - Interfacing (inport/export work lists)

Programming

- Very time consuming iterative process



- Some software has virtual run environment – this can expedite testing steps
- **If process well defined**, can commission manufacturer to help with programming
- **Good design of process and minimal requirement for protocols pays off here!!**

System integration

- Different levels of integration
  - Integration of peripheral instruments (on/off deck)
  - Work lists generated by LIMS, audit trail and results fed back to LIMS - manual or automatic bar code tracking.
  - Different processes linked by conveyors or manipulator arms, full LIMS integration - fully automated bar code tracking.

System integration

- Full spec for how integration will work.

3.3. To ensure all tube transfers are correctly carried out and recorded the following protocol will be adopted:

3.3.1. For each tube transfer (regardless of what process is being carried out) the main database will generate a work list for the appropriate robot (pre/post-PCR)

3.3.2. The user will scan pre-bar coded labware which will then be allocated to the work list.

3.3.3. Before the robot performs the allocate task it will first check both the source and destination labware for the barcodes in the work list.

3.3.4. If there is any discrepancy the process will be halted and details of the error fed back to the main database.

3.3.5. The task will only be performed if the deck of the robot is correctly set up.

Sample tracking

- What type of sample tracking is required?
  - Manual checking
  - Worksheet & manual barcode scan
  - Complete setup of variable number of PCRs dependent on current work load

Summary

- In general liquid handling capability of robotics will not be challenged: