



Simplifying Automated Liquid Handler Integration and Programming using Mosaic Software's VSLH Application

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INTRODUCTION

Automated liquid handlers are an essential component of the modern laboratory, significantly improving pipetting speed and accuracy while reducing error rates by automating tedious tasks. However, liquid handlers still need to be programmed and set up for operation, and the data they generate needs to be combined with other process data and interpreted. These tasks can be distracting and time consuming for research scientists.

WITHOUT INTEGRATION

If automated liquid handlers are not integrated into lab workflows, they can present some challenges for their operators, such as:

- Requiring experts to write machine scripts for different operations
- Inventory errors caused by inaccurate manual transfers of data files
- Time consuming inventory updates to synchronise inventory data
- Human error in setting up the liquid handler ready for transfers
- Human error in calculations, such as half log serialization volumes
- Difficulties connecting information from stores holding the source samples used for dispensing
- Managing occasional equipment errors and updating the inventory accordingly

WITH MOSAIC SOFTWARE INTEGRATION

Titian's Mosaic sample management software has a VSLH application (Variable Span Liquid Handling) designed to easily and seamlessly integrate automated liquid handlers with your sample inventory and lab workflow operations. Off-the-shelf integrations are



available for many automated liquid handlers, including:

- Beckman Biomek, FX and NX systems
- Hamilton Star systems
- Tecan Fluent and EVO



Once your liquid handler is integrated with Mosaic's VSLH application, as a lab scientist you will see the following benefits:

- You simply select the pipetting operations you want rather than wrestle with writing scripts
- You can order assay plates and tubes knowing that the inventory amounts are automatically tracked and updated for you
- You can't make mistakes in setting up the liquid handler transfers, such as when calculating logarithmic dilution factors, as it is all managed by Mosaic
- You don't need to manage data files or perform data transfers, which eliminates a common source of errors
- If there is an error or blockage during the liquid handler run, you can intervene to solve the problem, and then a new script is automatically written to carry on processing from where the error occurred

The powerful Mosaic workflow management system also allows your liquid handler to be used in a multi-stage workflow. This includes sample processing involving other instrumentation such as automated stores, weighing stations and plate stackers. Used this way, Mosaic sample management software brings the benefits of end-to-end sample tracking and inventory management to your liquid handler.

SUPPORTED OPERATIONS

Integrating your automated liquid handler using Mosaic's VSLH application ensures that you are guided through each step of the following process:

- Setting up a run on the liquid handler. This guidance is provided by the Mosaic order, which specifies
 - Workflow segments (these include: cherry picking, dilution, solubilization, serialization, reagent addition and solvent transfers)
 - Labware and tip placement and tracking
 - Reagent sources



- Standard and control positions and required volumes
- Support for block replication operations with 96 and 384 tip heads
- Mosaic's VSLH application validates the run and writes the liquid handling instrument control scripts based on the user's requirements. No additional programming is needed
- Mosaic's VSLH application performs inventory and workflow updates in real-time
- Mosaic's VSLH application manages error handling
 - You can intervene to handle machine failures, and the inventory is only updated when transfers are completed
 - A new script will be written to complete the work from where the interruption occurred
- Mosaic's VSLH application can integrate subsystems
 - Several peripherals can also be integrated with your liquid handler and controlled through scripting to provide further automation

EXAMPLE OF INTEGRATED WORKING:

Preparation of a Serialised 384 Well Plate with DMSO Controls and Standards

For example, a scientist may place a Mosaic order for assay plates where the workflow contains:

- A cherry pick process from a tube to a plate
- Addition of standard substances
- Dispensing of DMSO control wells

The last step of the run is to serialise the substances and standards.

To produce the scientist's assay plates using the Mosaic VSLH application, the liquid handler operator selects the appropriate order (which includes the necessary scripts for liquid handler).



Choose Orders

Please select orders to process.



Order ID	Required By	Comment	Items	Template
<input checked="" type="checkbox"/> 39	17/10/2017	transfer to plate...	2	from Tube to plate and serialise with controls
<input type="checkbox"/> 25	28/04/2017		1	End to End Process
<input type="checkbox"/> 8	07/04/2017		1	Mosquito Serialise
<input type="checkbox"/> 9	07/04/2017		4	ECHO End to End Test
<input type="checkbox"/> 10	07/04/2017		4	[ST-SP D/B] From Solutions in Tubes transfe...

View all orders
 View selected orders
 View orders for barcode...

Find orders

Orders selected: 1

Clear selection

Key

- Input
- Output
- Finished
- Liquid
- Unused
- Error
- Vacant
- Selected

System

Flush Machine Unload Ad hoc mode Next >

WORKFLOW SEGMENTS

The operator chooses which workflow process is to be run. In this case, the Cherry Pick operation is needed before the Serialisation (IC50) run.

Choose Run Parameters

Please select the process you wish to employ.



Process:

- Cherry Pick
- IC50



LABWARE, TIPS, REAGENTS AND VOLUMES

To carry out the order, the liquid handler must be prepared with labware in the correct positions, the input rack with the sample tubes ready, a destination plate and solvent loaded to the working bed.

Mosaic's VSLH application instructs the operator which positions on the bed to load labware, samples and solvent. The solvent volume is automatically calculated based on the consumption for the selected process. When the operator presses "Start Run" the cherry picking process will be carried out by the liquid handler.

Load Solvents, Standards and Controls

Please load the following:

Solution	Stream	Loaded	Required
✓ 100% DMSO	Solvent	Yes	48µL

Load Trough Load Untracked Tubes Unload Untracked Tubes

SWP 384 HR Tube (2.5 mL)

Key

- Input
- Output
- Finished
- Liquid
- Unused
- Error
- Vacant
- Selected

System: 39 (Cherry Pick)

Flush Machine Unload Load Refresh < Back Start Run >>

However, the assay plate is not ready yet: dilution, serialisation and adding the standard compounds still needs to be done. Mosaic's VSLH application flags this to the operator who selects which process should be fulfilled next.



For each of these processes, Mosaic guides the user where to load the liquid handler with solvent, necessary standard compounds for dilution and calculates the volumes needed automatically.

STANDARDS AND CONTROL POSITIONS

When a scientist places the assay order, they can specify standards and control positions for the plates to be created. Mosaic's VSLH application passes these through to the liquid handler so that the operator is instructed to load the standards and controls onto the workbed for pipetting, the volumes are calculated automatically, and the liquid handler transfers them to the correct wells. As the liquid handling operations are carried out, the plate map is updated in real time.

The screenshot displays the Mosaic VSLH application interface. At the top, a navigation bar includes icons for SampleBank, Ordering, Inventory, Stores, Query, Fulfillment, Shipping, and Admin. Below this, the main header reads "Plate TestP_3001".

The interface is divided into several sections:

- CONTENT MAP:** A 96-well plate grid (rows A-H, columns 1-12) with blue circles representing wells. Well A9 is highlighted in a darker blue.
- A09 SAMPLE:** A table of sample details:

Position:	A09
Substance Type:	Small Molecule
CompoundBatch:	TST00000001-001
Name:	
Sample Amount:	100 µL
Available Amount:	100 µL
Concentration:	0.00316 mM
Solvent:	100.0 % DMSO
Total Thaw Count:	0
Filled Date:	28/04/2020 17:13:33

An "Edit Sample" button is located below the table.
- CONTENT LIST:** A dropdown menu currently set to "Expand to view".
- PLATE DETAILS:** A table of plate information:

Barcode:	TestP_3001
Type:	SWP 96
Creation Date:	28-Apr-2020 17:13:30
Thaw Count:	0
Comment:	
- LOCATION:** A table showing the location path:

Location Path:	\\Home
----------------	--------
- SET DETAILS:** A table showing folder and name information:

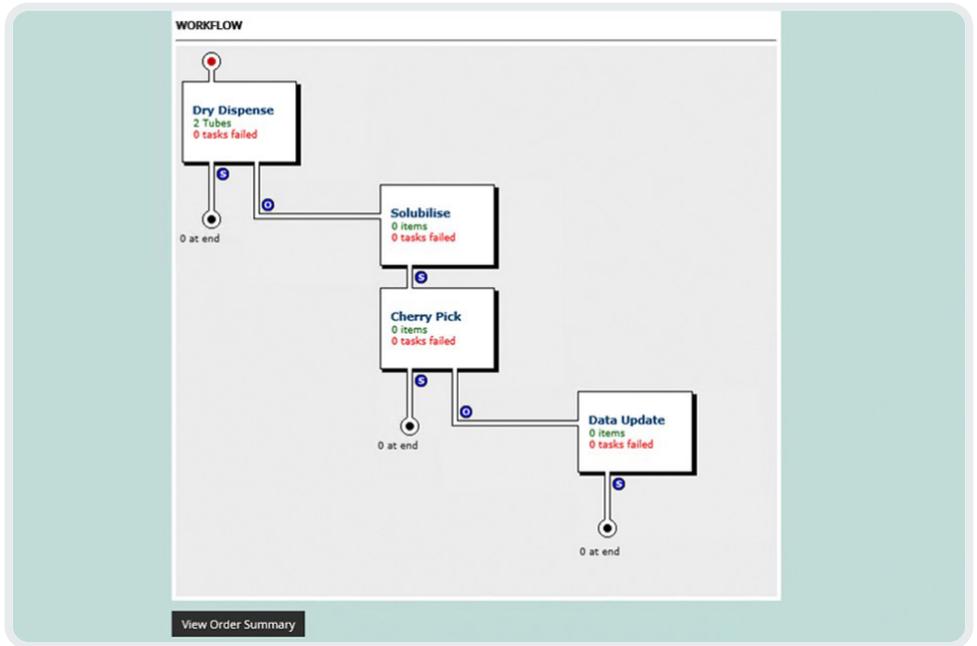
Folder:	\\Sets\Non-Orderable
Name:	Non-Orderable Plates

At the bottom, a toolbar contains several action buttons: Edit Plate, View Audit Trail, Solubilise, Dry Down, Add to Pick List, Pick, Add to Place List, Create Child Plates, and Dispose.



INVENTORY AND WORKFLOW UPDATES

Mosaic's workflows are updated in real time, showing the operator what the next steps in the sequence are and what tasks can be carried out next.



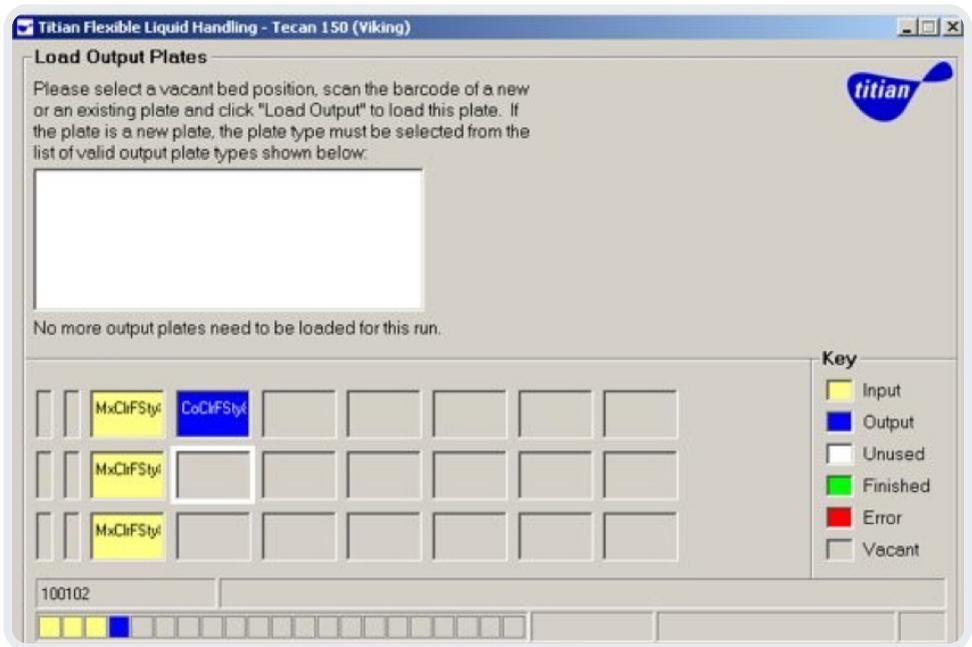
Mosaic's VSLH application offers additional advantages for managing liquid handling workflows. For instance, if one tube is currently in use elsewhere, the operator can choose to dispense, solubilize and cherry pick the rest of the order, and then do the missing tube when it becomes available.

This flexibility becomes particularly useful for larger HTS-type runs where an order of 5000 plates can't be fitted on one liquid handler. Alternatively, the assay may only have a daily capacity of 50 plates so Mosaic's workflow management allows a large order to be split into multiple runs.



ERROR HANDLING

Mosaic's VSLH application maintains details of work in progress during a liquid handling run. If the run is interrupted by power failure or a tip crash, for instance, the operator is asked to check and confirm any suspect transfers at the time of the interruption. Mosaic has logged the work done so far and automatically writes a new script to complete the order. The inventory is only updated when transfers are completed.



This ensures there is no need to abandon processing done so far and start again.



INTEGRATING SUBSYSTEMS

Mosaic's VSLH application software can also help to smoothly integrate a range of subsystems with your automated liquid handler in order to automate tedious aspects of assay plate preparation or provide unattended operation. Subsystems include carousels, heaters, centrifuges, cappers, decappers, sealers and de-sealers. For example, integrating a carousel and capper/decapper to your liquid handler could enable overnight runs so that requested assay plates are ready to run next day.



SUMMARY

Using Mosaic sample management software with its VSLH application to integrate your automated liquid handlers provides a range of benefits in addition to fast and accurate dispensing. These include error-free pipetting, work list creation, advanced tip usage/ tracking, volume tracking and automated data processing, resulting in auditable inventory updates. Workflow management, error handling and subsystem integration also provide efficient processing and promote unattended operation.

For scientists, using Mosaic's VSLH application means they don't have to understand how to program each liquid handler, they just specify the transfers in Mosaic and the rest is handled by Mosaic.

Mosaic's VLSH application helps liquid handler operators to:

- Provide on time delivery of requested substances, with the outputs defined, in the order that the scientists are looking for
- Maintain a highly accurate inventory by capturing volume transfer information on-the-fly without any user interaction. Data updates are carried out live, which removes any delays in downstream processing or analysis. This supersedes error-prone manual tracking of volumes and concentrations
- Track every sample preparation step via Mosaic's comprehensive audit trail, to capture data for quality security processes

An additional benefit is that Titian works in partnership with automated liquid handler vendors to continually evolve the VSLH application, so it is responsive to customer requirements and the development of new liquid handler types and software.



ABOUT TITIAN SOFTWARE

Titian Software is the industry leader in providing sample management software for the life sciences. Using Mosaic software, our customers see significant benefits in terms of their throughput, response times, error rates, labor costs as well as in sample conservation. Titian have done this by producing an application that can process multiple requests with varying sources, and labware output formats. It can easily be run by any operators, instead of tying up an automation expert to write new protocols. We also use our extensive experience in interfacing laboratory instrumentation and robotic systems with our software to ensure that customers make best use of their investment in research and development technologies.

At Titian, our development efforts never stop as we continue to advance Mosaic toward higher levels of efficiency and practicality for the user. The ongoing collaborative relationship between Titian and liquid handling hardware suppliers continues to ensure that new applications are made available on a timely basis to fulfill our customer's research goals. We pride ourselves on taking into account customer feedback for all of our Mosaic applications to drive our product to be the best it can be. It's all part of Titian's commitment to providing innovative solutions that make life easier for sample management professionals.

AUTHOR

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Steffen Koehler ran the compound management department at Evotec for 10 years before spending 4 years focusing on HTS, screening and automation as Director Industrial Applications at Direvo Industrial Biotechnology. He joined Titian Software in 2013 as a business application consultant.

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