

The Titian logo consists of the word "titian" in a lowercase, sans-serif font, enclosed within a white, teardrop-shaped graphic element that tapers to the right.

titian

The word "Access" is written in a bold, black, sans-serif font, positioned above the Labcyte logo.

Access

The Labcyte logo features the word "LABCYTE" in a bold, black, sans-serif font, followed by a circular icon containing a stylized, curved shape.

LABCYTE

{ APPLICATION NOTE }

# TFM: A New Approach for Integrating Mosaic with Labcyte Automation Platforms

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Mosaic Sample Management is Titian Software's comprehensive, customisable, modular software product to control and monitor all aspects of sample storage, preparation and delivery. From small biotech to global pharma, Mosaic helps to provide a seamless, error-free sample supply chain and audit trail.

Mosaic Sample Management is a tailored solution for all sample management requirements, configured through expert consulting services.

Mosaic SampleBank and Mosaic FreezerManagement are Mosaic packages, optimised and pre-configured for rapid deployment:

- FreezerManagement keeps track of samples in freezers and provides a comprehensive audit trail as samples are accessed and aliquoted.
- SampleBank provides full inventory tracking capabilities coupled with sample ordering and workflow management in a simple package. It offers seamless start-up and ongoing performance for busy sample managers.

Mosaic's modular approach means that it is simple to upgrade or extend the software's functionality whenever it is needed.

# Introduction



Acoustic transfer instrumentation has been at the forefront of liquid handling technology for the life sciences since 2004. The ability to reliably transfer nanolitre quantities of DMSO and aqueous solutions has enabled the scientific community to perform research on a scale not previously achievable at a practical level. This unique technology has been successfully developed by Labcyte Inc to apply to a wide variety of scientific uses – from drug discovery to cancer research to genomics – and continues to expand as innovative techniques are developed in the industry.

These advantages can come with drawbacks; such as how to manage bringing the new instruments and the new information flows into your existing sample management system. Titian Software brings its extensive experience of integrating laboratory instrumentation and robotics into Mosaic sample management software to ensure that it is easy for customers to make best use of their investment in research and development technologies.



For many years, Labcyte and Titian have enjoyed a collaborative partnership which provides robust solutions when integrating Labcyte's Echo instrumentation with Titian's Mosaic software. Here, we describe the latest development in our goal to provide seamless integration solutions for sample management professionals: the Mosaic Tempo Fulfilment Module or TFM.

## The Labcyte Echo<sup>®</sup> Liquid Handler

At the centre of every Labcyte system is their flagship product, the Echo liquid handler. This has transformed research by using sound energy to provide highly accurate, fully automated, non-contact dispensing of fluids. The Echo can transfer very low volumes of a variety of solutions from any acoustic compatible microplate well or AcoustiX tube, to any destination well. This greatly facilitates sample management processes. The Echo's flexible sample transfer capabilities range from simple reformatting operations, through creating dose-response curves for potency determination, to assembling complex assays – all while minimising reagent costs and sample waste.

The advantages of Echo's acoustic approach include:

- Non-contact, contamination free liquid transfers
- Fast, accurate and precise liquid transfers on a nanolitre scale
- Able to transfer a wide variety of solutions (e.g. DMSO, aqueous buffers, etc.)
- Preserves sample integrity and viability during transfer
- No pipette tip requirements
  - Reduces operating costs and waste
  - Eliminates time and effort associated with tip changing
  - Saves robotic work cell space (no tip box storage needed)
- Sample sources can be acoustic friendly microplates or tubes

When using your Echo at the heart of an Access™ robotic solution:

- All plate handling operations are automatically done for you. Labcyte's Tempo™ software coordinates bulk diluent additions, plate sealing, labelling and storage
- Operators are freed up to "walk away" and perform other essential tasks while the automated system creates your plates to your specification

# Considerations When Integrating New Equipment into Sample Management

Sample management professionals face a number of challenges in the performance of their jobs. Bringing in new instrumentation can give them the physical tools that they need, but can also present issues with handling the new data streams that the new instruments provide.

Some of these issues are:

- How to incorporate the new technology into your sample management workflows
- Managing and processing multiple output files of various types
- The consumption of the information contained in these files
- Relying on MS Excel workbooks and macros to track samples and create reports
- Keeping up to date internally developed, custom solutions that can become inefficient as laboratory workflows change and instrumentation is improved
- Establishing IT support of bespoke systems (often a challenge for smaller research lab applications)
- Assuming that all sample preparation workflow steps are carried out as prescribed, without the ability to audit and investigate data anomalies
- Ensuring data integrity while managing multiple workflows involving multiple systems with confidence

To address these issues, sample management professionals need a proven partner for sample management who can provide a robust system to meet their sample preparation needs.

## Combining the Improved Power of Mosaic's TFM with your Labcyte Automation System

Titian's Mosaic software is the perfect solution for managing and tracking both large, complex and/or high throughput sample orders as well as smaller, more varied workflows. When a Labcyte Access automation workcell has its software directly integrated with Mosaic through Mosaic's TFM, sample management groups can fulfil workflow steps best suited to the acoustic platform in a user-friendly and intuitive manner. The work is presented to you in Mosaic and requires only a handful of operator steps to carry out. This, followed by Mosaic's automated results processing, will complete the sample management workflow, accurately update your inventory and maintain traceability in a comprehensive audit trail.

The key benefits of the TFM integration are:

- Dynamic creation of Tempo and Echo files based on the Mosaic workflow, resulting in fewer mouse clicks to start a run
- Users select sources for fulfilment in one simple step, as TFM reads the Tempo inventory to know what resources are directly available on the Access workcell
- Multiple similar orders can be bundled into the same Tempo run
- Results are processed automatically, which means no manual file editing or copying steps
- The Echo Dose-Response protocol is now guaranteed to match the Mosaic Order which avoids the possibility of human error
- The exact volume transfers reported by the Echo are captured in the Mosaic inventory and in the audit trail
- The creation of intermediate plates in EDR protocols is minimised. TFM allows transfers from source plates where the same sources are present at multiple concentrations. This thereby conserves samples, reduces fulfilment times and increases the accuracy of concentration curves.
- All intermediate plates used by the Echo platform are tracked in Mosaic inventory and in the audit trail

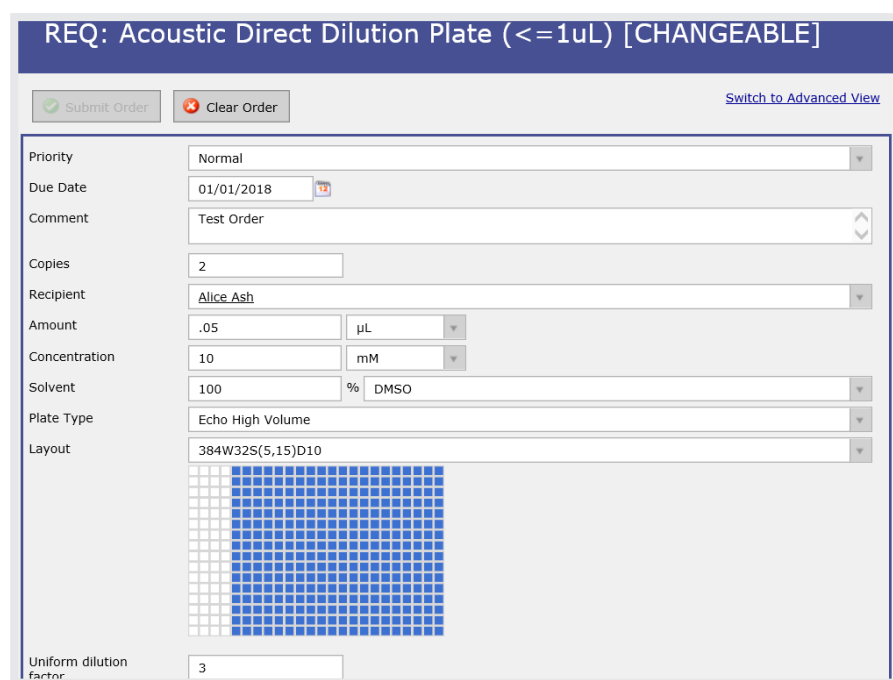
- Survey volumes of source plate wells are used to update the Mosaic inventory
- Any Echo transfer failures are tracked and visibly highlighted in Mosaic inventory
  - Email reports are generated of any transfer errors during the automatic results file import
- Transfers of controls and standards, if present, are reported and used to update the Mosaic inventory
- To identify your plates, TFM can drive the plate labeller within the Access workcell as part of a Tempo run
- TFM also supports the following Labcyte Software applications: Echo Cherry Pick (ECP), Echo Reformat (EPR), Echo Dose-Response (EDR), Echo Plate Audit (EPA), and Echo Combination Screen (ECS)

## Example: Using TFM to Fulfil Mosaic Reformat Series Nanolitre Orders on Your Labcyte System

### Create your Mosaic Order

First, create your acoustic transfer order using the Mosaic interface

- Populate your request to match your desired output
- Once your Order is submitted, these values are fed to the Labcyte Tempo software to automatically insert parameters



REQ: Acoustic Direct Dilution Plate (<=1uL) [CHANGEABLE]

Submit Order Clear Order [Switch to Advanced View](#)

Priority: Normal

Due Date: 01/01/2018

Comment: Test Order

Copies: 2

Recipient: Alice Ash

Amount: .05  $\mu$ L

Concentration: 10 mM

Solvent: 100% DMSO

Plate Type: Echo High Volume

Layout: 384W32S(5,15)D10

Uniform dilution factor: 3

Detailed preferences for how you use your Access system can be stored in Mosaic Stream templates, which are provided to Tempo every time you perform a fulfilment. These include specifics such as: preferred Tempo batch size, concentration tolerances for points in dose-response curves, maximum number of intermediate templates allowed, etc.

## Process your Order Using TFM

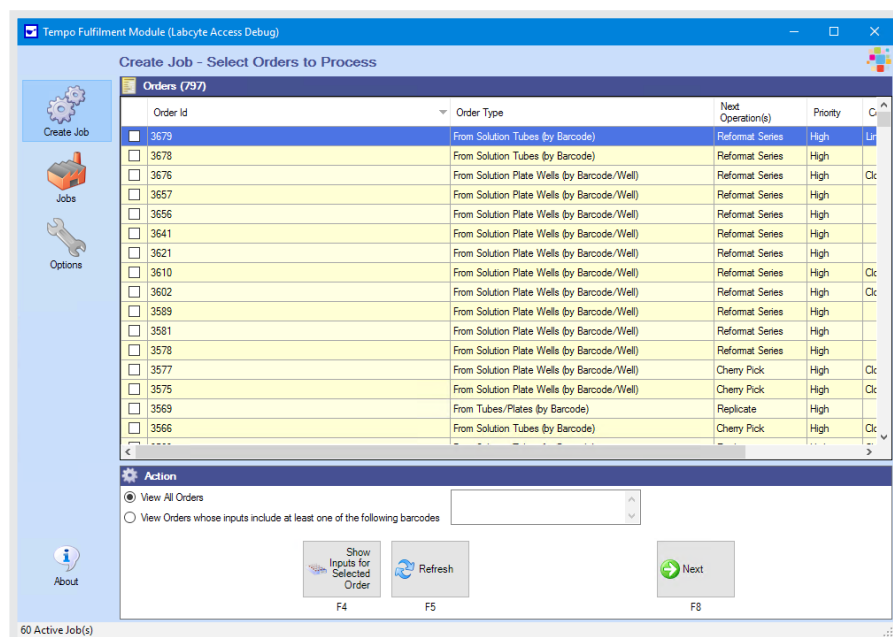
Once your Mosaic Order is accepted, go directly to the TFM to start the Tempo run

- No need to go through workflow processing and off-line runs, so fewer mouse clicks are needed
- TFM uses the newly available Labcyte APIs to create specific Tempo protocols from a list of pre-defined run definition templates. The same templates can be used for workflows with varying:
  - Target volumes / concentration
  - Dilution series (uniform or not)
  - Destination labware type
  - Curve accuracy requirements
  - Output copies

## Select Orders

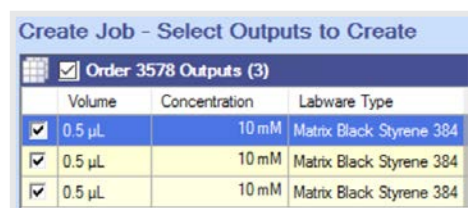
Mosaic orders that can be fulfilled on the Labcyte automated platform will be shown in the TFM user interface.

- Users can select a single order, or multiple orders that are similar
  - When multiple like orders are selected, TFM will fulfil these in a single Tempo run. This saves the operator queuing each job individually, as well as providing walk away time for scientists to perform other tasks while the automation is processing.



## Select Outputs

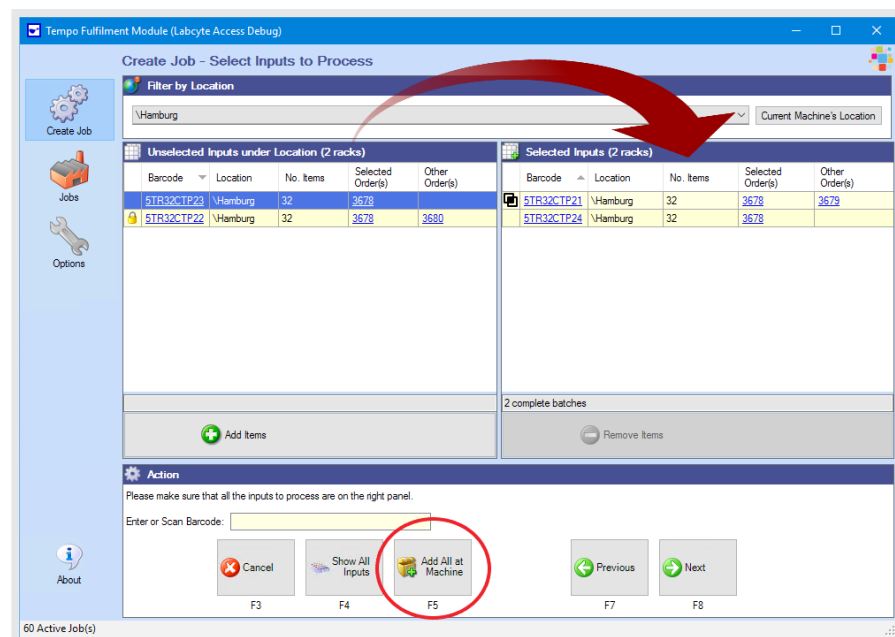
Once the work is selected, the necessary output plates for the orders will be displayed.



## Select Inputs

Select input plates capable for fulfilling the order.

- The “Add All at Machine” feature
  - TFM reads Tempo inventory reports to see which labware is already loaded on the workcell. A single button press adds these items to the job being created. This allows operators to streamline their run creation by pre-loading the system with the plate sets they know will be used for testing (e.g. library sets, activity confirmation sets, etc.).
- Plates are filtered according to their location, allowing you to hide items not available in your lab (or on your Labcyte system)
- Icons tell the user if plates are locked by other processes or are part of additional Mosaic orders
  - Labware locked
  - Labware used in multiple Orders



## Add Assay Controls and Standards

Controls and standards are easy to add to the Tempo run

- You can manually scan the barcodes of the desired samples or automatically add those already present in storage on your Labcyte workcell
- Single point controls will be transferred to your plates via a secondary ECP protocol within your Tempo run
- Solvent controls can also be added via the bulk reagent dispenser, if desired
- Reference standards requiring the same dose-response curve parameters as test samples are added within the main EDR protocol and can share any required intermediate plates
- The user interface will summarise the total wells and volume of each control per plate

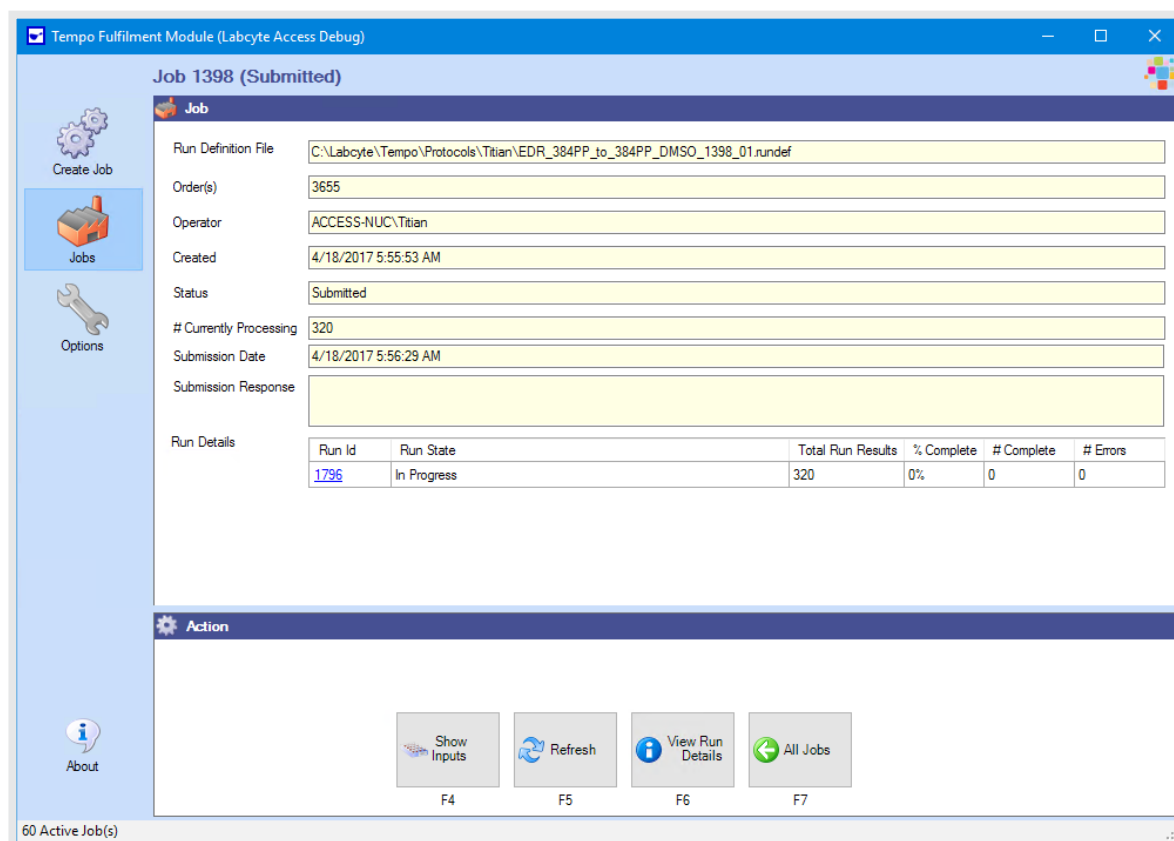
Control: Set4-Plate49-Well4 @ 5 mM, 100% DMSO					
Substance	Set4-Plate49-Well4	Barcode	Location	Samples	Amount (µL)
Concentration	5 mM	<input checked="" type="checkbox"/> NHP-0425-02	\\London	1	99.0
Solvent	100% DMSO	<input type="checkbox"/> NHP-0427-01	\\London	1	197.0
Required Volume	0.5 µL				

Standard: Set4-Plate49-Well4 @ 10 mM, 100% DMSO					
Substance	Set4-Plate49-Well4	Barcode	Location	Samples	Amount (µL)
Concentration	10 mM	<input type="checkbox"/> NHP-0425-01	\\London	8	100.0
Solvent	100% DMSO	<input checked="" type="checkbox"/> NHP-0425-02	\\London	11	99.0
Required Volume	0.5 µL	<input type="checkbox"/> NHP-0425-03	\\London	12	99.0
		<input type="checkbox"/> NHP-0425-04	\\London	12	99.0
		<input type="checkbox"/> NHP-0427-01	\\London	23	97.0

## Create Job

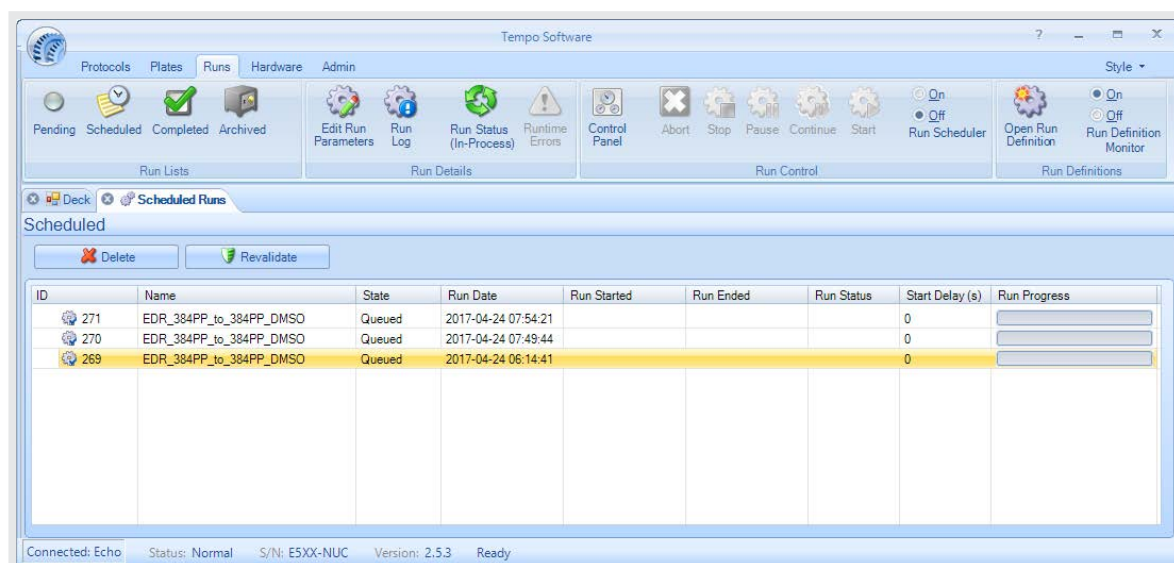
The last step in the TFM process is the final confirmation of your inputs and creation of the Mosaic job. The files are then written out to the Tempo Inbox for automatic queuing of the Tempo runs.



## Fulfil Your Work on Your Labcyte System

Once ported to Tempo, Mosaic jobs are queued and automatically fulfilled as soon as the system is available

- No further user input is required
- TFM is able to make use of sources of different concentrations in EDR protocols (i.e. plates containing a sample solution at 10mM, 1mM and 0.1mM) such that the creation of intermediate plates is minimised
- TFM also now drives microplate labelling within Tempo to clearly identify your plates



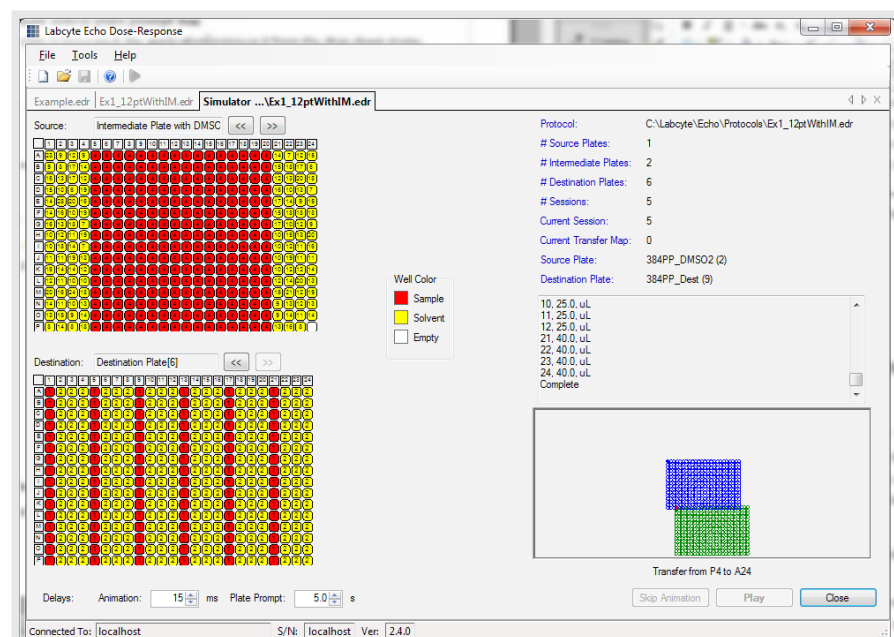
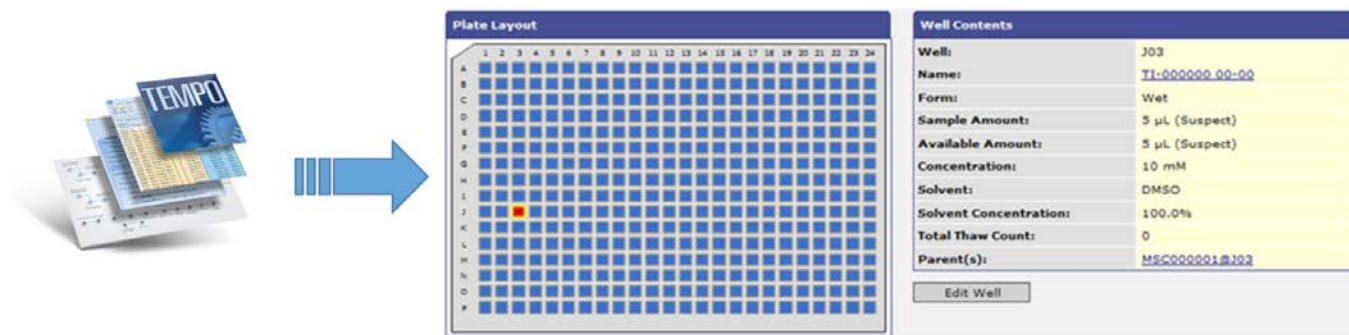


## Data Processing



When acoustic transfer operations for a plate are completed, the plate data is updated immediately in Mosaic

- You don't have to wait for the end of a Tempo run to look at your plate data
- Mosaic registers and tracks the inventory of any intermediate plates involved in serialisation protocols
- Mosaic captures material transfers exactly as they are physically performed, reflecting the discrete 2.5nL volumes that the Echo instruments can transfer. This results in an accurate plate inventory, both in terms of volumes and concentrations, as well as provision of a precise audit trail.
- Any Echo transfer errors, from air bubbles or other causes, are highlighted in the inventory and only affect the explicit well(s) and any subsequent doses dependent on them



## Combination Screening

For complex sample transfer protocols, such as those used in combination screening (using the ECS), TFM generates the source picklists so ECS can determine how the order line items will be layered on top of one another using a pre-configured ECS protocol. The results of the ECS run are automatically imported into Mosaic to update the inventory.

# Summary

The use of the Mosaic sample management software and its Tempo Fulfilment Module, along with Labcyte's acoustic transfer automated platforms, allow for full integration of the sample preparation workflow with Labcyte's suite of Echo applications software. Mosaic's tight coupling with these systems through APIs and automated processing of the result files means that users are able to:

- Easily and seamlessly add Labcyte technologies to Mosaic sample management workflows
- Define and obtain the outputs they are looking for
- Easily setup Tempo runs through Mosaic, with no manual file handling
- Bundle multiple similar orders into one Tempo run
- Create and use intermediate plates as an integral part of the Tempo process, without any need for external calculations to find the best transfer volumes and intermediate concentrations
- Maintain a highly accurate inventory by capturing the precise volume transfer and plate survey data provided by the Echo
- Provide a comprehensive audit trail that tracks every sample preparation step; including intermediate plates and standards and controls
- Capture liquid handling error information



## About Mosaic

Mosaic sample management is Titian Software's comprehensive, customisable, modular software product to control and monitor all aspects of sample storage, preparation and delivery. From small biotech to global pharma, Mosaic helps to provide a seamless, error-free sample supply chain and audit trail. Mosaic sample management is a tailored solution for all sample management requirements, configured through expert consulting services.

Mosaic's modular approach means that it is simple to upgrade or extend the software's functionality whenever it is needed.

# Titian Software and Collaborations



Titian is the industry leader in providing sample management software for the Life Sciences. Using our Mosaic software, our customers see significant benefits in terms of throughput, response times, error rate reduction, sample conservation and cost savings due to markedly reducing the labour associated with managing sample collections. Titian Software's development efforts never stop as we continue to advance Mosaic toward higher levels of efficiency and practicality for the user.

The collaborative relationship between Titian and Labcyte continues to ensure that new applications are made available on a timely basis, and we pride ourselves on taking into account customer feedback for all Mosaic modules to drive our product to be the best it can be. It's all part of Titian's commitment to providing innovative solutions to make life easier for sample management professionals.

## About the authors

### Arthur Yarwood

Fascinated by mathematics and programming, Arthur spent 11 years at Sony, specialising in tools programming, asset management and databases. He joined Titian in 2012 and is now a team leader and project manager on Mosaic.

### Mark Doring

Mark Doring worked for Schering Plough for 25 years as a biochemist in new lead discovery, focusing on high throughput screening assay performance, development and compound preparation with an emphasis on automation and informatics. He joined Titian Software in 2015 as a business application consultant.

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