Poster Reprint

ASMS 2022
Poster number MP329

High fidelity legacy-to-modern method transfer on the 6475 triple quadrupole LC/MS platform for large output production labs

Lauren Seymour, Zirui Kuan, Cathy Henderson, Erik Lopez,
Linfeng Wu, Patrick M. Batoon

Agilent Technologies, Santa Clara, CA

Introduction

Large output production labs often resist changes in physical hardware or software revision despite improved performance or enhanced features due to the time consuming nature of re-verification, re-validation, or reconstruction of the analytical method. Often, the method needs to be "rebuilt", using the former method as a template – possibly leading to transcription errors or unexpected performance differences.

The new **6475 triple quadrupole LC/MS system with MassHunter 12 utilizes a unique metadata framework that assists in the direct transfer, import, and resolution of previously created methods.** Methods are meant to be directly opened in the acquisition system, such that production labs with a large library of in-use methods require minimum effort for transfer into the new platform.

Here we present a demonstration and metadata framework to handle the direct method transfer from a "legacy" triple quadrupole LC/MS instrument to a novel triple quadrupole LC/MS hardware and software platform with minimal adjustments and similar performance for accelerated incorporation into the production environment.

Experimental

Representative dMRM methods used for routine analysis in a production lab was developed and validated using a ("legacy") 6470 triple quadrupole LC/MS system containing optimal MRM transitions, collision energies, fragmentor voltages, and ion source parameters. The method was loaded onto a 6475 triple quadrupole LC/MS system with MassHunter 12 acquisition, with no input of chemical data.

Metadata in the unique XML structure was systematically parsed to ensure fidelity and transfer. Lastly, verification of analytes were compared between the existing and novel triple quadrupole LC/MS systems to ensure MRM targets are properly observed and parameters require minimal fine tuning.

If the signal was not within the expected range, automated collision energy and fragmentor optimization was carried out to ensure that signals were recovered.

Experimental

The 6475 triple quadrupole LC/MS system and MassHunter 12 data system

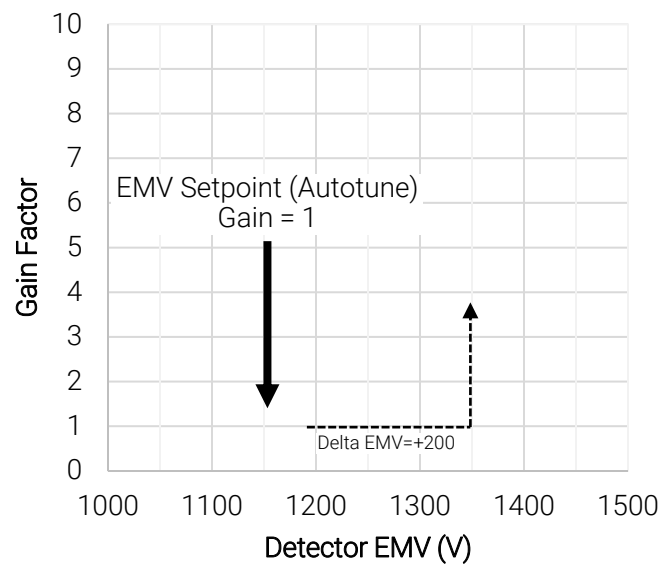
DeltaEMV to Gain Factor Translation

A notable difference between legacy systems is the transition from a commonly applied "DeltaEMV" parameter to "Gain Factor" found on the 6475 LC/TQ using MassHunter 12.

- DeltaEMV – provides a linear voltage increase to the optimally defined EMV voltage. As the detector ages, additional voltage has diminishing effect.
  - Ex. DeltaEMV=+200V results in 5x signal boost on a new detector, but 2x signal boost on an aged detector.

- Gain Factor – provides a signal boost multiplier using a variable increase in detector voltage, regardless of detector age.
  - Ex. Gain Factor=2 results in a 2x signal boost throughout the detector's lifetime.

To assist in the transition from DeltaEMV to Gain Factor, **a Gain Factor vs Detector EMV curve table is included in the Autotune report**. In this example, the former DeltaEMV=+200V parameter is roughly equivalent to Gain Factor=4.



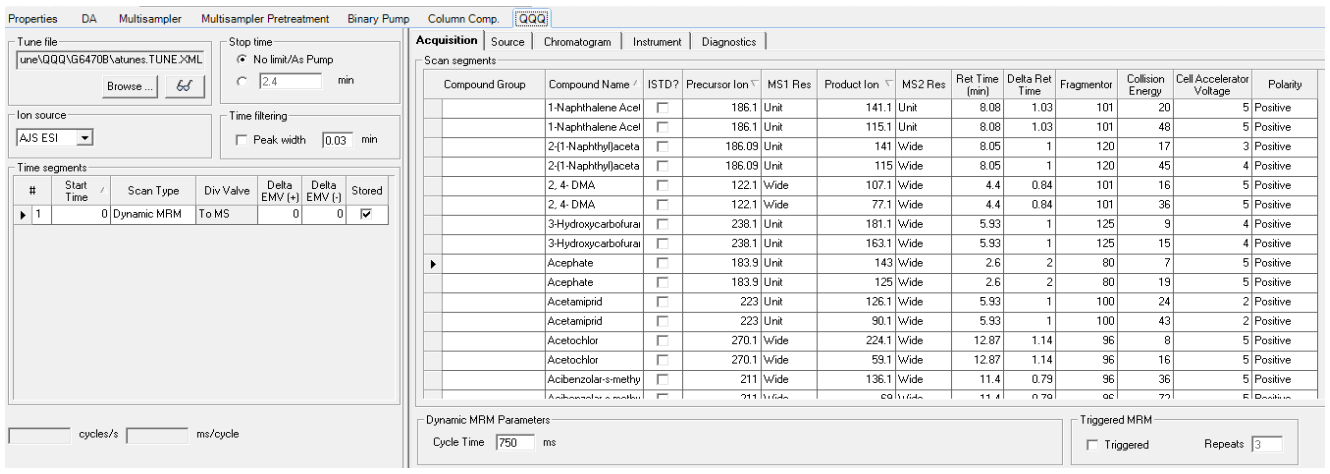
Gain Factor	EMV(V)
1	1157
2	1249
3	1306
4	1346
5	1378
6	1405
7	1428
8	1448
9	1466
10	1482

Direct transfer of a 6470 LC/TQ method on MassHunter 10.1 to a 6475 LC/TQ method on MassHunter 12

Method transfer from a legacy system to the 6475 LC/TQ is done by “opening” an existing method in the MassHunter 12 data system. Through the available metadata, the system understands that the method did not originate from the original model, opening a method resolution window to correct any invalid method parameters. Method resolution displays method inconsistencies on the inconsistency report, red error symbols on the tree item, and the invalid parameters with a red background. After all the invalid parameters are changed (i.e “resolved”), the user is able to accept the changes and complete the migration. The method will be displayed in the MassHunter 12 method UI format.

If new parameters are present from the legacy method in the 6475 LC/TQ with MassHunter 12 interface, the default values of those parameters are added to the method, i.e., gain factor, method override tune parameters, and optimization settings. The user is able to see the new parameters in the method resolution window and method UI.

Method Loaded under MassHunter 10.1



Example XML Metadata Structure per Analyte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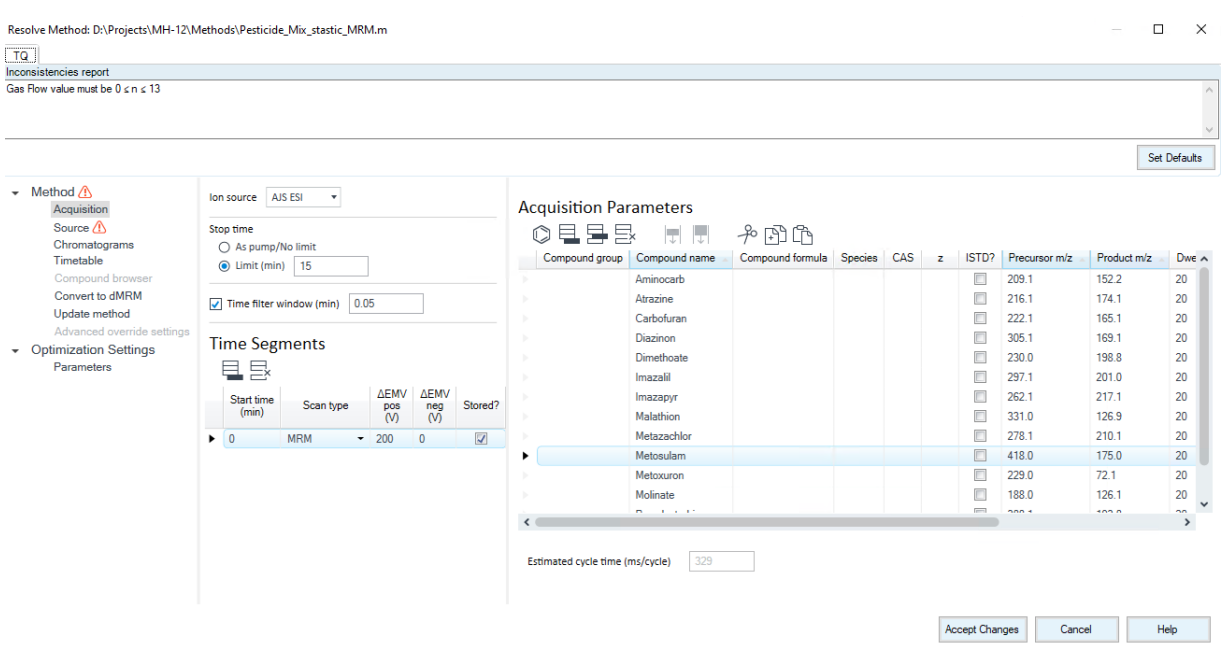
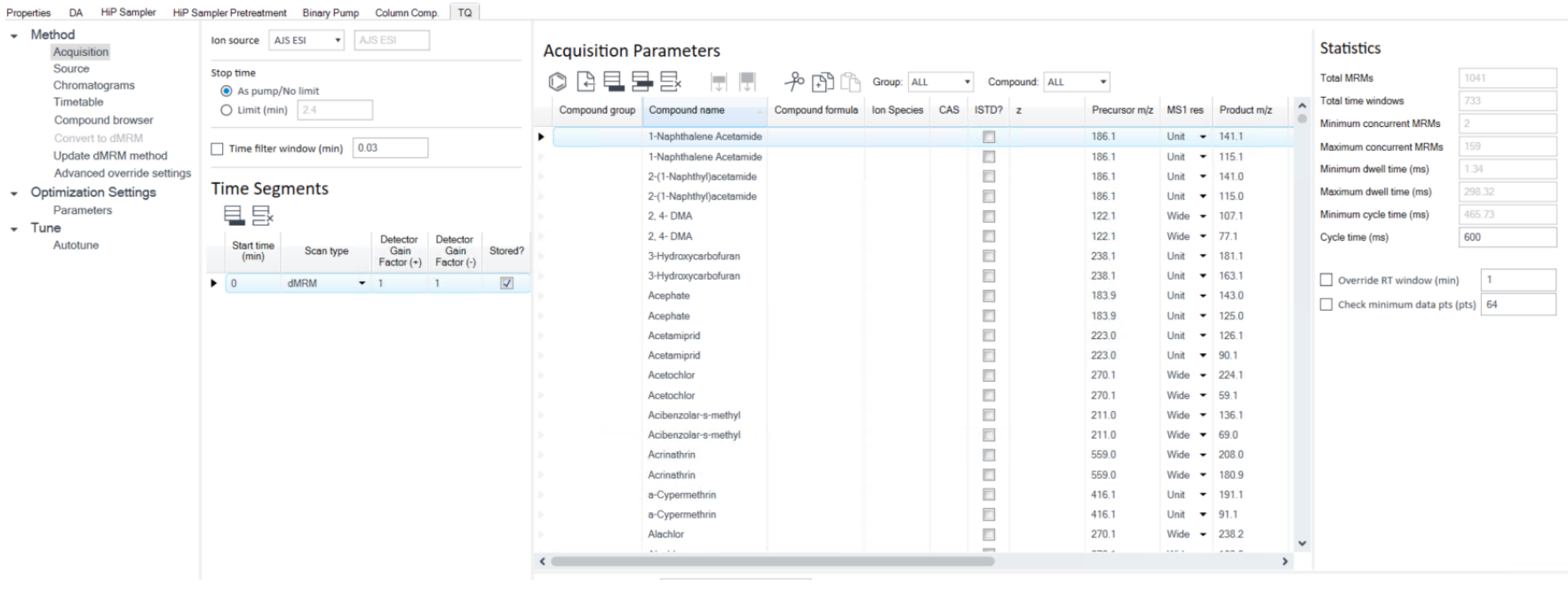
Method Resolution window under MassHunter 12



Fully resolved legacy method loaded under MassHunter 12

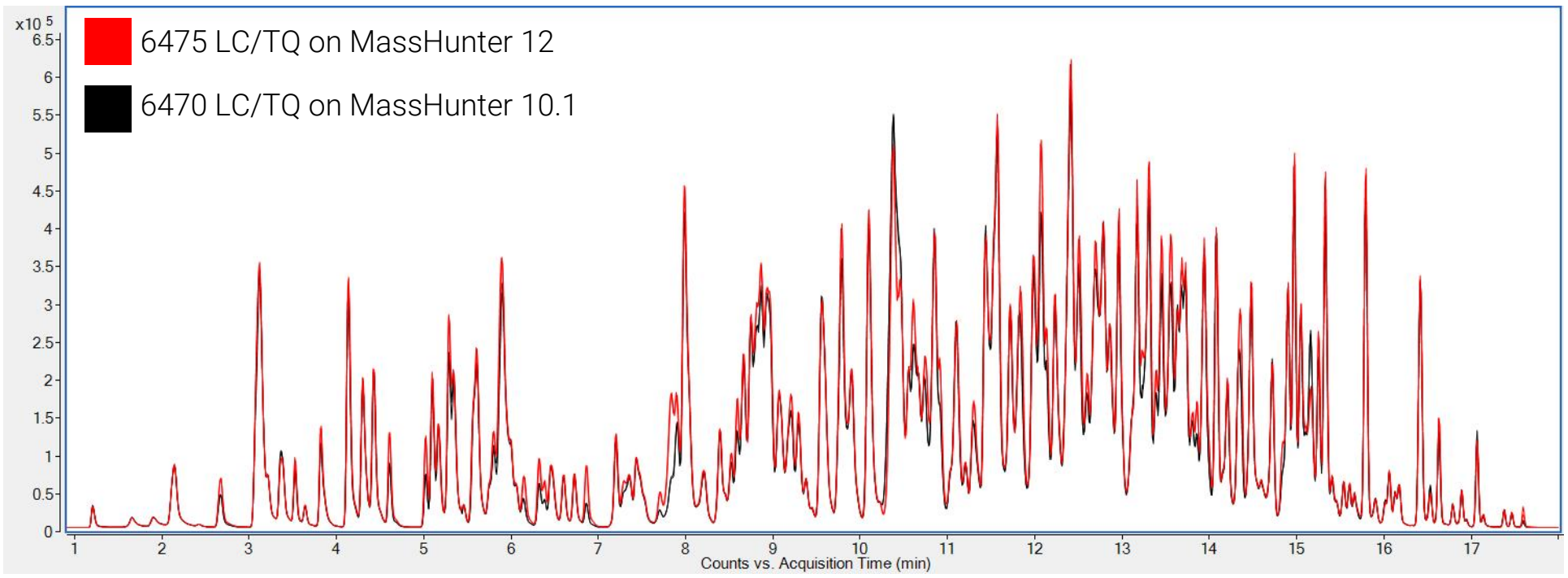


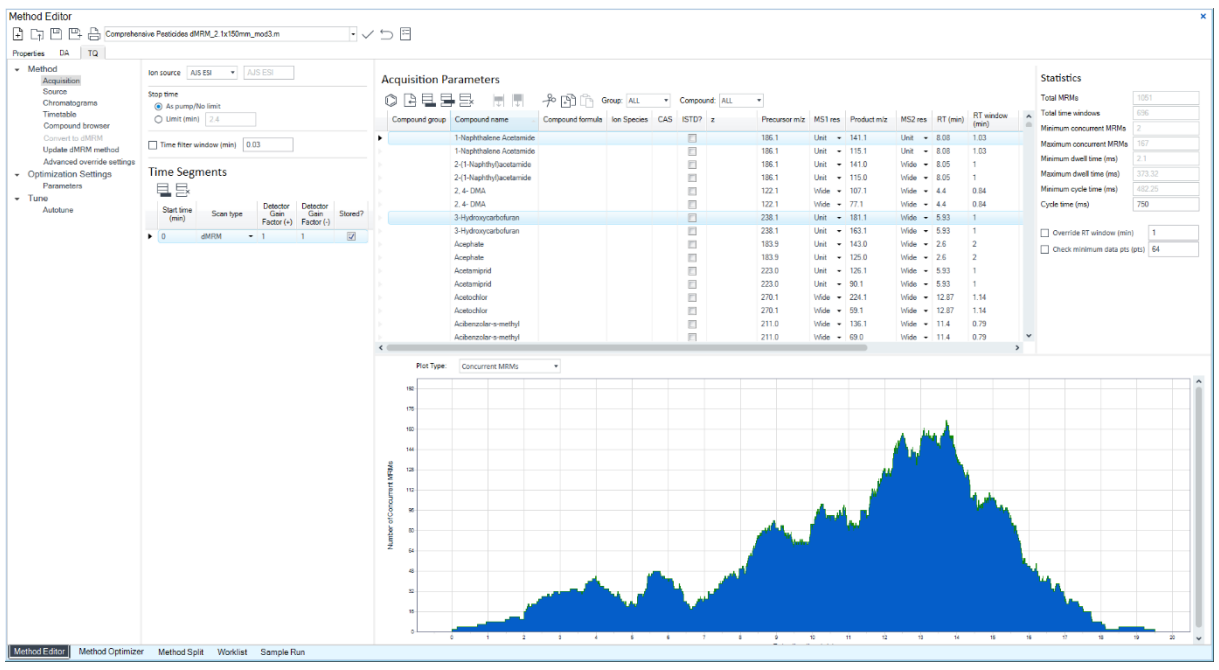
Results and Discussion

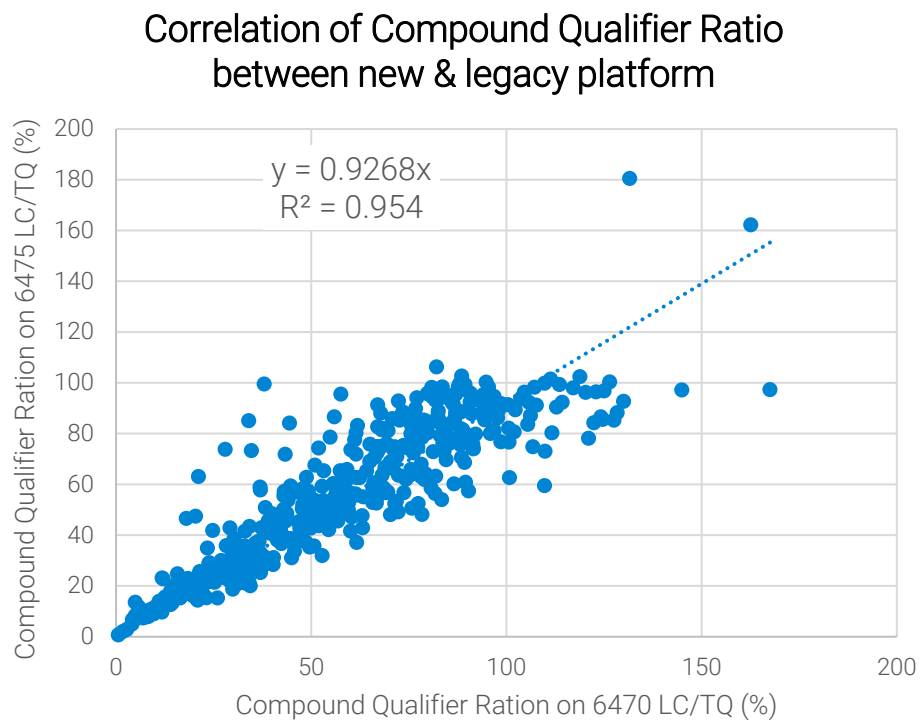
Example using a comprehensive multiresidue pesticide screening method (+1000 MRMs, +500 compounds)

To test the validity of the method transfer, an original production-ready MRM method with Qual/Quant transitions and optimized CE values on a legacy 6470 LC/TQ system with MassHunter 10.1 was directly imported onto the new 6475 LC/TQ system with MassHunter 12. Using the same HPLC and sample vials, fragmentor and CE voltage fine-tuning was carried out to account for instrument-to-instrument variation on each model.

The overlaid chromatograms below show excellent agreement between the two instrument and data systems, with slightly higher abundances on the 6475 LC/TQ. Close examination of the analyte-by-analyte data shows a strong linear correlation between Quant/Qual ratios for each instrument, with some variation due to instrument and model differences.







Conclusions

- Method import and resolution is done in a high-fidelity manner due to the unique metadata structure that is automatically parsed for relevant information
- DeltaEMV can be converted to Gain Factor using the table embedded in the instrument's autotune report. Gain Factor applies a consistent signal boost multiplier for consistent ion abundances as the detector ages
- A +500 analyte pesticide method developed on a legacy system was successfully resolved, imported, and demonstrated to have strong agreement and data correlation when run on the new 6475 LC/TQ with MassHunter 12

https://explore.agilent.com/asms

DE84865786

Published in USA, May 20, 2022

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