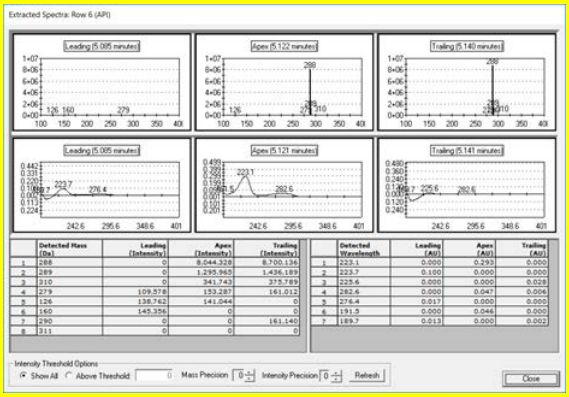
S-Matrix®

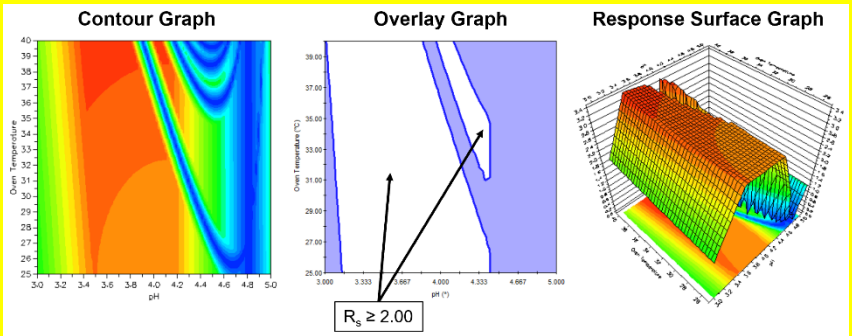
Fusion QbD®

Amazing New Features

PeakTracker™ – Automated UV & MS Based Peak Tracking



Rs-Map Response – Instant R_s Prediction Chromatograms and Graphs for all Compounds



Forced Deg Studies – closed-loop automation support for forced degradation studies

S-Matrix Corporation
www.smatrix.com

Fusion QbD – *PeakTracker*™

S-Matrix has developed a powerful new peak tracking technology which automates, optimizes, and simplifies the use of PDA and MS data in LC and LC/MS method development. ***PeakTracker*** can be used for all Fusion QbD method development experiments run on Waters LC systems controlled by the Empower CDS. ***PeakTracker*** automatically identifies each peak in each experiment chromatogram using 3D PDA spectral data, and also fully utilizing 3D mass spectral data when the LC system is configured with the Acquity QDa Mass Detector (QDa). Complex separation and tracking challenges ***PeakTracker*** can automatically address include:

- Auto-deconvolution of Partially and Completely Co-eluted Peaks.
  When two peaks co-elute, one peak of the co-eluted peak pair will be "hidden" in the UV chromatogram. Standard UV results data such as Retention Time and Resolution will be missing for this peak for all experiment runs in which the peaks co-elute. Using PDA and MS spectral data to automatically locate "hidden" peaks and fill in missing results data can dramatically improve the quality of prediction models.

- Two or More Peaks with Identical Mass Data.
  There are many circumstances in which two peaks will have the same parent mass value, and therefore the same mass-to-charge ratio (m/z). A solution in these cases would be to use a mass spectrometer capable of fully fragmenting all ionizable compounds coupled with a spectral library for identification. However, this capability is unavailable in many labs charged with developing LC methods. Utilizing an economical mass detector, and coupling it with automated diagnostics utilizing UV spectral data and standard peak results data provides a unique solution to this problem.

- Non-absorbing and Non-ionizing Compounds.
  In most cases it is desirable to have an MS- LC method which resolves all sample compounds. This goal is complicated when the sample contains compounds which either do not absorb, as shown in Figure 1 (no UV data), or do not ionize, as shown in Figure 2 (no MS data). These cases require coupling the PDA and MS spectral data into the automated peak tracking protocol. This enables creating a merged chromatogram which contains all of the peaks and the associated results data needed for data modeling.

Figure 1 – Non-absorbing Peak

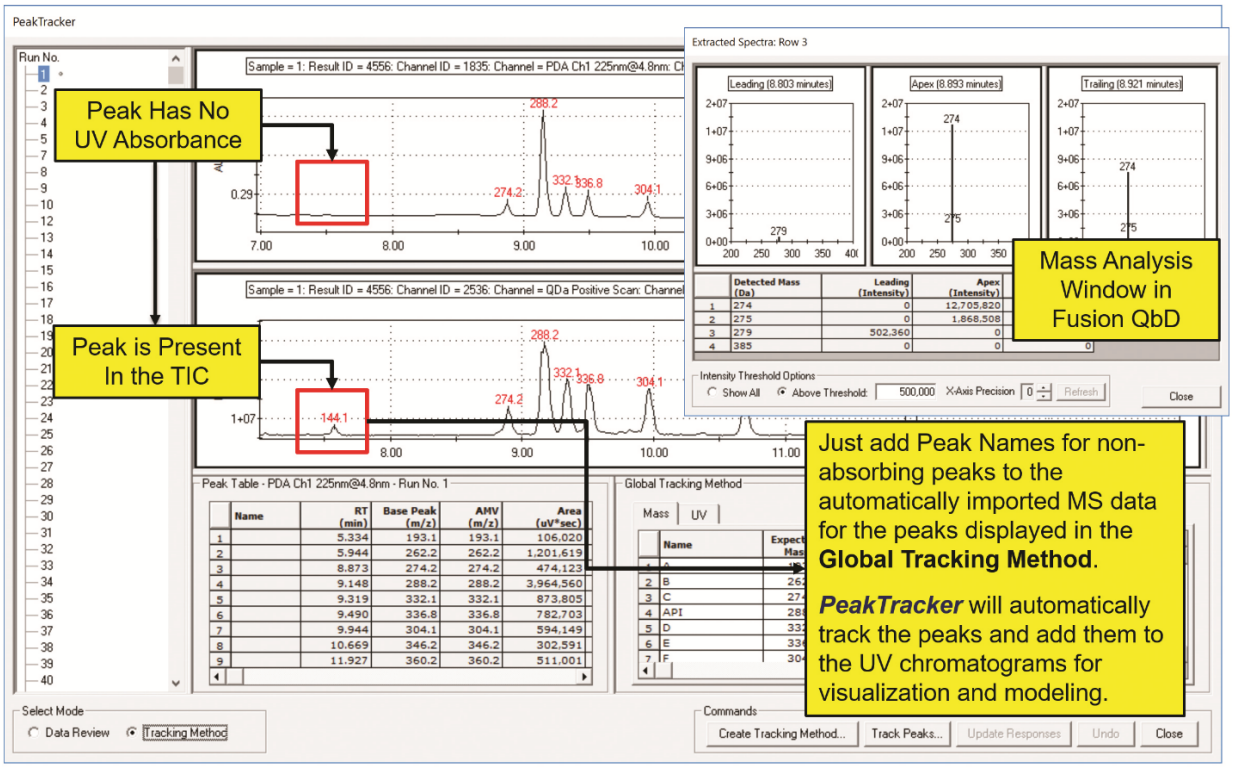
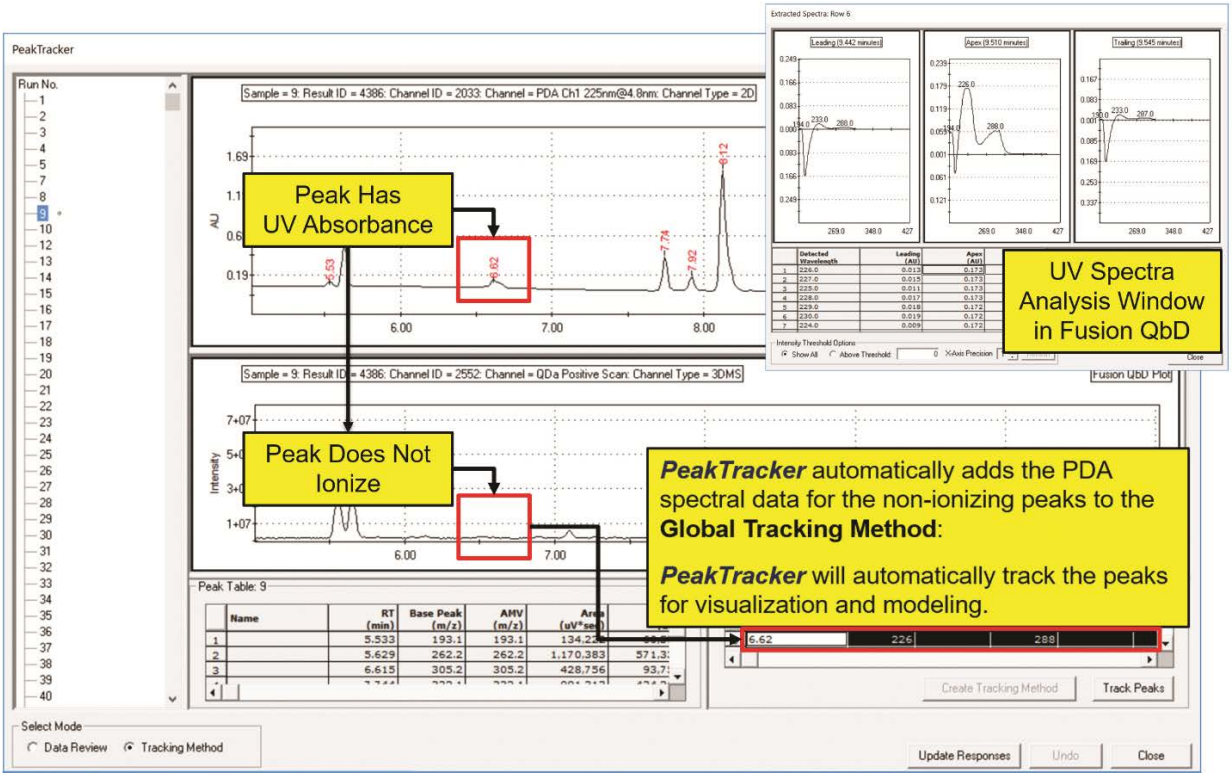
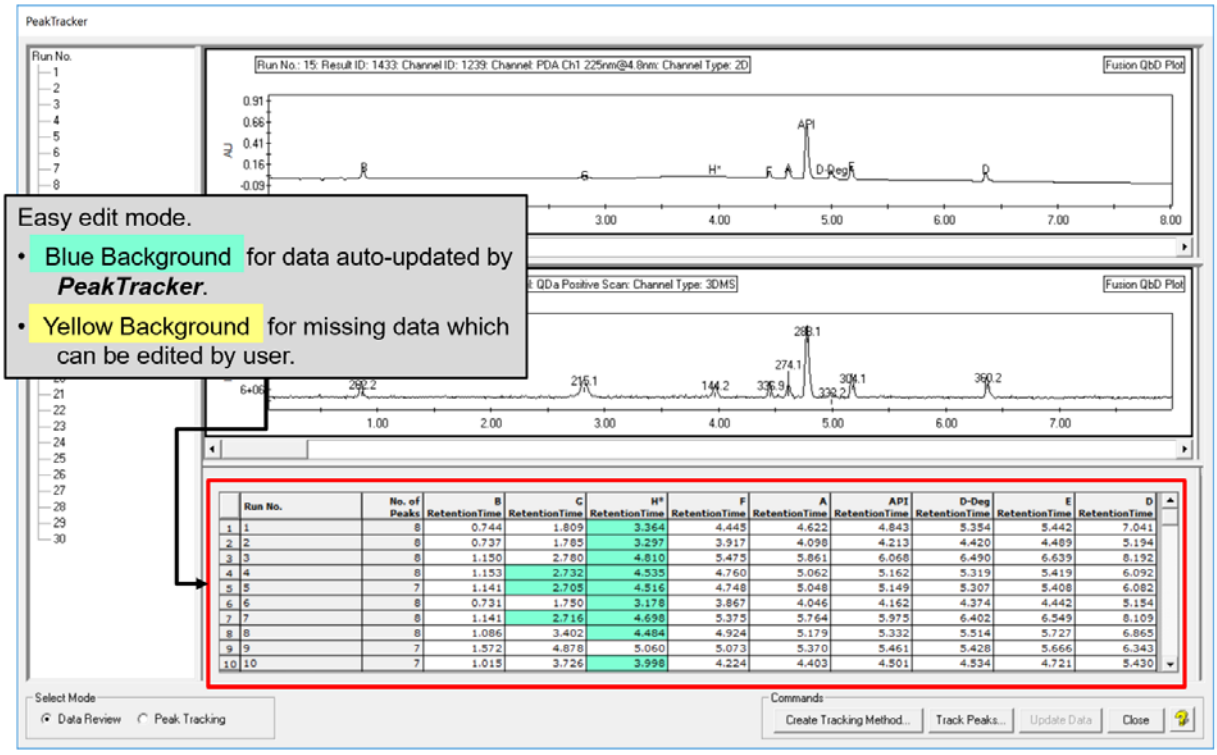


Figure 2 – Non-ionizing Peak



PeakTracker also incorporates the additional features and functions needed to complete the tracking workflow. These include (1) a paired graphical and numerical display of the MS and PDA spectra data for each peak, as shown in Figures 1 and 2, respectively, along with facilitation tools for manual manipulations to tracking results, and (2) a stacked display of the the UV chromatogram and Total Ion Chromatogram (TIC) for each experiment run for simple visual comparisons and tracking confirmation. In addition, as shown in Figure 3, ***PeakTracker*** displays a user-filterable table of the UV peak results with highlight colors to easily identify tracking updates to peak data – for example, updates to missing data for co-eluted peaks and added data for non-absorbing peaks merged into the UV chromatogram. Once tracking is complete, ***PeakTracker*** automatically maps compound names to all of UV results data computed by the CDS for all identified peaks in the experiment chromatograms for automated modeling and visualization. Automated peak tracking which fully utilizes PDA and MS data within a chromatography data framework greatly simplifies the integration of MS data into the method development workflow. Further, the ability to incorporate non-absorbing peaks into UV experiment chromatograms directly supports the development of MS compatible HPLC methods, which can be of great benefit to both production and quality control.

Figure 3 – Simple Data Review



Fusion QbD – *Rs-Map Response*

NEW

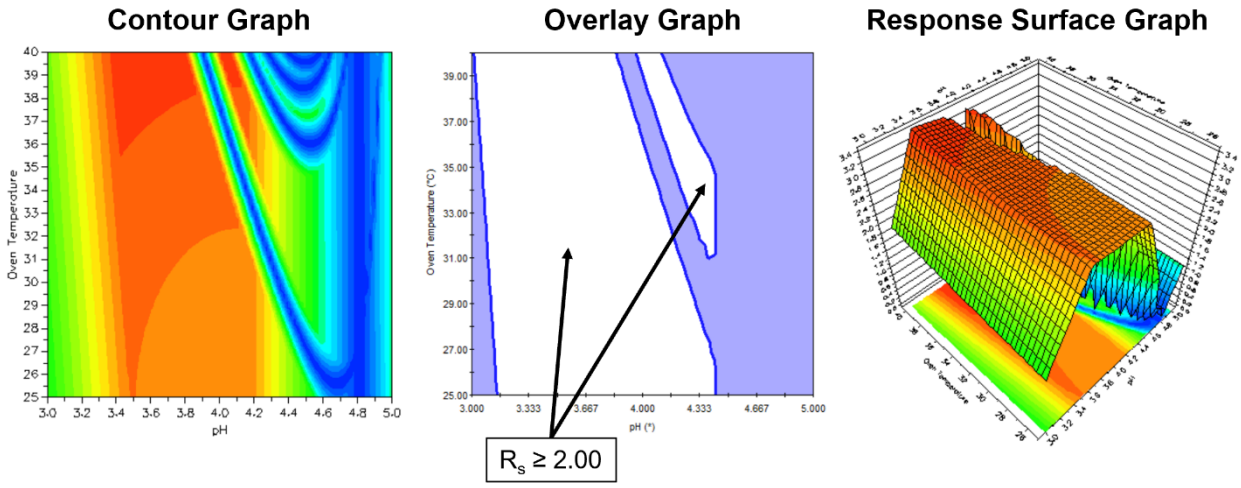
Fusion QbD now uses its hyper-accurate modeling technologies to predict the resolutions of all identified peaks for any given set of experimental conditions using standard USP or EP resolution equations. As shown in Figure 1, Fusion QbD then displays the predicted resolution results for all identified peaks in multiple graphics formats: – all of which update in real time as you change chromatographic method conditions.

2D Contour (left graph)– Rs-Map Response: Rs of least resolved peak).

2D Overlay (center graph) – Unshaded region: methods which exceed user set goals.

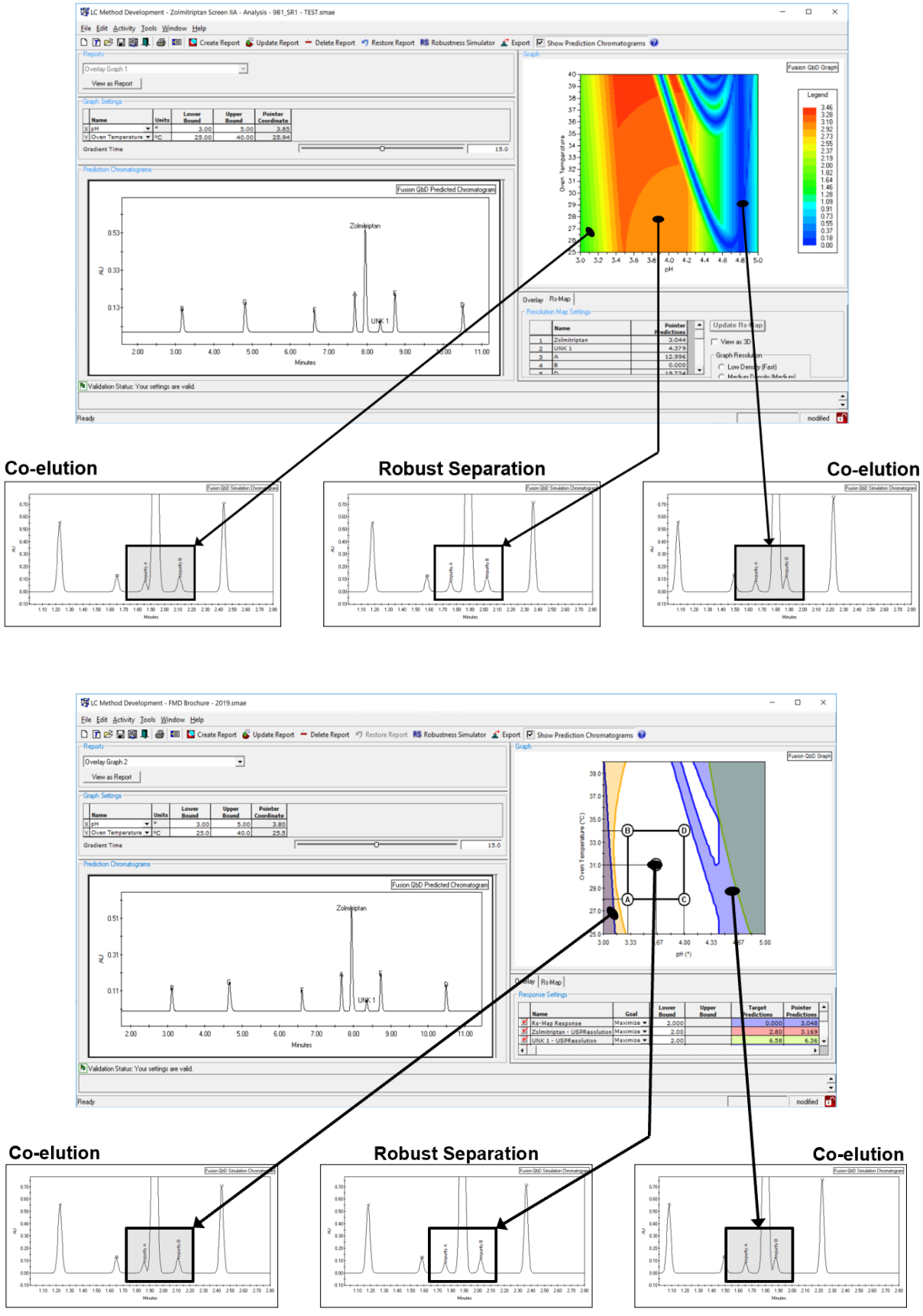
3D Surface (right graph) – 3D (X-Y-Z) graph: Z axis = Rs-Map Response.

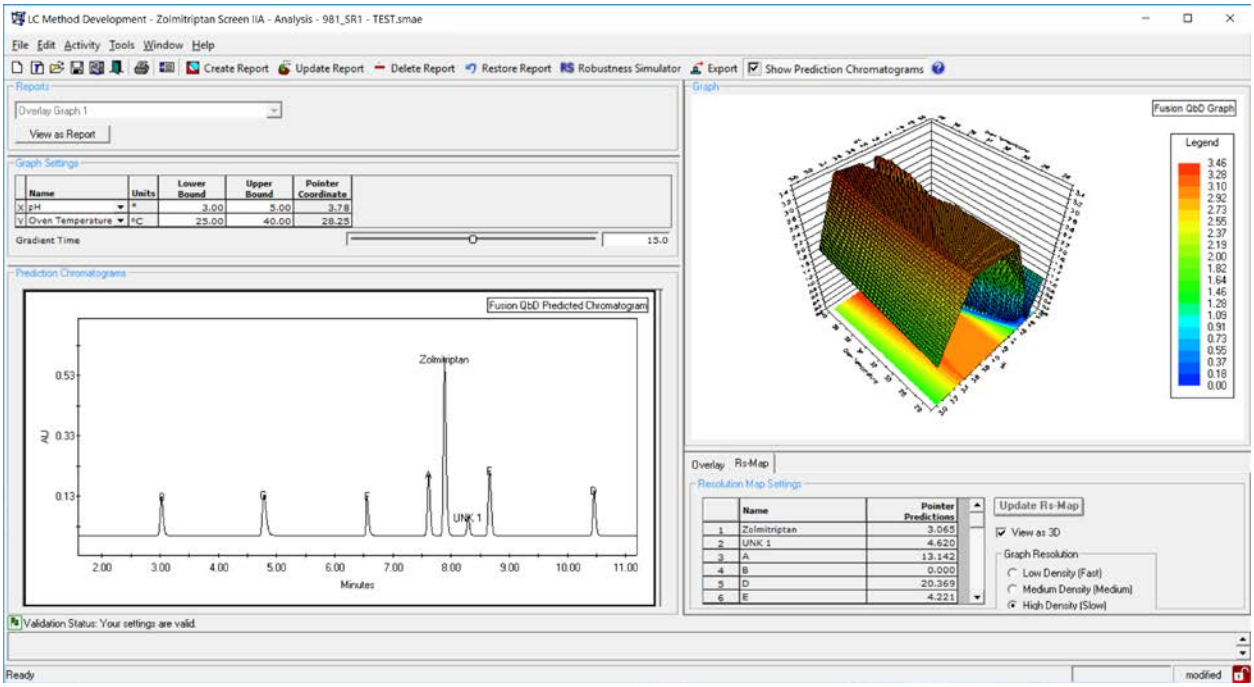
Figure 1 – ***Rs–Map Response*** : – Contour, Overlay, and Response Surface Graphs



You can dynamically set a minimum Rs requirement threshold, and Fusion QbD will update the ***Rs–Map*** data to visually display the peaks which do – and do not – meet your specified performance requirement. Your threshold will also be reflected in the Overlay graph. The ***Rs–Map Response*** data can also be coupled with Fusion QbD's numerical and graphical Best Answer search capabilities, as well as its fully integrated Robustness Simulator capability.

Figure 2 – Prediction Data and Chromatogram Visualization

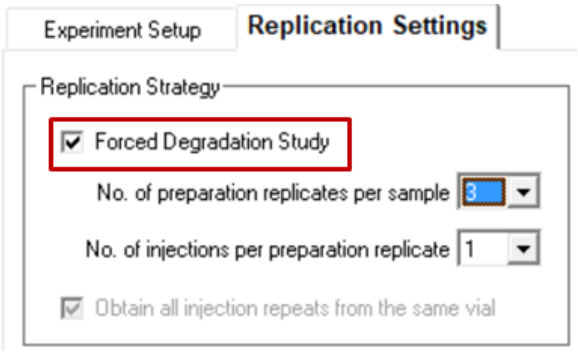




Fusion QbD – *Forced Degradation Studies*

NEW

Fusion QbD enables users to set up an experiment execution protocol in which each experiment run will be repeated according to user-specified Replication Strategy which can be any combination of Sample Preparation and/or Injection replicates – with the replicates taken from the same vial or assigned different vials.



S-Matrix has now created a new "Forced Degradation Study" mode to support experiments in which the different Sample Preparation replicates represent different degradation paths such as photo degradation, acid degradation, and peroxide degradation. This activates an entirely new technology which aggregates peak data from the replicates for each run into a "Composite Chromatogram" data set for the run to be used in robust method optimization and prediction chromatogram visualization.

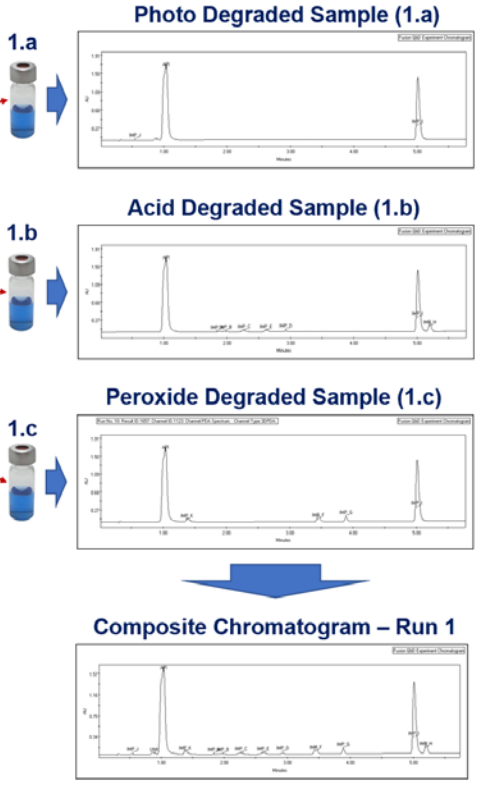
Forced Degradation Studies – Full Automation Support

Experiment Design Matrix

Run No.	Pump Flow Rate (mL/min)	Gradient Time (min)	Oven Temperature (°C)	pH
Condition Column - 1	0.400	2.0	35.0	3.20
1.a	0.300	5.0	35.0	3.20
1.b	0.300	5.0	35.0	3.20
1.c	0.300	5.0	35.0	3.20
2.a	0.500	5.0	35.0	3.20
2.b	0.500	5.0	35.0	3.20
2.c	0.500	5.0	35.0	3.20
3.a	0.300	15.0	35.0	3.20
3.b	0.300	15.0	35.0	3.20
3.c	0.300	15.0	35.0	3.20

Full Automation Support

- ✓ Each experiment run is replicated for each degradation path sample.
- ✓ Each peak is tracked in each degradation path sample chromatogram.
- ✓ All peaks from all degradation path sample chromatograms are aggregated into one chromatogram for the run.



S-Matrix has also linked the new ***PeakTracker*** and ***Rs–Map Response*** features to the new “Forced Degradation Study” operating mode.

PeakTracker tracks the peaks in each Sample Preparation replicate injection chromatogram for a given experiment run, and then aggregates all peak data into a composite chromatogram for the run which contains all peaks from all degradation paths.

The ***Rs–Map Response*** feature uses hyper-accurate retention and peak shape modeling to predict peak resolutions under all experimental conditions for robust method optimization and prediction chromatogram visualization.