Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

FUSION METHOD DEVELOPMENT FROM S-MATRIX

The only automated, Quality by Design solution for rapid LC method development

Chromatographic method development is performed throughout the drug development process. To decrease time-to-market, increase profitability, and meet regulatory requirements, organizations are continually working to improve the efficiency of analytical testing. Reducing chromatographic method development time can have a significant impact on drug development productivity.

Fusion Method Development™ Software from S-Matrix® streamlines LC method development by automating this process using Waters® ACQUITY UPLC® System and Empower™ 2 Chromatography Software, according to Quality by Design (QbD) guidelines recommended by the U.S. FDA and the International Conference on Harmonization (ICH). Fusion transparently manages complex statistics and mathematical models used for method optimization experiments. It also integrates method robustness testing into method development, as suggested by ICH guidelines.[1,2]

BENEFITS

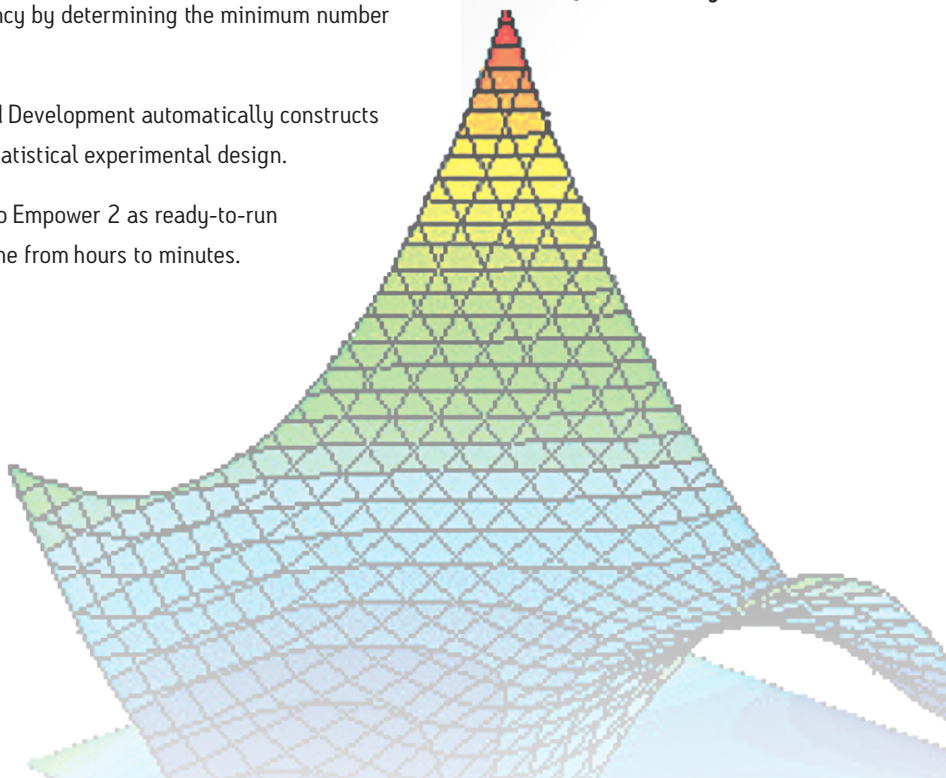
- Quickly develop robust methods according to Quality by Design guidelines
- Automate the method development workflow with seamless integration with Waters Empower 2 Software and ACQUITY UPLC
- Ensure reliability by testing and visually confirming LC method robustness prior to validation
- Reduce method development time from weeks to days
- Save time and reduce solvent usage with the ACQUITY UPLC System

QUICKLY DESIGN AND RUN AUTOMATED EXPERIMENTS

Fusion Method Development automatically builds and runs experiments using standard or user-customized templates. Study chromatographic parameters in combination by simply selecting them from a list. Fusion maximizes experimental efficiency by determining the minimum number of experiments required for valid results.

Incorporating a systematic QbD approach, Fusion Method Development automatically constructs the experimental region and selects the most efficient statistical experimental design.

With one click, Fusion exports the experimental design to Empower 2 as ready-to-run methods and sample sets, reducing experiment setup time from hours to minutes.



FUSION METHOD DEVELOPMENT IMPROVES PRODUCTIVITY

Implement an efficient two-phase method development strategy

Quickly develop optimized LC methods with Fusion Method Development using a two-phase strategy. For each phase, statistically rigorous and quantitative results are used to identify the best method.

PHASE 1

COLUMN AND SOLVENT SCREENING

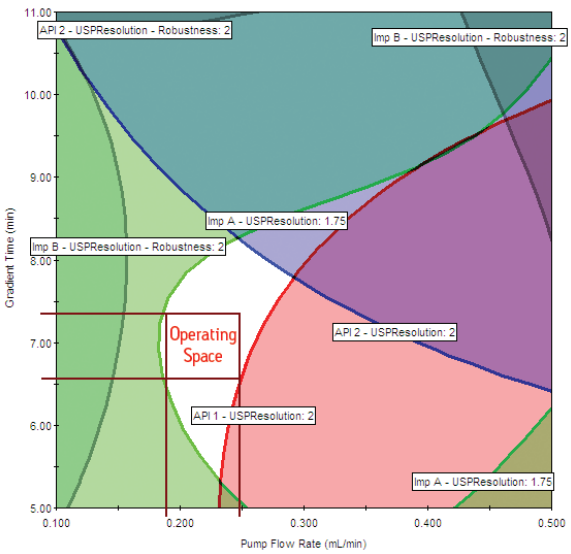
Rapid screening experiments study the major chromatographic selectivity factors, including column type, pH, and mobile phase composition.

PHASE 2

METHOD OPTIMIZATION

Phase 2 experiments use the results from Phase 1 plus additional variables with tighter ranges to determine the optimum LC method. Fusion Method Development applies a unique combination of Monte Carlo Simulation and Process Capability statistics to quantitatively evaluate method robustness.

Visualize method performance and robustness



Visualize method performance and robustness with Fusion Method Development's overlay graphics. The color-coded response maps define the QbD Knowledge, Design, and Operating spaces. With these spaces defined, users can automatically predict robust LC methods.

Analyze data without tracking peaks

Fusion Trend Response™ operators are numerical interpretations that sort the data by characterizing the quality of the separation. Operators that can be associated with any chromatographic result include:

- Total number of peaks
- Number of resolved peaks
- Max peak area-tracked resolution
- Max peak area-tracked symmetry
- Last peak retention time

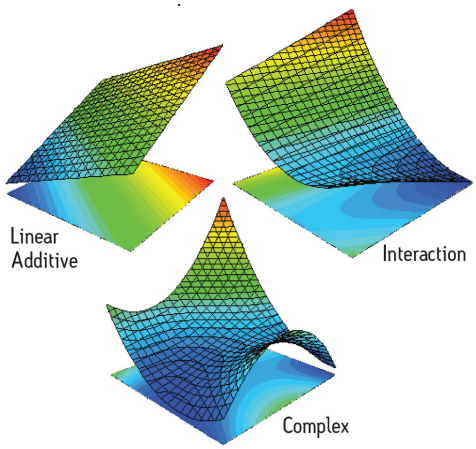
With statistical engines that are transparent to the user, Fusion Method Development analyzes and models critical method performance characteristics and predicts the optimal LC method. Data are automatically presented as numerical and graphical reports for easy visualization of results.

Instantly identify regions of optimal method performance

Fusion Method Development is the only application to account for all key chromatographic interaction effects. Response surface plots show the combined effects of variables on key chromatographic responses such as peak resolution, tailing, and retention. Color gradation represents the magnitude of interactions with curvature indicating the type of interaction. Fusion Method Development automatically analyzes data, generates response surface plots, and identifies regions where methods will optimally perform.

User-defined method performance goals are quickly tested with the automated Optimizer Wizard that searches for the LC method that meets all performance requirements goals simultaneously. Results are instantly ranked and reported.

3D Response Surface Plots



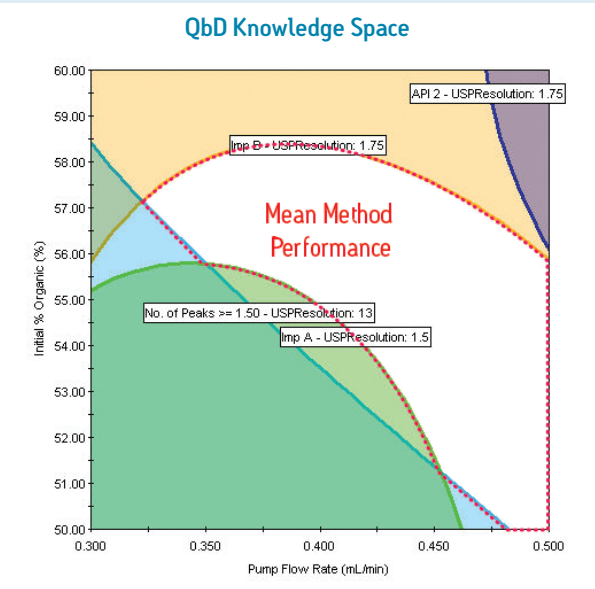
Response surface plots show the combined effects of variables on key chromatographic responses.

Automatically predict mean method performance and robustness

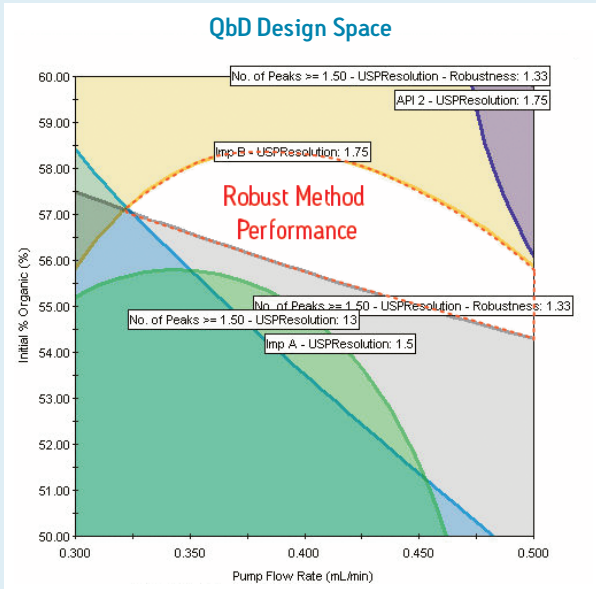
Fusion Method Development's overlay graphs are used to automatically predict mean method performance and robustness. The unshaded area in the QbD knowledge space corresponds to variable ranges that meet or exceed all goals for mean method performance.

Using the Robustness Simulator,™ Fusion Method Development integrates robustness into the method development process without the need for any additional experiments. Mean method performance and robustness models are then linked to establish the QbD design space. The design space defines the ranges of the chromatographic parameters that will generate a robust method.

TURN KNOWLEDGE SPACE...



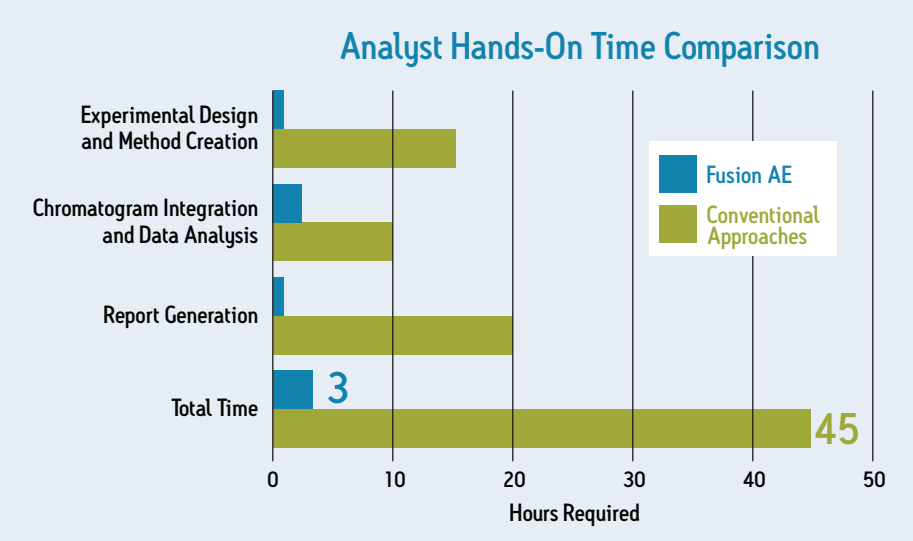
...INTO DESIGN SPACE



Unshaded areas identify where mean method and robust method performance goals are met.

Save time and reduce solvent usage with ACQUITY UPLC

The combination of ACQUITY UPLC and Fusion Method Development can result in significant solvent and time savings. Solvent usage can be reduced by more than 80% using the ACQUITY UPLC. When paired with the ACQUITY UPLC, Fusion Method Development can result in a 15-fold time savings when compared to conventional HPLC and traditional, one factor at a time (OFAT) method development.



MAXIMIZE LABORATORY EFFICIENCY

The template-driven Fusion Method Development front-end reduces the time required to design experiments and build the associated Empower 2 instrument methods and sample sets from hours to minutes. Fusion Trend Response operators significantly simplify and speed up post-run data processing and analysis. With overlay graphs, analysts can quickly identify, test, and report regions of optimum method performance and robustness. The result is a robust method that is defined by a well-characterized design space that meets ICH's Quality by Design guidelines.

References

1. ICH Q2 (R1) Validation of Analytical Procedures: Text and Methodology.
2. ICH Q8 (R2) Pharmaceutical Development.

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