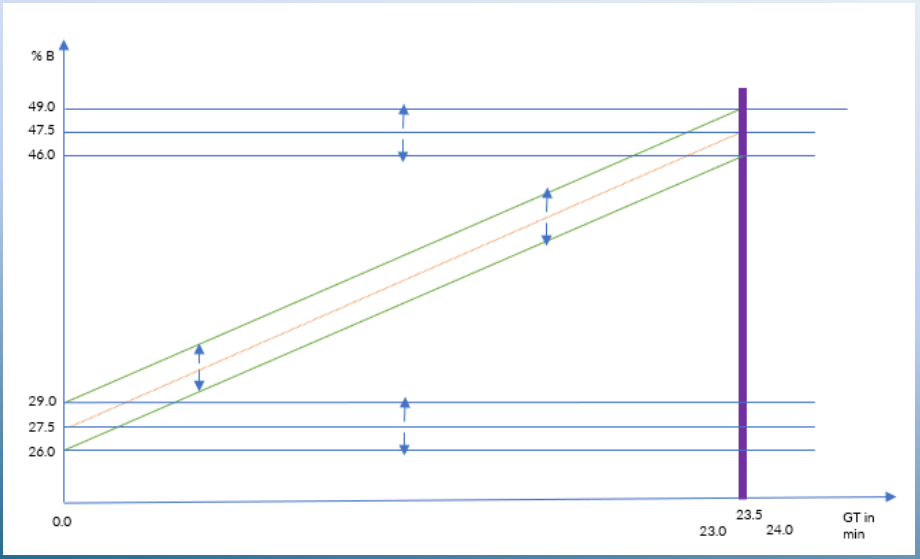
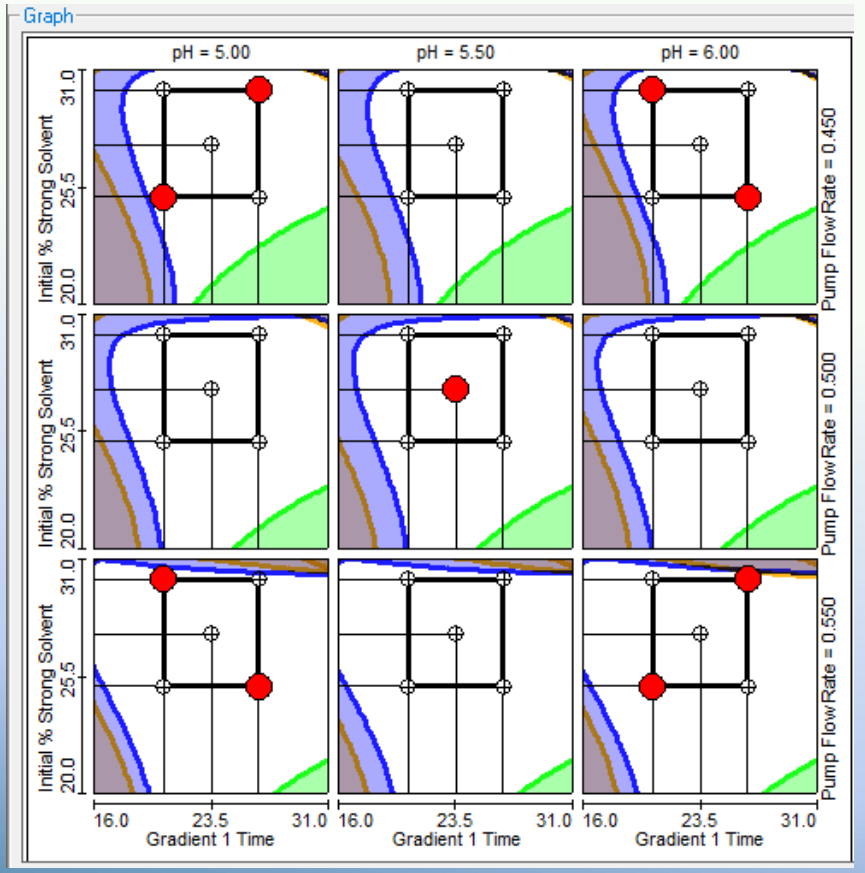
Assessing Gradient Robustness in Fusion QbD 9.9.2

cromingo

Traditional (Shifting a Gradient) **vs.** **Modern (Multivariate Experiment)**

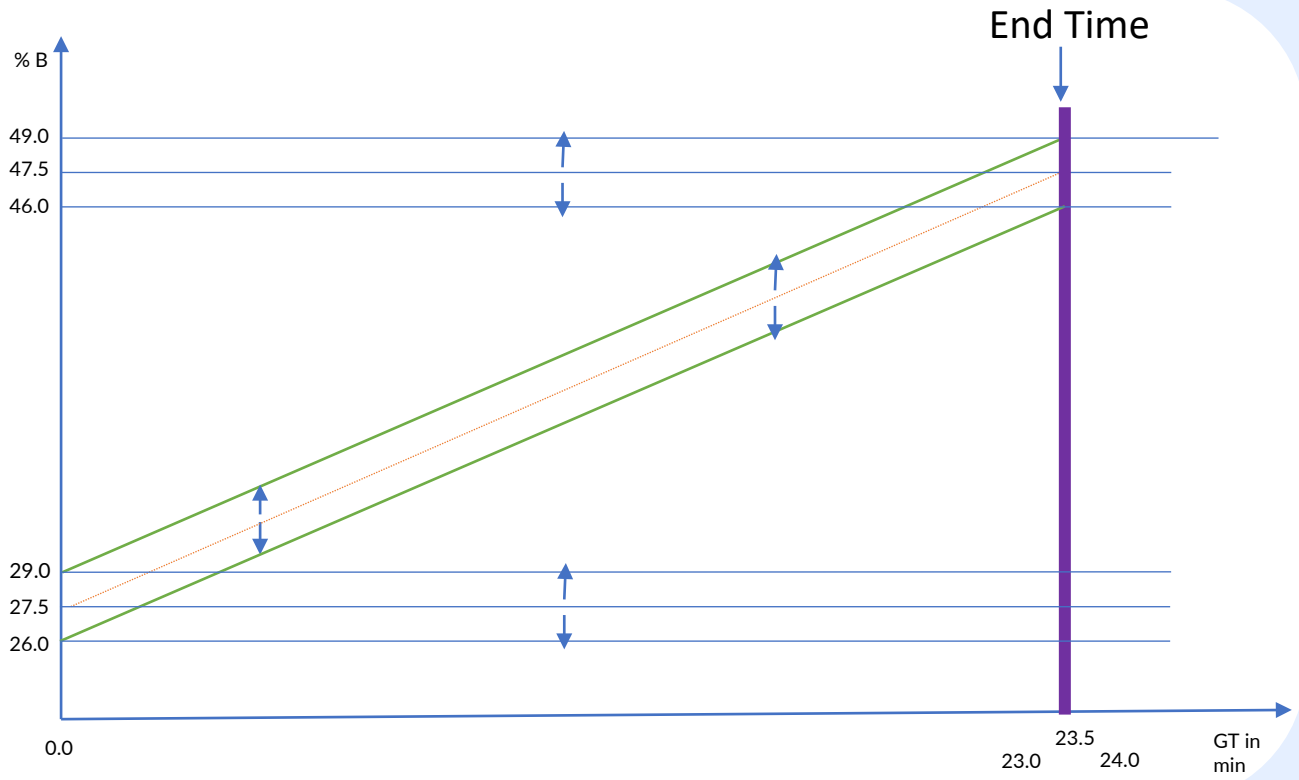




How to Characterize Robustness for a Gradient?

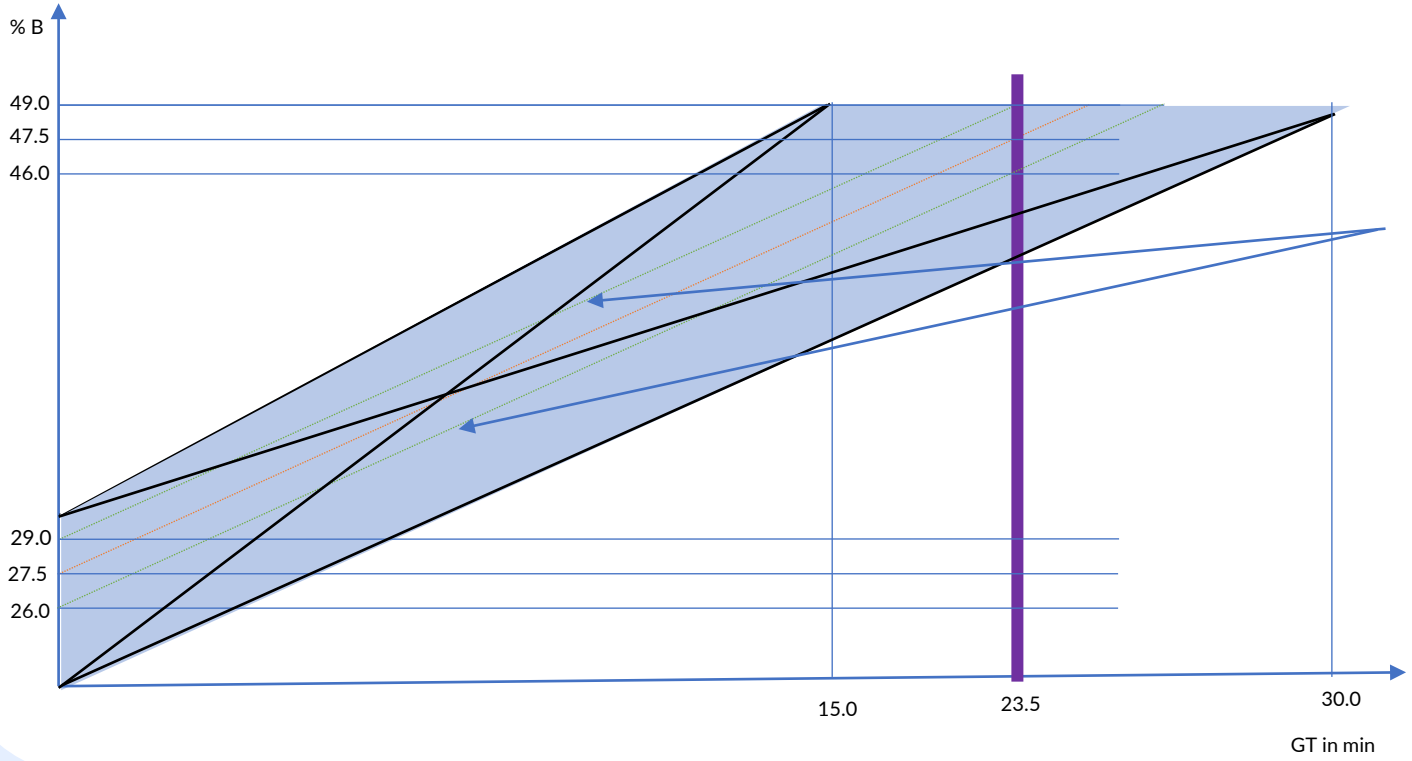
With a traditional approach analysts usually study the robustness of a gradient by simply shifting the initial and final percentage of the around the setpoint of the organic mobile phase while keeping Gradient Time and Slope as a constant, e.g.:

- %Bi = 26 – 29%;
- GT = 23.5 min
- %Be = 46 – 29%



However, in Fusion QbD such an approach is not required and for that reason a design like this is not provided by the software.

Optimization Design for Gradient Variation in Fusion QbD 9.9.2

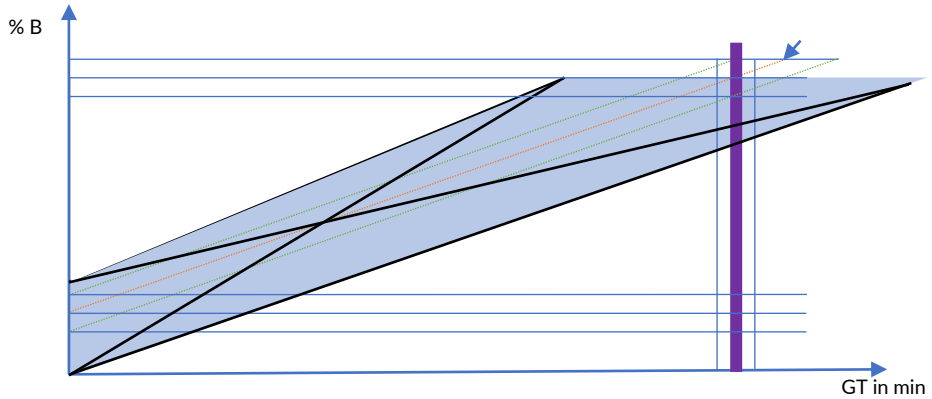


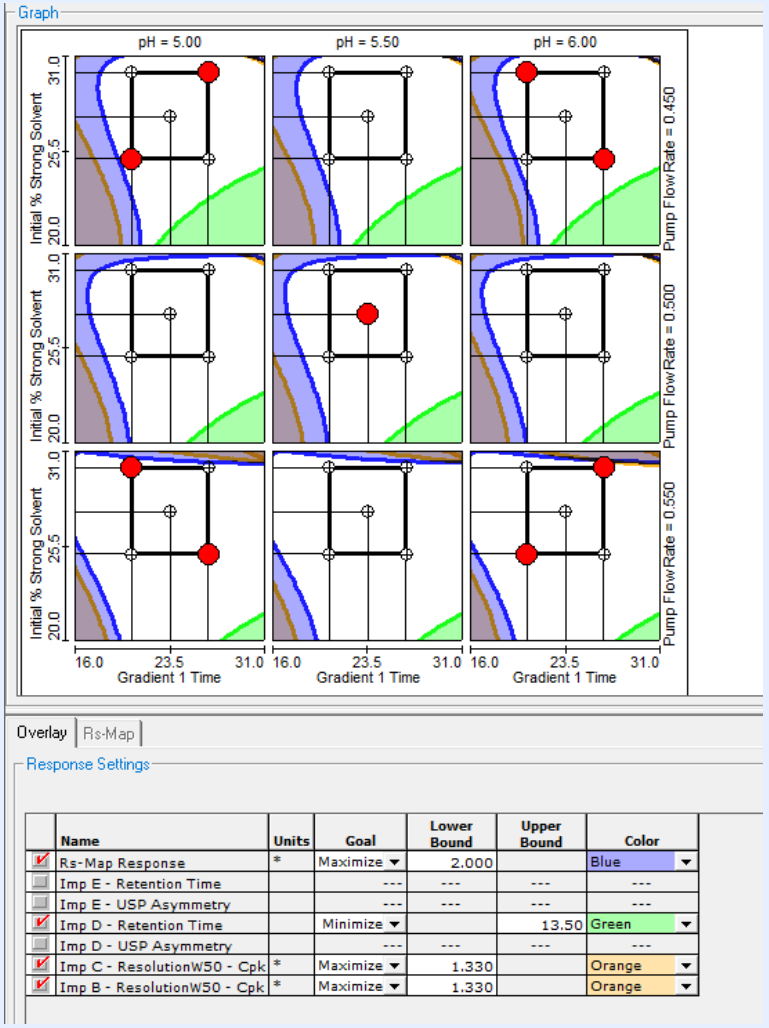
The shifted gradient ramps from the traditional approach (green lines) are both included in the studied gradient variation.

In an multivariate experiment %Bi and GT can be studied simulatenously by covering a much broader range (shaded region below) compared to a traditional approach, e.g.

- %Bi = 20 – 30%
- GT = 15 - 30 min

Fusion QbD: Full Characterization of the Method Operable Design Region (MODR) also in Terms of Robustness

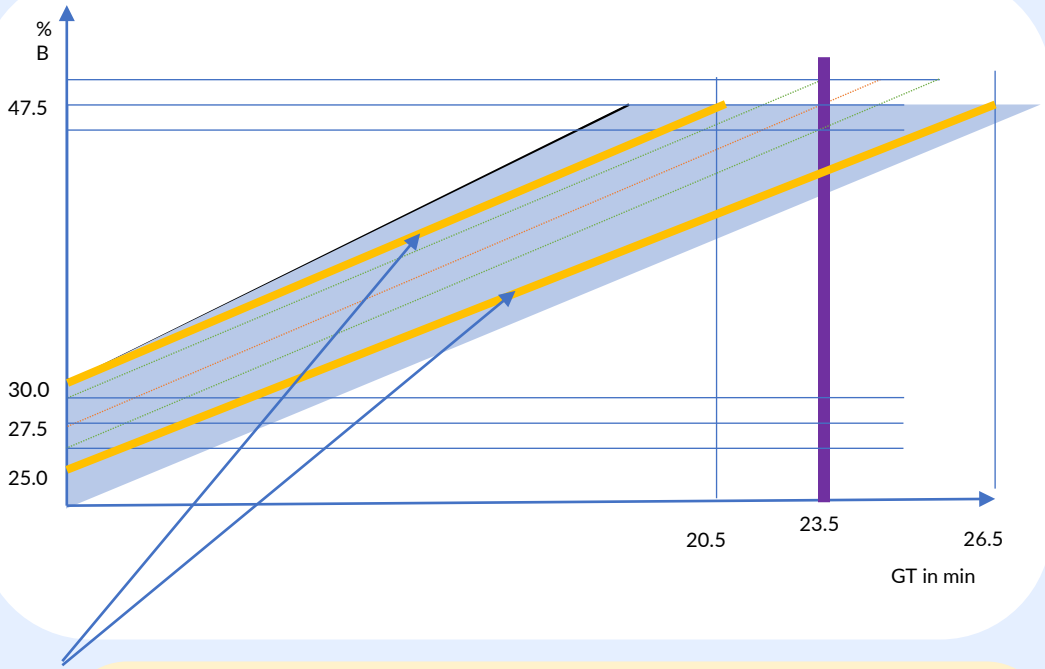


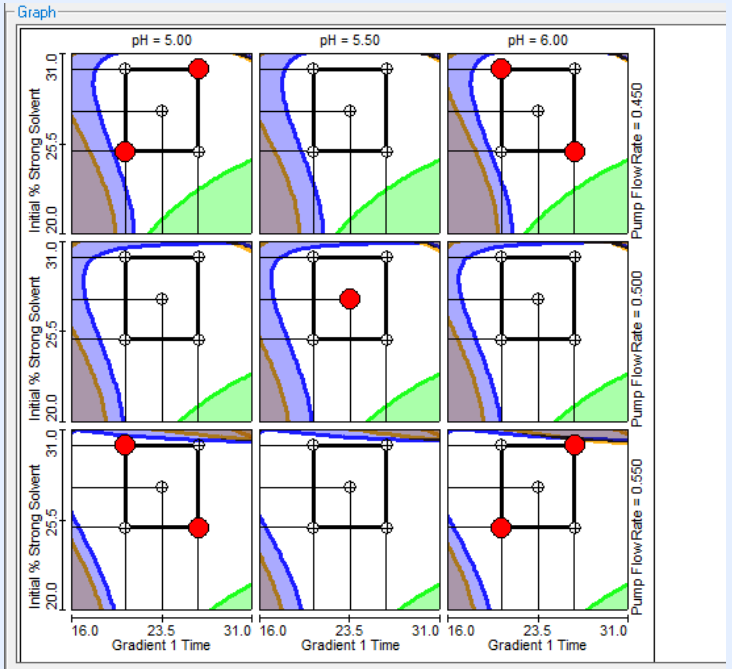


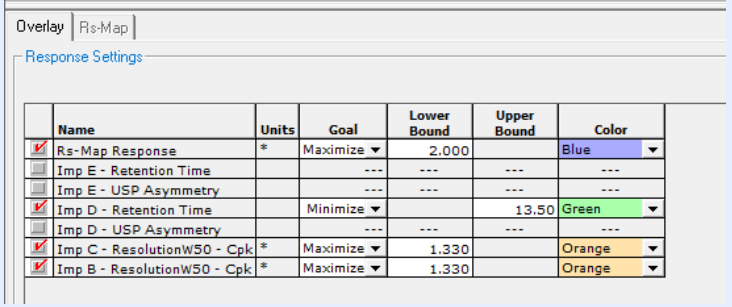
	Name	Units	Goal	Lower Bound	Upper Bound	Color
☑	Rs-Map Response	*	Maximize	2.000		Blue
☐	Imp E - Retention Time		---	---	---	---
☐	Imp E - USP Asymmetry		---	---	---	---
☑	Imp D - Retention Time		Minimize		13.50	Green
☐	Imp D - USP Asymmetry		---	---	---	---
☑	Imp C - ResolutionW50 - Cpk	*	Maximize	1.330		Orange
☑	Imp B - ResolutionW50 - Cpk	*	Maximize	1.330		Orange

- From a single optimization experiment the entire range can be characterized in terms of mean performance and robustness.
- In a multivariate study, not only the combination of single parameters such as %BI and GT is characterized, but the entire multivariate design region. The example shows us different pH and flow settings as well.
- The shaded regions stand for method settings, where our method goals are not met, the combined unshaded region shows us, where all method goals are met simulatenously.
- Cpk - Robustness Responses are included as method goals (orange shadows).

Identifying Settings for a Robust Method







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☑	Rs-Map Response	*	Maximize	2.000		Blue
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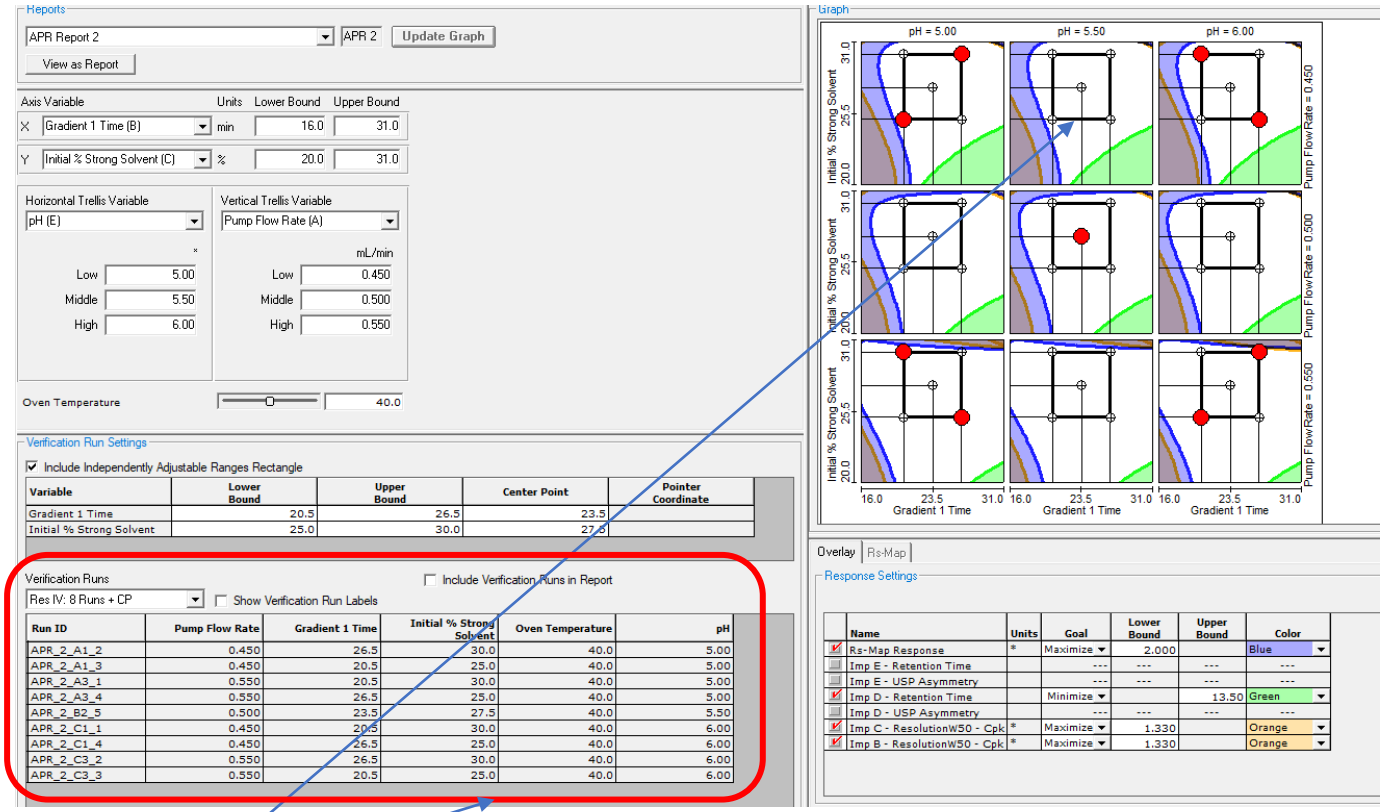
☑	Imp D - Retention Time		Minimize		13.50	Green
☐	Imp D - USP Asymmetry		---	---	---	---
☑	Imp C - ResolutionW50 - Cpk	*	Maximize	1.330		Orange
☑	Imp B - ResolutionW50 - Cpk	*	Maximize	1.330		Orange

- A rectangel can be inserted into the overlay graphs in a way, that it is located inside the unshaded region in all 9 plots.
- Yellow lines in the gradient plot above reflect the rectangle settings in the Fusion overlay graphs.
- Robust method settings are identified for the following conditions:
  - Bi [%] = 25 – 30
  - GT [min] = 20.5 – 26.5
  - pH = 5.00 – 6.00
  - Flow [ml/min] = 0.450 – 0.550
  - Temperature [°C] = 40*

*Only 4 variable factors can be displayed in the trellis graph at a time.

Verification Runs



In Fusion 9.9.2

- Verification runs can easily be exported for a subset of representative methods (red spots on the rectangles)
- After data acquisition and processing the processed results and chromatograms can be imported back to Fusion for reporting purposes.

Contact us for more Information

Fusion QbD® is a mature LC method development software especially designed for AQbD approaches in the pharmaceutical industry.

If you want to better understand, how robustness of an analytical method can be simulated and characterized for the entire design region, please contact us for **a free software demo**.

Cromingo e.K. – All Fusion products and services from a single source in close collaboration with S-Matrix Corporation.

Reach out to us directly for further information **info@cromingo.com**