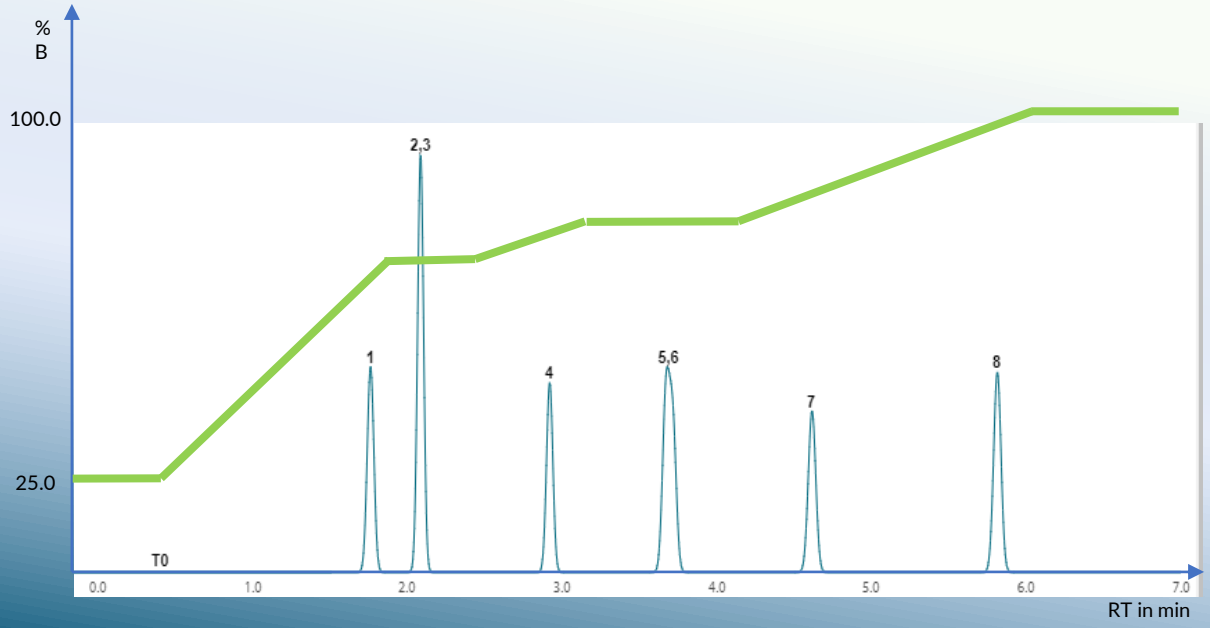
Why LC Methods developed with Fusion QbD® usually do not have gradient segments



…, and can segmented gradients be reconciled at all with the basic idea of AQbD?

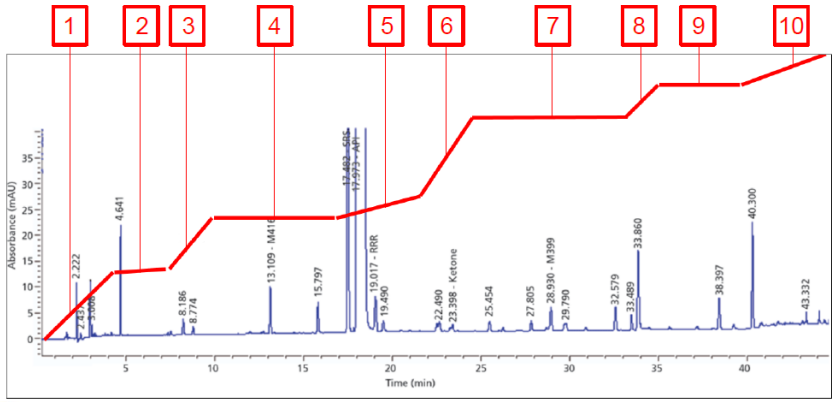
Why LC Methods developed with Fusion QbD usually do not have gradient segments?

Segmented Gradient

6 Months Full Time: 2 Analysts Working Independently.

Result: Non-robust 10-step Gradient Method.

10-step Gradient = **10 Critical Robustness Parameters**

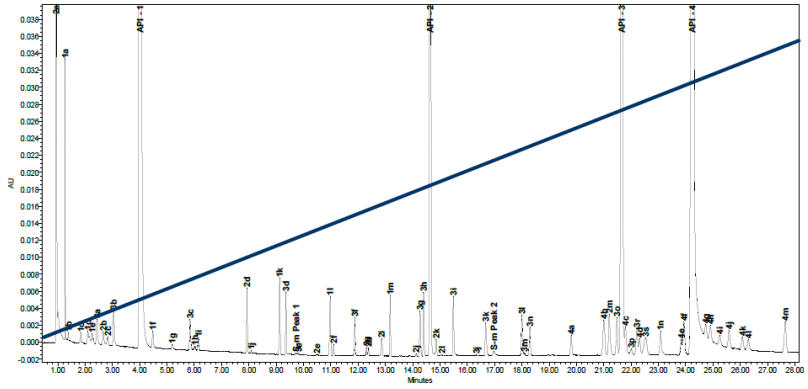


Single Gradient Ramp developed using Fusion QbD

Total Time: **2 Weeks** – 1 Analyst (versus 6 months) !

Result: Robust Single gradient method

1-step Gradient = **1 Critical Robustness Parameter !**



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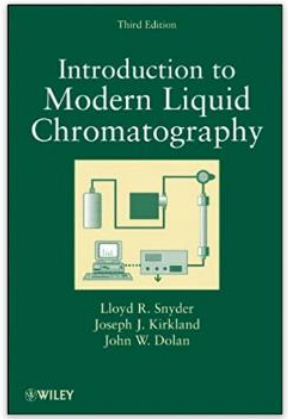
The example shows, that with the Fusion QbD approach it was possible to develop an LC method with a single gradient ramp in a shorter time having even a shorter run time. This is because in a multivariate study, there are many more optimization parameters than only the slope factor.

But this is not the only reason!

Why LC Methods developed with Fusion QbD usually do not have gradient segments?

As with each additional step the pump valve needs to switch and causes small perturbations in the mobile phase composition and by that leads to poor robustness in that region and makes a future transfer more difficult.

This risk has even been in acknowledged already in 2010 in the 3rd edition of handbook "Introduction to Modern Liquid Chromatography - by Snyder, Kirkland, Dolan [page 427-428]:



"Increasing resolution by adjusting selectivity for different parts of the chromatogram can sometimes be achieved with a segmented gradient; … Segmented gradients are not often used for improving resolution as in figure 9.12 because their ability to enhance resolution without increasing run time is usually limited…However, there are other – generally more useful – means of optimizing resolution by changing selectivity and relative retention. Also, separations that use segmented gradients to improve resolution are likely to be less reproducible when transferred to another piece of equipment."

Conclusion: LC methods with segemented gradients have an intrinsic risk to fail reproducibility requirements and future method transfers.

Why does it work in Fusion?

In a real multivariate study as it is conducted with Fusion QbD you obtain many more optimization parameters and this makes it more probable to identify method conditions in the characterized design region, where a single gradient ramp already fulfills your requirements in terms of selectivity and method run time.

Further on we take the QbD in Fusion seriously and therefore want to avoid any quality issues in the final method already from the beginning.

This is why, for LC methods developed with Fusion QbD, the unsegmented gradient ramp is the rule.

The introduction of further segments should therefore be a well-considered exception.

Can segmented gradients be reconciled at all with the basic idea of AQbD?

Can segmented gradients be reconciled at all with the basic idea of AQbD?

In our opinion the introduction of gradient segments is contradictory to an AQbD approach, as a potential risk for reproducibility and transferability of your analytical method is deliberately introduced already during the design phase of the analytical method.

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 the design region is modelled in Fusion, 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**