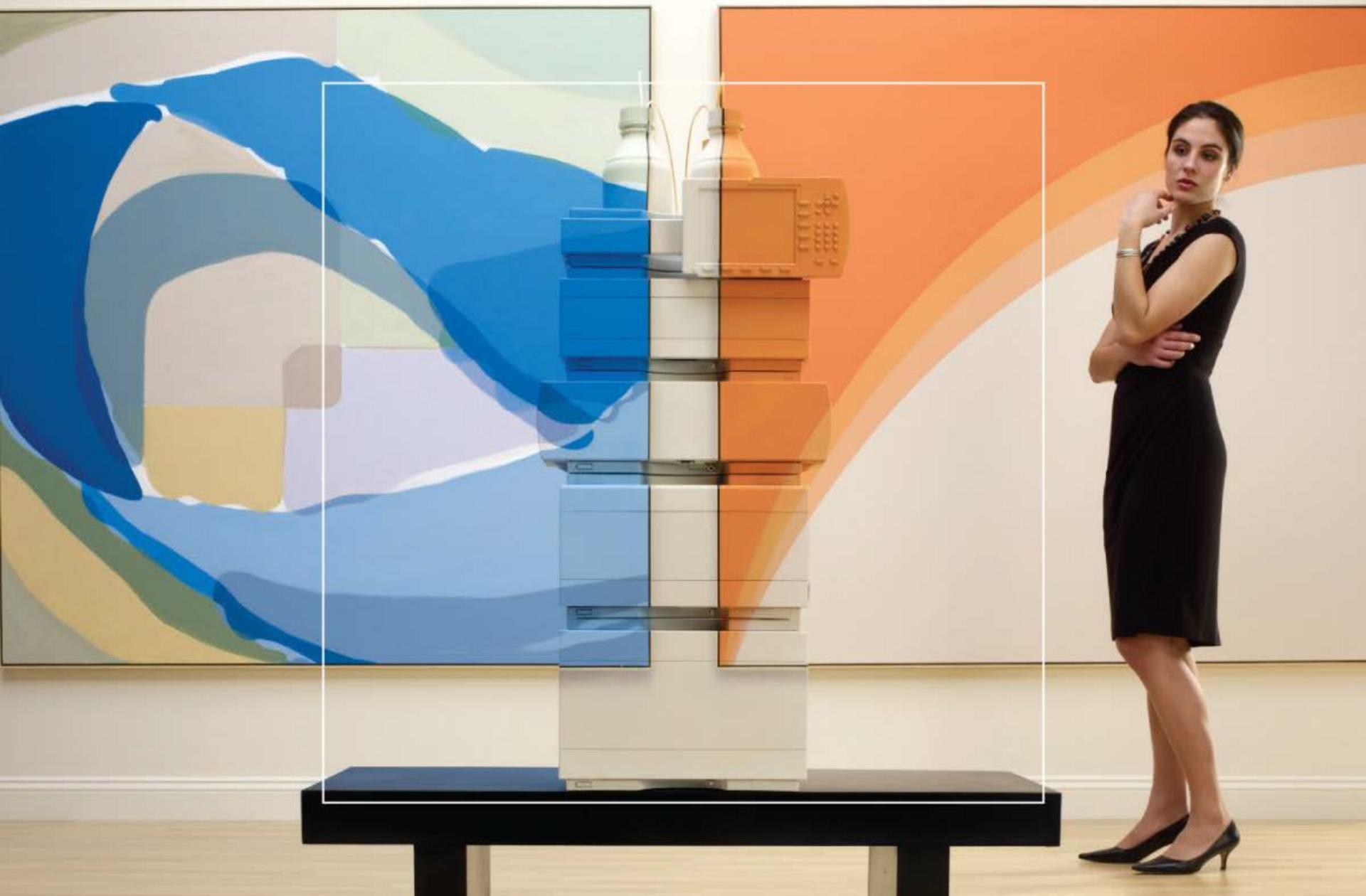
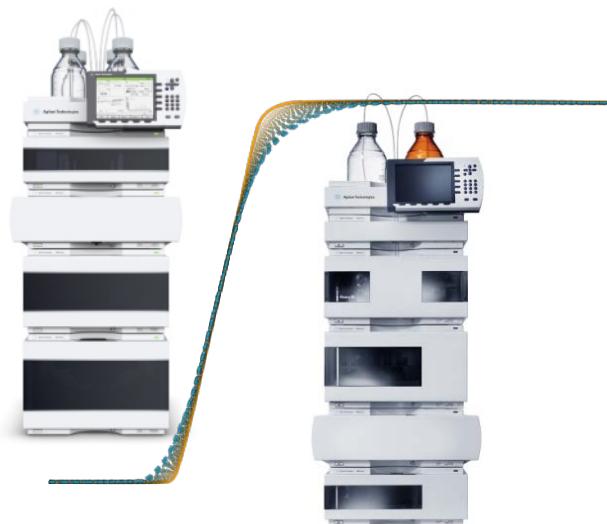


THE ART OF EMULATION



*Infinitely better
method transfer*



Agilent 1290 Infinity with
**Intelligent System Emulation
Technology (ISET)**



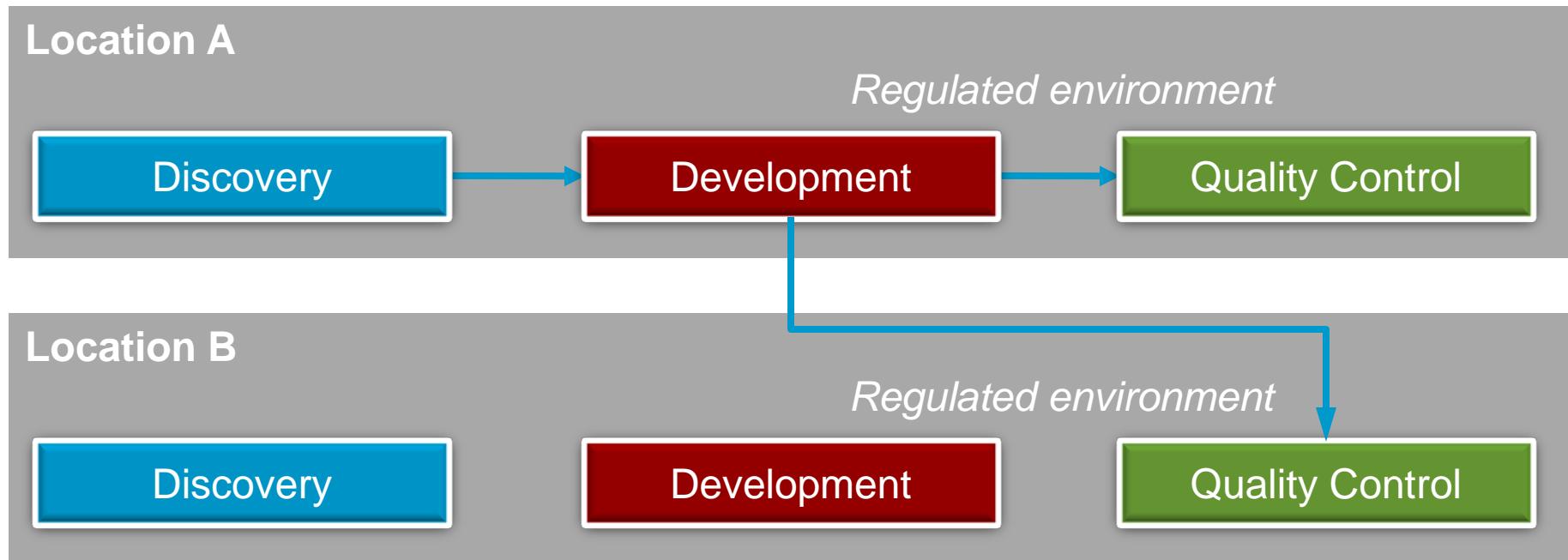
Agilent Technologies

Agenda

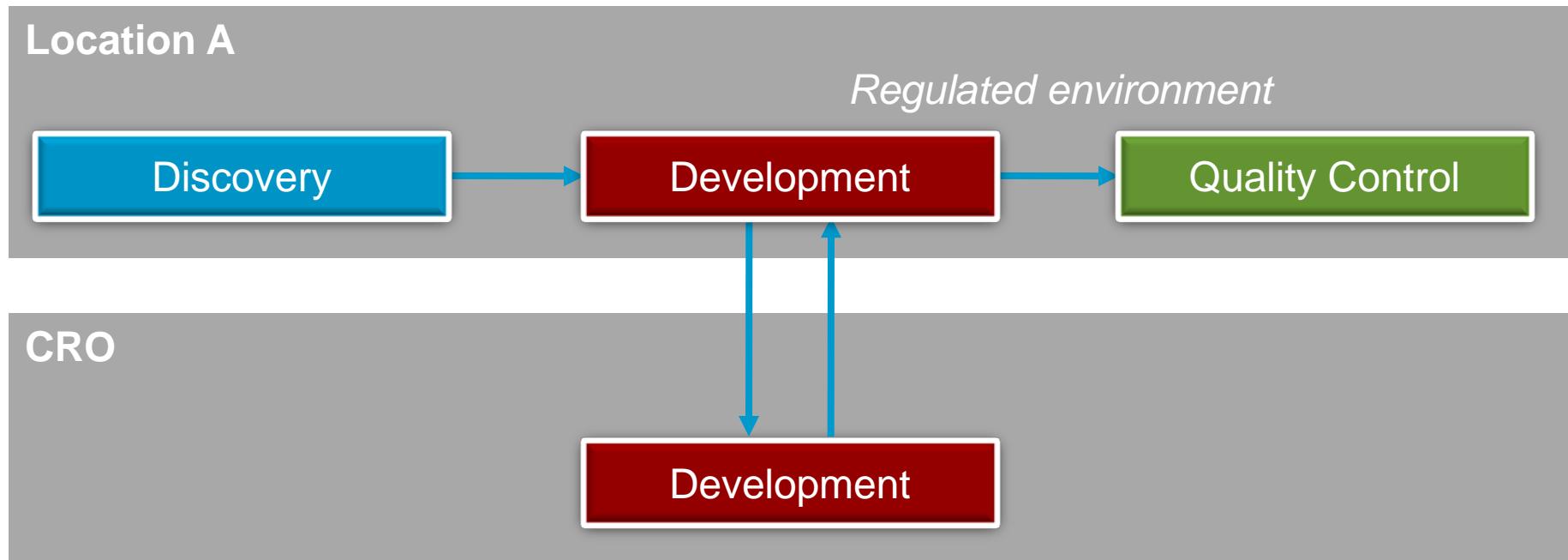
- Method transfer workflows
- Parameter affecting instrument to instrument method transfer
- Current solutions
- What is ISET
- Performance examples
- Summary



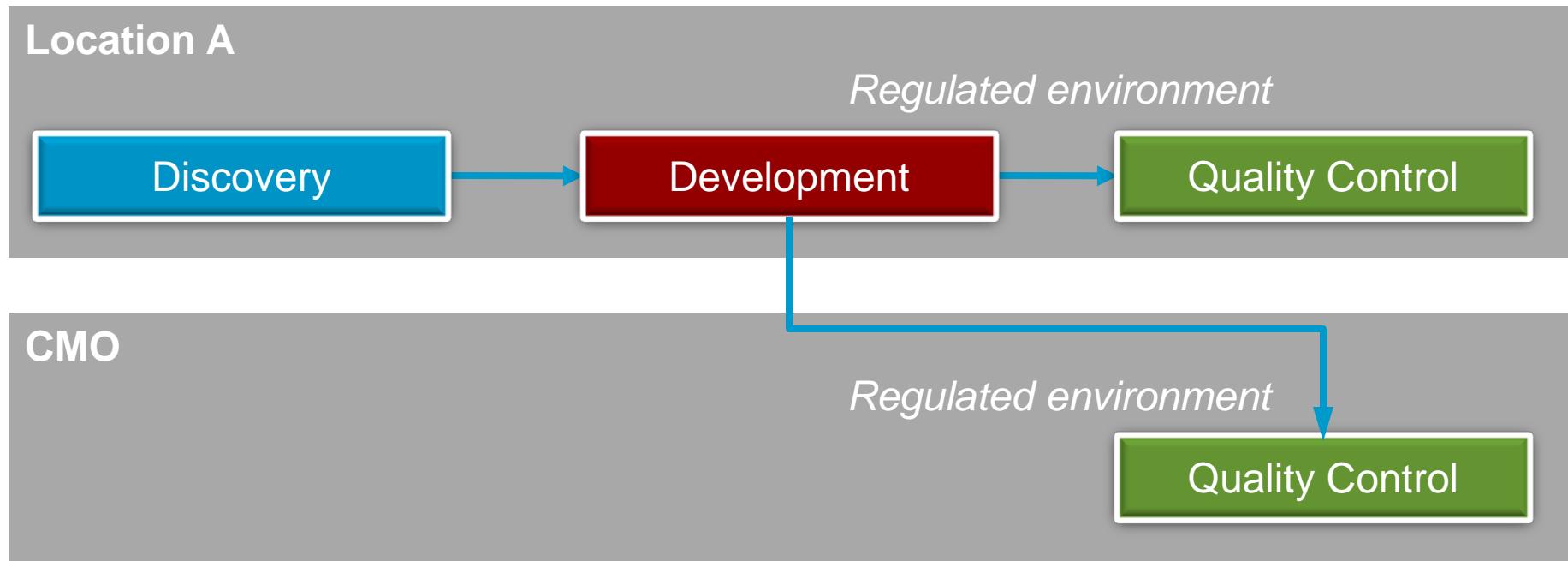
Method Transfer Workflow



Method Transfer Workflow



Method Transfer Workflow



Method Transfer Workflow

Application of Very-High Pre-Chromatography for Development and More Efficient Separation

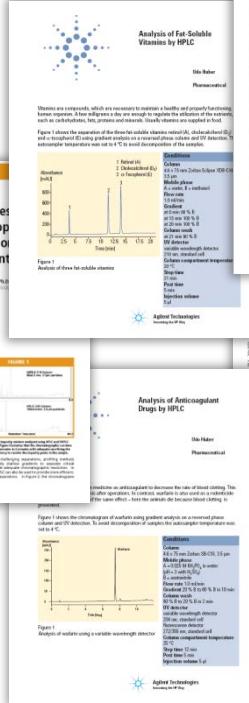
Pharmaceutical Development

By

Brent L. Kistner, PhD

Agilent Technologies

High performance liquid chromatography (HPLC) is a well-established technique for the separation and analysis of pharmaceutical compounds. However, the process of method development can be time-consuming and costly. One way to improve the efficiency of method development is to use very-high pre-chromatography (VHPC) to separate the sample into different fractions before performing the final HPLC analysis. This can significantly reduce the time and cost of method development, as well as improve the overall quality of the final product.



Methods from Literature:
Scientific journals, application notes, etc

Instrumentation:
1100 Series, 1200 Series, Alliance,
Acuity, etc



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Design Differences (U)HPLC Systems

- Delay volumes
(gradient formation)
- Power range
(flow x pressure)
- Extra column volume
- Temperature
- Data rates
- Sensitivity



Problem:

Instrument to Instrument Method Transferability

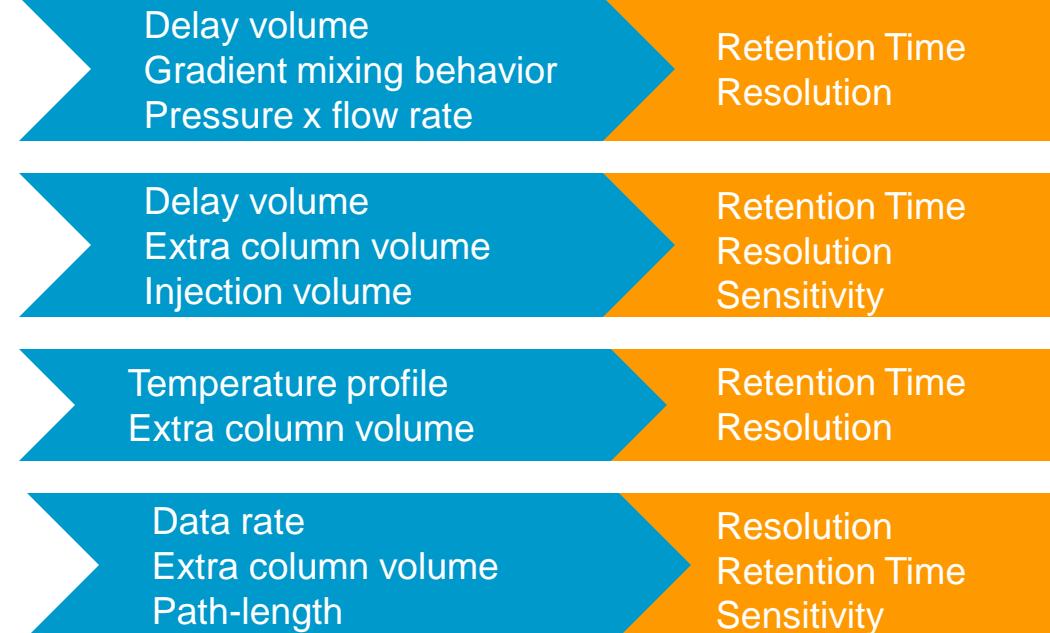
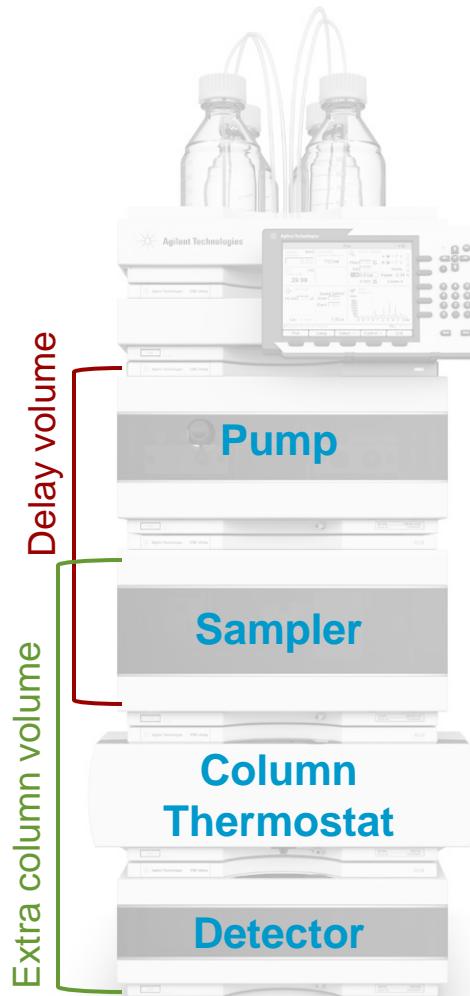
- Not possible
- Requires Re-development
- Requires Re-validation

Resulting in huge additional cost factor:



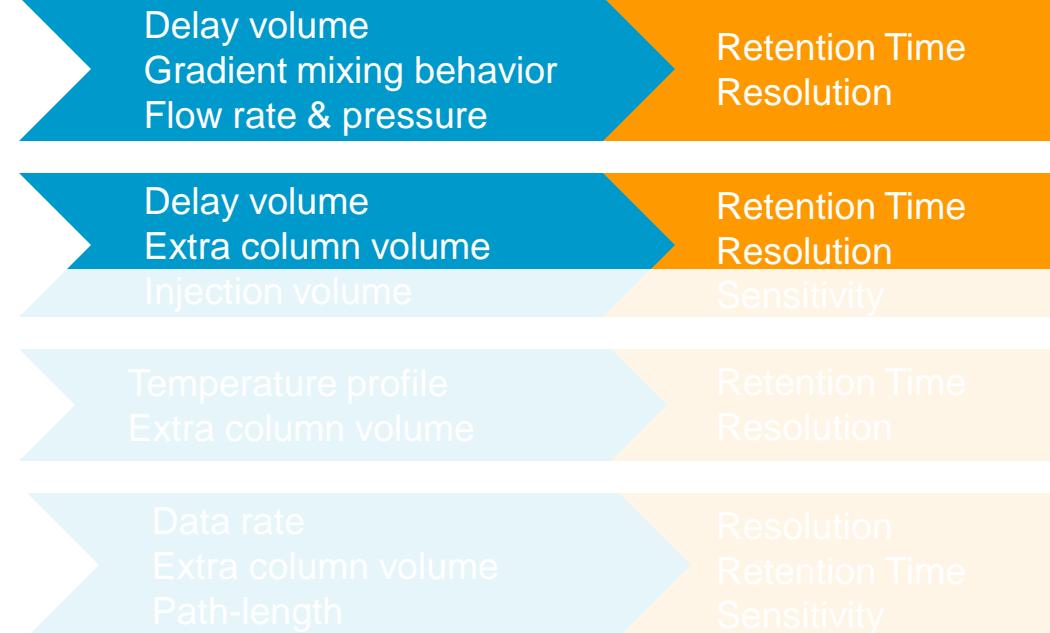
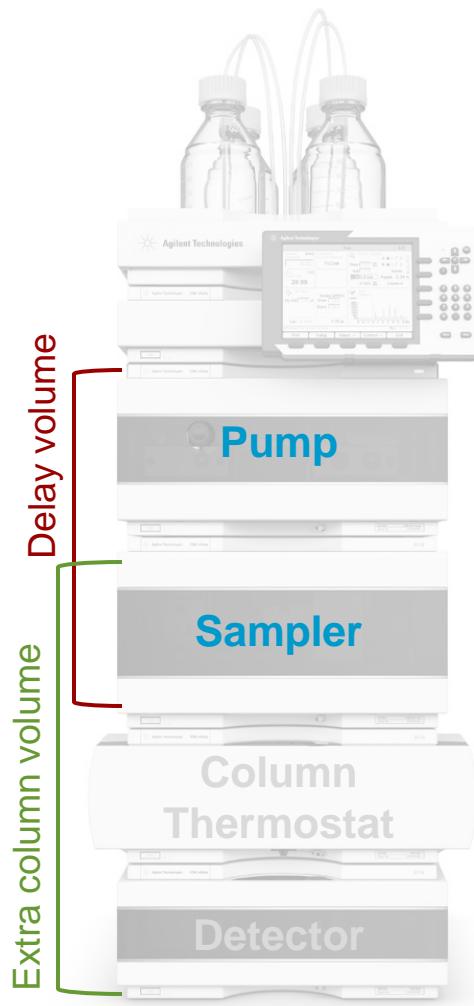
Instrument to Instrument Method Transferability

- *Important Parameters*



Instrument to Instrument Method Transferability

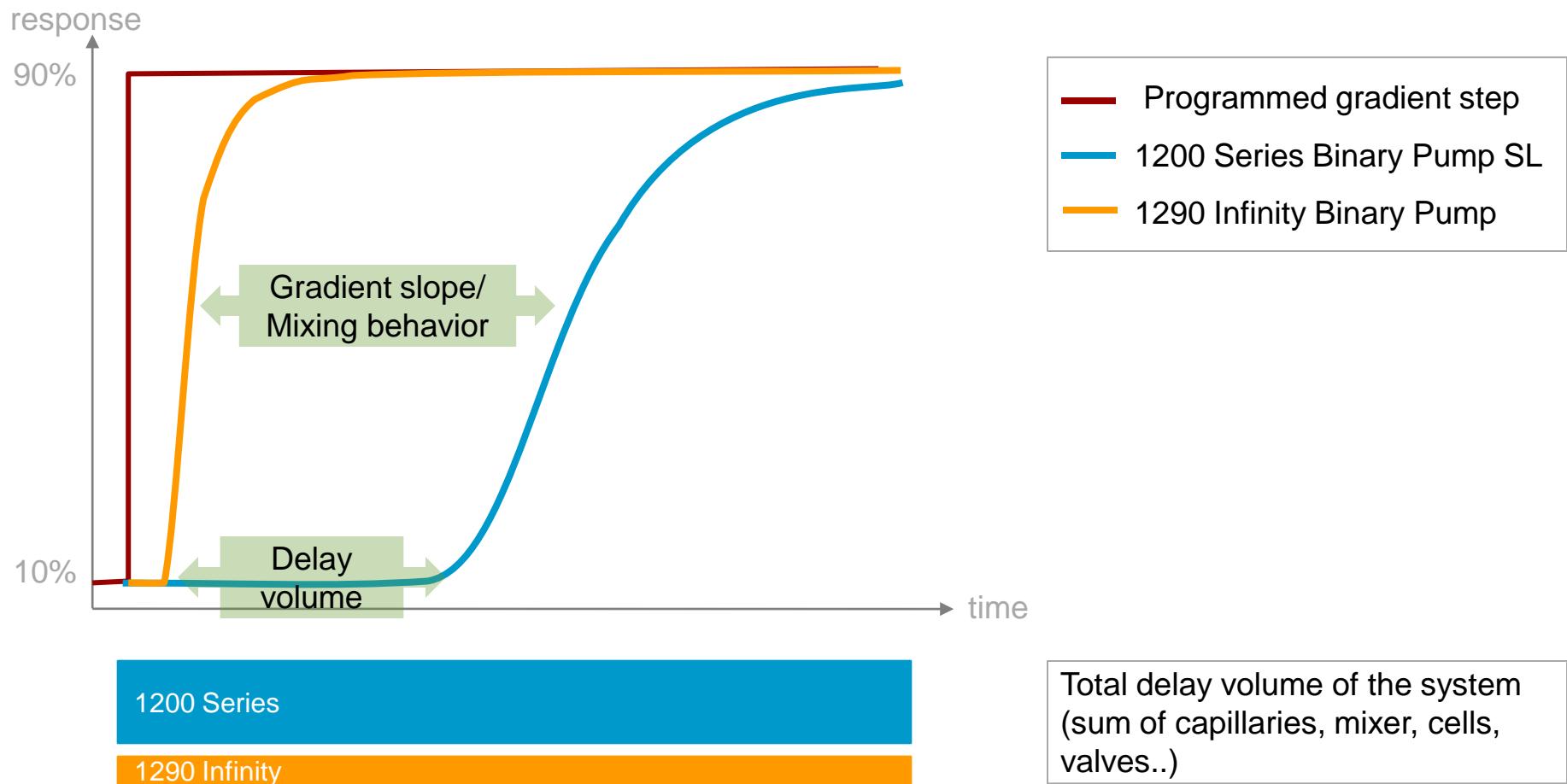
- *Important Parameters*



Instrument to Instrument Method Transferability

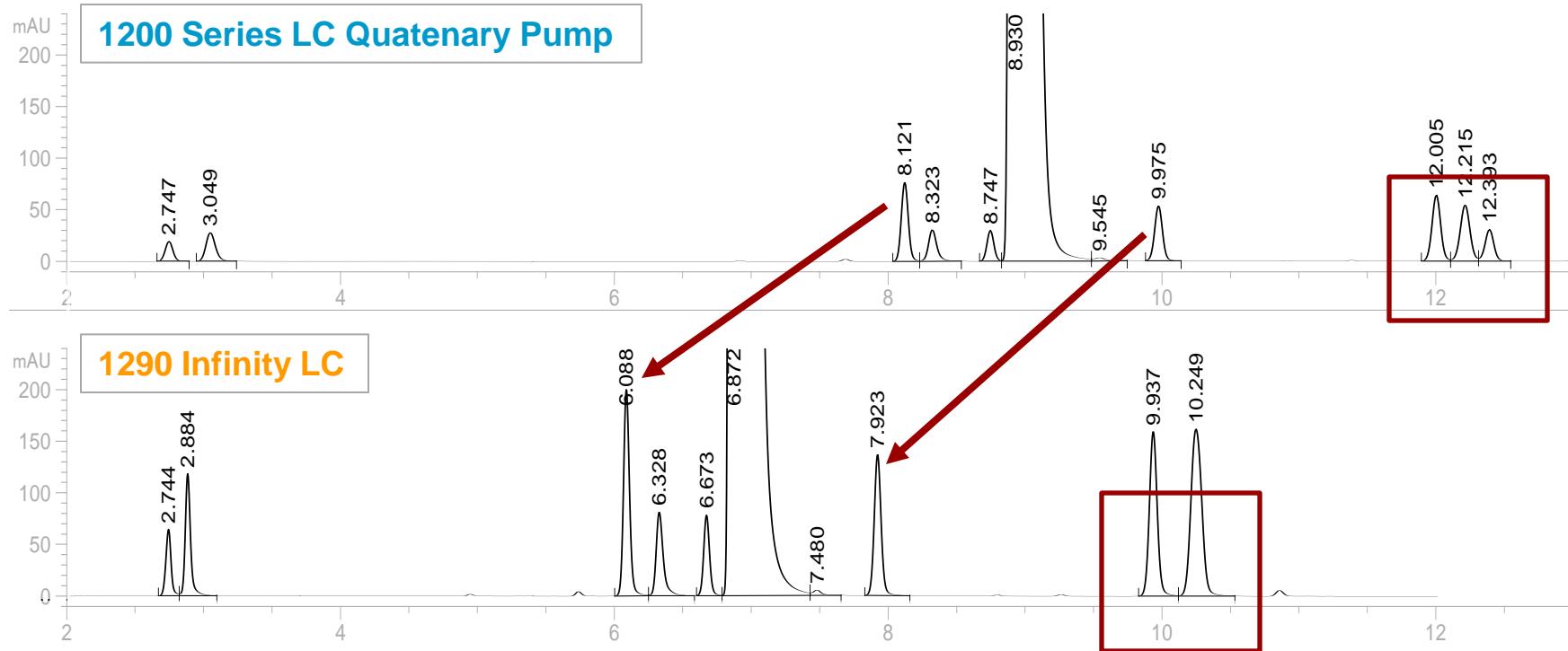
- Impact of delay volume and mixing behavior

What happens with a programmed gradient?



Gradient Analyses with Different LC Systems

- *Impact of delay volume and mixing behavior*



Sample: 0.5% impurities in formulation (metoclopramide)
Xbridge C18, 150x3 mm, 3.5 μ m dp,
0.45 ml/min, Eluent: A = 0.25 % AmAc, B = ACN,
Gradient: 0-15 min; 5-57 % B

The result:

- Difference in RT and Resolution
- One peak is missing!



Instrument to Instrument Method Transferability

- *What can you do today?*

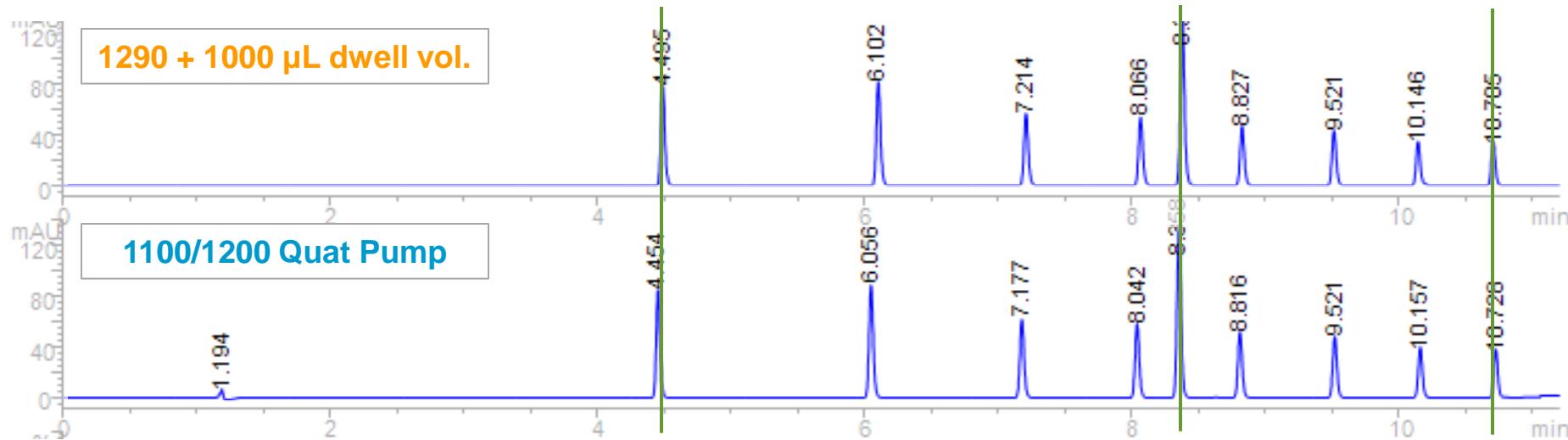
- From a *lower to higher* dwell volume LC system
 - A) Adding physical volume (plumbing solution)
 - B) Modifying your gradient table with isocratic hold
- From a *higher to lower* dwell volume LC system
 - C) Delay the injection (see appendix)



Method Transfer Possibilities Today

- A) Adding physical volume (plumbing solution)

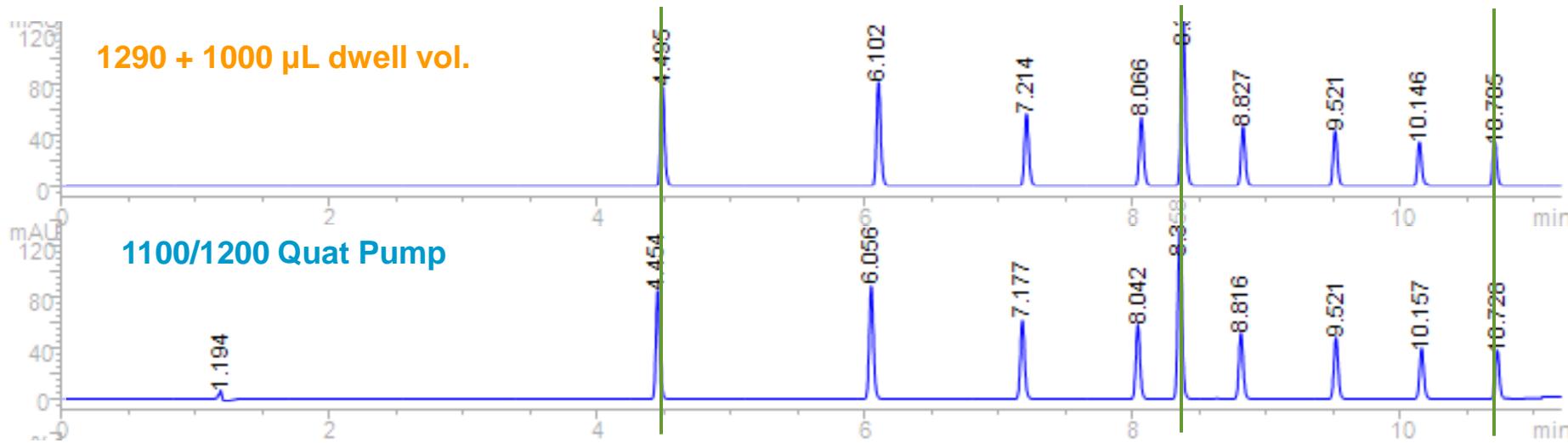
Example: 1290 Infinity LC



Method Transfer Possibilities Today

- A) Adding physical volume (plumbing solution)

Example: 1290 Infinity LC



Advantages

- Works well for not so fast analysis
- No Method change

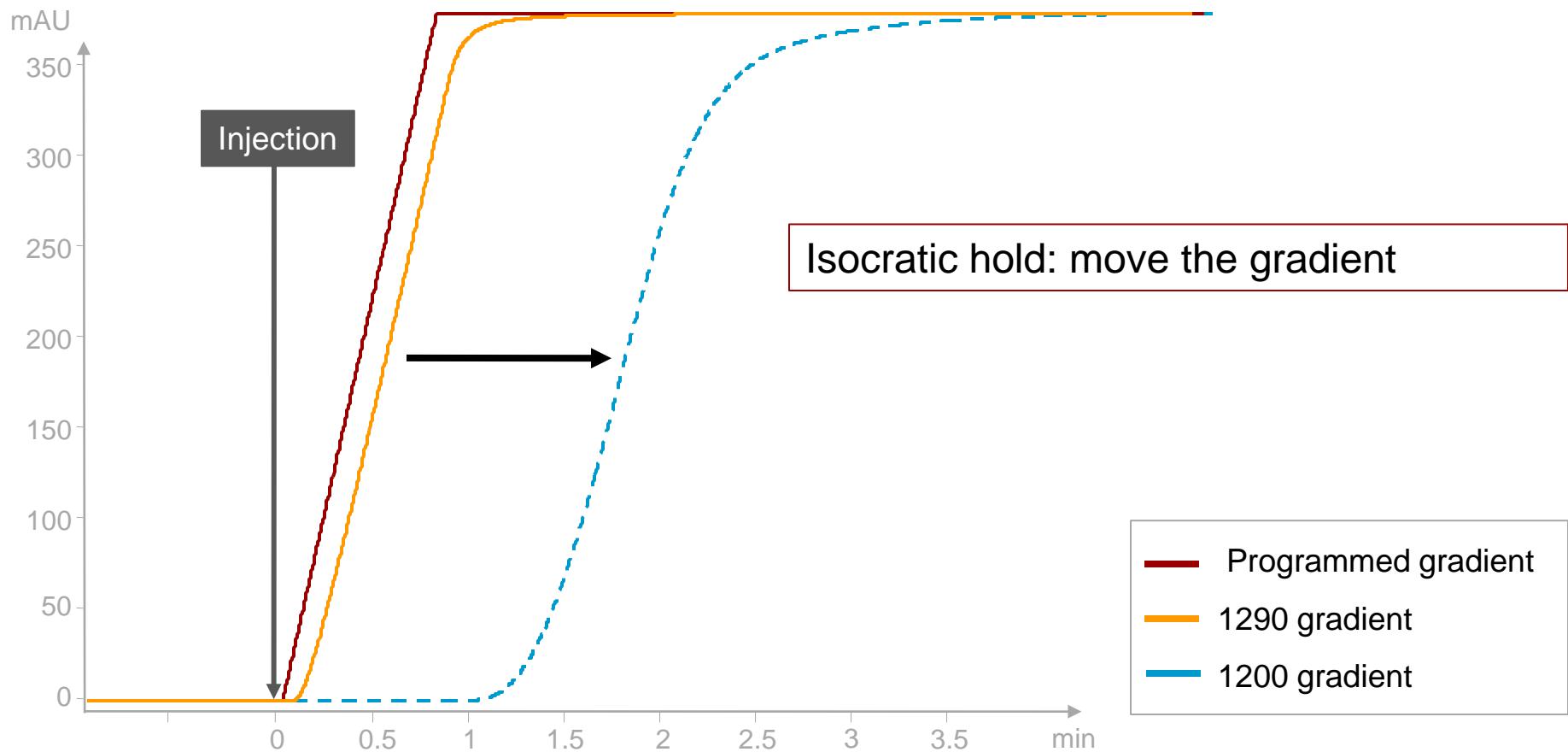
Disadvantages

- Requires hardware change, no flexibility
- Requires manual determination of the dwell volume (Pumps with damper the dwell volume is not constant and depends on pressure)
- Hardware change difficult in validated environment

Method Transfer Possibilities Today

- B) Isocratic Hold

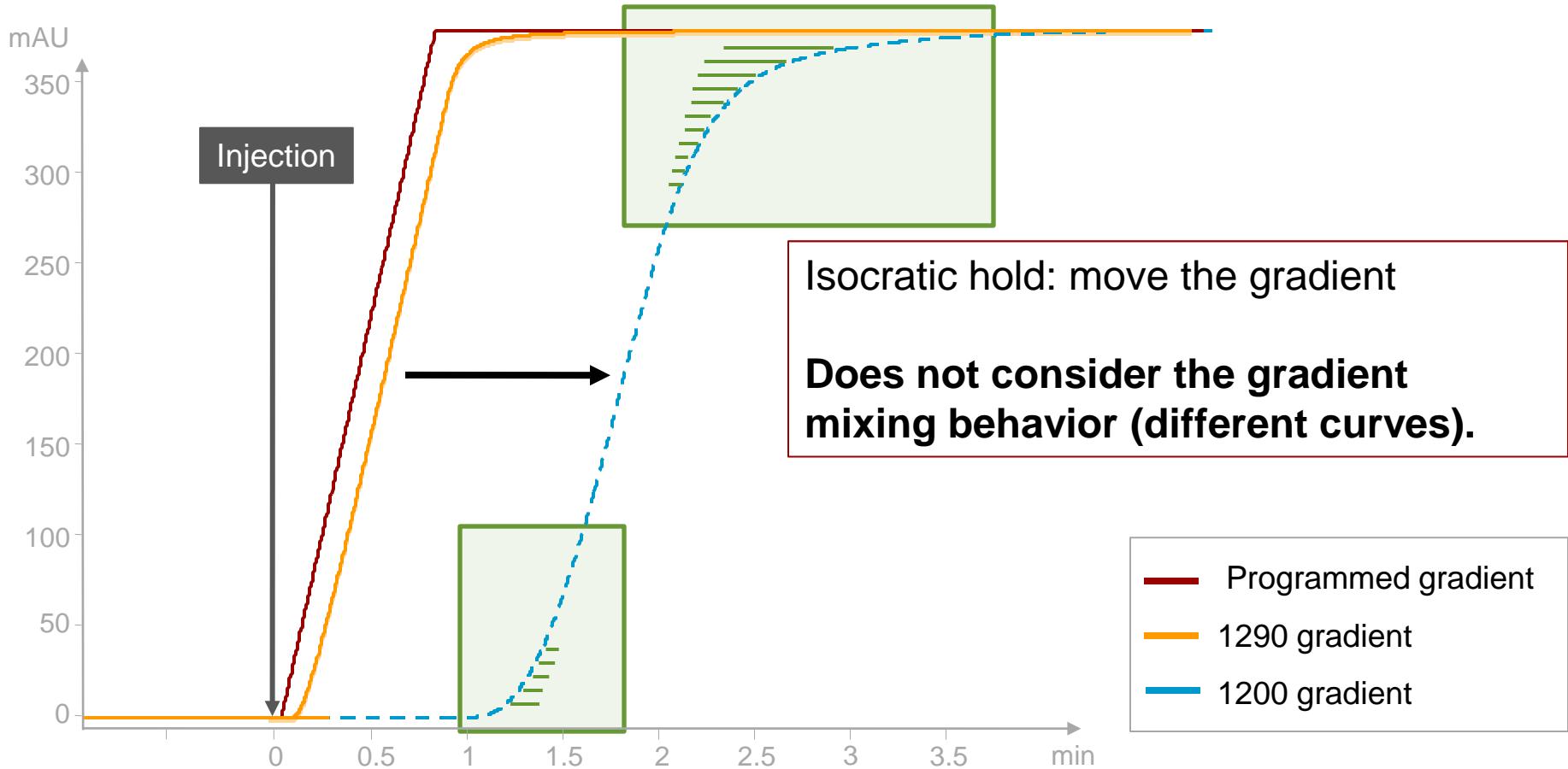
Example: 1290 to 1200



Method Transfer Possibilities Today

- B) Isocratic Hold

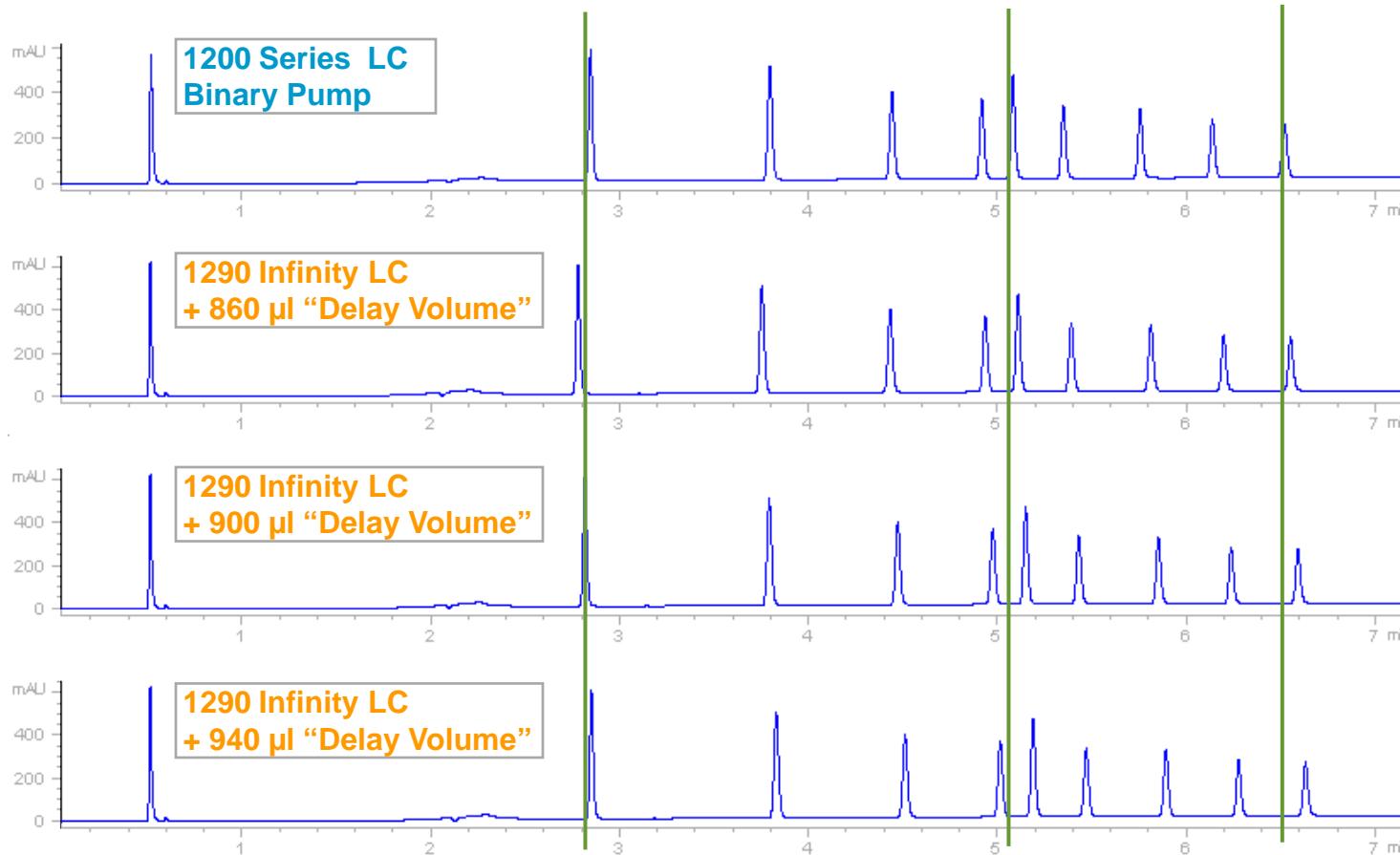
Example: 1290 to 1200



Method Transfer Possibilities Today

- B) Isocratic Hold

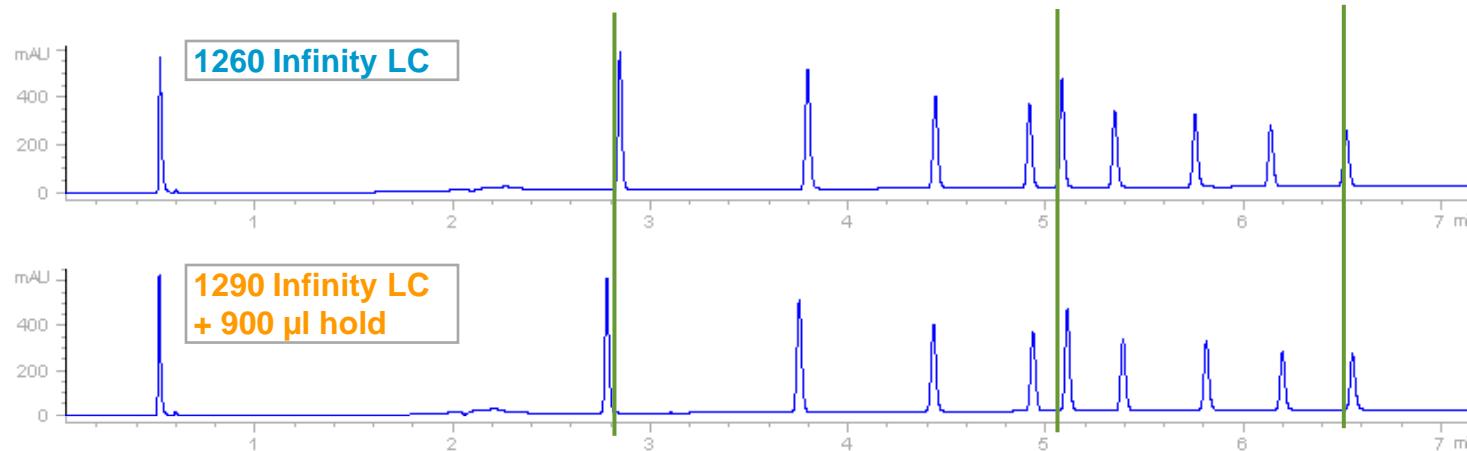
Example: 1290 to 1200



Method Transfer Possibilities Today

- B) Isocratic Hold

Example: 1290 to 1200



Advantages

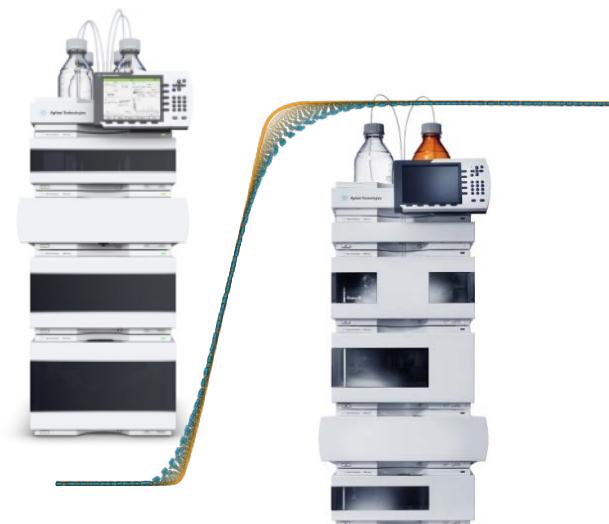
- Flexible, *Isocratic Hold* is part of the method

Disadvantages

- Works not in all cases
- Requires manual determination of the dwell volume/ isocratic hold (Pumps with damper the dwell volume is not constant and depends on pressure)
- Requires modification of the methods (should be avoided in validated environment, but doesn't require revalidation USP Chapter <621>)

NEW

Intelligent System Emulation Technology (ISET)



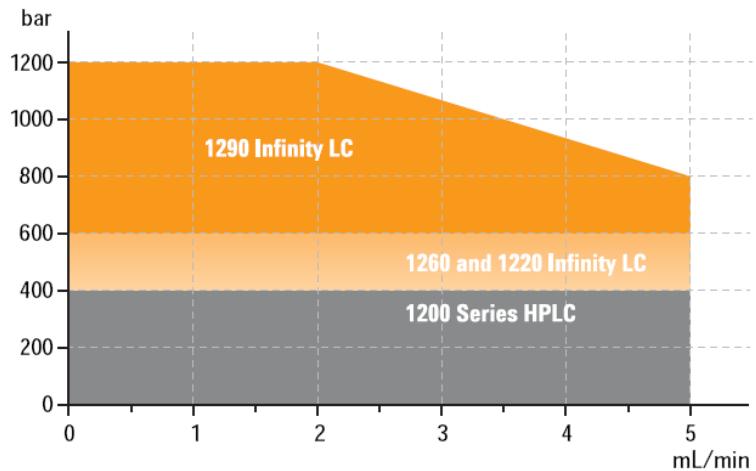
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What is ISET?

- *Two components*

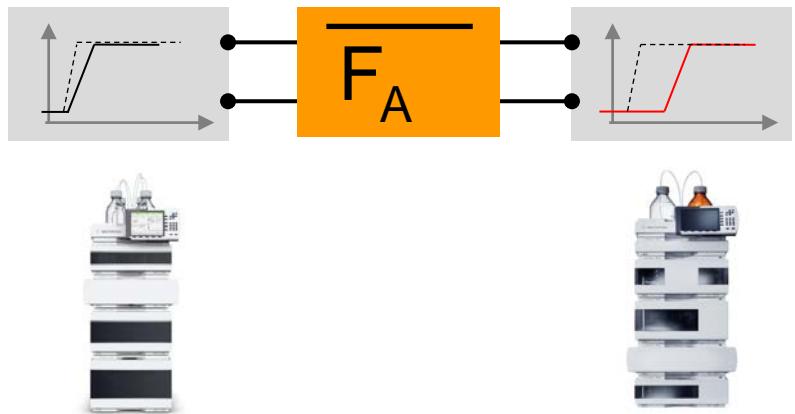
A. Best in class performance of the 1290 Infinity LC

Broad power range, ultra-low delay volume, superior sensitivity, unmatched flow and composition accuracy



B. The revolutionary ISET emulation algorithm

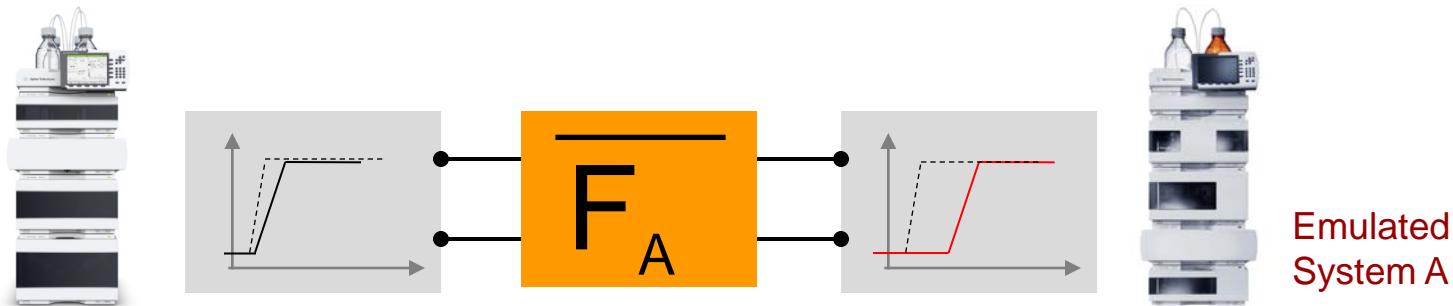
Full characterization of target LC systems
Creation of emulation function



Method Transferability: 1290 Infinity LC

- System Emulation Technology

Concept



Select System to be emulated by a simple mouse click:



Agilent
1100 Series



Agilent 1200
Series LC



Agilent 1260
Infinity LC



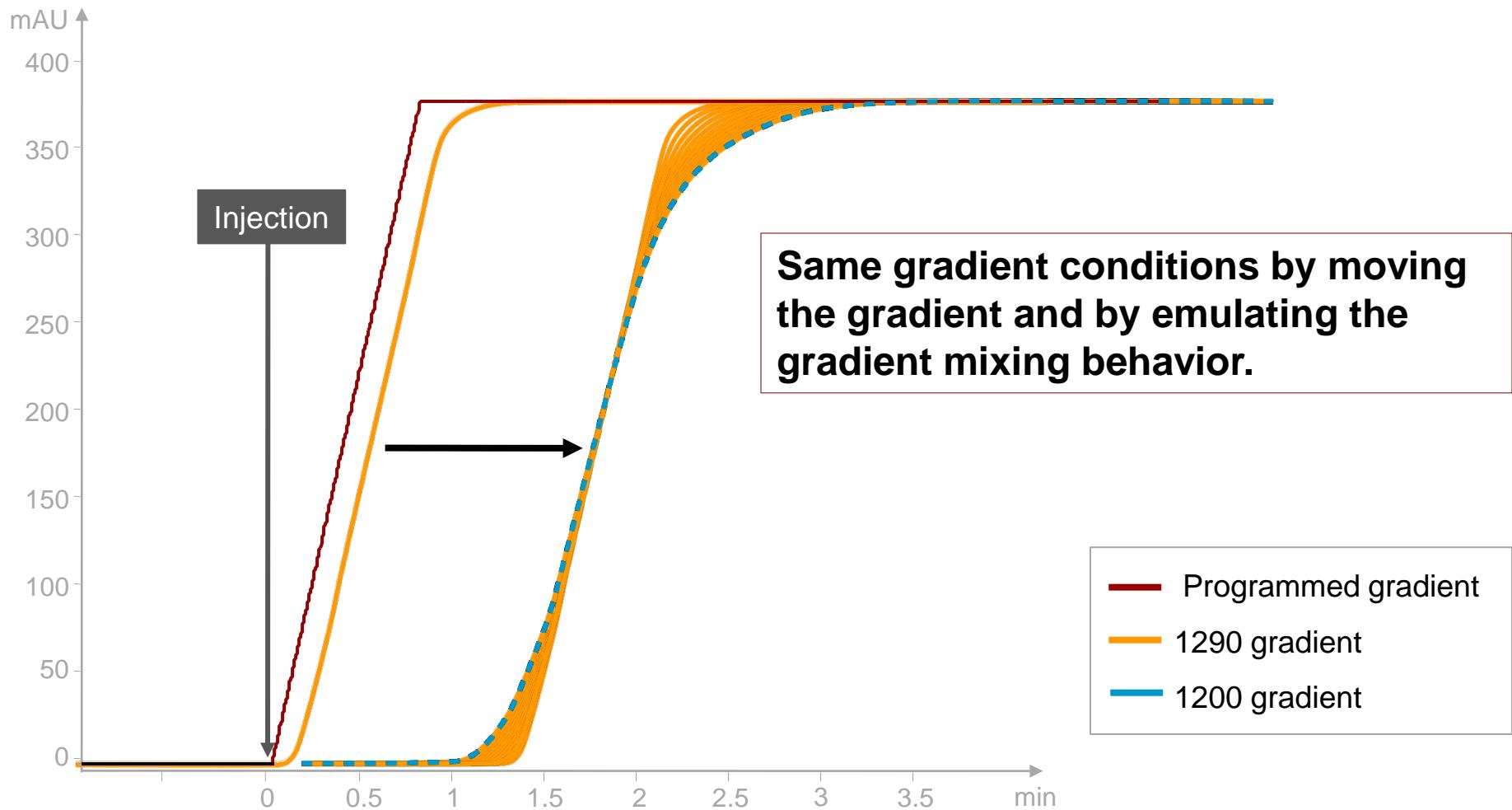
Agilent 1220
Infinity LC



Other

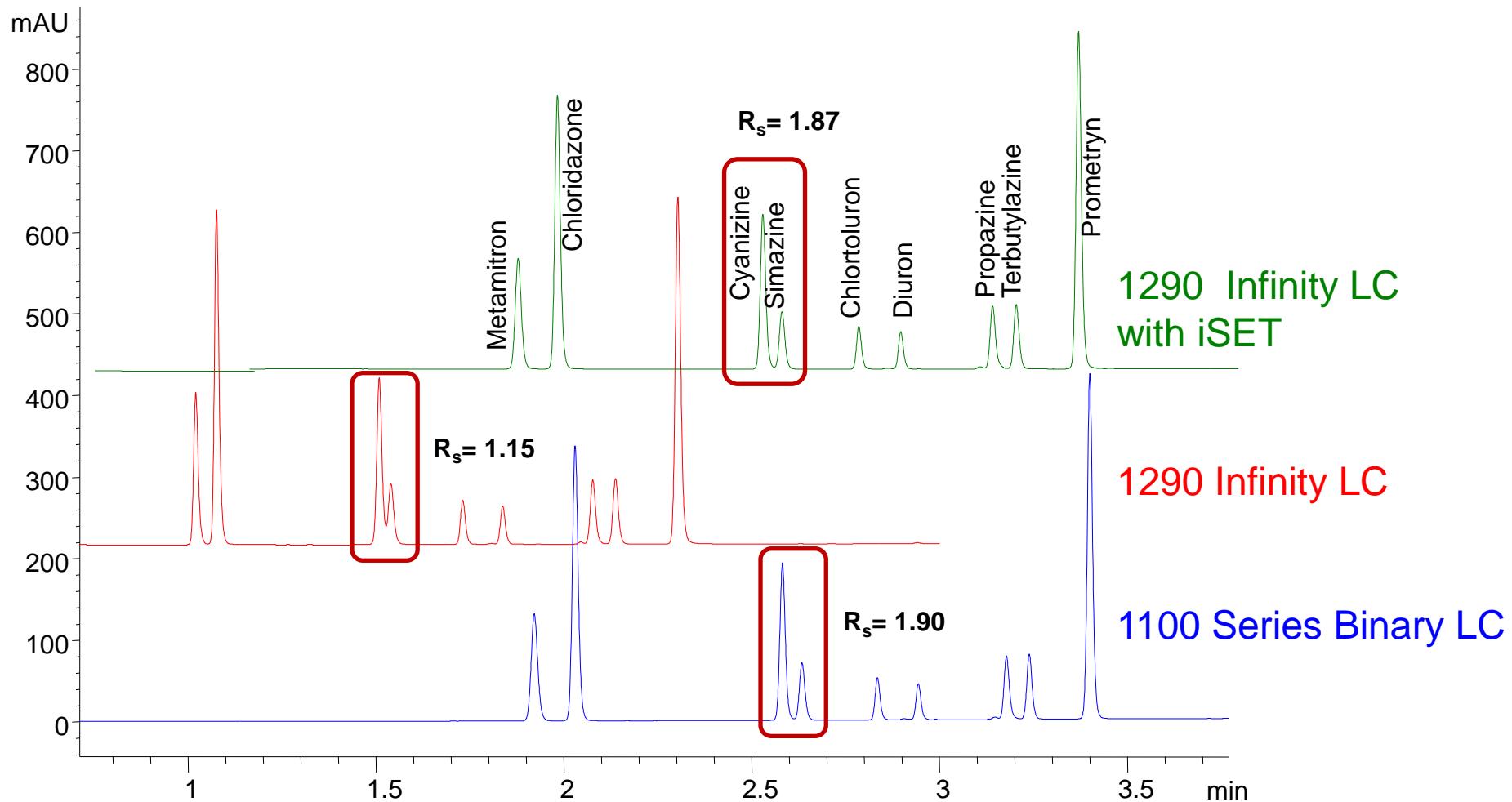
Intelligent System emulation technology

- How it works (1290 to 1200)



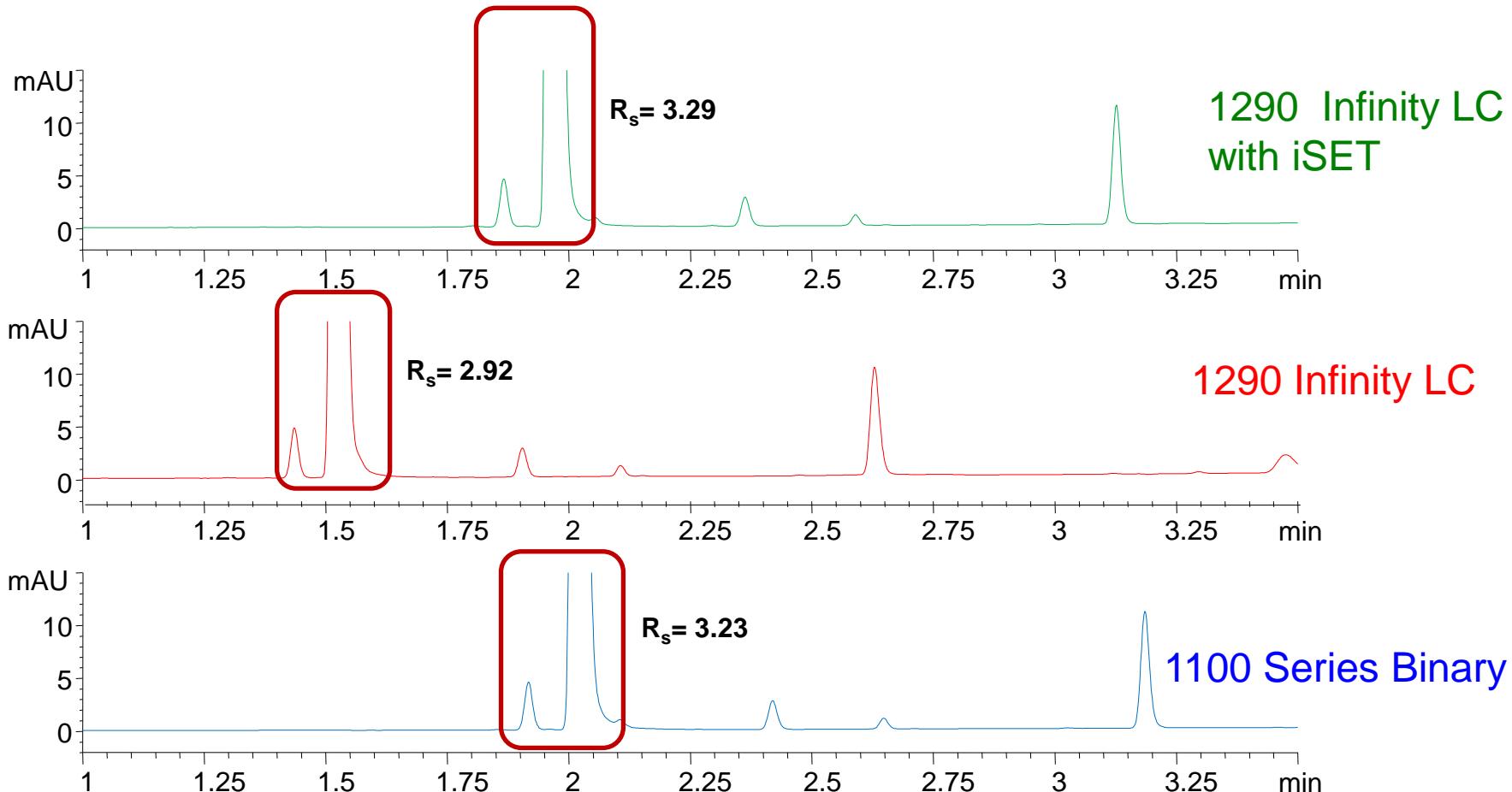
Pesticides

Column: 3 x 50 mm, 2.7 μ m Poroshell



Impurities analysis

Column: 4.6 x 50 mm, 1.8 μ m



LC Method Transfer Possibilities *Tomorrow*

- LC System Emulation Technology

Advantages

- Simple and flexible
(select the emulated LC system simply by a mouse click)
- No determination of the dwell volume etc. required
(perfectly covers pumps with damper and not constant dwell volume)
- Works perfectly in all cases
- Requires no modification of the methods
(no conflicts in regulated environment)



Intelligent System Emulation Technology ISET

- Benefits

➤ **Accelerate your method transfer**

No more method transfer problems! Simply emulate the LC system on which the original method was developed –with a single mouse click.

➤ **Make a safe investment**

Run your legacy methods with ISET and at the same time take full advantage of the UHPLC speed, resolution and sensitivity of the 1290 Infinity LC .

➤ **Achieve higher productivity**

Speed up your method development with UHPLC performance and then fine-tune your method by emulating the target system – and be confident that the method will run as intended.



Agilent 1290 Infinity LC with ISET inside

- *The Art of Emulation*

- **Emulates other (U)HPLC instruments**
 - *by a simple mouse click*
- **Runs existing (U)HPLC methods**
 - *without modifying method or system*
- **Delivers same retention times and peak resolution**
 - *for infinitely better method transfer*

