

Pump Program

No. of Gradient Steps: Time Precision:

No.	Step Name	Time State	Time - Lower Bound	Time - Upper Bound	% Strong Solvent	
<input checked="" type="checkbox"/>	1	Equilibration	Constant	1.00	---	5.0
<input type="checkbox"/>	2	Initial Hold	Variable	0.50	1.50	5.0
<input type="checkbox"/>	3	Gradient 1	Variable	1.00	3.00	35.0
<input checked="" type="checkbox"/>	4	Intermediate Hold	Constant	0.50	---	35.0
<input type="checkbox"/>	5					
<input type="checkbox"/>	6					
<input type="checkbox"/>	7					
<input checked="" type="checkbox"/>	8					
<input type="checkbox"/>	9					
<input checked="" type="checkbox"/>	10					

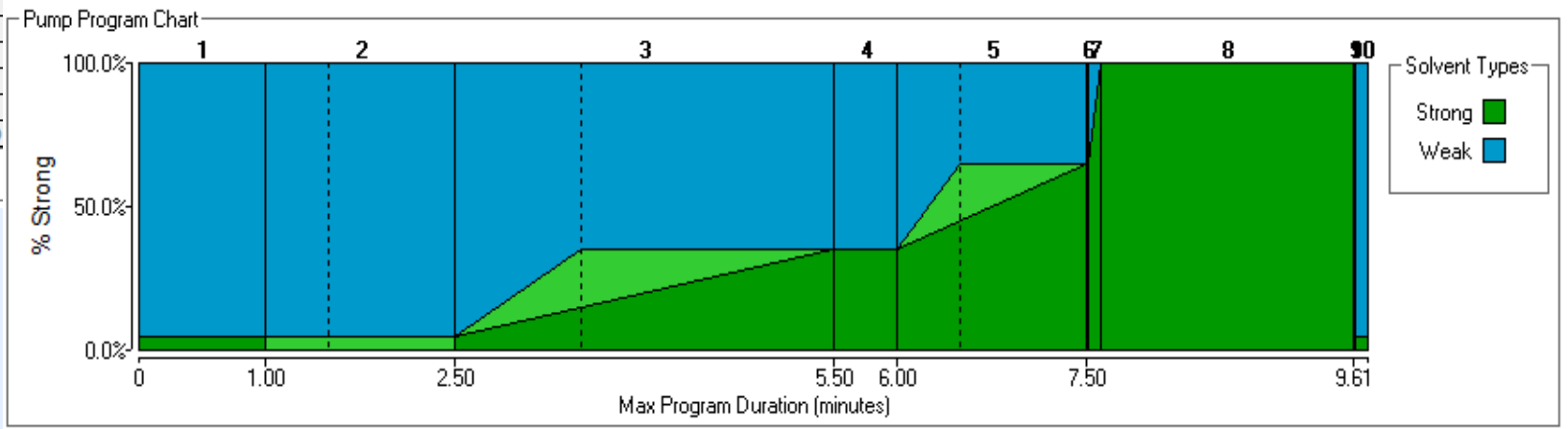
Gradient Study Factor: Gradient Time

Setting Mode: Time Slope

Gradient 1

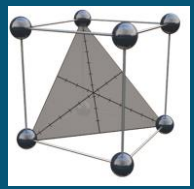
Time (min)	Slope (%/min)
1.00	30.00
2.00	15.00
3.00	10.00

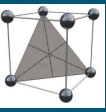
No. of Levels:



FUSION QBD[®] - GRADIENT STEPS

Variation Flexibilities in Classical DOE





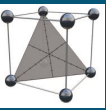
Beyond others, you can now include a **second gradient step** as a pump program variable in a single DOE experiment.

The following two options are available in Fusion QbD 9.9.2:

- (1) Varying Slope for both Gradients** in a single study by keeping initial and final %Strong Solvent constant.
- (2) Varying either initial or final % Strong Solvent of a Gradient and varying Slope for both Gradients.**

- ! Note, usually we ask our customers not to include any segments in the gradient ramp, as quality of the method might be compromised from that and in a multivariate experiment other optimization parameters than slope can often be used and should then be preferred.*
- But no rule without exceptions. Therefore in the case where it doesn't go without gradient steps, Fusion now provides more flexibility in including study factors from the pump program in your DOE experiment.

*Compare our technical note on segmented gradient.



Varying **Slope for both Gradients** in a single study by keeping initial and final %Strong Solvent constant

- (1) The example shows a gradient program, where **Initial Hold**, **Gradient 1** and **Gradient 2** are included as a study factor.
- (2) In addition the **Blending of two Strong Solvents** is included in the study.
- (3) The light green region stands for the study space. Prediction inside this region will be provided by such an experiment in all study factor combinations of the selected range.
- (4) Note: **Intermediate Hold Time** can be included as a study factor.

No. of Strong Solvents: No. of Weak Solvents:

OK to Blend Strong Solvents OK to Blend Weak Solvents Mobile Phase Precision

Mobile Phase Name	Solvent Type	State	Lower Bound	Upper Bound	Reservoir
Acetonitrile	Strong (Organic)	Variable	35.0	45.0	---
Methanole	Strong (Organic)	Variable	55.0	65.0	---
Aqueous Solution	Weak (Aqueous)	---	---	---	---

A D

B D-1 D-2 D-3

C D-4 D-5 D-6

Pump Program

No. of Gradient Steps: Time Precision

No.	Step Name	Time State	Time - Lower Bound	Time - Upper Bound	% Strong Solvent
<input checked="" type="checkbox"/>	1 Equilibration	Constant	5.00	---	5.0
<input type="checkbox"/>	2 Initial Hold	Variable	0.50	1.50	5.0
<input type="checkbox"/>	3 Gradient 1	Variable	1.00	3.00	45.0
<input checked="" type="checkbox"/>	4 Intermediate Hold	Constant	0.50	---	45.0
<input type="checkbox"/>	5 Gradient 2	Variable	0.50	1.50	---
<input type="checkbox"/>	6 Final Hold	Constant	0.01	---	65.0
<input type="checkbox"/>	7 Ramp Up to Wash	Constant	0.10	---	---
<input checked="" type="checkbox"/>	8 Column Wash	Constant	2.00	---	100.0
<input type="checkbox"/>	9 Ramp Down from Wash	Constant	0.01	---	---
<input checked="" type="checkbox"/>	10 Re-equilibration	Constant	0.10	---	5.0

Program duration: Min = 9.72 minutes, Max = 13.72 minutes

Gradient Study Factor: Gradient Time

Setting Mode: Time Slope Update

Gradient 1

Time (min)	Slope (%/min)
1.00	40.00
2.00	20.00
3.00	13.33

No. of Levels:

Gradient 2

Time (min)	Slope (%/min)
0.50	40.00
1.00	20.00
1.50	13.33

No. of Levels:

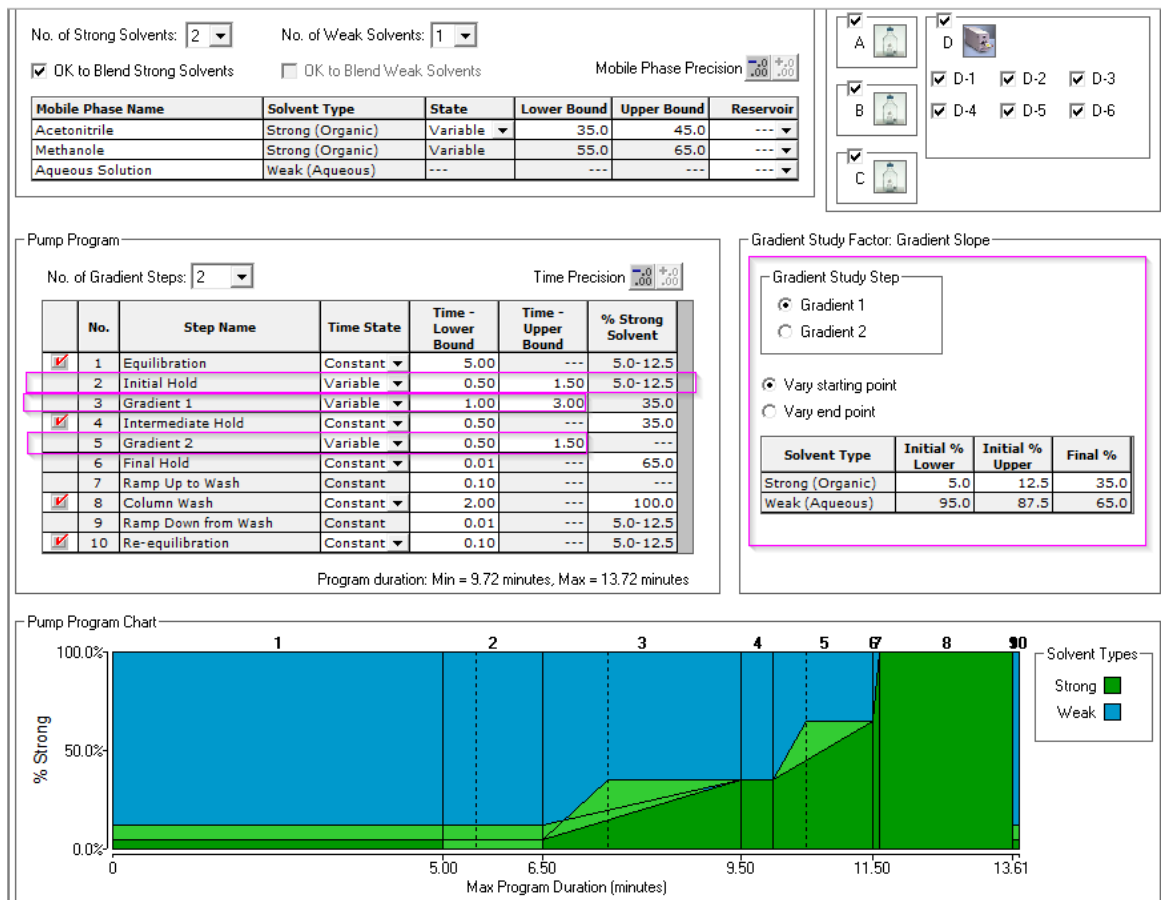
Pump Program Chart

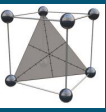
Legend: Solvent Types: Strong (Green), Weak (Blue)



Varying initial or final % Strong Solvent for a Gradient by varying Gradient Slope

- (1) The example shows a gradient program, where **Initial Hold**, **Gradient 1** and **Gradient 2** are included as a study factor.
- (2) In addition the **Variation of the Initial % Strong Solvent** and **Blending of two Strong Solvents** is included in the study.
- (3) The light green region stands for the study space. Prediction inside this region will be provided by such an experiment.
- (4) Note: You can decide to which Gradient the variation of the %Strong Solvent should be applied.





Robustness Simulation with multiple pump program related study factors

- (1) As the expected variation for all pump program related study factors finally results from the variation of the **Mobile Phase Composition** a new MPC Variable has been implemented that can serve as a single parameter for Robustness Simulation.

Robustness Simulator

Maximum Expected Variation ($\pm 3\sigma$):
The $\pm 3\sigma$ value defines the "total" setpoint error. This is the maximum variation around a given setpoint expected during ongoing use over time due to random error.

Maximum Expected Variation Around Setpoint for Each Variable

Setpoint

LCL

UCL

Δ

Maximum Expected Variation (Control Limit Delta = $\pm 3\sigma$)

IMPORTANT: Use manufacturer's specs for the setpoint Control Limit value or extend it based on the least-capable system in use.

$5\sigma = 99.7\%$

Study Variable

Variable Settings

Enabled	Experiment Variable	Units	Maximum Expected Variation ($\pm 3\sigma$ Value)
<input checked="" type="checkbox"/>	Acetonitrile	%	2.0
<input checked="" type="checkbox"/>	pH	*	0.15
<input checked="" type="checkbox"/>	Mobile Phase Composition (MPC)*	%	2.0

* - MPC variation is composition (blend) variation due to pump precision limits. A commonly used $\pm 3\sigma$ value = $\pm 2.0\%$.
The value you enter will be applied to all Gradient Slope factors (e.g., Time, Slope, and Ramp Steps) in the experiment design.

Select All Select None Restore

The settings are valid.

Back Next Cancel

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