Fusion QbD® – Interaction Effects

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Interaction Effects – ICH Q8(R2)

Sample and Mobile Phase Parameters

Design Space*:

The multidimensional combination and **interaction** of **input variables** (e.g., material attributes) and **process parameters** that have been demonstrated to provide assurance of **quality**.

LC Instrument Parameters

Robust Method Performance

* – Many recent documents dealing with Analytical QbD refer to the Analytical Method Design Space as the Method Operable Design Region (**MODR**).

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Interaction Effects – ICH Q8(R2)

Formal Experimental Design:

A structured, organized method for determining the

relationship between factors affecting a **process** ← **Method**

and the **output** of that process. Also known as “Design of Experiments”.

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Robust Method Performance

Interaction Effects

Pairwise Interaction Effects Explained

Pairwise (2-way) Interaction Effects

Pairwise interactions are the most common interactions occurring among standard LC method development parameters. A two-way interaction term has the general form:

$$X_i * X_j \qquad i \neq j$$

where X_i and X_j are two ***different*** study variables.

For example, for two variables X_1 and X_2, a quadratic model has the general form:

$$\hat{Y} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_1^2 + \beta_2^2 + \beta_{12}(X_1 * X_2)$$

where $\hat{Y}$ is the model-predicted response (e.g. R_s, Tailing, etc.), β_0 is the y intercept (the predicted response value when X_1 and X_2 = 0), and the β_i are the model term *coefficients* – the numerical estimates of the linear additive (independent) effects (β_1 and β_2), simple curvature effects (β_1^2 and β_2^2), and two-way interaction effect (β_{12}) of the two experiment variables on the response.

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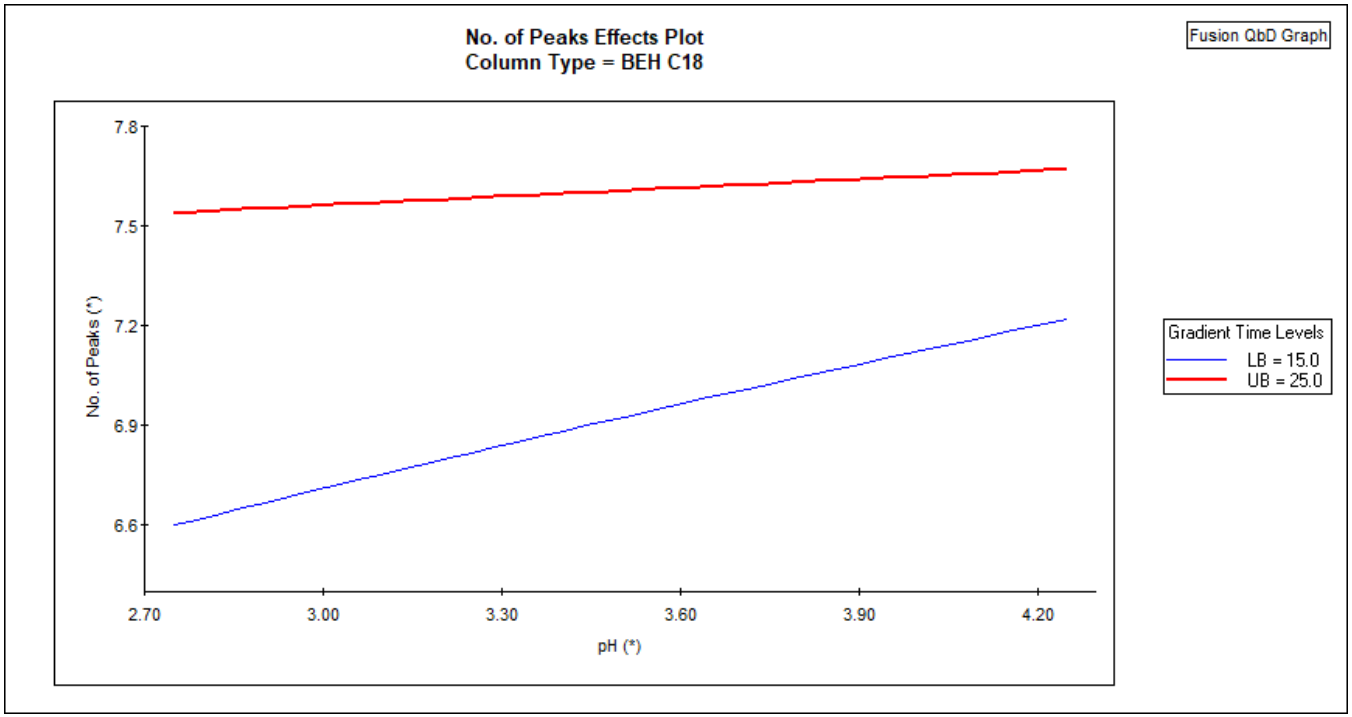
Pairwise Interaction Effect – pH and t_G

An interaction effect is a ***dependency*** between two (or more) variables – meaning that the effect of changing a variable on a given response is different at different levels of the other variable with which it interacts.

The graph below shows that effect of changing the pH across its range on the number of visualized (minimally separated) peaks is different for different t_G settings – i.e., the effect of pH ***depends*** on the t_G setting.



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Pairwise Interaction Effect – pH and t_G

The graph below demonstrates a different type of interaction effect between pH and t_G on the resolution of the largest peak ("Max Peak 1" = the API). As the graph below shows, a dependency between two factors can also extend to the curvature effects of the factors. The flexible modeling capability within Fusion QbD can include interaction terms of the form below to even characterize interactions affecting curvature:

$$\left(X_i^2\right)X_j \quad \text{I} \neq \text{j}$$