Fusion QbD® – Interaction Effects
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.

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

A structured, organized method for determining the relationship between factors affecting a process and the output of that process. Also known as “Design of Experiments”.

Robust Method
Performance

Interaction Effects
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:

$$X_i \times X_j \quad i \neq j$$

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:

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

where $\hat{Y}$ is the model-predicted response (e.g. $R_s$, Tailing, etc.), $\beta_0$ is the $y$ intercept (the predicted response value when $X_1$ and $X_2 = 0$), and the $\beta_i$ are the model term coefficients – the numerical estimates of the linear additive (independent) effects ($\beta_1$ and $\beta_2$), simple curvature effects ($\beta_1^2$ and $\beta_2^2$), and two-way interaction effect ($\beta_{12}$) of the two experiment variables on the response.
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 tG settings – i.e., the effect of pH depends on the tG setting.
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:

$$(X_i^2)X_j\quad 1 \neq j$$