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StatLIA®

FULL LOGISTIC CURVE PARALLELISM

Full curve parallelism analyzes the parallelism of the entire dilution curves, including both linear and non-linear regions. This method provides greater accuracy, reliability, and assurance that all corresponding areas of bioactivity in the reportable range are included in the parallelism analysis.

Parallelism Methodology Used in StatLIA

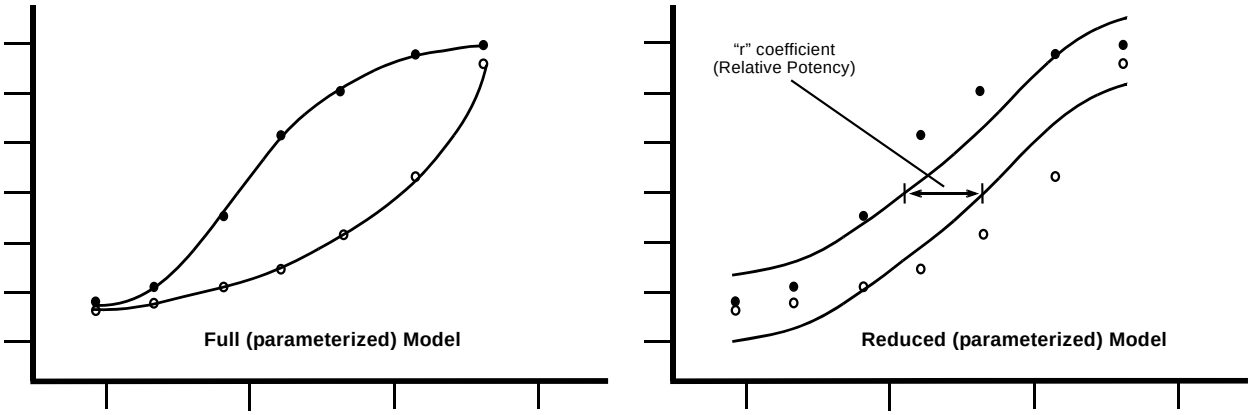

Figure 1. *In the Full Model, two sets of parameters (one for each curve) are computed to provide a best fit for each curve. In the Reduced Model, the same curve parameters (and shape) are used to provide the best curve fit for both sets of data points. The relative potency ("r" coefficient) in the Reduced Model defines the difference in position between the two curves. (The more parallel the curves, the better fit the same curve will have for both the unknown dilution and standard data points.) The error is computed between all of the data points and their respective curves in each model to measure any significant difference in the total error between the two models. If the curves are parallel, then the error between the data points and their respective curves will be insignificant. If they are not parallel, as illustrated above, then the error between the data points and the curves in the Reduced Model will be significantly larger than the error in the Full Model.*

StatLIA uses powerful weighted logistic curve fitting models and robust statistics to measure full curve parallelism, which can be summed up into 3 basic steps:

1) StatLIA computes the error (Sum of Squares Error or SSE) between the data points and the curve fits for both the unknown dilution and standard curves.

(StatLIA makes these computations for each curve by using a *Full* parameterized model. (*See Figure 1.*) If a 5 parameter curve fit model is selected for the test method, the Full model uses 10 parameters, 5 for each curve. If a 4 parameter is selected, then the Full model uses 8 parameters, 4 for each curve.)

2) StatLIA also computes the error between the data points and both curves using the same parameters, or curve fit, for both the unknown dilution data and the standard data. This is called the Reduced model in StatLIA and includes only the 5 (or 4) parameters in a logistic model and an additional "r" parameter for relative potency, which defines the distance along the x-axis between the two curves. StatLIA computes the best fit curve to accommodate both sets of data points. (If the curves are parallel, then a single curve fitting model should fit both sets of data the same.)

3) StatLIA measures the difference between the error (SSE's) in the Full parameterized model and the error in the Reduced parameterized model. If both curves are parallel, then the difference in error between the two models will be acceptable. If they are not parallel, then the error will be significantly different.

(To determine whether the difference in error is acceptable or statistically different, StatLIA uses a chi-square methodology for computing the parallelism. Using the well characterized extra-sum-of-squares approach, this method provides, for the first time, a direct measure of the amount of nonparallelism. StatLIA computes both a χ^2 Statistic and a χ^2 Probability.)

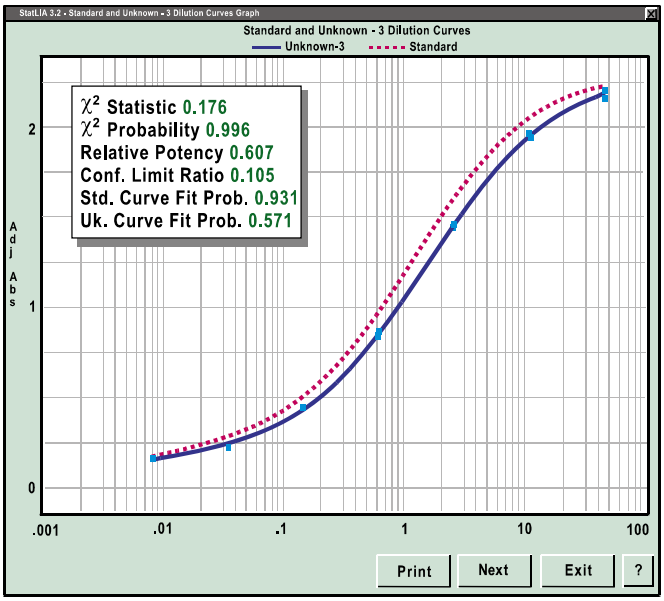

Figure 2. *StatLIA graphs the Full (parameterized) Model, as shown, with the unknown dilution curve and data points (solid line and boxes) and standard curve (dotted line). For parallelism analysis, a 5 parameter or a 4 parameter logistic model can be selected for the curve fitting. In addition to the parallelism analysis (χ^2 Statistic and χ^2 Probability), StatLIA automatically calculates IC25, IC50, IC75, Relative Potency and Confidence Limits, Fit Probabilities to measure the reliability of the standard and unknown dilution curves, Maximum Response, Minimum and Maximum Detectable Concentrations, and much more.*

Reference. ***Measuring Parallelism, Linearity and Relative Potency in Bioassay and Immunoassay Data***, *Gottschalk PG, Dunn JR*, Journal of Biopharmaceutical Statistics, *2005; 3:437-463.*

Importance of Weighting

Weighting is used to compute the expected variance of each data point in the standard and unknown dilution curves. The weighting for each assay is based on either a default weighting, a user-defined weighting, or one computed by StatLIA based on the lab's own data. After running a sufficient number of assays, the laboratory can use StatLIA to automatically determine an optimum weighting function and coefficients from among 16 different weighting functions for each test method. (The default weighting is used unless changed by the laboratory.)

Weighting is a measurement of the acceptable variation normally observed for each data point on the standard and unknown dilution curves. The weighting is needed to adjust the sensitivity of the parallelism computations by reflecting the appropriate variance inherent for each test methodology.