Taking a deeper look into MDC and RDL

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The Minimum Detectable Concentration (MDC) and Reliable Detection Limit (RDL) are important measures of assay performance. The MDC for an increasing curve is defined as the lowest concentration which results in an expected response significantly greater then the expected response at 0 concentration. RDL is defined, again for an increasing curve, as the lowest concentration that has a high probability of the producing a response that is significantly greater than the response at 0. Below we outline the mathematical details of MDC and RDL. Note for the purposes of this discussion we restrict our attention to increasing curves.

For m replicates at each concentration x_i the estimated (1 - α)% confidence interval (CI) for the four parameter logistic (FPL) model, $f(x_i, \hat{\beta}) = \hat{\beta}_2 + (\hat{\beta}_1 - \hat{\beta}_2)/[1 + (x_i/\hat{\beta}_3)^{\hat{\beta}_4}]$ (or the alternative log parameterization of the FPL model, which is the same as the latter but replacing β_3 with β_3^* where $\beta_3^* = \exp\beta_3$) are given by

$$\mathrm{lcl}_\alpha(x_i, \hat{\beta}) = f(x_i, \hat{\beta}) - t_{1-\alpha/2,\mathrm{df}} \times q_{nm}$$
$$\mathrm{ucl}_\alpha(x_i, \hat{\beta}) = f(x_i, \hat{\beta}) + t_{1-\alpha/2,\mathrm{df}} \times q_{nm}$$

where

$$q_{nm} = \hat{\sigma}\sqrt{1/m + f_\beta^T(x)\hat{\Sigma}f_\beta(x)}$$

Here, $f_\beta(x)$ denotes the gradient vector of the FPL function $f(x, \hat{\beta})$ at x, $\hat{\Sigma}$ is the estimated covariance matrix for $\hat{\beta}$, unscaled by $\hat{\sigma}$; and $t_{1-\alpha/2,\mathrm{df}}$ is the $(1-\alpha/2)$% point of the t-distribution with df $=$ $N - 4$ degrees of freedom where n is the total number of obervations.

A row of the gradient matrix $f_\beta(x)$ is

$$\begin{aligned} f_\beta(x) &= \frac{\partial f(x)}{\partial \beta} \\ &= \Bigg(\frac{1}{(x/\beta_3)^{\beta_4}}, 1 - \frac{1}{(x/\beta_3)^{\beta_4}}, \\ & \frac{(\beta_1 - \beta_2)(\beta_4/\beta_3)(x/\beta_3)^{\beta_4}}{[1 + (x/\beta_3)^{\beta_4}]^2}, \\ & \frac{-(\beta_1 - \beta_2)(x/\beta_3)^{\beta_4}\log(x/\beta_3)}{[1 + (x/\beta_3)^{\beta_4}]^2} \Bigg) \end{aligned}$$

For power of the mean variance model (POM)

$$\hat{\Sigma} = [f_\beta(x)^T \mathbf{G}^{-1} f_\beta(x)]^{-1}$$

where $\mathbf{G}$ is a $(n \times n)$ diagonal matrix with elements $f(x_i, \hat{\beta})^{2\hat{\theta}}$, $i = 1, \ldots, n$. This reduces to the constant variance model for $\mathbf{G} = \mathbf{I}$, where $\mathbf{I}$ is the identity matrix.

With the above notation and derivation we are now able to explicitly define the MDC and RDL. Taking the physical definition of MDC and RDL from above we write

$$x_{\text{MDC}} = \min\{x : f(x, \hat{\beta}) > \text{ucl}_\alpha(0, \hat{\beta})\}$$
$$x_{\text{RDL}} = \min\{x : \text{lcl}_\alpha(x, \hat{\beta}) > \text{ucl}_\alpha(0, \hat{\beta})\}$$

The MDC has the following analytic solution

$$x_{\text{MDC}} = \left(\frac{\beta_1 - \text{ucl}(0, \hat{\beta})}{\text{ucl}(0, \hat{\beta}) - \beta_2}\right)^{1/\beta_4} \times \beta_3$$

The extension to the log parameterization of the FPL model is straightforward. The RDL on the other hand does not have an equivalent closed form solution.