Parametric Linear Regression: Accuracy and Power Simulations

(for Windows NT/95 and later)

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Regression Accuracy and Power Simulations (RAPS.exe)

This program assesses the accuracy and power of parametric linear regression using X, Y pairs randomly generated by the program itself, or imported X, Y pairs generated externally by the user. The program incorporates ordinary (unweighted) least squares regression (OLS), iteratively reweighted least squares regression (WLS) and iteratively reweighted Deming (1) regression (errors in X and Y). Significance testing is based on confidence intervals for slope and intercept and also the joint slope, intercept confidence region and is primarily concerned with contrasting these two approaches; in particular the improved statistical power that can be realised in most situations by using the joint confidence region rather than confidence intervals.

This document gives a broad description of the program. The fine detail of using the program is given in program on-line help. A brief popup description of all controls on all dialogs can be obtained by pressing F1 when the control has focus, or by clicking the right mouse button over the control (provided it is enabled), or by using the ? icon at the top right of the dialog. All dialogs have a Help button which gives access to detailed information about the dialog. Print copies of help topics as required.

Confidence Intervals and Regions

Figure 1 illustrates the results of a sampling experiment in which OLS was applied to 50 sets of randomly drawn X, Y pairs from a hypothetical Y = X relationship. The characteristic ‘bow-tie’ appearance (the same pattern is seen with WLS and Deming regression). Highest values of slope are associated with lowest values of intercept and vice versa. High values of slope and intercept are not jointly observed. Likewise, low values of slope and intercept are not jointly observed. Figure 1 illustrates the correlation of slope and intercept. For any given error characteristics, the smaller the range of X-values the higher the slope, intercept correlation (increasingly pronounced bow-tie shape). Conversely, increasing the range of X-values reduces slope, intercept correlation.

![Figure 1. Results of OLS regression on 50 sets of X, Y values (each N = 20) randomly drawn from a hypothetical Y = X relationship. X-values were concentrated in the central part of the range and Y-values were drawn from a Gaussian distribution with SD = 10% of the range of the X-values. The dashed line is the line of identity.](image)

![Figure 2. Slope, intercept parameter space typically observed with a narrow range of X-values (high slope, intercept correlation). The data point represents the estimated slope and intercept and is accompanied by slope and intercept confidence intervals (dashed lines) and corresponding joint slope, intercept confidence ellipse.](image)

Confidence intervals and regions are identical in the sense that in sampling experiments, such as illustrated in Fig. 1, a specified proportion of intervals and regions (depending in the significance level) are expected to enclose the true underlying [slope, intercept] point (eg. the point [1, 0] in the case of Fig. 1). Either could be used as the basis of significance tests. Intuition suggests that the confidence region is preferable because it takes account of parameter correlation, but there is a further consideration. The usual purpose of significance tests is to detect differences from a hypothetical X, Y relationship (such as the line of identity) and this is determined by the failure of confidence intervals or confidence regions to enclose the hypothetical [slope, intercept] point. The relative shapes in Fig 2 clearly indicate that confidence ellipses will detect smaller horizontal or vertical shifts.
from a target point (pure proportional bias and pure constant bias, respectively). A mixture of constant and proportional bias is represented by diagonal differences from a target [slope, intercept] point and it is true that if the difference we are seeking to detect has slope and intercept values that lie roughly along the major axis of the confidence ellipse, then confidence regions may have slightly reduced power relative to confidence intervals. Overall, however, the use of confidence regions can be expected to confer substantially improved statistical power, particularly with narrow range data. This implies the ability to detect smaller differences with a given sample size (N) or, alternatively, require smaller sample sizes to detect a specified difference.

The idea of using the joint parameter confidence region is far from new. Thirty years ago Munson and Rodbard wrote an excellent paper (2) advocating the use of confidence regions in an immunoassay context. Moreover, a number of text books give general guidelines for the calculations (eg. Refs. 3, 4). However, for one reason or another, confidence intervals appear to have become entrenched as the standard mode of significance testing in medical laboratory regression analysis. This computer program is a tool for acquiring a feel for the properties of confidence regions and can also be used to formally estimate necessary sample size by simulating data whose properties are based on the range and error characteristics of real method comparison data. A separate computer program (5) estimates variance (weighting) functions and offers OLS, WLS and Deming analysis of real data, including plots of joint parameter confidence regions at user defined significance levels.

To give a more complete picture, Fig. 3 illustrates a typical parameter space when the maximum:minimum ratio of X-values is several thousand-fold (very low slope, intercept correlation). In these cases the more circular joint confidence region confers no statistical power advantage. However, Fig. 3 illustrates an extreme case that is only likely to be relevant for a small number of medical laboratory analytes measured by immunoassay.

**Figure 3.** Slope, intercept parameter space typically observed with a very wide range of X-values (low slope, intercept correlation). The data point represents the estimated slope and intercept and is accompanied by slope and intercept confidence intervals (dashed lines) and corresponding joint slope, intercept confidence ellipse.

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### Accuracy

Accuracy in this context refers to the reliability of recovery of the slope and intercept values that were used to generate sets of paired X, Y data and also the concordance between expected and observed frequencies of confidence intervals and confidence regions enclosing target values. Figure 4 illustrates the program Accuracy dialog. Use the Data box to specify properties of the X, Y data that the program will randomly generate, or to import X, Y pairs generated externally. Use the Regression Type and Weighting box to specify error properties of the Y-variate (OLS or WLS) or both the X- and Y-variates (Deming). An explanation of how to specify error properties is given in program on-line help. The lower panel displays the current date and time. Use the adjacent buttons to produce a permanent copy of the design and outcome of a simulation run by copying an image of the dialog to the Windows clipboard for subsequent pasting into another application, such as Word, or directly printing an image of the dialog.

### Power

The program Power dialog, illustrated in Fig. 5, follows the same principles. Data can be either generated by the program or imported from an external source. The focus here is on the Actual slope and intercept values which are used by the program to generate sets of data. The resulting confidence intervals and regions are assessed for enclosure of the Target slope and intercept values. The issue is the sample size required to reliably detect a difference between Actual and Target (hypothetical) values when such a difference actually exists. The program offers automatic sample size determination (as illustrated).

It is important to appreciate that since the program is based on randomly generated data, there will always be some variation between results of simulation runs of the same design. Obviously the larger the number of samples and/or sample size (N), the smaller the run-to-run variation in outcomes, and vice versa. The manual sample size option on the Power dialog can be used repetitively to quickly get a feel for the variation associated with a particular design and sample size.
Figure 4. The program Accuracy dialog illustrating the options available, plus the results from an OLS simulation run using data generated by the program according to the Data box specifications.

Figure 5. The program Power dialog illustrating a simulation run which automatically determined the smallest sample sizes (confidence intervals versus joint confidence region) necessary to achieve 90% detection of a statistically significant difference (p < 0.05) when the hypothetical slope is 1 and the actual slope is 1.01 (i.e. 1% proportional bias). In this OLS example, uniformly distributed (error-free) X-values cover a 10-fold range and Y-values were randomly drawn from a Gaussian distribution with variance = 1.
**External Data**

Externally generated data must be presented in the form of a text file with a single $X$, $Y$ pair on each line. The $X$, $Y$ values must be separated by a single character (any character can used except 0 – 9, + (plus), - (minus) or period). The intention is allow distributions of $X$-values that are more extreme than those offered by the program and which may more accurately reflect real data. In the Accuracy dialog the option is given to either randomly draw $X$, $Y$ pairs from the imported data or to draw sequential sets of $X$, $Y$ pairs of a specified size. The latter could be used to compare results produced by this program with those produced elsewhere with the same data.

Data generated by the program are randomly drawn from Gaussian distributions with precise error properties as defined in the Regression Type and Weighting box. Consequently, weighting functions used in subsequent calculations are exact. Data generated by the program represent an ideal situation. Imported data could be used to systematically assess the effect on both accuracy and power, of data drawn from non-Gaussian distributions, or the misspecification of errors, eg. generate and import data with certain error properties, then test the effect of deliberately specifying alternative error properties in the Regression Type and Weighting box.

**Simulations versus Direct Calculation**

Linnet (6) studied the statistical power of regression analysis in medical laboratory method comparison studies and drew attention to the fact that required sample sizes might be larger than generally realised. He derived power formulae which allow direct calculation of minimum sample sizes based on the use of confidence intervals. The high accuracy of Linnet’s equations is easily confirmed using simulation results from this program. However, Linnet’s equations assume identical $X$ and $Y$ errors and are restricted to cases of either constant variance or constant coefficient of variation. Completely general power equations for confidence intervals and confidence regions are less tractable. This program therefore uses simulations throughout.

**Technical Notes**

- The program requires error properties (weights) to be expressed as one of the following variance functions;
  
  \[ V = (\beta_1 + \beta_2 U)^J \]
  
  or
  
  \[ V = \beta_1 + \beta_2 U^J \]

  where $V$ denotes variance, $U$ denotes the mean and $\beta_1$, $\beta_2$ and $J$ are variance function parameters. These functions describe how variance (measurement error) changes with the concentration. They are taken from the immunoassay environment (7) where error properties are usually more complicated than those for other medical laboratory tests. However, these relationships readily reduce to simpler forms such as constant variance (set $\beta_1$ = value, $\beta_2$ = 0, $J$ = 1). Full details are given in program on-line help.

- Deming estimation and confidence interval calculations are performed according to the method of Press et al. (3) which is based on arctan transformation of the data. However, rather than using a single estimation cycle, the process is iteratively reweighted according to adjusted $X$, $Y$ values. York (8) gave formulae for adjusted $X$, $Y$ values and these were systematically evaluated by Martin (9).

- Joint slope, intercept confidence regions are estimated using the ‘extra sum-of-squares’ method (4).

- Many text books define confidence intervals for slope and intercept as $t \times s.e.$ where $t$ is a Student’s $t$-variate with $N – 2$ degrees-of-freedom (df) and $s.e.$ is the standard error of slope or intercept. That is certainly correct for OLS where $N – 2$ refers to the df associated with the error term, which is estimated from the data itself as the residual mean square about the fitted line. However, in the WLS and weighted Deming cases the errors are assumed to be known and confidence intervals are therefore calculated as $Z \times s.e.$ where $Z$ is a normal deviate.

**References**


**Program Delivery, Installation and Removal**

The program is delivered (by a mutually agreed file transfer mechanism) as file RAPSInstallFiles.exe (1017 Kb). This is a self-extracting zip file. Just double click it and the 10 installation files listed below will be unzipped into C:\Temp (which will be created if necessary). Note that if Windows Explorer is already open a newly created C:\Temp directory may not appear immediately; click Explorer menu item View > Refresh. You can specify an alternative location for the 10 installation files if you wish. Copy the 10 files to a CD/DVD if you wish to create an installation CD or DVD.

```
_INST32I.EXE_ 288 Kb
_ISDEL.EXE 8 Kb
SETUP.EXE 45 Kb
_SETUP.DLL 6 Kb
SETUP.INS 80 Kb
_SETUP.I 330 Kb
_SETUP.LIB 200 Kb
DISK1.ID 1 Kb
SETUP.INI 1 Kb
SETUP.PKG 1 Kb
```

Install RAPS.exe by double clicking SETUP.EXE and following the prompts. It is recommended that you accept C:\RAPS as the program home directory but you are free to specify any alternative location. RAPS is suggested as the program icon name during installation but you can change this or choose to include the program in an existing program group. The following files are installed into the specified home directory;

```
RAPS.exe 614 Kb (The program described in this document)
RAPS.hlp 37 Kb (On-line help file)
RAPS.cnt 1 Kb (On-line help contents file)
```

Use the Add/Remove Programs icon in the system Control Panel to remove the program icon and the installed files. Files created after program installation will not be included in the clean up operation and must be deleted manually (eg. auxiliary files created by on-line Help).