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Use of Deming Regression in Method-Comparison Studies

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Introduction

In many clinical laboratories, a significant amount of time and effort is devoted to the evaluation of methods. To accent the importance of this phase of testing a method, the IFCC Expert Panel on Nomenclature and Principles of Quality Control in Clinical Chemistry published a document on this subject [1]. The Panel states that 'information about the performance of an analytical method must be obtained before it is used routinely with patients' specimens' and published a document which establishes guidelines. More detailed information on this subject appeared in the literature and the reader is referred to a recent review [2] on this topic.

The present essay deals with one aspect: the accuracy and precision of a 'test method', by performing a comparison of methods experiment.

Regression as Statistical Tool

Accuracy is closeness to the true value [3] but the determination of the true value for a component of a biological specimen is difficult or sometimes impossible. It is now well accepted to determine the accuracy of a 'test method' with use of the results of patients samples in a comparison study [4].

Precision is closeness of the results of a repeated analysis performed on the same material and is expressed in such terms as standard deviation, coefficient of variation and standard error [3].

The whole evaluation procedure is planned carefully: the choice of the 'reference' method is critical and this method is set up and tested well in advance. For making decisions on the acceptability of the 'test method' with regard to accuracy and precision, the comparison data are subjected to statistical analysis. For that, one has to choose between parametric and nonparametric statistics, which depends on the frequency distribution of the data.

The Pearson product moment (correlation coefficient) and the 'classical' regression analysis are parametric tests and assume a normal distribution, while nonparametric tests such as the sign test and Spearman's rank correlation coefficient can be applied to normal and nonnormal data alike. However, it has been shown [5] that the use of a recommended method [6] to test whether clinical laboratory data have a Gaussian frequency distribution was either overly sensitive or inappropriate. The authors have modified this method to give a lower frequency of non-normality.

Table I. Data from a comparison and precision study of two methods

Point No.	x	y
1	0.15	0.17
2	0.50	0.45
3	0.40	0.30
4	1.39	1.24
5	0.75	0.78
6	0.79	0.88
7	0.35	0.42
8	0.45	0.35
9	0.12	0.16
10	0.62	0.69
11	0.60	0.50
12	0.81	0.64
	$x = 0.58$	$y = 0.55$
	$S_x = 0.34$	$S_y = 0.32$
	$r = 0.9636$	
	$n = 12$	

$S_{ex} = 0.040$ of $x = 0.62$.
$S_{ey} = 0.069$ of $y = 0.50$.

Table II. Calculation of Deming regression line $Y = b_{yx} X + a_{yx}$ and of S_{yx}

Substitute data of table I in:

$$b_{yx} = U + \sqrt{U^2 + S_{ey}^2/S_{ex}^2}$$

$$U = \frac{S_y^2 S_{ex}^2 - S_x^2 S_{ey}^2}{2 r S_x S_y S_{ex}^2}$$

$$a_{yx} = y - b_{yx} x$$

$$S_{yx} = \sqrt{\frac{n-1}{n-2} (S_y^2 - b_{yx} r S_x S_y)}$$

Thus $U = 1.152$, $b_{yx} = 0.92$, $a_{yx} = 0.02$, and $S_{yx} = 0.08$.

The advantage of the knowledge of regression results is the estimation of the types (random, constant or proportional error) and magnitude of errors, as was shown by *Westgard and Hunt* [7]. The 'classical' least-squares analysis in which the 'line of the best fit' is chosen to minimize the residuals for all data points in the Y direction is only appropriate if the independent variable, x, is measured (almost) without random error. We mention the use of a 'reference method' with very precise results or the use of preassigned values, e.g. with standard solutions. In most method comparison studies, however, some random error in both x and y values appear and thus the 'classical' least-squares procedure will always yield *two* different lines. This feature is often overlooked in the literature! According to *Cornbleet and Gochman* [8], an alternate regression procedure should be considered if the slopes of the two lines are not related in a reciprocal manner. The procedure of *Deming* [9], an alternate method, has been mentioned before [8, 10]. Now, the sum of the squares of the perpendicular distances from the data points to the line are minimized. *Deming's* method always results in *one* regression line, because the error of measurement of both variables is taken into account.

Calculations in Deming Regression

To calculate the slope and the Y intercept of the line, one has to know r, S_x, S_y and, with some approximations [8], the ratio S_{ex}^2/S_{ey}^2. We do not endorse the opinion [11] of putting the ratio equal to 1, if such precision data are lacking. Finally, the standard deviation of the residual error of regression in the Y direction is calculated. This value is a quantitative

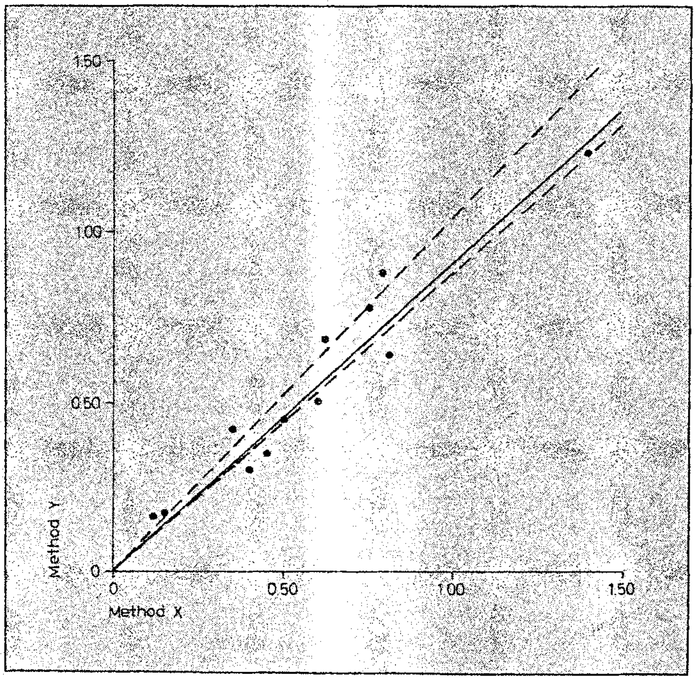

Fig. 1. Comparison of results with method X and method Y. —— = Regression line, Deming's method; - - - = regression lines, classical method.

measure of the scatter of the data about the regression line. To demonstrate the correct use of Deming's method, twelve points are given in table I, merely to illustrate the technique. It is assumed that the data may be subjected to parametric statistics. We use the formulas given by *Cornbleet and Gochman* [8] to compute the slope (b_{yx}) and the Y intercept (a_{yx}) of the line (table II), and find the equation of the line to be $Y = 0.92X + 0.02$ with $S_{yx} = 0.08$. With the use of the same data points, the slopes of the 'classical' line are 0.89 and 1.05 (fig. 1).

In some recent volumes *(35–45)* of the *Journal of Immunological Methods*, 30 papers deal with method comparisons. It was astonishing that only one author [12] employed Deming regression as a statistical tool. Moreover, standard deviations and sometimes scatter diagrams were lacking. Testing normality of the method comparison data is not at all popular because of the obliged use of statistical tables. It is to be hoped that the information and calculations given in this paper will contribute to the increased use of Deming regression, even in the field of immunochemistry.

Abbreviations used:

a_{yx}	Y intercept of the linear relationship between x and y data
b_{yx}	slope of the line
S_{yx}	standard error of estimate
S_y, S_x	standard deviation of y and x data, respectively
S_{ey}, S_{ex}	standard deviation of repeated measurement of a single y and x value near the mean of all y and all x data, respectively
r	Pearson's product moment or correlation coefficient
x, y	mean of all x and y data, respectively

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