Within group and between group correlation: Application to noninvasive estimation of intracranial pressure

Caren Marzban, Paul R. Illian, David Morison, Pierre D. Mourad

***Abstract*—The linear association between two continuous quantities is often assessed in terms of Pearson's correlation coefficient, r. However, if the data are not homogeneous, i.e., consist of groups, then it is important to decompose r into components that measure the correlation within the groups, and the correlation between the groups. We point out the importance of examining these components, and present a method for computing them. Our approach has several attractive features. First, all three measures of correlation are computed in a unified framework based on the analysis of (co)variance in a single linear model. Second, it allows one to measure nonlinear correlations. Finally, p-values, traditionally computed in linear modeling can be utilized to test the statistical significance of the three measures of correlation. The method is applied to assess the correlation between invasive observations and noninvasive estimates of intracranial pressure (ICP), with individual patients representing each group. The total correlation is 0.506, while the within-group and between-group correlations are 0.053 and 0.518, respectively. As such, the ICP predictions are useful for estimating/predicting the mean (over time) ICP for any patient, but they are useless for monitoring an individual's ICP at any time.**

***Index Terms*—Performance evaluation, correlation, analysis of variance, noninvasive treatment, intracranial pressure sensors**

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I. Introduction

GIVEN data on two continuous quantities x and y, the strength of the (linear) association between them is often assessed by a scatterplot of y vs. x. A strong linear pattern along the diagonal of the scatterplot indicates strong association. If x and y are observations and corresponding predictions, respectively, then the overall position of the points on a scatterplot, relative to the diagonal, is a measure of the accuracy of the predictions, and the amount of scatter about the diagonal gauges the precision of the predictions. A popular, scalar measure of the latter is Pearson's correlation coefficient [1], here denoted r.

If the data are not homogeneous, then the scatterplot displays clusters/groups. In such a case, then there are three different correlations: 1) correlation, ignoring the existence of clusters altogether; 2) correlation within the groups; and 3) correlation across the groups. Borrowing from the language of analysis of variance [2], in this paper we refer to these as *total correlation*, *within-group correlation*, and *between-group correlation*, respectively. Each of these three correlations has a different meaning, and the appropriate choice depends on the problem at hand.

At the simplest level, the total correlation can be measured by computing r across the entire data, ignoring the groups altogether. The within-group correlation may be measured by computing r within each of the groups, and then averaging them. Similarly, a measure of the between-group correlation can be obtained by averaging the x and y values for each group (leading to a scatterplot where each group is replaced by the average of the corresponding x and y), and then computing r across them. Although these specific measures provide intuitive gauges of the respective correlations, they lack a desirable feature characteristic to analysis of variance: the sum of these within-group and between-group correlations is not readily related to the total correlation. Furthermore, correlations measured with r have two additional ``defects:" r gauges only linear associations, and statistical tests of r are often sensitive to violations of their respective assumptions [3], [4]. In this paper, we propose a decomposition that does embody a simple relation between the three measures of correlation. Additionally, the proposed method readily allows for nonlinear associations, and effortlessly performs statistical

tests on each component.

The importance of the distinction between the three correlations is best illustrated through Simpson's paradox [5]: Consider the simulated data shown in Fig 1. The *r* for each of the two groups (i.e., measuring correlation within-group) is 0.9. But the total *r* for the entire data set is zero. In other words, by examining only the total correlation, one can miss the fact that the correlation within group is very high.

Moreover, the three correlations have very different meanings and interpretations, as illustrated in the next section.

The "causes" of groups in scatterplots can vary, but a common situation in which clustering occurs is when multiple measurements (and predictions) are made on multiple subjects, in which case each group corresponds to a unique subject. An example of data from such an experimental design is shown in Fig. 2. Here ZFP (Zero-Flow Pressure; further discussed below) is used as a noninvasive estimate/prediction of ICP.

I. Intracranial pressure (ICP)

ICP is an important factor in monitoring patients who have experienced head trauma as well as other conditions [6], [7]. Direct measures of ICP are invasive, requiring the placement of pressure sensors within the cranium. Therefore, there is great interest in finding noninvasive measures of ICP [8]-[22]. One particular noninvasive measure of ICP is ZFP, and the relation between the two has been examined in [23]-[26]. Most measures of ZFP involve linearly extrapolating arterial blood pressure (ABP) to the point where blood flow is zero (hence, the name zero-flow-pressure). In a recent article, we examined a nonlinear extrapolation method for defining ZFP [26]. Here, only the linear extrapolation results from that work will be considered, in order to focus on the matter at hand, namely the assessment and meaning of correlations. Details of the nonlinear extrapolation method can be found in [26]; suffice it to say that ICP and ZFP were computed for 200 random samples (at different times) taken from each of 104 patients. Said differently, there are 104 clusters/groups in Fig. 2, each consisting of 200 points.

As mentioned previously, given the existence of clusters in this scatterplot, there exist different notions of correlation. Each has a different meaning, and its utility depends on the problem at hand. If one is interested in predicting the mean (over time) ICP for a patient, then the correlation between-group is appropriate for assessing the quality of the predictions. On the other hand, if one is interested in predicting ICP, for a given patient, across time, then the appropriate quantity is the correlation within-group.

The ICP literature abounds with instances where only the total correlation is reported. Czosnyka, et al [9] report r=0.41, Thees, et al [10] find r=0.91, and Buhre, et al [24] report r=0.93. For the data in Fig.2 the total r is 0.506 [26]. But this single number obscures the visually evident fact that the data are not homogeneous. It is, therefore, important to compute some measures of the within-group and between-group correlations.

As mentioned above, intuitive measures of the two correlations can be computed as follows: One may average over the x and y of the 200 cases for each patient, leading to a scatterplot containing 104 points, corresponding to the 104 patients (Fig. 3). The r corresponding to that scatterplot is 0.519, and it provides a measure of between-group correlation. Fig. 4 shows the histogram of the r values for each of the 104 patients. Each of these r values is an estimate of the within-group correlation, and their average provides a more precise estimate. The mean ± 1 Standard deviation of these r values is 0.07 ± 0.47.

As mentioned previously, the first aim of this paper is to highlight the importance of examining all three correlations. The second aim is to present a method for computing these correlations in a unified fashion which also allows for nonlinear associations.

II. Method

A. Correlation defined as $\sqrt{R^2}$ of a linear model

In multiple linear regression, the coefficient of determination, R^2, accounts for the variation in the response that can be explained by the predictors. It is well-known that for simple linear regression, R^2 is exactly equal to the square of the correlation coefficient, r^2. This connection between R^2 and r^2 can be used to define measures of nonlinear correlation [27]. Specifically, a (nonlinear) correlation coefficient can be defined as the square root of R^2 of *any* regression model, even if the model includes nonlinear terms. For example, the square root of the R^2 of a polynomial regression model relating two variables serves as a measure of nonlinear correlation between the variables.

Defining the correlation coefficient as $\sqrt{R^2}$ has the additional advantage of utilizing *partial sum-squared* and *extra sum-of-squares* to measure *partial correlations* between a response and each of multiple predictors [1], [28]. Loosely speaking, a partial correlation between y and a given predictor measures the association between the two but after the remaining predictors have been taken into account.

B. Within-group and between-group correlation via extra sum-of-squares

Having established that $\sqrt{R^2}$ of a linear model is a more general and flexible measure of correlation than r, we turn to the problem of decomposing R^2 into components measuring within-group and between-group correlation. The details of the decomposition are presented in the Appendix; here, we will show that R^2_{total}, R^2_{within} and $R^2_{between}$ can all be computed from variations on a single linear model.

In multiple regression, the analysis of variance is often performed in what is called *sequential analysis of variance* [1]. A common format for presenting the results of that analysis is shown in (1). The first line shows the equation of the model; the response is denoted by y, the predictors are x_1, x_2, …, and ε is the error term. The term $SS(\beta_i \mid \beta_j, \beta_k, ...)$ is called the extra sum-of-squares (SS), and it measures the

contribution to the total sum-squared of y that can be explained by x_i above and beyond the amount already explained by x_j , x_k , etc. The estimates of the parameters are usually based on a least-squares criterion, in which case $SSE(\beta_0,\beta_1,\beta_2,...)$ is the minimum value of the sum of the squared errors. The quantities reported in this format are precisely the necessary ingredients for computing the R^2 contribution of each of the predictors in the regression model [1].

$$\begin{aligned} &y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + ... + \varepsilon \\ &x_1 : SS(\beta_1 \mid \beta_0) \\ &x_2 : SS(\beta_2 \mid \beta_0, \beta_1) \\ &... \\ &Error : SSE(\beta_0, \beta_1, \beta_2). \end{aligned} \tag{1}$$

Specializing the format in (1) to the problem at hand, the ith response (ICP) for the jth patient is denoted y_{ij} , and the two predictors are the patient label i, and ZFP, denoted x_{ij} . Then, the model in (1) can be written in notation more traditional in linear modeling:

$$\begin{aligned} &y_{ij} = \mu + \tau_i + \beta x_{ij} + \varepsilon_{ij} \\ &\tau : SS(\tau \mid \mu) \\ &x : SS(\beta \mid \mu, \tau) \\ &Error : SSE(\mu, \tau, \beta), \end{aligned} \tag{2}$$

where τ_i is a factor encoding the group corresponding to the ith patient, β is a slope parameter common to all patients, and μ is the y-intercept. All of these parameters are estimated from data, via some criterion - usually the ordinary least-squares (but, see below).

In performing statistical hypothesis testing, the total R^2 of this *full model* is contrasted with that of a *reduced model* [1]. For example, to test the significance of the factor τ_i the reduced model is that shown in (3):

$$\begin{aligned} &y_{ij} = \mu' + \beta' x_{ij} + \varepsilon'_{ij} \\ &x : SS(\beta' \mid \mu') \\ &Error : SSE(\mu', \beta'). \end{aligned} \tag{3}$$

Similar reduced models, excluding other parameters, are used to test the significance of the "missing" parameter.

A special case of the model shown in (3) is obtained by summing over the j index:

$$\begin{aligned} &y_{i.} = \mu'' + \beta'' x_{i.} + \varepsilon_{i.} \\ &x : SS(\beta'' \mid \mu'') \\ &Error : SSE(\mu'', \beta''). \end{aligned} \tag{4}$$

where "." denotes sample average over the corresponding index.

As shown in the Appendix, the full model in (2), and the two reduced models (3) and (4), each lead to the following R^2 values:

$$\begin{aligned} R^2_{total} &= \frac{SS(\beta' \mid \mu')}{SS(\beta' \mid \mu') + SSE(\mu', \beta')} \\ R^2_{within} &= \frac{SS(\beta \mid \mu, \tau)}{SS(\beta \mid \mu, \tau) + SSE(\mu, \beta, \tau)} \\ R^2_{between} &= \frac{SS(\beta'' \mid \mu'')}{SS(\beta'' \mid \mu'') + SSE(\mu'', \beta'')} \end{aligned} \tag{5}$$

That R^2 can be written as ratios of the form *SS/(SS+SSE)* is not surprising [1], [2]; however, it is somewhat unexpected that the full model in (2) in fact leads to the *within*-group contribution to R^2, and it is the reduced models which yield the total and the between-group contributions. This may seem counter-intuitive, but it can be understood by noting that the slope parameter in the full model (2) is common to all patients, and so, any *SS* computed from that model is apt to refer to some within-group characteristic. The linear model (2) for computing the within-group correlation has also been considered in [28]. Further motivation for why we have called the specific ratios in (5) "total", "within", and "between" can be found in the appendix. Then, we define the respective correlations as the square-root of the corresponding R^2:

$$\begin{aligned} r_{total} &= \sqrt{R^2_{total}} \\ r_{within} &= \sqrt{R^2_{within}} \\ r_{between} &= \sqrt{R^2_{between}} \end{aligned} \tag{6}$$

Recall that in the standard analysis of variance, it is the sum-of-squares (*SS*), *not* variance, which is decomposed and written as $SS_{total} = SS_{within} + SS_{between}$; the total, within-group, and between-group variances (derived from the corresponding *SS*) do not follow this type of additive property. Similarly, in decomposing correlation, r_{total} is not equal to the sum of r_{within} and $r_{between}$. However, there does exist a simple relationship between them; see (10).

III. Application to ICP

Table 1 shows all the relevant quantities arising in the full model and reduced models shown in (2), (3), and (4). It is important to point out that the R^2 values shown in that table are not the R^2 that would ordinarily accompany the analysis of variance for each of the models shown in the table; the latter are usually *total* R^2 values for the respective models. The R^2 values reported in Table 1 are computed from (5). Similarly, the quantities reported as *r* are computed from (6).

As mentioned previously, an advantage of defining correlation in terms of R^2, and therefore *SS*, of linear models is that each *SS* is generally accompanied by a p-value, testing the null hypothesis that the true/population *SS* is zero. As such, the p-values corresponding to the *SS* terms in the models (2), (3), (4), provide a test of the corresponding correlation. For the problem at hand, all three p-values are smaller than any conventional choice of significance level (e.g., 0.05, or 0.01). As such, there is considerable evidence from data that the

true/population correlations are nonzero.

The total, within-group, and between-group correlations reported in Table 1 (i.e., 0.506, 0.053, 0.519) may be compared with the naive measures discussed in the Introduction: 0.506, 0.070, 0.519. Evidently, for the problem at hand, the total and between-group correlations obtained from the proposed method are equal (to at least three decimal places) to the naive estimates; but the two within-group correlations are different. This result is not a general result, but is approximately true if/when the group-conditional sample sizes are comparable across the different groups. Given this close agreement between the intuitive measures and those obtained from linear modeling, one may wonder what has been gained by the proposed method, as compared to using the naive estimates. The answer is that the three estimates in (6) are based on a rigorous decomposition of variation and covariation (see (8)), leading to an additive property (see (10)) that is not satisfied by the naive estimates.

IV. Summary, Conclusion and Discussion

We have shown that it is important to assess the correlation between two quantities in terms of within-group and between-group correlations. A method is put forth which allows the computation of these quantities from a sequential analysis of variance performed on a single, linear model. Defining correlation in this manner has the advantage of allowing nonlinear correlations; all one must do is to add nonlinear terms to the right-hand-side of the linear model. (Note: such an addition still yields a linear model, because the model is linear in its parameters.) Additionally, significance testing of the correlations is then equivalent to significance testing of sum-squared terms, which are commonly reported in analysis of variance tables generated by most modern statistical routines. Finally, the three correlations defined this way follow the desirable feature of being based on an exact decomposition of sample variation and covariation.

The application of the method to a data set of 200 invasive measurements and noninvasive estimations/predictions of ICP, on 104 patients, yields $r_{total}=0.506$, $r_{within}=0.053$, $r_{between}=0.519$, all with near-zero p-values. As such, data provide significant evidence that all three correlations are nonzero. However, the relatively small magnitude of the within-group correlation suggests that ZFP is not useful for estimating ICP at any given time, for any given patient. By contrast, the relatively larger between-group correlation suggests that ZFP is more useful for estimating the mean (over time) ICP of individual patients.

For the data set at hand, nonlinear extensions of the models (2), (3), and (4), do not lead to significantly different results, and are therefore not presented here.

Appendix

In this appendix, we will show the relationship satisfied by the three correlations. To that end, it is convenient to define the following quantities:

$$
\begin{aligned}
T_{xx} &= \sum_{ij} (x_{ij} - x_{..})^2 \\
T_{yy} &= \sum_{ij} (y_{ij} - y_{..})^2 \\
T_{xy} &= \sum_{ij} (x_{ij} - x_{..})(y_{ij} - y_{..}) \\
W_{xx} &= \sum_{ij} (x_{ij} - x_{i.})^2 \\
W_{yy} &= \sum_{ij} (y_{ij} - y_{i.})^2 \\
W_{xy} &= \sum_{ij} (x_{ij} - x_{i.})(y_{ij} - y_{i.}) \\
B_{xx} &= \sum_{i} (x_{i.} - x_{..})^2 \\
B_{yy} &= \sum_{i} (y_{i.} - y_{..})^2 \\
B_{xy} &= \sum_{i} (x_{i.} - x_{..})(y_{i.} - y_{..}).
\end{aligned}
\tag{7}
$$

In these expressions x_{ij} and y_{ij} refer to the j[th] value of x (ZFP) and y (ICP) for the i[th] patient. A "." indicates the sample average over the corresponding index. For example, $x_{i.}$ is the sample mean (over time) of x for the i[th] patient. Note that these quantities satisfy the desirable additive property:

$$
\begin{aligned}
T_{xx} &= W_{xx} + B_{xx} \\
T_{yy} &= W_{yy} + B_{yy} \\
T_{xy} &= W_{xy} + B_{xy}.
\end{aligned}
\tag{8}
$$

The labels *T, W*, and *B* are intended to correspond to Total, Within, and Between. The quantities with "*xx*" and "*yy*" subscripts are measures of sample variation, and the terms with "*xy*" subscripts measure sample covariation [2, p. 576]. It follows from (5) that

$$
\begin{aligned}
R^2_{total} &= \frac{T_{xy}^2}{T_{xx}T_{yy}} \\
R^2_{within} &= \frac{W_{xy}^2}{W_{xx}W_{yy}} \\
R^2_{between} &= \frac{B_{xy}^2}{B_{xx}B_{yy}}.
\end{aligned}
\tag{9}
$$

When the quantities *T, W* are estimated via a least-squares criterion, and the quantities *B* are estimated via a weighted least-squares criterion, then it follows that

$$
\begin{aligned}
&\sqrt{T_{xx}T_{yy}}\, r_{total} = \\
&\sqrt{W_{xx}W_{yy}}\, r_{within} + \sqrt{B_{xx}B_{yy}}\, r_{between}.
\end{aligned}
\tag{10}
$$

It is worth emphasizing that this (desirable) decomposition of correlation is possible only if the expressions for B_{xx}, B_{yy}, B_{xy} in (7) include the term n_i . In turn, the presence of this term requires minimizing the *weighted SSE*, with n_i as the weights. In short, an ordinary least-squares fit of models (2) and (3), but a weighted least-squares fit of model (4), is necessary for the decomposition of correlation in (10) to be possible. Such a decomposition of correlation has also been considered in [29], but without proof or derivation.

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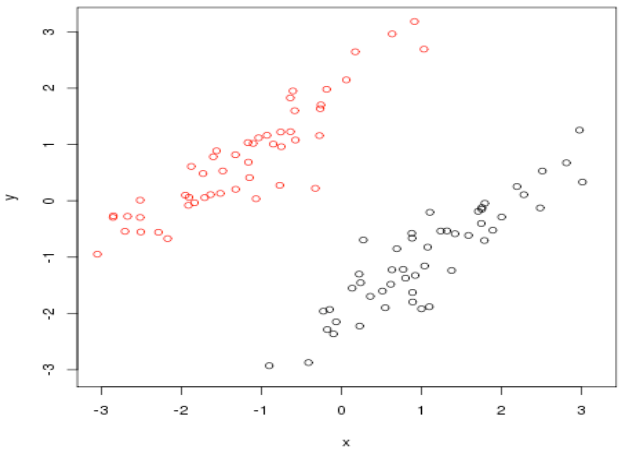

Fig. 1. Illustration of Simpson's paradox. The correlation coefficient between *x* and *y* within each cluster is 0.9, but the overall correlation coefficient is 0.

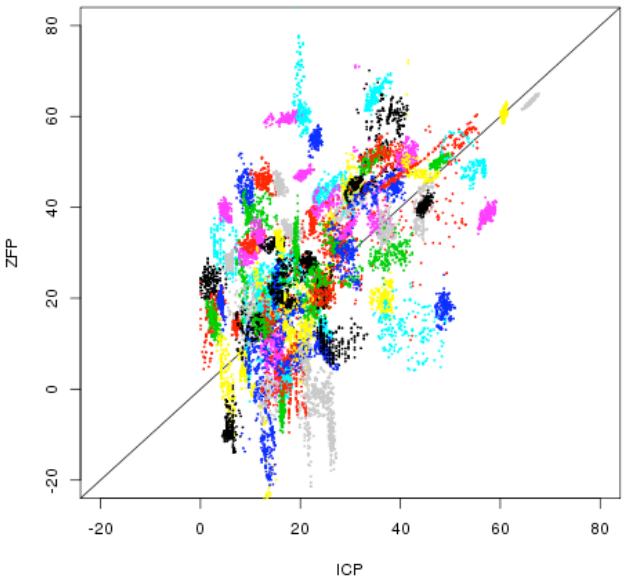

Fig. 2. Scatterplot of 200 measurements of ICP and ZFP for 104 patients (in different colors). Depending on the patient, there is a positive correlation, a negative correlation, or no correlation at all between ICP and ZFP. Overall, i.e., between the patients, there is a positive correlation between ICP and ZFP.

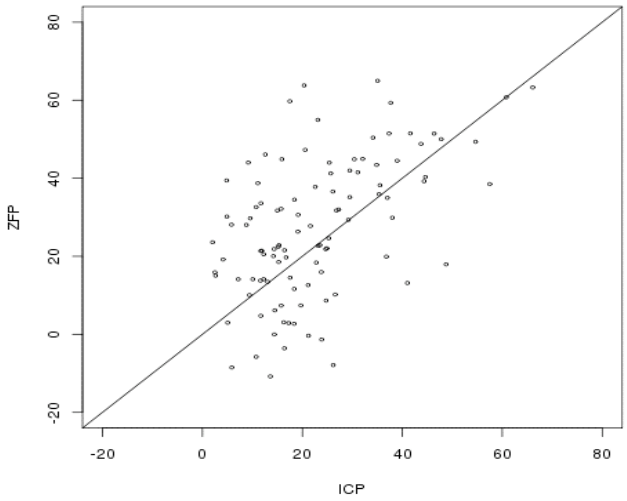

Fig. 3. Scatterplot of mean ICP and mean ZFP for 104 patients, with the mean taken over different times. The appropriate measure of association is the correlation coefficient between group, here 0.519.

TABLE I
CORRELATION TOTAL, WITHIN, AND BETWEEN GROUPS

Model	SS	R^2	r	p
Total	$SS(\beta' \mid \mu') = 981800.1$ $SSE(\mu', \beta') = 2857453$	0.256	0.506	~0
Within	$SS(\beta \mid \mu, \tau) = 210.4$ $SSE(\mu, \tau, \beta) = 74190.2$	0.003	0.053	~0
Between	$SS(\beta'' \mid \mu'') = 1013173$ $SSE(\mu, '' \beta'') = 2751680$	0.269	0.519	~0

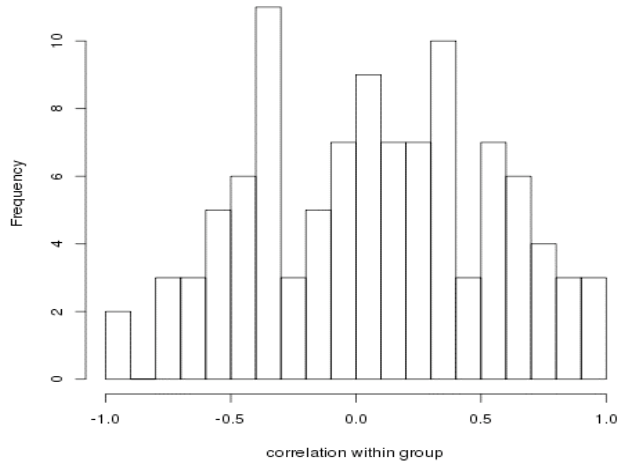

Fig. 4. Histogram of the104 correlations within group.