The longitudinal concordance correlation

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Abstract: We present the `lcc` package, available from the Comprehensive R Archive Network (CRAN). The package implements estimation procedures for the longitudinal concordance correlation (LCC), using fixed effects and variance components estimates from linear mixed models. The LCC is a quantity that measures the extent of agreement between two (or more) methods used to evaluate a response variable of interest and is frequently applied in medicine, pharmacology, and agronomy. The main features of the package are the estimation and inference of the extent of agreement using numerical and graphical summaries. Moreover, our approach presents flexibility in the sense that it accommodates both balanced and unbalanced experimental designs, allows for different within-group error structures, while also allowing for the inclusion of covariates in the linear predictor to control systematic variations in the response. We illustrate our methodology by comparing different methods used to measure the peel colour of fruit as an assessment of ripeness.

Keywords: Extent of agreement; Polynomial mixed-effects regression model; Bootstrap procedures; Heteroscedasticity; R

1 Introduction

Agreement indices are generally used when the same experimental unit is measured by at least two methods or observers. The concordance correlation coefficient (ρ_{CCC}) introduced by Lin (1989) is a statistic commonly used to measure the agreement between methods when the response is

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continuous and is given by

$$\rho_{CCC} = 1 - \frac{E\left[\left(Y_1 - Y_2\right)^2\right]}{\sigma_1^2 + \sigma_2^2 + \left(\mu_1 - \mu_2\right)^2} = \frac{2\sigma_{12}}{\sigma_1^2 + \sigma_2^2 + \left(\mu_1 - \mu_2\right)^2} = \rho C_b,$$

where $\mu_1 = \mathrm{E}\left(Y_1\right)$, $\mu_2 = \mathrm{E}\left(Y_2\right)$, $\sigma_1^2 = \mathrm{Var}\left(Y_1\right)$, $\sigma_2^2 = \mathrm{Var}\left(Y_2\right)$, and $\sigma_{12} = \mathrm{Cov}\left(Y_1, Y_2\right)$. The coefficient takes the value -1 when there is perfect disagreement, zero when there is no agreement, and 1 when there is perfect agreement. Moreover, ρ is the Pearson correlation coefficient ($|\rho| \leq 1$) that measures how far each observation deviates from the best-fit line (precision measure), and C_b is the accuracy ($0 < C_b \leq 1$) that measures how far the best-fit line deviates from the line of perfect agreement, the 45° line through the origin.

When it is necessary to include extra variability sources due to within-subject measurements and/or other covariates in the model, the ρ_{CCC} can be estimated through the variance components (VC) and fixed effects from a mixed-effects model (Carrasco et al., 2009; Oliveira et al., 2018). For longitudinal data, Rathnayake and Choudhary (2017) and Oliveira et al. (2018) considered models for the response that included a linear or non-linear function of time and/or other covariates. Here, we present the implementation of the Oliveira et al. (2018) methodology as the `R` (R Core Team, 2019) package `lcc` (Oliveira et al., 2019).

2 The longitudinal concordance correlation ($\rho_{jj'}\left(t_k\right)$)

Suppose a researcher is interested in investigating the extent of measurement agreement between two or more methods, indexed as $j = 1, 2, \ldots, J$. Let N be the number of subjects in the experiment, or observational study, indexed as $i = 1, 2, \ldots, N$, and suppose that each subject is observed n_i times. Also, let y_{ijk} be a realization of a random variable Y_{ijk} measured on the i-th subject by the j-th method at time t_k, $k = 1, 2, \ldots, n_i$. Here the times t_k are specific values of the time covariate $t \in \mathcal{T}$, measured in seconds, minutes, days, etc. Hence, the linear mixed-effects model with a polynomial function of time, fixed effects for method, as well as their interactions and subject-specific random polynomial coefficients is given by

$$\begin{gathered} Y_{ijk} = \sum_{h=0}^{p} \beta_{hj} t_{ik}^{h} + \sum_{h=0}^{q} b_{hi} t_{ik}^{h} + \epsilon_{ijk}, \\ \text{with } \mathbf{b}_i \sim \mathrm{MVN}\left(\mathbf{0}, \mathbf{G}\right) \text{ and } \epsilon_i \sim \mathrm{MVN}\left(\mathbf{0}, \mathbf{R}_i\right), \end{gathered} \tag{1}$$

where $h = 1, 2, \ldots, q, q+1, \ldots, p$ is an index for the terms in the fixed and random polynomials of degree p and q, respectively, with $q \leq p$; $\beta_j = \left[\beta_{0j}, \beta_{1j}, ..., \beta_{pj}\right]^T$ is a $(p+1)$-dimensional vector of fixed effects for the j-th method; $\mathbf{b}_i = \left[b_{0i}, b_{1i}, ..., b_{qi}\right]^T$ is a $(q+1)$-dimensional vector of random

effects with mean vector $\mathbf{0}$ and covariance matrix $\mathbf{G}$; ϵ_i is a $(J \times n_i)$-dimensional vector with mean vector $\mathbf{0}$ and covariance matrix $\mathbf{R}_i$ assumed to be independent for different i, and independent of the random effects, and often also assumed to be independent over j and k with $\mathbf{R}_i = \sigma_\epsilon^2 I$.
Under model (1), the $\rho_{jj'}(t_k)$ function between methods j and j', $j \neq j'$, is given by

$$\rho_{jj'}(t_k) = \frac{\mathbf{t}_k \mathbf{G} \mathbf{t}_k^T}{\mathbf{t}_k \mathbf{G} \mathbf{t}_k^T + \frac{1}{2}\left\{\sigma_\epsilon^2 \left[g(t_k, \delta_j) + g(t_k, \delta_{j'})\right] + S_{jj'}^2(t_k)\right\}} \tag{2}$$

where $S_{jj'}(t_k) = \mathbf{t_k}^T(\beta_j - \beta_{j'})$ is the systematic difference between methods j and j'; $\mathbf{t}_k^T = \left(t_k^0, t_k^1, \ldots, t_k^q\right)$; $g(\cdot)$ is a variance function assumed continuous in δ; δ_j is a vector of variance parameters for observations measured by j-th method or observer. Furthermore, as the $\rho_{jj'}(t_k)$ can be rewritten as $\rho_{jj'}(t_k) = \rho_{jj'}^{(p)}(t_k) C_{jj'}(t_k)$, we also obtain the longitudinal Pearson Correlation, $\rho_{jj'}^{(p)}(t_k)$, and the longitudinal accuracy, $C_{jj'}(t_k)$, functions.
The `lcc` package uses the REML method, as default, for parameter estimations because it is less biased, less sensitive to outliers, and deals more effectively with high correlations when compared to ML estimation. However, the function includes the option to change the estimation method to ML because this approach is required for comparing nested fixed effects models under the same common random structure.

3 Specifying models

In the `lcc` package, to estimate the $\rho_{jj'}(t_k)$ we need to specify the subject, response, method, time, a polynomial mixed-effect model, and the dataset. This arguments are specified through easy-to-use syntax. Consider a first degree polynomial model with a subject-specific random intercept for a continuous dependent variable Y observed on ith fruit $(i = 1, 2, \ldots, N)$ by J methods at times t_k $(k = 1, 2, \ldots, n_i)$:

$$\begin{gathered} Y_{ijk} = \beta_{0j} + b_{0i} + \beta_{1j} t_k + \epsilon_{ijk} \\ b_{0i} \sim N(0, \sigma_{b_0}^2) \quad \text{and} \quad \epsilon_{ijk} \sim N\left(0, \sigma_\epsilon^2\right) \end{gathered}$$

Here the LCC is given by

$$\rho_{jj'}(t_k) = \frac{\sigma_{b_0}^2}{\sigma_{b_0}^2 + \sigma_\epsilon^2 + \frac{1}{2}\left[\beta_{01} - \beta_{02} + (\beta_{11} - \beta_{12}) t_k\right]^2}$$

and the syntax to specify this model in the `lcc()` function is:

```
R> fit1 <- lcc(dataset = data, subject = "Subject", resp = "y",
               method = "Method", time = "Time", qf = 1, qr = 0)
```

where qf=1 represents the polynomial degree for the fixed part, qr=0 a subject-specific random intercept. Suppose that the experimental design in the previous example was randomized block designs, then the fixed effect of blocks can be included in the model as

```
R> fit2 <- lcc(dataset = data, subject = "Subject", resp = "y",
               covar ="Block", method = "Method", time = "Time",
               qf = 1, qr = 0)
```

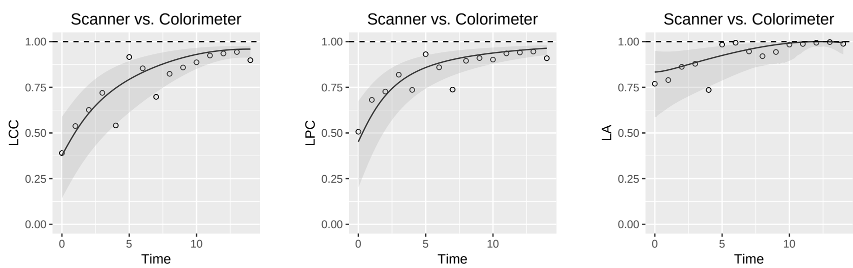
3.1 Output

Numerical and graphical summaries of the fitted object and associated confidence intervals can be obtained by using `summary`, and `lccPlot` methods implemented for `lcc` objects. The generic function summary is specified as `summary(obj, type)`, where `obj` is a object of class `lcc` and `type` is a character string defining of required `LCC` components, such as model, or fitted and sample values. When `type = "model"`, the summary function gives the model used in the `lcc()` function whereas `type = "lcc"` gives the fitted and sampled values for the LCC component, its 95% bootstrap confidence intervals, and the ρ_{CCC} between fitted and sampled values as a goodness-of-fit statistic.
The `summary` method output depends on whether the components argument was set as TRUE or FALSE in the `lcc` call. If the `components` argument is TRUE, the generic function summary with `type = "lcc"` gives a list containing the following components: the fitted values of (i) $\rho_{jj'}(t_k)$, the longitudinal concordance correlation; (ii) $\rho^{(p)}_{jj'}(t_k)$, the longitudinal Pearson correlation; and (iii) $C_{jj'}(t_k)$, the longitudinal accuracy; the upper and lower limits of 95% bootstrap confidence intervals; (iv) the sample values for ρ_{CCC}, the Pearson correlation coefficient, and the accuracy measure C_b (Lin, 1989); and (v) the ρ_{CCC} between the fitted and sample values as a goodness-of-fit statistic.
The fitted $\rho_{jj'}(t_k)$ versus the time covariate as well as its bootstrap confidence interval can be visualized using the generic function `lccPlot`, which uses the package `ggplot2`. In addition, predicted values are connected by lines while sample observations are represented by circles. If the argument `components = TRUE` is set in the `lcc` call, single plots of the $\rho_{jj'}(t_k)$, $\rho^{(p)}_{jj'}(t_k)$, and LA are returned on separate pages.

3.2 The papaya peel hue analysis

The aim of this agreement study was to determine whether a colorimeter can compete with a scanner in measuring the response variable mean hue of papaya peel over time (Oliveira et al., 2018). This because it is much faster to obtain the measurements using a colorimeter than a flatbed scanner. The importance of this study is to evaluate the magnitude of agreement over time. For this datat set we used a quadratic polynomial model with random effect on all coefficients considering different variances for each level of the factor `Method`. Under this model we estimate the $\rho_{jj'}(t_k)$, $\rho^{(p)}_{jj'}(t_k)$ and $C_{jj'}(t_k)$ statistics as well as compute their 95% bootstrap confidence intervals based on 8.000 pseudo-samples using the `lcc()` function call:

```
R> fit2 <- lcc(dataset = hue, subject = "Fruit",resp = "H_mean",
               factorA = "Method",time = "Time", qf = 2,
               qr = 2, components = TRUE, var.class = varIdent,
               weights.form = "method", ci=TRUE, nboot = 8000,
               lme.control =lmeControl(opt="optim"))
R> lccPlot(fit2)
```



(a) (b) (c)

FIGURE 1. Estimate and 95% bootstrap confidence interval for the (a) $\rho_{jj'}(t_k)$ (LCC); (b) $\rho^{(p)}_{jj'}(t_k)$ (LPC); and (c) $C_{jj'}(t_k)$ (LA) between observations measured on the equatorial region by the scanner and colorimeter, and points representing sampled observations

Figure 1 shows that the agreement profile changes over time, being smaller at the beginning of the experiment and increasing over time to values close to 1. If we consider values above 0.80 for the lower bound of the CI as an indicator of possible interchangeability between their ability to measure papaya peel color, the colorimeter could be used from day 12 onwards.

4 Final remarks

The proposed longitudinal concordance correlation is a useful statistic to describe the agreement between methods over time based on polynomial mixed-effects models, allowing the detection of changes in the extent of agreement over time. Our approach is flexible because it can accommodate balanced or unbalanced (dropouts) experimental designs and multiple methods. The argument `covar` included in the `lcc()` function allows for the inclusion of covariates in the linear predictor of the mixed-effects model to control systematic variations in the response. Another helpful feature of the `lcc` package is its flexibility to estimate the $\rho_{jj'}(t_k)$, $\rho^{(p)}_{jj'}(t_k)$ and $C_{jj'}(t_k)$ for models with heterogeneous residual variance structures for different groups of observations. This can give differences in results and conclusions. Therefore, these arguments make the `lcc()` function much more flexible for working with different types of datasets and experimental settings.

Statistical inference for estimators of $\rho_{jj'}(t_k)$, $\rho^{(p)}_{jj'}(t_k)$, and $C_{jj'}(t_k)$ can be obtained using bootstrap confidence intervals based on approximation of their empirical distributions by the normal distribution or from percentiles of their bootstrap sampling distribution. These methods are computationally intensive. The computations for the hue data analysis (Section 3.2) took about 45 minutes to construct the confidence intervals based on 8,000 bootstrap samples on a Linux platform version 4.13.0-21-generic with an Intel® Core™ 2.40GHz i7 processor and 4GB of RAM.

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References

Carrasco, J. L., King, T. S. and Chinchilli, V. M. (2009). The concordance correlation coefficient for repeated measures estimated by variance components. *Journal of Biopharmaceutical Statistics*, **19**, 90 – 105.

Lin, L. I. (1989). A Concordance Correlation Coefficient to Evaluate Reproducibility. *Biometrics*, **45**, 255 – 268.

Oliveira, T. P., Hinde, J. and Zocchi, S. S. (2018). Longitudinal concordance correlation function based on variance components: an application in fruit color analysis. *Journal of Agricultural, Biological and Environmental Statistics*, **23**, 233 – 254.

Oliveira, T. P., Moral, R. A., Hinde, J., Zocchi, S. S. and Demetrio, C. G. B. (2019). lcc: Longitudinal Concordance Correlation. R package version 1.0.2. CRAN `//R-project.org/package=lcc`

R core Team (2019). The R environment. `//www.r-project.org/`

Rathnayake, L. N. and Choudhary, P. K. (2017). Semiparametric modeling and analysis of longitudinal method comparison data. *Statistics in Medicine*, **36**, 2003 – 2015