Assessment of local influence for the analysis of agreement

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Outline

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Let $(x_{11}, x_{12}), \ldots, (x_{n1}, x_{n2})$ be a bivariate random sample from a population with mean vector μ and covariance matrix Σ .

A method to quantify the degree of agreement between the variables x_1 and x_2 corresponds to the CCC $(\textsf{Lin},\,1989).^1$ which is defined as

$$
\rho_{\rm c} = \frac{2\sigma_{12}}{\sigma_{11} + \sigma_{22} + (\mu_1 - \mu_2)^2},
$$

where μ_j and σ_{jj} are the mean and variance of the measurements obtained by the jth method or instrument of measurement $(j = 1, 2)$, and σ_{12} is the covariance between the measurements from methods 1 and 2.

It is easy to see that the CCC can be written as

$$
\rho_{\rm c} = \rho_{12} C_{12}, \qquad C_{12} = 2 \left[\frac{\sqrt{\sigma_{11} \sigma_{22}}}{\sigma_{11} + \sigma_{22} + (\mu_1 - \mu_2)^2} \right].
$$

Moreover, a nice property of CCC is $-1 < \rho_c < 1$.

¹Biometrics 45, 225-268

Let $D_i = x_{i1} - x_{i2}$ for $i = 1, ..., n$, be the differences between the measurements obtained by the two instruments. Stevens et al. $(2017)^2$ introduced the probability of agreement defined as:

$$
\psi_{\mathsf{c}} = \mathsf{P}(|D_i| \le c), \qquad c > 0,
$$

where $CAD = (-c, c)$ represents a clinically acceptable difference. Assuming that the observations $(x_{i1}, x_{i2}), i = 1, \ldots, n$, were selected from a bivariate normal population yields

$$
\psi_{\rm c} = \Phi\left(\frac{c - \mu_D}{\sigma_D}\right) - \Phi\left(-\frac{c - \mu_D}{\sigma_D}\right),\,
$$

where $\Phi(\cdot)$ denotes the cumulative distribution function of the standard normal, and $\mu_D = \mu_1 - \mu_2, \sigma_D^2 = \sigma_{11} + \sigma_{22} - 2\sigma_{12}.$

²Statistical Methods in Medical Research 26, 2487-2504.

Svetnik et al. $(2007)^3$ conducted a clinical study designed to compare the automated and semi-automated scoring of Polysomnographic (PSG) recordings used to diagnose transient sleep disorders.

The study considered 82 patients who were given a sleep-inducing drug (Zolpidem 10 mg). Measurements of latency to persistent sleep (LPS: lights out to the beginning of 10 consecutive minutes of uninterrupted sleep) were obtained using six different methods.

We focus on two of these methods: fully manual scoring (Manual) and automated scoring by the Morpheus software (Automatic).

Let $x_i = (x_{i1}, x_{i2})^\top$, for $i = 1, ..., 82$, be the log(LPS) measurements obtained with the manual and automatic methods, respectively.

³SLEEP 30, 1562-1574.

Motivating example (Svetnik et al., 2007)

Sample estimators for ρ_c and ψ_c

If subjects 1, 30 and 79 are eliminated from the dataset, the degree of agreement is increased by 28% mainly due to an increase in ρ_{12} (also called precision).

⁴McBride (2005) suggested 0.650 as a cutt-off for the CCC.

Motivating example (Svetnik et al., 2007)

To assess the influence of extreme observations on the maximum likelihood estimates, Cook (1986)⁵ proposed to study the likelihood displacement

$$
LD(\omega) = 2\{\ell(\widehat{\boldsymbol{\theta}}) - \ell(\widehat{\boldsymbol{\theta}}(\boldsymbol{\omega}))\},
$$

where $\widehat{\theta}$ and $\widehat{\theta}(\omega)$ are the MLE based on the postulated and perturbated models, which are defined as

$$
\mathcal{P} = \{p(\bm{x};\bm{\theta}): \bm{\theta} \in \Theta\}
$$

and,

$$
\mathcal{P}_\omega = \{p(\boldsymbol{x};\boldsymbol{\theta},\boldsymbol{\omega}): \boldsymbol{\theta} \in \Theta, \boldsymbol{\omega} \in \Omega\},
$$

respectively, with $\bm{\omega}\in\Omega\subset\mathbb{R}^q$ satisfying $\mathcal{P}_{\omega_0}=\mathcal{P}$, for a null perturbation, $\bm{\omega}_0$.

⁵ Journal of the Royal Statistical Society, Series B 48, 133-169

Let $f(\omega)$ be a measure of influence. The main aim of the local influence is to analyze the curvature of the influence surface $\varphi(\omega) = (\omega^{\top}, f(\omega))^{\top}$ at the critical point ω_0 .

Consider $\omega = \omega_0 + \varepsilon h$, where h is a unitary direction $(\Vert h \Vert = 1)$ and $\varepsilon \in \mathbb{R}$. When $f(\omega) = LD(\omega)$ its local behavior around $\varepsilon = 0$ for a direction h can be characterized by

$$
C_h = \mathbf{h}^\top \ddot{\mathbf{F}} \mathbf{h}, \qquad \ddot{\mathbf{F}} = \frac{\partial^2 \ell(\widehat{\boldsymbol{\theta}}(\boldsymbol{\omega}))}{\partial \boldsymbol{\omega} \partial \boldsymbol{\omega}^\top}\Big|_{\boldsymbol{\omega} = \boldsymbol{\omega}_0}.
$$

Moreover, Cook (1986) shows that

$$
\ddot{\mathbf{F}} = 2\boldsymbol{\Delta}^{\top}(-\ddot{\mathbf{L}})^{-1}\boldsymbol{\Delta},
$$

with

$$
\ddot{L} = \frac{\partial^2 \ell(\boldsymbol{\theta})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\theta}^\top}, \qquad \qquad \boldsymbol{\Delta} = \frac{\partial^2 \ell(\boldsymbol{\theta}|\boldsymbol{\omega})}{\partial \boldsymbol{\theta} \partial \boldsymbol{\omega}^\top},
$$

which must be evaluated at $\theta = \widehat{\theta}$ and $\omega = \omega_0$, and $\ell(\theta)$ and $\ell(\theta|\omega)$ denote the log-likelihood functions arising from P and P_{ω} .

For general objective functions, $f(\omega)$, we have that (Cook, 1986) the normal curvature assumes the form

$$
C_{f,h} = \frac{\boldsymbol{h}^\top \boldsymbol{H}_f \boldsymbol{h}}{(1 + \nabla_f^\top \nabla_f) \boldsymbol{h}^\top (\boldsymbol{I} + \nabla_f \nabla_f^\top) \boldsymbol{h}},
$$

where $\nabla_f=\partial f(\bm{\omega})/\partial \bm{\omega}\big|_{\omega=\omega_0}$ and $\bm{H}_f=\partial^2 f(\bm{\omega})/\partial \bm{\omega}\partial \bm{\omega}^\top\big|_{\omega=\omega_0}$, whereas the conformal normal curvature in the direction h evaluated at ω_0 (Poon and Poon, $(1999)^6$ is given by

$$
B_{f,h} = \frac{\boldsymbol{h}^\top \boldsymbol{H}_f \boldsymbol{h}}{\|\boldsymbol{H}_f\|_M \boldsymbol{h}^\top (\boldsymbol{I} + \nabla_f \nabla_f^\top) \boldsymbol{h}}.
$$

An interesting property of the conformal curvature is that $0 \leq |B_{f,h}| \leq 1$.

 6 Journal of the Royal Statistical Society, Series B 61 , 51-61

The first-order approach for local influence (Cadigan and Farrell, 2002) 7 is measured using the directional derivative of $f(\omega)$, which is given by

$$
S_{f,h} = \frac{\partial f(\boldsymbol{\omega})}{\partial \varepsilon}\Big|_{\varepsilon=0} = \boldsymbol{h}^\top \nabla_f,
$$

where $\nabla_f=\partial f(\bm{\omega})/\partial \bm{\omega}|_{\omega=\omega_0}.$ In the case that $\nabla_f\neq\bm{0},$ the direction of the maximum local slope is

$$
\boldsymbol{h}_{\text{max}} = \frac{\nabla_f}{\|\nabla_f\|}.
$$

Remark:

First-order local influence may be unable to detect some significant directions with large curvature (see Wu and Luo 19938 and Cadigan and Farrell, 2002).

8 Journal of the Royal Statistical Society, Series B 55, 929-936.

⁷Applied Statistics 51, 469-483.

To construct influence measures of the first and second order, Zhu et al. $(2007)^9$ introduced the matrix $G(\omega)$ defined as the Fisher information matrix with respect to ω , with elements

$$
g_{ij}(\boldsymbol{\omega}) = \mathsf{E}_{\omega} \left\{ \frac{\partial \ell(\boldsymbol{\theta}|\boldsymbol{\omega})}{\partial \omega_i} \frac{\partial \ell(\boldsymbol{\theta}|\boldsymbol{\omega})}{\partial \omega_j} \right\}, \qquad i, j = 1, \dots, n,
$$

where $E_{\omega}(\cdot)$ indicates that the expectation is taken with respect to the density function $p(x; \theta, \omega)$.

The first-order influence measure (FI) in the direction h is given by

$$
\mathrm{FI}_{f,h} = \frac{\mathbf{h}^\top \nabla_f \nabla_f^\top \mathbf{h}}{\mathbf{h}^\top \mathbf{G}(\boldsymbol{\omega}_0) \mathbf{h}},
$$

The second-order influence measure (SI) in the direction h is given by

$$
\mathrm{SI}_{f,h} = \frac{\mathbf{h}^\top \tilde{\mathbf{H}}_f \mathbf{h}}{\mathbf{h}^\top \mathbf{G}(\boldsymbol{\omega}_0) \mathbf{h}},
$$

where $G(\omega_0)$ is the metric tensor matrix evaluated at ω_0 .

⁹The Annals of Statistics 35, 2565-2588.

In the definition of $\mathrm{SI}_{f,h}$, $\tilde{\bm{H}}_f$ denotes the covariant Hessian matrix at $\bm{\omega}_0$, with (i, j) th element given by

$$
\left(\tilde{\pmb{H}}_{f}\right)_{ij}=\frac{\partial}{\partial \omega_{i}}\Big(\frac{\partial f(\pmb{\omega})}{\partial \omega_{j}}\Big)\Big|_{\omega=\omega_{0}}-\sum_{s,r}g^{r,s}(\pmb{\omega})\Gamma_{ijs}^{0}(\pmb{\omega})\Big(\frac{\partial f(\pmb{\omega})}{\partial \omega_{r}}\Big)\Big|_{\omega=\omega_{0}},
$$

in which $g^{r,s}(\boldsymbol \omega)$ is the (r,s) th element of $\boldsymbol G(\boldsymbol \omega)^{-1}$ and

$$
\Gamma^0_{ijs}(\omega) = \frac{1}{2} \bigg\{ \frac{\partial}{\partial \omega_i} g(\omega)_{js} + \frac{\partial}{\partial \omega_j} g_{is}(\omega) - \frac{\partial}{\partial \omega_s} g_{ij}(\omega) \bigg\},\,
$$

denotes the Christoffel symbol for the Lévi-Civita connection.

Influence measures for CCC and PA

We consider $\widehat{\rho}_c(\omega)$ and $\widehat{\psi}_c(\omega)$ as objective functions

$$
\widehat{\rho}_c(\boldsymbol{\omega}) = \frac{2\widehat{\sigma}_{12}(\boldsymbol{\omega})}{\widehat{\sigma}_{11}(\boldsymbol{\omega}) + \widehat{\sigma}_{22}(\boldsymbol{\omega}) + (\widehat{\mu}_1(\boldsymbol{\omega}) - \widehat{\mu}_2(\boldsymbol{\omega}))^2},
$$

and

$$
\widehat{\psi}_c(\boldsymbol{\omega}) = \Phi\Big(\frac{c - \widehat{\mu}_D(\boldsymbol{\omega})}{\widehat{\sigma}_D(\boldsymbol{\omega})}\Big) - \Phi\Big(-\frac{c - \widehat{\mu}_D(\boldsymbol{\omega})}{\widehat{\sigma}_D(\boldsymbol{\omega})}\Big),
$$

where $\widehat{\mu}_D(\omega) = \widehat{\mu}_1(\omega) - \widehat{\mu}_2(\omega)$, $\widehat{\sigma}_D^2(\omega) = \widehat{\sigma}_{11}(\omega) + \widehat{\sigma}_{22}(\omega) - 2\widehat{\sigma}_{12}(\omega)$, and

$$
\widehat{\mu}_j(\omega) = \frac{1}{\sum_{i=1}^n \omega_i} \sum_{i=1}^n \omega_i x_{ij},
$$

$$
\widehat{\sigma}_{jk}(\omega) = \frac{1}{\sum_{i=1}^n \omega_i} \sum_{i=1}^n \omega_i (x_{ij} - \widehat{\mu}_j(\omega)) (x_{ik} - \widehat{\mu}_k(\omega)),
$$

for $j, k = 1, 2$, and $\boldsymbol{\omega} = (\omega_1, \dots, \omega_n)^\top$.

The density of the perturbed model, is given by

$$
p(\boldsymbol{x};\boldsymbol{\theta},\boldsymbol{\omega}) = \prod_{i=1}^n \left[(2\pi)^{-d/2} |\omega_i^{-1} \boldsymbol{\Sigma}|^{-1/2} \exp \big\{ -\frac{1}{2} \omega_i (\boldsymbol{x}_i - \boldsymbol{\mu})^\top \boldsymbol{\Sigma}^{-1} (\boldsymbol{x}_i - \boldsymbol{\mu}) \big\} \right].
$$

The null perturbation is $\omega_0 = 1_n$ in which case $\mathcal{P}_{\omega_0} = \mathcal{P}$ and $\ell(\theta|\omega_0) = \ell(\theta)$.

This yields to the matrix $G(\omega_0) = I_n$, and we verify that the perturbation scheme induced by the model P_{ω} is appropiate.

The first- and second-order influence measures are reduced to

$$
\mathrm{FI}_{f,h} = \mathbf{h}^\top \nabla_f \nabla_f^\top \mathbf{h}
$$
, and $\mathrm{SI}_{f,h} = \mathbf{h}^\top \tilde{\mathbf{H}}_f \mathbf{h}$,

respectively, for each objective function, either $\widehat{\rho}_c(\omega)$ or $\widehat{\psi}_c(\omega)$.

The first-order derivative required in $FI_{\hat{\rho}_c,h}$, as well as $C_{\hat{\rho}_c,h}$ and $B_{\hat{\rho}_c,h}$, assumes the form

$$
\nabla_{\widehat{\rho}_c} = \frac{\widehat{\rho}_c}{n\widehat{\sigma}_{12}} \left(\boldsymbol{z}_1 \odot \boldsymbol{z}_2 - \widehat{\sigma}_{12} \boldsymbol{1} \right) - \frac{\widehat{\rho}_c^2}{2n\widehat{\sigma}_{12}} \boldsymbol{z}_*,
$$
\nwhere $\boldsymbol{z}_j = (z_{1j}, \ldots, z_{nj})^\top$ with $z_{ij} = z_{ij} - \widehat{\mu}_j$, for $i = 1, \ldots, n; j = 1, 2$,
\n $\boldsymbol{z}_* = (\boldsymbol{z}_1 \odot \boldsymbol{z}_1 - \widehat{\sigma}_{11} \boldsymbol{1}_n) + (\boldsymbol{z}_2 \odot \boldsymbol{z}_2 - \widehat{\sigma}_{22} \boldsymbol{1}_n) + 2(\widehat{\mu}_1 - \widehat{\mu}_2)(\boldsymbol{z}_1 - \boldsymbol{z}_2),$

and \odot represents the Hadamard product.

Moreover, $\tilde{\bm{H}}_{\widehat{\rho}_c} = \bm{H}_{\widehat{\rho}_c} + \text{diag}(\nabla_{\widehat{\rho}_c}),$ with $H_{\widehat{\theta}} = \Gamma_1 - \Gamma_2 - \Gamma_3.$

For definition of Γ_1 , Γ_2 and Γ_3 see Leal et al. (2019).

Influence measures for CCC and PA

Furthermore $\nabla_{\widehat{\psi}_c}=\partial\psi_c(\boldsymbol\omega)/\partial\boldsymbol\omega|_{\omega=\omega_0}$ assumes the form

$$
\nabla_{\widehat{\psi}_c} = -\frac{2}{\widehat{\sigma}_D^2} \phi \left(\frac{c - \widehat{\mu}_D}{\widehat{\sigma}_D} \right) \mathbf{s},\,
$$

with

$$
\boldsymbol{s} = \widehat{\sigma}_D(\boldsymbol{Z}_1 - \boldsymbol{Z}_2) + \frac{1}{2} \Big(\frac{c - \widehat{\mu}_D}{\widehat{\sigma}_D} \Big) \Big\{ \frac{n-2}{n} (\boldsymbol{Z}_1 - \boldsymbol{Z}_2) \odot (\boldsymbol{Z}_1 - \boldsymbol{Z}_2) - \widehat{\sigma}_D^2 \boldsymbol{1} \Big\},
$$

where $\phi(\cdot)$ denotes the density funtion of the standard normal.

$$
\begin{aligned} \boldsymbol{H}_{\widehat{\psi}_c} &= \partial^2 \widehat{\psi}_c(\boldsymbol{\omega}) / \partial \boldsymbol{\omega} \partial \boldsymbol{\omega}^\top |_{\boldsymbol{\omega} = \omega_0} \text{ can be written as,} \\ \boldsymbol{H}_{\widehat{\psi}_c} &= 2 \phi \Big(\frac{c - \widehat{\mu}_D}{\widehat{\sigma}_D} \Big) \Big\{ \boldsymbol{\Delta}_1 - \frac{1}{\widehat{\sigma}_D^2} (\boldsymbol{\Delta}_2 + \boldsymbol{\Delta}_3 + \boldsymbol{\Delta}_4) - \frac{1}{\widehat{\sigma}_D^4} \boldsymbol{s} \boldsymbol{s}^\top \Big\}. \end{aligned}
$$

Details on the definition of $\Delta_1, \Delta_2, \Delta_3$ and Δ_4 can be found in Leal et al. (2019).

We generate 500 datasets of sample sizes $n = 25, 50, 100$ and 200 from $N_2(\mu, \Sigma)$, with

$$
\boldsymbol{\mu} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \qquad \boldsymbol{\Sigma} = \begin{pmatrix} 1 & 0.95 \\ 0.95 & 1 \end{pmatrix}.
$$

To introduce an outlier, for each dataset, a single observation of the second variable x_2 was changed to $x_2 + \delta$, where $\delta = 0.5, 1.5, 2.0, 2.5, 3.0$ and 3.5.

We find the unitary direction related to the maximum local slope, normal and conformal curvatures and first- and second-order influence measures for $\widehat{\rho}_c(\omega)$ and $\widehat{\psi}(\omega)$.

For each δ , the percentages of detecting the outlier were computed using the following threshold:

$$
M_j=|\boldsymbol{h}_{\text{max}}|_j>\overline{M}+2\,\text{sd}(M),
$$

where sd(M) denotes the standard deviation of M_j , $j = 1, \ldots, n$.

All the diagnostic measures described in our work have been implemented in an R code available at github¹⁰

¹⁰URL: <https://github.com/faosorios/CCC/>

Monte Carlo simulation study: A typical dataset

Scatter plot of a typical dataset (with $\delta = 2$) from the simulation experiment:

Monte Carlo simulation study

Outlier detection percentage using $\psi_c(\boldsymbol{\omega})^{11}$ as objective function

Monte Carlo simulation study: Index plot of $|h_{\sf max}|$ for $\widehat{\bm{\rho}}_c(\bm{\omega})$ O [Slide 20](#page-19-0)

Monte Carlo simulation study: Index plot of $|h_{\sf max}|$ for $\psi_c(\omega)$

This dataset was previously analyzed by Feng et al. $(2015)^{12}$ using a robust approach within a Bayesian framework.

Figure \triangleright [Slide 6](#page-5-0) reveals that observations 1, 30 and 79 are outside the limits of agreement and therefore can be identified as potential outliers.

Consider the percentage of change of the ML estimates for the fitted model:

¹²Journal of Biopharmaceutical Statistics 25, 490-507.

Percentage of change for $\widehat{\rho}_c$, $\widehat{\psi}_c$ and the log-likelihood function:

Transient sleep disorder: Index plot of $|h_{\sf max}|$ for $\widehat\rho_c(\omega)$

Transient sleep disorder: Index plot of $|h_{\sf max}|$ for $\psi_c(\omega)$

Concluding remarks and future work

- Influential data may distort the estimation of the CCC and PA leading to incorrect decisions (replacing one measurement method with another when their degree of agreement is not really true).
- \triangleright Several diagnostic measures to detect influential data on the estimates of the CCC and PA were proposed.
- \triangleright A computational implementation of such diagnostic techniques has been made publicly available.
- \blacktriangleright The empirical results seem to suggest that for our problem, first-order influence measures are efficient for the identification of influential observations.
- \triangleright Extend the estimation and diagnostics for the CCC and PA considering a
- \blacktriangleright Influence diagnostics for the matrix-based concordance correlation coefficient.

Concluding remarks and future work

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- \blacktriangleright The empirical results seem to suggest that for our problem, first-order influence measures are efficient for the identification of influential observations.
- \triangleright Extend the estimation and diagnostics for the CCC and PA considering a multivariate t-distribution.
- Influence diagnostics for the matrix-based concordance correlation coefficient.

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