A repeated measures concordance correlation coefficient

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Presented by Yan Ma
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- Blood draw data example

Background

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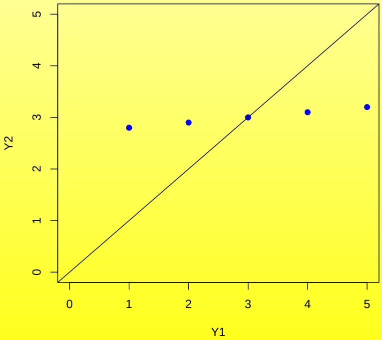

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- Kendall's *tau* =1;
- Spearman's *rho*=1.

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- Lin (1989),

$$\begin{aligned}\rho_c &= 1 - \frac{E(Y_1 - Y_2)^2}{E_{indep}(Y_1 - Y_2)^2} \\ &= \frac{2\sigma_{Y_1 Y_2}}{\sigma_{Y_1 Y_1} + \sigma_{Y_2 Y_2} + (\mu_{Y_1} - \mu_{Y_2})^2}\end{aligned}$$

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- $-1 \leq -|\rho| \leq \rho_c \leq |\rho| \leq 1$

- $$\rho_c = \rho C_b$$

  where

$$\begin{aligned} C_b &= [(v + 1/v + u^2)/2]^{-1}, \\ v &= \sigma_1/\sigma_2, \\ u &= (\mu_1 - \mu_2)/\sqrt{\sigma_1\sigma_2}. \end{aligned}$$

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- $\hat{\rho}_c = 0.2$

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Table 1: A comparison of CCC, Pearson CC, Kendall's tau and Spearman's rho

Ex1. $(\mathbf{Y}_1, \mathbf{Y}_2) = \{(1, 2.8), (2, 2.9), (3, 3), (4, 3.1), (5, 3.2)\}$
Ex2. $(\mathbf{Y}_1, \mathbf{Y}_2) = \{(1, 21), (2, 22), (3, 23), (4, 24), (5, 25)\}$
Ex3. $(\mathbf{Y}_1, \mathbf{Y}_2) = \{(1, 1), (2, 12), (3, 93), (4, 124), (5, 95)\}$

Example	CCC	Pearson CC	Kendall's tau	Spearman's rho
1	0.2	1	1	1
2	0.01	1	1	1
3	0.02	0.86	0.8	0.9

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- has been expanded to assess the amount of agreement among more than two raters or methods (King and Chinchilli,2001; and Barnhart *et al.*, 2002);
- has been shown to be equivalent to a particular specification of the intraclass correlation coefficient (ICC) (Carrasco and Jover, 2003).

King *et al.*, 2007

This paper proposes an approach to assessing agreement between two responses in the presence of repeated measures which is based on obtaining population estimates. We incorporate an unstructured correlation structure of the repeated measurements, and use the population estimates, rather than subject-specific estimates, to construct a repeated measures CCC.

Notations and Assumptions

- **X(Y)**$(x(y)_{ij})$: ith subject and jth repeated measure of the first (second) method of measurement, $i = 1, 2, .., n$; $j = 1, 2, ..., p$.

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- **X(Y)**$(x(y)_{ij})$: ith subject and jth repeated measure of the first (second) method of measurement, $i = 1, 2, .., n$; $j = 1, 2, ..., p$.
- Assume $[X_i, Y_i]$ are selected from a multivariate normal population with $2p \times 1$ mean vector $[\mu_X, \mu_Y]$, and $2p \times 2p$ covariance matrix Σ, which consists of the following four $p \times p$ matrices: Σ_{XX}, Σ_{XY}, Σ_{YX} and Σ_{YY}.

A repeated measures CCC

$$\rho_{c,rm} = 1 - \frac{E[(\mathbf{X}\text{-}\mathbf{Y})^\top \mathbf{D}(\mathbf{X}\text{-}\mathbf{Y})]}{E_{indep}[(\mathbf{X}\text{-}\mathbf{Y})^\top \mathbf{D}(\mathbf{X}\text{-}\mathbf{Y})]}$$
$$= \frac{\sum_{j=1}^p \sum_{k=1}^p d_{jk}(\sigma_{X_jY_k} + \sigma_{Y_jX_k})}{\sum_{j=1}^p \sum_{k=1}^p d_{jk}(\sigma_{X_jX_k} + \sigma_{Y_jY_k}) + \sum_{j=1}^p \sum_{k=1}^p d_{jk}(\mu_{X_j} - \mu_{Y_j})(\mu_{X_k} - \mu_{Y_k})}$$

where **D** is a $p \times p$ non-negative definite matrix of weight between the different repeated measurements. This parameter is a generalization of that described by Lin (1989), and reduces to Lins CCC if $p = 1$ for $i = 1, 2, ..., n$

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To consider the measurement of agreement in a variety of paired and unpaired data situations, we can specify different definitions of **D** which incorporate strictly within-visit (X_j versus Y_j) or between- and within-visit agreement (X_j versus Y_k). Four options we consider for the **D** matrix are as follows:

(1) $\mathbf{D} = \mathbf{I}_{p \times p}$.

(2) $\mathbf{D} = ((d_{jk}))$

$$\text{where } d_{jk} = \begin{cases} p & \text{for } j = k \text{ of greatest interest} \\ p-1 & \\ \vdots & \\ 1 & \text{for } j = k \text{ of least interest} \end{cases}$$

and $d_{jk} = 0$ when $j \neq k$.

(3) $\mathbf{D} = ((d_{jk}))$ where $d_{jk} = d^{|j-k|}$ $0 < d < 1$.

(4) $\mathbf{D} = ((d_{jk}))$ where $d_{jk} = 1$

An estimator of ρ_c

$$\hat{\rho}_{c,rm} = \frac{\sum_{j=1}^{p}\sum_{k=1}^{p} d_{jk}(\hat{\sigma}_{X_j Y_k} + \hat{\sigma}_{Y_j X_k})}{\sum_{j=1}^{p}\sum_{k=1}^{p} d_{jk}(\hat{\sigma}_{X_j X_k} + \hat{\sigma}_{Y_j Y_k}) + \sum_{j=1}^{p}\sum_{k=1}^{p} d_{jk}(\hat{\mu}_{X_j} - \hat{\mu}_{Y_j})(\hat{\mu}_{X_k} - \hat{\mu}_{Y_k})}$$

A basic consideration for statistical inference concerning $\rho_{c,rm}$ is to recognize that the estimator $\hat{\rho}_{c,rm}$ can be expressed as a ratio of functions of U-statistics.

$$\hat{\rho}_{c,rm} = \frac{(n-1)(V-U)}{U+(n-1)V}$$

Apply the theory of U-statistics, $\hat{\rho}_{c,rm}$ has a normal distribution asymptotically with mean $\rho_{c,rm}$ and a variance that can be consistently estimated using the delta method with

$$Var(\hat{\rho}_{c,rm}) = \mathbf{d}\Sigma\mathbf{d}^{\top}$$

$$\hat{Z} = \frac{1}{2} ln \left(\frac{1+\hat{\rho}_{c,rm}}{1-\hat{\rho}_{c,rm}} \right)$$

Scenario

The simulation was performed for three cases evaluating different location and scale shifts, with sample sizes of $n = 20, 40$ and 80, considering scenarios with three repeated measurements per unit.

- Case 1: Means $\mu_x = (4, 6, 8)$ and $\mu_y = (5, 7, 9)$, within-visit covariance matrix

$$\begin{pmatrix} 8 & 0.95 \times \sqrt{8} \times \sqrt{10} \\ 0.95 \times \sqrt{8} \times \sqrt{10} & 10 \end{pmatrix}$$

  and a 3×3 compound symmetric within-subject correlation structure with $\rho = 0.4$.

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- Case 2:Means $\mu_x = (4, 6, 8)$ and $\mu_y = (6, 8, 12)$, within-visit covariance matrix

$$\begin{pmatrix} 8 & 0.8 \times \sqrt{8} \times \sqrt{12} \\ 0.8 \times \sqrt{8} \times \sqrt{12} & 12 \end{pmatrix}$$

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- Case 3:Means $\mu_x = (4, 6, 8)$ and $\mu_y = (7, 9, 11)$, within-visit covariance matrix

$$\begin{pmatrix} 8 & 0.5 \times \sqrt{8} \times \sqrt{15} \\ 0.5 \times \sqrt{8} \times \sqrt{15} & 15 \end{pmatrix}$$

Table I. Average estimates of $\hat{\rho}_{c,rm}$, average asymptotic $\hat{\sigma}^2_Z$, and the empirical variance of $\hat{Z}$ based on simulation of 1000 runs generated from normal distribution: three repeated measurements.

Within-unit correlation	Case	Measure	$\rho_{c,rm1}$ 20	40	80	$\rho_{c,rm}$	$\rho_{c,rm2}$ 20	40	80	$\rho_{c,rm}$	$\rho_{c,rm3}$ 20	40	80	$\rho_{c,rm}$	$\rho_{c,rm4}$ 20	40	80	$\rho_{c,rm}$
0.4	1	$\hat{\rho}_{c,rm}$	0.891	0.895	0.897	0.900	0.890	0.895	0.897	0.900	0.870	0.876	0.879	0.882	0.852	0.861	0.865	0.869
		$\hat{\sigma}^2_Z$	0.015	0.008	0.004		0.016	0.009	0.004		0.023	0.012	0.006		0.032	0.017	0.009	
		$\mathrm{var}(\hat{Z})$	0.019	0.009	0.005		0.021	0.010	0.006		0.027	0.012	0.007		0.035	0.016	0.009	
	2	$\hat{\rho}_{c,rm}$	0.646	0.655	0.659	0.664	0.644	0.654	0.658	0.664	0.603	0.614	0.618	0.625	0.570	0.584	0.599	0.597
		$\hat{\sigma}^2_Z$	0.022	0.011	0.006		0.024	0.012	0.006		0.034	0.018	0.009		0.047	0.025	0.012	
		$\mathrm{var}(\hat{Z})$	0.016	0.008	0.004		0.017	0.008	0.005		0.021	0.010	0.006		0.027	0.013	0.007	
	3	$\hat{\rho}_{c,rm}$	0.339	0.346	0.350	0.354	0.337	0.345	0.349	0.354	0.303	0.311	0.315	0.320	0.279	0.288	0.292	0.297
		$\hat{\sigma}^2_Z$	0.031	0.016	0.008		0.033	0.017	0.009		0.046	0.024	0.012		0.061	0.032	0.016	
		$\mathrm{var}(\hat{Z})$	0.012	0.006	0.003		0.013	0.007	0.004		0.015	0.007	0.004		0.018	0.009	0.005	
0.8	1	$\hat{\rho}_{c,rm}$	0.888	0.894	0.897	0.900	0.888	0.894	0.897	0.900	0.881	0.889	0.892	0.895	0.878	0.886	0.889	0.892
		$\hat{\sigma}^2_Z$	0.024	0.013	0.006		0.024	0.013	0.007		0.028	0.015	0.008		0.031	0.017	0.008	
		$\mathrm{var}(\hat{Z})$	0.031	0.014	0.008		0.032	0.015	0.009		0.036	0.017	0.009		0.039	0.018	0.010	
	2	$\hat{\rho}_{c,rm}$	0.640	0.653	0.658	0.664	0.640	0.652	0.658	0.664	0.627	0.640	0.646	0.653	0.619	0.634	0.640	0.647
		$\hat{\sigma}^2_Z$	0.034	0.018	0.009		0.035	0.018	0.009		0.040	0.021	0.010		0.044	0.023	0.011	
		$\mathrm{var}(\hat{Z})$	0.026	0.013	0.007		0.027	0.013	0.007		0.030	0.014	0.008		0.032	0.015	0.009	
	3	$\hat{\rho}_{c,rm}$	0.334	0.344	0.349	0.354	0.334	0.344	0.349	0.354	0.323	0.334	0.339	0.344	0.317	0.328	0.334	0.339
		$\hat{\sigma}^2_Z$	0.048	0.025	0.012		0.049	0.025	0.013		0.055	0.029	0.014		0.060	0.031	0.015	
		$\mathrm{var}(\hat{Z})$	0.020	0.010	0.006		0.021	0.011	0.006		0.023	0.011	0.006		0.024	0.012	0.007	

Table II. Coverage probabilities for the 95 per cent confidence interval around $\rho_{c,rm}$ based on simulation of 1000 runs generated from normal distribution.

Within-unit correlation	Case	n	Three repeated measures				Five repeated measures			
			$\rho_{c,rm1}$	$\rho_{c,rm2}$	$\rho_{c,rm3}$	$\rho_{c,rm4}$	$\rho_{c,rm1}$	$\rho_{c,rm2}$	$\rho_{c,rm3}$	$\rho_{c,rm4}$
0.4	1	20	0.911	0.910	0.923	0.935	0.909	0.897	0.921	0.934
		40	0.930	0.922	0.940	0.950	0.914	0.907	0.933	0.939
		80	0.909	0.903	0.926	0.937	0.912	0.917	0.920	0.937
	2	20	0.972	0.971	0.978	0.986	0.972	0.972	0.978	0.980
		40	0.974	0.975	0.986	0.992	0.970	0.974	0.983	0.991
		80	0.973	0.972	0.983	0.989	0.971	0.971	0.985	0.990
	3	20	0.994	0.991	0.997	0.996	0.995	0.990	0.994	0.995
		40	0.998	0.997	1.000	1.000	0.998	0.997	1.000	1.000
		80	0.997	0.996	0.999	0.999	0.996	0.995	0.999	1.000
0.8	1	20	0.901	0.909	0.916	0.921	0.905	0.901	0.912	0.917
		40	0.925	0.916	0.926	0.926	0.911	0.911	0.917	0.924
		80	0.903	0.904	0.907	0.910	0.907	0.902	0.906	0.911
	2	20	0.965	0.970	0.969	0.970	0.966	0.966	0.975	0.978
		40	0.975	0.977	0.981	0.980	0.974	0.972	0.974	0.973
		80	0.967	0.967	0.971	0.971	0.968	0.968	0.972	0.973
	3	20	0.991	0.990	0.992	0.992	0.986	0.989	0.986	0.988
		40	0.997	0.995	0.997	0.998	0.992	0.994	0.993	0.993
		80	0.994	0.994	0.995	0.994	0.992	0.993	0.993	0.993

Penn State Young Women's Health Study

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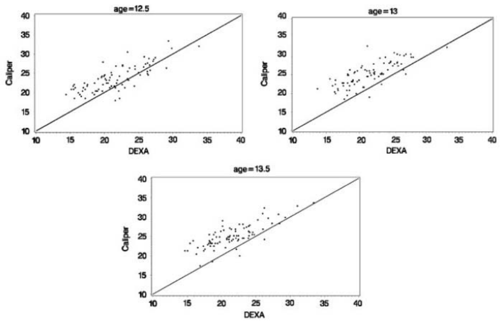
- Body fat was estimated from skinfolds calipers and DEXA on a cohort of 90 adolescent girls whose initial visit occurred at age 12;
- Skinfolds calipers and DEXA measurements were taken for the subsequent visits, which occurred every 6 months.



	Visit2	Visit3	Visit4
Visit 2	0.667	0.584	0.545
Visit 3	0.497	0.481	0.457
Visit 4	0.438	0.432	0.486

$\widehat{\rho}_{c,rm} = 0.568$ with 95% CI = (0.406, 0.695)*

Figure 2. Scatter plots of bodyfat data. *Using the D matrix based on the uneven weighting of the diagonal elements (D_2) with a degradation of emphasis from visits 2 to 4.

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- Weighted average of the pair-wise estimates of the CCC among the repeated measurements of the two variables X and Y.

$$\rho_{c,w} = \sum_{j=1}^{p} \sum_{k=1}^{p} w_{jk} \rho_{cjk}$$

  - intuitively more appealing, based on a distance function, similar to Lin's original coefficient;
  - The asymptotic variance of $\rho_{c,w}$ would be difficult to derive.

- $\rho_{c,rm}$ is an aggregated index.

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- If there is a pattern in these pair-wise CCCs, one may be interested in modeling agreement over time(Barnhart and Williamson , 2001).