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SYMMETRICALLY DEPENDENT MODELS ARISING IN VISUAL ASSESSMENT DATA

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ABSTRACT. Given data from bilateral visual assessments on N subjects at k occasions, we consider inference for contralateral correlations (C) between fellow eyes and lateral correlations (L) among p different assessments of the same eye. Under permutation symmetric dependence structure between observations from fellow eyes and among observations from the same eye, we obtain maximum likelihood estimates of L, C, and L-C. Based on the large-sample estimates of the corresponding covariance structures, we test the hypothesis that the association between fellow eyes is constant across time and the hypothesis that lateral and contralateral associations between at any two occasions are the same.

1. Introduction

Observations between related measurements, such as with eyes, ears, siblings, etc. possess intrinsic symmetries which may be relevant for assessing an underlying physiological process. This article is concerned with the assessment of symmetrically dependent models arising in human vision-related data. The symmetry with which a given biological or physiological condition is observed on fellow eyes (namely, right and left eyes from one person) often contributes to the understanding of the etiology of that condition. In fact, as discussed in Wood and Bullimore (1996), a commonly used clinical technique for determining whether visual function is abnormal, particularly when a patient is suspected of having unilateral or asymmetric disease, is to compare the visual function of the 'suspect' eye to that of the normal eye. This implies the assessment of the assumption that visual function in each eye is equal and that this symmetry is maintained, for example, across time-periods. Similarly, the bilateral or symmetric presence or progression of a given condition is often part of its differential characterization. The characterization of Marfan's syndrome (an

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autosomal dominant disorder characterized by superior lens dislocation) includes a symmetrical retinal detachment and tears (Detrelova 1998) and the symmetry of the clinical manifestations in nephropathia epidemica reflects the systemic nature of the underlying infection (Kontkanen, Puustjarvi, Kauppi and Lahdevirta 1996).

The presence or absence of contra-lateral (opposing eyes) conditions may also contribute to the understanding of the underlying physiological process. Various forms of albinism frequently have misrouting of their optic nerve fibers and visual evoked potential studies show that monocular stimulation tends to result in asymmetrical rather than symmetrical occipital response. The most likely explanation of this phenomenon is that the visual pathway misrouting is complete or nearly complete in some children with albinism so that one rather than both occipital lobes receive visual information from each eye (Smith 1998). The occurrence of monocular naso-to-temporal optokinetic nystagmus (OKN) asymmetry, as a reflection of the immature oculomotor system in infants has been linked with poor bilateral function, as reported by Shawkat, Harris, Taylor, Thompson, Russell-Eggitt and Kriss (1995). The study also concluded that unequal input from the two eyes and between-eye rivalry lead to OKN asymmetry, thus suggesting that if vision from one eye is so negligible that it does not compete with the neuroanatomic connections of the fellow eye, then the input from this eye remains undisturbed, and OKN remains symmetric.

Experimental data from these and similar examples have certain notions in common, such as lateral and contra-lateral observations or symmetry between fellow eyes. To represent these notions, we need the following notation. Let $(\mathrm{Y}_{\mathrm{t1}}, \mathrm{Y}_{\mathrm{t2}})$ represent a visual response in the left $(\mathrm{Y}_{\mathrm{t1}})$ and right $(\mathrm{Y}_{\mathrm{t2}})$ eye at time-points $\mathrm{t} = 1, 2, \ldots, \mathrm{k}$. The two k-variate vectors $(\mathrm{Y}_{11}, \mathrm{Y}_{21}, \ldots, \mathrm{Y}_{\mathrm{k1}})$ and $(\mathrm{Y}_{12}, \mathrm{Y}_{22}, \ldots, \mathrm{Y}_{\mathrm{k2}})$ representing left and right eye observations at time-points $\mathrm{t} = 1, 2, \ldots \mathrm{k}$ are called *lateral* observations whereas the k bivariate vectors $(\mathrm{Y}_{\mathrm{t1}}, \mathrm{Y}_{\mathrm{t2}}), \mathrm{t} = 1, \ldots, \mathrm{k}$ are called *contra-lateral* (or fellow) observations. The concern is with correlational inferences for these two types of observations. We assume a sample of size N from an underlying multivariate normal distribution in which the contra-lateral correlations between any two time-points t and u are vision-symmetric, that is, $\mathrm{corr}(\mathrm{Y}_{\mathrm{t1}}, \mathrm{Y}_{\mathrm{u2}}) = \mathrm{corr}(\mathrm{Y}_{\mathrm{t2}}, \mathrm{Y}_{\mathrm{u1}}) = \gamma_{\mathrm{tu}}$, whereas the lateral correlations between any two time points t and u depend only on t and u, that is, $\mathrm{corr}(\mathrm{Y}_{\mathrm{t1}}, \mathrm{Y}_{\mathrm{u1}}) = \mathrm{corr}(\mathrm{Y}_{\mathrm{t2}}, \mathrm{Y}_{\mathrm{u2}}) = \lambda_{\mathrm{tu}}$. Furthermore, we assume that $\mathrm{var}(\mathrm{Y}_{\mathrm{t1}}) = \mathrm{var}(\mathrm{Y}_{\mathrm{t2}}) = \sigma_{\mathrm{t}}^2$. These conditions are equivalent to assuming that the covariance structure between fellow eyes may depend on the time-points, and that the left-right labeling is irrelevant at each time-point. Equivalently, we say that the observations are (block) permutation-symmetric.

The following example will serve to clarify the model. Let Σ denote the covariance matrix of $\mathbf{Y}' = (\mathrm{Y}_{11}, \mathrm{Y}_{12}, \ldots, \mathrm{Y}_{k1}, \mathrm{Y}_{k2})$. The 2×2 diagonal and off-diagonal blocks have the form

$$\Sigma_{tt} = \sigma_t^2 \begin{bmatrix} 1 & \gamma_{tt} \\ \gamma_{tt} & 1 \end{bmatrix}, \quad \Sigma_{tu} = \sigma_t \sigma_u \begin{bmatrix} \lambda_{tu} & \gamma_{tu} \\ \gamma_{tu} & \lambda_{tu} \end{bmatrix}, \quad t \neq u.$$

For example, when k=3, the joint covariance matrix becomes

$$\Sigma = \begin{bmatrix} \sigma_1^2 \begin{bmatrix} 1 & \gamma_{11} \\ \gamma_{11} & 1 \end{bmatrix} & \sigma_1\sigma_2 \begin{bmatrix} \lambda_{12} & \gamma_{12} \\ \gamma_{12} & \lambda_{12} \end{bmatrix} & \sigma_1\sigma_3 \begin{bmatrix} \lambda_{13} & \gamma_{13} \\ \gamma_{13} & \lambda_{13} \end{bmatrix} \\ \sigma_1\sigma_2 \begin{bmatrix} \lambda_{12} & \gamma_{12} \\ \gamma_{12} & \lambda_{12} \end{bmatrix} & \sigma_2^2 \begin{bmatrix} 1 & \gamma_{22} \\ \gamma_{22} & 1 \end{bmatrix} & \sigma_2\sigma_3 \begin{bmatrix} \lambda_{23} & \gamma_{23} \\ \gamma_{23} & \lambda_{23} \end{bmatrix} \\ \sigma_1\sigma_3 \begin{bmatrix} \lambda_{13} & \gamma_{13} \\ \gamma_{13} & \lambda_{13} \end{bmatrix} & \sigma_2\sigma_3 \begin{bmatrix} \lambda_{23} & \gamma_{23} \\ \gamma_{23} & \lambda_{23} \end{bmatrix} & \sigma_3^2 \begin{bmatrix} 1 & \gamma_{33} \\ \gamma_{33} & 1 \end{bmatrix} \end{bmatrix}.$$

In the general case, with p observations at time points t or u,

$$\Sigma_{tt} = \sigma_t^2[\gamma_{tt}\mathbf{e}\mathbf{e}' + (1 - \gamma_{tt})\mathbf{I}], \quad \Sigma_{tu} = \sigma_t\sigma_u[\gamma_{tu}\mathbf{e}\mathbf{e}' + (\lambda_{tu} - \gamma_{tu})\mathbf{I}], \quad t \neq u, \tag{1.1}$$

where $\mathbf{e}' = (1, \ldots, 1)$, and each block is of dimension p. The matrix,$\mathrm{C} = \{\gamma_{ij}\}$, of contralateral correlations includes the relations between left and right eyes at different times, whereas the matrix, $\mathrm{L} = \{\lambda_{ij}\}$, with $\lambda_{ii} = 1$, of lateral correlations includes the relations of a left eye (or right) eye at different points. Both $\mathbf{C}$ and $\mathbf{L}$ are symmetric. Let $\Delta = \mathrm{diag}\ (\sigma_{ij})$.

2. Estimates and Large-sample Distributions

The unrestricted maximum likelihood (ML) estimates $\widehat{\mathrm{L}}$, $\widehat{\mathrm{C}}$ and $\widehat{\Delta}$ of L, C and Δ follow from the canonical decomposition of the sample covariance matrix S. More specifically (as detailed in Appendix A), under the assumption of a multivariate normal distribution, the distribution of nS decomposes into two independent Wishart components $n\mathcal{E}$ and $n\mathcal{F}$, with respective parameters $\mathrm{E} = \Delta(\mathrm{L} + (\mathrm{p}-1)\mathrm{C})\Delta$ and $\mathrm{F} = \Delta(\mathrm{L} - \mathrm{C})\Delta$, so that $\widehat{\mathrm{E}} = \mathcal{E}/\mathrm{n}$ and $\widehat{\mathrm{F}} = \mathcal{F}/\mathrm{n}$ are the ML estimates of E and F, respectively, based on the data $\mathcal{E}, \mathcal{F}$. The functional relation between E, F and $\mathcal{E}, \mathcal{F}$

leads to the ML estimates of C, L and Δ. The connection with the original data comes from the fact that $\mathrm{p}\mathcal{E}_{\mathrm{tu}} = \mathbf{e}'\mathrm{S}_{\mathrm{tu}}\mathbf{e}$ (the sum of the entries of S_{tu}) and $\mathrm{p}\ \ \mathrm{tr}\ \mathrm{S}_{\mathrm{tu}} - \mathbf{e}'\mathrm{S}_{\mathrm{tu}}\mathbf{e} = \mathrm{p}\mathcal{F}_{\mathrm{tu}}$, where $\mathcal{E}_{\mathrm{tu}}$ and $\mathcal{F}_{\mathrm{tu}}$ indicate the (t,u) entries of $\mathcal{E}$ and $\mathcal{F}$, respectively, and S_{tu} indicates the corresponding block submatrix of S. This leads to the maximum likelihood estimates of the component parameters in Δ, C and L, namely

$$\widehat{\sigma}^2_{\mathrm{tt}} = \frac{1}{\mathrm{p}}\ \mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}, \tag{2.1a}$$

$$\widehat{\gamma}_{\mathrm{tt}} = \frac{\mathbf{e}'\mathrm{S}_{\mathrm{tt}}\mathbf{e} -\ \mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}}{(\mathrm{p}-1)\ \mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}}, \quad \widehat{\gamma}_{\mathrm{tu}} = \frac{\mathbf{e}'\mathrm{S}_{\mathrm{tu}}\mathbf{e} -\ \mathrm{tr}\ \mathrm{S}_{\mathrm{tu}}}{(\mathrm{p}-1)\sqrt{\mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}\ \mathrm{tr}\ \mathrm{S}_{\mathrm{uu}}}}, \quad \mathrm{t} \neq \mathrm{u}, \tag{2.1b}$$

$$\widehat{\lambda}_{\mathrm{tu}} = \frac{\mathrm{tr}\ \mathrm{S}_{\mathrm{tu}}}{\sqrt{\mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}\ \mathrm{tr}\ \mathrm{S}_{\mathrm{uu}}}}, \quad \mathrm{t} \neq \mathrm{u}. \tag{2.1c}$$

Note that the ML estimates depend on the data only through the maximal invariants under block-permutation symmetry, namely, the sum ($\mathbf{e}'\mathrm{S}_{\mathrm{tu}}\mathbf{e}$) of the entries and the trace of the block sample covariance matrices.

Let $\mathrm{G} \equiv \mathrm{L} - \mathrm{C}$. In order to carry out the analyses we require the large-sample distribution of $\widehat{\mathrm{G}} \equiv \widehat{\mathrm{L}} - \widehat{\mathrm{C}}$. The proof of the corresponding result is based on the standard delta method (see also Proposition 21.5.1 in Viana and Olkin (1997)). Because this development leads to lengthy expressions, we provide the details in Viana and Olkin (1998).

3. Hypotheses

We are interested in assessing two main hypotheses, namely, $\mathrm{H}_1 : \gamma_{11} = \ldots = \gamma_{\mathrm{kk}} = \gamma$ and $\mathrm{H}_2 : \gamma_{\mathrm{tu}} = \lambda_{\mathrm{tu}},\ \ \mathrm{t} \neq \mathrm{u}$. Hypothesis H_1 states that the association between fellow eyes is constant across time - an important differential characterization of bilateral progression. Hypothesis H_2 states that lateral and colateral associations between any two time-points are the same (equivalently, the disease progression should be equally felt at either fellow or contralateral eyes, if present). Note that H_2 is equivalent to $\mathrm{G} \equiv \mathbf{L} - \mathbf{C} = \mathrm{diag}\ (1-\gamma_{11}, \ldots, 1-\gamma_{\mathrm{kk}})$, whereas $\mathrm{H}_1 \cap \mathrm{H}_2$ is equivalent to $\mathbf{L} - \mathbf{C} = (1-\gamma)\mathbf{I}$. Alternative hypotheses in the context of this model are (i) H_1 vs $\overline{\mathrm{H}}_1$, (ii) H_2 vs $\overline{\mathrm{H}}_2$, (iii) $\mathrm{H}_{12} \equiv \mathrm{H}_2 \cap \mathrm{H}_1$ vs $\overline{\mathrm{H}}_{12}$, (iv) H_{12} vs H_2, (v) H_{12} vs H_1.

To obtain the ML estimates of interest under the hypothesis H_1, note that the MLE of γ_{tt} in equation (2.1b) is equivalently obtained from the relation

$$\frac{1+(\mathrm{p}-1)\widehat{\gamma}_{\mathrm{tt}}}{(\mathrm{p}-1)(1-\widehat{\gamma}_{\mathrm{tt}})} = \frac{\mathcal{E}_{\mathrm{tt}}}{\mathcal{F}_{\mathrm{tt}}}. \tag{3.1}$$

It then follows that, under H_1, the ML estimate of the common correlation γ is obtained from the relation

$$\frac{1+(\mathrm{p}-1)\widehat{\gamma}}{(\mathrm{p}-1)(1-\widehat{\gamma})} = \frac{\mathrm{tr}\ \mathcal{E}}{\mathrm{tr}\ \mathcal{F}}. \tag{3.2}$$

Under the hypothesis H_2 of lateral-contralateral homogeneity, we obtain

$$\widehat{\gamma}_{\mathrm{tu}} = \widehat{\lambda}_{\mathrm{tu}} = \frac{1}{\mathrm{p}}\,\frac{\mathbf{e}'\mathrm{S}_{\mathrm{tu}}\mathbf{e}}{\sqrt{\mathrm{tr}\ \mathrm{S}_{\mathrm{tt}}\ \mathrm{tr}\ \mathrm{S}_{\mathrm{uu}}}}, \quad \mathrm{t} \neq \mathrm{u}, \tag{3.3}$$

which is a weighted linear combination of the estimates (2.1b) and (2.1c) with weights $(\mathrm{p}-1)/\mathrm{p}$ and $1/\mathrm{p}$.

The assessment of permutation symmetry in the covariance structure, namely $\Sigma = \sigma^2[\gamma\mathbf{e}\mathbf{e}' + (1-\gamma)\mathbf{I}]$, is due to Wilks (1946). The model was extended by Votaw (1947) to a block covariance matrix in which each block was permutation symmetric. The important point to note is that although the compound symmetry structure is maintained, the hypotheses of interest in the context of visual outcomes are different.

4. Intra-ocular Pressure Data

Consider the study described by Sonty, Sonty and Viana (1996), in which intra-ocular pressure (IOP) measurements at pre-treatment ($\mathbf{Y}_1$) and post treatment ($\mathbf{Y}_2$) conditions were obtained from fellow glaucomatous eyes of $\mathrm{N} = 15$ subjects on topical beta blocker therapy. The primary question addresses the therapy mean effect in IOP response from fellow eyes. However, there is also interest, both clinical and methodological, in assessing the therapy's effect on the association between fellow eyes. For example, weaker-than-normal associations may indicate a different etiology. In the present example, to assess hypotheses H_1, H_2 and H_{12}, we start with the observed covariance matrices for IOP between fellow eyes and cross-covariance matrix are, respectively,

$$\mathrm{S}_{11} = \begin{bmatrix} 12.410 & 7.019 \\ 7.019 & 12.924 \end{bmatrix}, \quad \mathrm{S}_{22} = \begin{bmatrix} 17.029 & 15.371 \\ 15.371 & 17.352 \end{bmatrix}, \quad \mathrm{S}_{12} = \begin{bmatrix} 11.671 & 9.348 \\ 8.200 & 10.076 \end{bmatrix}.$$

Direct application of Votaw's test supports the assumption of block permutation symmetry, as described by equation (1.1) (large-sample Chi-square of 1.91, with 4 degrees of freedom). From

Section 2, the estimated variances are $\widehat{\sigma}_1^2 = 12.667$, $\widehat{\sigma}_2^2 = 17.190$, whereas the estimated correlations are $\widehat{\gamma}_{11} = 0.554$, $\widehat{\gamma}_{22} = 0.894$, $\widehat{\lambda}_{12} = 0.736$, $\widehat{\gamma}_{12} = 0.594$.

Writing, in vector form, $\mathrm{G}' = (1-\gamma_{11}, \lambda_{12}-\gamma_{12}, 1-\gamma_{22})$, the asymptotic joint distribution of $\sqrt{\mathrm{N}}[\widehat{\mathrm{G}} - \mathrm{G}]$ is bivariate normal with mean zero and approximate large-sample covariance matrix

$$\mathrm{Cov}_\infty(\widehat{\mathrm{G}}) = \begin{bmatrix} 0.48037 & 0.15257 & 0.07150 \\ 0.15257 & 0.08103 & 0.046556 \\ 0.07150 & 0.046556 & 0.040306 \end{bmatrix}, \tag{4.1}$$

so that approximate confidence intervals for γ_{11}, γ_{22} and $\lambda_{12} - \gamma_{12}$ follow directly from $\widehat{\mathrm{G}}$ and $\mathrm{Cov}_\infty(\widehat{\mathrm{G}})$ above. To assess the hypothesis $\mathrm{H}_1 : \gamma_{11} = \gamma_{22}$, let $\mathrm{M} = [-1, 0, 1]$, so that (writing G in vector form) $\mathrm{MG} = 0$ represents H_1. Then, asymptotically,

$$\mathrm{Q} = \mathrm{N}(\widehat{\mathrm{G}}'\mathrm{M}')(\mathrm{M}\ \mathrm{Cov}_\infty(\widehat{\mathrm{G}})\ \mathrm{M}')^{-1}(\mathrm{M}\widehat{\mathrm{G}}) \ \sim\ \chi_1^2,$$

and can be used to assess H_1. In the present case, we obtain Q=4.57, with 1 degree of freedom, thus suggesting a strengthening in association between left and right eye response during the experimental period, that is, the beta blocker therapy did improve the association between the IOP responses from fellow eyes (thus turning each eye into a better indicator of the progression of glaucoma in the fellow eye). To assess the lateral-contralateral homogeneity hypotheses (H_2), let $\mathrm{M} = [0, 1, 0]$, so that, similarly, $\mathrm{MG} = 0$ represents H_2 and, asymptotically, $\mathrm{Q} \sim \chi_1^2$. We obtain Q=3.73, with 1 degree of freedom, thus suggesting a heterogeneous (not proportional to $\mathbf{ee}'$) covariance structure Σ_{12} between pre-treatment and post-treatment. To assess H_{12} we define $\mathrm{M} = \begin{bmatrix} -1 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix}$, so that, similarly, $\mathrm{MG} = 0$ represents H_{12} and, asymptotically, $\mathrm{Q} \sim \chi_2^2$. We obtain Q=5.22, with 2 degrees of freedom, in joint support of the hypotheses that beta blocker therapy did alter the association between the IOP responses from fellow eyes, and that the covariance structure Σ_{12} between pre-treatment and post-treatment is heterogeneous.

Appendix A. Canonical Forms and Elementary Estimates

The covariance matrix Σ of $\mathbf{Y}$ is expressed as $\Sigma = (\Delta \otimes \mathbf{I}_\mathrm{p})(\mathbf{C} \otimes \mathbf{ee}' + (\mathbf{L} - \mathbf{C}) \otimes \mathbf{I}_\mathrm{p})(\Delta \otimes \mathbf{I}_\mathrm{p})$, where $\mathbf{I}_\mathrm{p}$ is the identity matrix of dimension p and $\mathbf{e}' = (1, \ldots, 1)$ has dimension p. To obtain a canonical form for Σ, let $\Gamma = \mathbf{I}_\mathrm{k} \otimes \mathbf{Q}$, where $\mathbf{Q}$ of dimension $\mathrm{p} \times \mathrm{p}$ is orthogonal with first row equal to $\mathbf{e}'/\sqrt{\mathrm{p}}$. It then follows that $\Gamma\Sigma\Gamma' = (\Delta\mathbf{C}\Delta) \otimes \mathrm{diag}(\mathrm{p}, 0, \ldots, 0) + (\Delta(\mathbf{L} - \mathbf{C})\Delta) \otimes \mathbf{I}_\mathrm{k}$. Moreover, there is a permutation g (conjugating $\Delta \otimes \mathbf{I}_p$ and $\mathbf{I}_p \otimes \Delta$) such that

$$g\Gamma\Sigma\Gamma' g' = \mathrm{diag}(p, 0, \ldots, 0) \otimes (\Delta\mathbf{C}\Delta) + \mathbf{I}_k \otimes (\Delta(\mathbf{L} - \mathbf{C})\Delta).$$

The resulting canonical form is $\mathrm{diag}(E, F, \ldots, F)$, where $E = \Delta(\mathbf{L}+(p-1)\mathbf{C})\Delta$ and $F = \Delta(\mathbf{L}-\mathbf{C})\Delta$. Both E and F have dimension $k \times k$ and the block F is repeated p-1 times. In the simplest case (p=k=2) the canonical form is diag (E, F), with

$$E = \begin{bmatrix} \sigma_1^2(1+\gamma_{11}) & \sigma_1\sigma_2(\lambda_{12}+\gamma_{12}) \\ \sigma_1\sigma_2(\lambda_{21}+\gamma_{21}) & \sigma_2^2(1+\gamma_{22}) \end{bmatrix}, \quad F = \begin{bmatrix} \sigma_1^2(1-\gamma_{11}) & \sigma_1\sigma_2(\lambda_{12}-\gamma_{12}) \\ \sigma_1\sigma_2(\lambda_{21}-\gamma_{21}) & \sigma_2^2(1-\gamma_{22}) \end{bmatrix}.$$

Because $E + (p-1)F = p\mathbf{\Delta L \Delta}$ and $E - F = p\mathbf{\Delta C \Delta}$, it then follows that

$$\frac{1}{p}(E + (p-1)F)_{tt} = \sigma_t^2, \quad \frac{(E-F)_{tt}}{(E+(p-1)F)_{tt}} = \gamma_{tt}, \quad t = 1, \ldots, k, \tag{A.1}$$

$$\frac{((E-F)_{tu})^2}{(E+(p-1)F)_{tt}(E+(p-1)F)_{uu}} = \gamma_{tu}^2, \quad t \neq u, \tag{A.2}$$

$$\frac{((E+(p-1)F)_{tu})^2}{(E+(p-1)F)_{tt}(E+(p-1)F)_{uu}} = \lambda_{tu}^2, \quad t \neq u. \tag{A.3}$$

In addition, for $\gamma_{tu} \neq 0$,

$$\frac{(E+(p-1)F)_{tu}}{(E-F)_{tu}} = \frac{\lambda_{tu}}{\gamma_{tu}} \quad t \neq u. \tag{A.4}$$

To obtain the ML estimates of interest, let S indicate the sample covariance matrix associated with Σ and S_{tu} the blocks of S corresponding to the blocks Σ_{tu} of Σ. Let $\mathcal{E}$ and $\mathcal{F}_1, \ldots, \mathcal{F}_{p-1}$ indicate the diagonal blocks of $g\Gamma S\Gamma' g'$ corresponding to the diagonal blocks of $g\Gamma\Sigma\Gamma' g'$. Direct computation shows that $p\mathcal{E}_{tu} = \mathbf{e}' S_{tu}\mathbf{e}$, the sum of the entries of S_{tu}, and that $p\mathcal{F}_{tu} = p \,\mathrm{tr}\, S_{tu} - \mathbf{e}' S_{tu}\mathbf{e}$, where $\mathcal{F} = \sum_{i=1}^{p-1} \mathcal{F}_i$. Note that $\mathcal{E}_{tu}$ refers to the (t,u) entries of $\mathcal{E}$, whereas S_{tu} indicates the (t,u) block submatrix of S. When the distribution of $\mathbf{Y}$ is multivariate normal then the distribution of $n\mathcal{E}$ is Wishart $W(E, n)$, the distribution of $n\mathcal{F}$ is Wishart $W(F, n(p-1))$, and $\mathcal{E}$ is independent of $\mathcal{F}$ (n=N-1). From the MLEs (based on the canonical transformation of sample covariance matrix) $\mathcal{E}$ and $\mathcal{F}$ of E and F and equations (A.1),(A.2),(A.3) and (A.4) we obtain the corresponding MLEs indicated by equations (2.1a),(2.1b) and (2.1c). For example,

$$\hat{\gamma}_{tt} = \frac{(\hat{E} - \hat{F})_{tt}}{(\hat{E} + (p-1)\hat{F})_{tt}} = \frac{(p-1)\mathcal{E}_{tt} - \mathcal{F}_{tt}}{(p-1)(\mathcal{E}_{tt} + \mathcal{F}_{tt})}.$$

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