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Testing Correlation in a Three-Level Model

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In this paper, we present a statistical approach to evaluate the relationship between variables observed in a two-factors experiment. We consider a three-level model with covariance structure $\boldsymbol{\Sigma} \otimes \boldsymbol{\Psi}_1 \otimes \boldsymbol{\Psi}_2$, where $\boldsymbol{\Sigma}$ is an arbitrary positive definite covariance matrix, and $\boldsymbol{\Psi}_1$ and $\boldsymbol{\Psi}_2$ are both correlation matrices with a compound symmetric structure corresponding to two different factors. The Rao's score test is used to test the hypotheses that observations grouped by one or two factors are uncorrelated. We analyze a fermentation process to illustrate the results.

Supplementary materials accompanying this paper appear online.

Key Words: Three-level model; Rao's score test; Maximum likelihood estimation; Independence test; Factorial design; Kronecker product structured covariance matrix.

1. INTRODUCTION

To analyze the influence of different factors in field experiments has been a problem in agricultural research (and not only) for many years (see, e.g., Verdooren 2020). For example, the influence of photoperiod and temperature into flowering responses (Imrie and Lawn 1990); the temperature and extracts on flowering and yield in cucumber (Sarhan and Ismael 2014); or the nutrients and salinity on the yield and growth of Faba beans (Haddad and Abahri 2022).

The relationship between variables can be found via the analysis of the structure of the covariance matrix (see Mieldzioc et al. 2019, 2021). In factorial experiments, the covariance matrix can be naturally expressed as a Kronecker product structure leading to less covariance parameters to estimate. The experiments where the variable can be cross-classified by two factors can be described by two-level models. The estimation and separability tests in these

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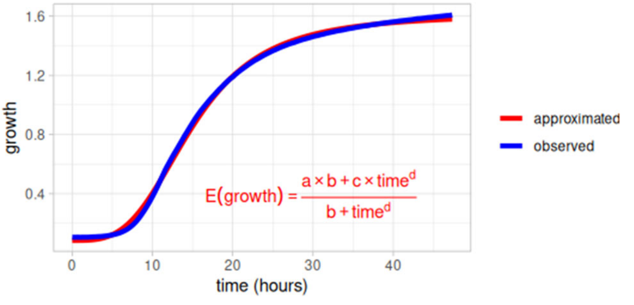

Figure 1. Example of response (growth curve) obtained from one well. The blue dots represent the measurements of the growth of yeast over time, and the red curve is an approximate model of the form $E(y) = \frac{ab+cx^d}{b+x^d}$ (Color figure online).

models has been widely discussed in the literature, see, e.g., Dutilleul (1999), Naik and Rao (2001), Lu and Zimmerman (2005), Roy and Khattree (2005), Srivastava et al. (2008), Simpson (2010), Soloveychik and Trushin (2016), Filipiak and Klein (2017), Szczepańska-Álvarez et al. (2017), Dutilleul (2021). Chen and Liu (2018) have been testing independence among a number of high-dimensional random samples.

Simultaneously with the development of the theory of the two-factor model, papers related to a three-level model appeared (e.g., see Mardia and Goodall 2013; Galecki 1994; Lu and Zimmerman 2005; Roy and Leiva 2008; Singull et al. 2012; Manceur and Dutilleul 2013; Leiva and Roy 2014).

In this paper, a three-level model is used to analyze the relationship between variables in a two-factor experiment involving a fermentation process. The studied data were collected during inoculation of yeast species using microplates. In the experiment, apple juice was mixed with one of three types of yeast species $\{A, B, C\}$, (the first factor) and was or was not supplemented by $K_2S_2O_5$ (the second factor). For each combination, the growth of yeast was observed. An example of response (growth curve) obtained from one of the wells is given in Fig. 1. From each curve, the following characteristic variables were determined: the time point where the growing process started, the speed of growth, and the asymptote of the growth curve. The presented experiment can then be described by a three-level model.

The main objective of this paper is to present statistical inference about the correlation of measurements in a two-factor design. Tests will be carried out with the help of Rao's score test (see Cox and Hinkley 1974; Rao 2005), since it is well known that one advantage of using the score test is that the maximum likelihood estimators (or asymptotically equivalent estimators) only have to be derived under the null hypothesis.

The structure of the paper is as follows: In Sect. 2, the statistical model of interest and the tested hypotheses are introduced. The likelihood function related to the considered model is presented in Sect. 3. In Sect. 4, maximum likelihood estimators and Rao's score test are applied to hypotheses about factor levels. In Sect. 5, the results are illustrated by data from the experiment that motivated this study. In the last section, the conclusions are formulated. Details connected to some of the calculations in the proofs are given in Appendix A and Appendix B.

Throughout the work, bold lower cases denote vectors, as applied above, such as $\mathbf{x}_1, \ldots, \mathbf{x}_n$, and bold upper cases denote matrices, e.g., $\mathbf{X}_1, \ldots, \mathbf{X}_n$. The Greek alphabet will be used to indicate parameters. Moreover, $\text{vec}(\cdot)$ is the usual vectorization operator, i.e., stacking columns of a matrix starting with the last one, and as noted above $\otimes$ denotes the Kronecker product. Other notations will be defined when they are introduced.

2. MODEL AND HYPOTHESES

Consider a two-factor experiment where r characteristics are measured. Let the factors have p and q levels, respectively. At hand are n independent r-valued measurements. Each set of independent observations can be written as a vector: for $d \in \{1, \ldots, n\}$,

$$\mathbf{x}_d = \sum_{i=1}^{p}\sum_{j=1}^{q}\sum_{k=1}^{r}(x_{ijk})_d\ \mathbf{e}_k^3 \otimes \mathbf{e}_j^2 \otimes \mathbf{e}_i^1,$$

where $(x_{ijk})_d$ is the element of the vector $\mathbf{x}_d$ and $\mathbf{e}_k^3, \mathbf{e}_j^2, \mathbf{e}_i^1$ are unit basis vectors of size r, q, p, respectively. We assume that $\mathbf{x}_d$ is independent of $\mathbf{x}_e$, $d \neq e$, and suppose that $\mathbf{x}_d$ follows a multivariate normal distribution, with $E[\mathbf{x}_d] = \boldsymbol{\mu}$: $pqr \times 1$, and $D[\mathbf{x}_d] = \boldsymbol{\Sigma} \otimes \boldsymbol{\Psi}_1 \otimes \boldsymbol{\Psi}_2$, where $\boldsymbol{\Sigma}$: $r \times r$ is an unstructured dispersion matrix, and $\boldsymbol{\Psi}_1$: $p \times p$ and $\boldsymbol{\Psi}_2$: $q \times q$ are correlation matrices. We also assume that both correlation matrices follow a compound symmetric structure corresponding to rotational invariance. With this choice of matrices, there is a unique parametrization and all parameters are estimable. The estimation equations will be derived, and then, a flip-flop algorithm delivers the estimators. Note that since $\boldsymbol{\Psi}_1$ and $\boldsymbol{\Psi}_2$ consist of only one unknown parameter it is a very simple case. However, even in this case the researcher has to be careful when carrying out inference. A stochastic representation of $\mathbf{x}_d$ equals $\mathbf{x}_d = \boldsymbol{\mu} + (\boldsymbol{\Sigma}^{1/2} \otimes (\boldsymbol{\Psi}_1)^{1/2} \otimes (\boldsymbol{\Psi}_2)^{1/2})\mathbf{e}$, where $\mathbf{e} \sim N_{pqr}(\mathbf{0}, \mathbf{I}_{pqr})$. In this model, we test the correlation matrices for factor levels and specifically consider the two null hypotheses

$$H_0^1 : D[\mathbf{x}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \boldsymbol{\Psi}_2, \quad H_0^2 : D[\mathbf{x}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \mathbf{I}_q.$$

Thus, the interest is to test hypothesis about a subset of the unknown parameters and Rao's score statistic (e.g., see Rao 2005) is going to be used.

In general, consider $\boldsymbol{\theta} = (\boldsymbol{\xi}', \boldsymbol{\psi}')'$ as the vector of unknown parameters, where $\boldsymbol{\xi} : t \times 1$, $\boldsymbol{\psi} : (s - t) \times 1$ and we would like to test $H_0 : \boldsymbol{\xi} = \boldsymbol{\xi}_0$. In this case, Rao's score statistic is given by

$$W_s = \mathbf{s}_{\boldsymbol{\xi}}(\widetilde{\boldsymbol{\theta}}_{\boldsymbol{\xi}_0})'[\mathcal{I}_{1.2}(\widetilde{\boldsymbol{\theta}}_{\boldsymbol{\xi}_0})]^{-1}\mathbf{s}_{\boldsymbol{\xi}}(\widetilde{\boldsymbol{\theta}}_{\boldsymbol{\xi}_0}),$$

where $\widetilde{\boldsymbol{\theta}}_{\boldsymbol{\xi}_0}$ is the maximum likelihood estimator of $\boldsymbol{\theta}$ under the null hypothesis and the score $\mathbf{s}_{\boldsymbol{\xi}} = \frac{\partial \ln L}{\partial \boldsymbol{\xi}}$: $t \times 1$ is the gradient of the log likelihood function. The matrix $\mathcal{I}_{1.2} = \mathcal{I}_{11} - \mathcal{I}_{12}(\mathcal{I}_{22})^{-1}\mathcal{I}_{12}'$ is the partial information matrix for $\boldsymbol{\xi}$, where $\mathcal{I}_{11}$: $t \times t$, $\mathcal{I}_{12}$: $t \times (s-t)$, $\mathcal{I}_{22}$:

$(s-t)\times(s-t)$ are the partitions of the information matrix for $\boldsymbol{\theta}$, given by $\mathcal{I}_{\boldsymbol{\theta}} = \begin{bmatrix} \mathcal{I}_{11} & \mathcal{I}_{12} \\ \mathcal{I}_{12}' & \mathcal{I}_{22} \end{bmatrix}$. Rao's score test statistic follows asymptotically a Chi-square distribution with t degrees of freedom.

3. LIKELIHOOD FUNCTION

To study the model, we will determine the maximum likelihood estimator of $\boldsymbol{\mu}$ and of the parameters in the dispersion matrix $\boldsymbol{\Sigma} \otimes \boldsymbol{\Psi}_1 \otimes \boldsymbol{\Psi}_2$. Let

$$\mathbf{G}_i^{\ell} = \mathbf{e}_i\mathbf{e}_i', \quad \mathbf{e}_i : \ell \times 1. \tag{1}$$

As it has been noted, the correlation matrices $\boldsymbol{\Psi}_1$ and $\boldsymbol{\Psi}_2$ are supposed to have a compound symmetric structure: $\boldsymbol{\Psi}_1 = (1-\phi_1)\mathbf{I}_p + \phi_1\mathbf{1}_p\mathbf{1}_p'$ and $\boldsymbol{\Psi}_2 = (1-\phi_2)\mathbf{I}_q + \phi_2\mathbf{1}_q\mathbf{1}_q'$, where ϕ_1 and ϕ_2 are unknown parameters. The eigendecompositions (spectral decomposition) of these matrices equal $\boldsymbol{\Psi}_1 = \boldsymbol{\Gamma}_1\boldsymbol{\Lambda}_1(\phi_1)\boldsymbol{\Gamma}_1'$ and $\boldsymbol{\Psi}_2 = \boldsymbol{\Gamma}_2\boldsymbol{\Lambda}_2(\phi_2)\boldsymbol{\Gamma}_2'$, where

$$\boldsymbol{\Lambda}_1(\phi_1) = (1+(p-1)\phi_1)\mathbf{G}_1^p + (1-\phi_1)\sum_{i=2}^{p}\mathbf{G}_i^p, \tag{2}$$

$$\boldsymbol{\Lambda}_2(\phi_2) = (1+(q-1)\phi_2)\mathbf{G}_1^q + (1-\phi_2)\sum_{i=2}^{q}\mathbf{G}_i^q. \tag{3}$$

Because of the compound symmetric structure, the eigenvector matrices $\boldsymbol{\Gamma}_1 : p \times p$ and $\boldsymbol{\Gamma}_2 : q \times q$ are completely known.

The correlation matrices $\boldsymbol{\Psi}_1$, $\boldsymbol{\Psi}_2$ and the vector of observations $\mathbf{x}_d$ can be jointly transformed to $\mathbf{y}_d \sim N_{pqr}(\boldsymbol{\xi}, \boldsymbol{\Sigma} \otimes \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))$, where

$$\boldsymbol{\xi} = (\mathbf{I}_r \otimes \boldsymbol{\Gamma}_1 \otimes \boldsymbol{\Gamma}_2)^{-1}\boldsymbol{\mu},$$
$$\mathbf{y}_d = (\mathbf{I}_r \otimes \boldsymbol{\Gamma}_1 \otimes \boldsymbol{\Gamma}_2)^{-1}\mathbf{x}_d.$$

Moreover, by rearranging the elements in $\mathbf{y}_d$ a matrix $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1)\otimes\boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$, appears where $\boldsymbol{\Xi}$ is obtained by restructuring $\boldsymbol{\xi}$ and

$$\mathrm{vec}\,\boldsymbol{\Xi} = (\mathbf{I}_r \otimes \boldsymbol{\Gamma}_1 \otimes \boldsymbol{\Gamma}_2)^{-1}\boldsymbol{\mu}, \quad \mathrm{vec}\mathbf{Y}_d = (\mathbf{I}_r \otimes \boldsymbol{\Gamma}_1 \otimes \boldsymbol{\Gamma}_2)^{-1}\mathbf{x}_d.$$

In the lemma below, the log likelihood function for $\mathbf{Y}_d$ is presented.

Lemma 1. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$, $d \in \{1, \dots, n\}$, *be independent and identically distributed observations, where* $\boldsymbol{\Xi} : pq \times r$ *is the mean,* $\boldsymbol{\Sigma}$ *is unknown covariance matrix and* $\boldsymbol{\Lambda}_1(\phi_1)$, $\boldsymbol{\Lambda}_2(\phi_2)$ *are unknown diagonal matrices. The log likelihood function can be written*

$$\ln(L(\boldsymbol{\Xi}, \boldsymbol{\Sigma}, \phi_1, \phi_2)) = \tfrac{1}{2}qrn \ln \mid \boldsymbol{\Lambda}_1(\phi_1) \mid^{-1} + \frac{1}{2}prn \ln \mid \boldsymbol{\Lambda}_2(\phi_2) \mid^{-1}$$

$$+\tfrac{1}{2}pqn\ln|\,\mathbf{\Sigma}\,|^{-1} - \tfrac{1}{2}\mathrm{tr}\{(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\mathbf{A}\},$$

where $\mathbf{A} = \sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})\mathbf{\Sigma}^{-1}(\mathbf{Y}_d - \mathbf{\Xi})'$.

4. SOLVING THE LIKELIHOOD EQUATIONS AND TESTING

We use the Rao score statistic which is based on the maximum likelihood estimators (or asymptotically equivalent estimators) derived under the null hypothesis.

In the next lemma, we formulate the likelihood equations corresponding to the likelihood in Lemma 1. Let $\lambda_k[i,i]$ be the ith diagonal element in $\mathbf{\Lambda}_k$, $k\in\{1,2\}$.

Lemma 2. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\mathbf{\Xi}, \mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2), \mathbf{\Sigma})$, $d\in\{1,\dots,n\}$, *be independent and identically distributed observations, where* $\mathbf{\Xi} : pq\times r$ *is the mean,* $\mathbf{\Sigma}$ *is an unknown dispersion matrix and* $\mathbf{\Lambda}_1(\phi_1)$, $\mathbf{\Lambda}_2(\phi_2)$ *are unknown diagonal matrices with elements:* $\lambda_1[1,1] = 1+(p-1)\phi_1$, $\lambda_1[i,i] = 1-\phi_1$ *for* $i\in\{2,\dots,p\}$, *and* $\lambda_2[1,1] = 1+(q-1)\phi_2$, $\lambda_2[j,j] = 1-\phi_2$ *for* $j\in\{2,\dots,q\}$, *respectively. Let* $L = L(\mathbf{\Xi},\mathbf{\Sigma},\phi_1,\phi_2)$ *denote the likelihood function. Then, the likelihood equations can be written:*

$$\frac{d\ln L}{d\mathbf{\Xi}} : \ \mathrm{vec}[(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\sum_{d=1}^{n}\mathbf{Y}_d\mathbf{\Sigma}^{-1}] - n\,\mathrm{vec}[(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\mathbf{\Xi}\mathbf{\Sigma}^{-1}] = \mathbf{0}, \tag{4}$$

$$\frac{d\ln L}{d(\mathbf{\Sigma}^{-1})^{\triangle}} : \ \tfrac{pqn}{2}\mathbf{H}_r\mathrm{vec}\mathbf{\Sigma} - \frac{1}{2}\mathbf{H}_r\mathrm{vec}\Bigg[\sum_{d=1}^{n}\mathbf{Y}_d'(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\mathbf{Y}_d - 2\sum_{d=1}^{n}\mathbf{Y}_d'(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\mathbf{\Xi} + n\mathbf{\Xi}'(\mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2))^{-1}\mathbf{\Xi}\Bigg] = \mathbf{0}, \tag{5}$$

$$\frac{d\ln L}{d\phi_1} : \ \tfrac{qrn(p-1)}{2}\left(\tfrac{1}{1-\phi_1} - \tfrac{1}{1+(p-1)\phi_1}\right) + \tfrac{(p-1)}{2(1+(p-1)\phi_1)^2}\mathrm{tr}\{(\mathbf{G}_1^p\otimes[\mathbf{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\} - \tfrac{1}{2}\sum_{i=2}^{p}\tfrac{1}{(1-\phi_1)^2}\mathrm{tr}\{(\mathbf{G}_i^p\otimes[\mathbf{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\} = 0, \tag{6}$$

$$\frac{d\ln L}{d\phi_2} : \ \tfrac{prn(q-1)}{2}\left(\tfrac{1}{1-\phi_2} - \tfrac{1}{1+(q-1)\phi_2}\right) + \tfrac{(q-1)}{2(1+(q-1)\phi_2)^2}\mathrm{tr}\{([\mathbf{\Lambda}_1(\phi_1)]^{-1}\otimes\mathbf{G}_1^q)\mathbf{A}\} - \tfrac{1}{2}\sum_{i=2}^{q}\tfrac{1}{(1-\phi_2)^2}\mathrm{tr}\{([\mathbf{\Lambda}_1(\phi_1)]^{-1}\otimes\mathbf{G}_i^q)\mathbf{A}\} = 0, \tag{7}$$

where $(\mathbf{\Sigma}^{-1})^{\triangle}$ *denotes the upper triangle of* $\mathbf{\Sigma}^{-1}$, $\mathbf{H}_r = \mathbf{V}_r(\mathbf{I}_{r^2} + \mathbf{K}_{r,r} - (\mathbf{K}_{r,r})_d)$, $\mathbf{V}_r : \frac{1}{2}r(r+1)\times r^2$, *is a block partitioned matrix,* $\mathbf{V}_r = ([\mathbf{V}_{11}],\dots,[\mathbf{V}_{rr}])_{[d]}$, $\mathbf{V}_{ii} = (\mathbf{e}_1,\dots,\mathbf{e}_i)'$, $i = \{1,2,\dots,r\}$, $\mathbf{e}_i$ *is the ith unit base vector,* $\mathbf{K}_{r,r}$ *is the commutation matrix,* $(\mathbf{K}_{r,r})_d$ *is the diagonal matrix obtained from* $\mathbf{K}_{r,r}$ *(for details see* Kollo and von Rosen 2005, p. 79, p. 99*) and* $\mathbf{A} = \sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})\mathbf{\Sigma}^{-1}(\mathbf{Y}_d - \mathbf{\Xi})'$.

Proof. When with the help of the derivatives given in Appendix A, differentiating the log likelihood function, presented in Lemma 1, establish the likelihood equations. □

Lemma 3. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$, *where* $d \in \{1, \ldots, n\}$. *Then,*

$$\mathrm{tr}\left[(\boldsymbol{\Lambda}_1(\widehat{\phi}_1) \otimes \boldsymbol{\Lambda}_2(\widehat{\phi}_2))^{-1}\mathbf{A}\right] = pqrn,$$

where $\mathbf{A} = \sum_{d=1}^{n}(\mathbf{Y}_d - \boldsymbol{\Xi})\boldsymbol{\Sigma}^{-1}(\mathbf{Y}_d - \boldsymbol{\Xi})'$ *and* $\widehat{\phi}_1$ *and* $\widehat{\phi}_2$ *satisfy* (6) *and* (7).

Proof. Lemma 2 yields $\frac{d \ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}} = \mathbf{0}$,

$$\frac{pqn}{2}\mathbf{H}_r \mathrm{vec}\boldsymbol{\Sigma} - \frac{1}{2}\mathbf{H}_r \mathrm{vec}\left[\sum_{d=1}^{n}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\mathbf{Y}_d \right.$$
$$\left. -2\sum_{d=1}^{n}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi} + n\boldsymbol{\Xi}'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi}\right] = \mathbf{0},$$

which is equivalent to

$$pqn\boldsymbol{\Sigma} = \sum_{d=1}^{n}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\mathbf{Y}_d - 2\sum_{d=1}^{n}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi}$$
$$+n\boldsymbol{\Xi}'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi}.$$

Multiplying by $\boldsymbol{\Sigma}^{-1}$ and taking the trace we get

$$pqnr = \mathrm{tr}\left[\sum_{d=1}^{n}\boldsymbol{\Sigma}^{-1}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\mathbf{Y}_d \right.$$
$$\left. -2\sum_{d=1}^{n}\boldsymbol{\Sigma}^{-1}\mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi} + n\boldsymbol{\Sigma}^{-1}\boldsymbol{\Xi}'(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi}\right].$$

$$pqnr = \mathrm{tr}\left[(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\sum_{d=1}^{n}\mathbf{Y}_d\boldsymbol{\Sigma}^{-1}\mathbf{Y}_d'\right]$$
$$-2\mathrm{tr}\left[(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\sum_{d=1}^{n}\boldsymbol{\Xi}\boldsymbol{\Sigma}^{-1}\mathbf{Y}_d'\right]$$
$$+n\mathrm{tr}\left[(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}\boldsymbol{\Xi}\boldsymbol{\Sigma}^{-1}\boldsymbol{\Xi}'\right].$$

After some calculations, the statement of the lemma is obtained. □

Now, necessary preparations have been taking place and likelihood equations are presented which can serve as a basis for estimation when, for example, the flip-flop algorithm is applied.

Theorem 1. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$, $d \in \{1, \ldots, n\}$, *with its likelihood given in Lemma 1. Then, the maximum likelihood estimators satisfy:*

$$\widehat{\boldsymbol{\Xi}} = \frac{1}{n}\sum_{d=1}^{n}\mathbf{Y}_d,$$

$$pqn\widehat{\boldsymbol{\Sigma}} = \sum_{d=1}^{n} \mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\widehat{\phi}_1) \otimes \boldsymbol{\Lambda}_2(\widehat{\phi}_2))^{-1}\mathbf{Y}_d - n\widehat{\boldsymbol{\Xi}}'(\boldsymbol{\Lambda}_1(\widehat{\phi}_1) \otimes \boldsymbol{\Lambda}_2(\widehat{\phi}_2))^{-1}\widehat{\boldsymbol{\Xi}},$$

$$\widehat{\phi}_1 = \frac{1}{p-1}\frac{(p-1)tr\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right] - \sum_{i=2}^{p} tr\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right]}{tr\left[(\mathbf{I}_p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right]},$$

$$\widehat{\phi}_2 = \frac{1}{q-1}\frac{(q-1)tr\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{G}_1^q)\widehat{\mathbf{A}}\right] - \sum_{i=2}^{q} tr\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{G}_i^q)\widehat{\mathbf{A}}\right]}{\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{I}_q)\widehat{\mathbf{A}}\right]},$$

where $\widehat{\mathbf{A}} = \sum_{d=1}^{n}(\mathbf{Y}_d - \widehat{\boldsymbol{\Xi}})\widehat{\boldsymbol{\Sigma}}^{-1}(\mathbf{Y}_d - \widehat{\boldsymbol{\Xi}})'$.

Proof. Notice that solving (4) and (5) given in Lemma 2 yields

$$\widehat{\boldsymbol{\Xi}} = \frac{1}{n}\sum_{d=1}^{n}\mathbf{Y}_d,$$

$$pqn\widehat{\boldsymbol{\Sigma}} = \sum_{d=1}^{n} \mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\widehat{\phi}_1) \otimes \boldsymbol{\Lambda}_2(\widehat{\phi}_2))^{-1}\mathbf{Y}_d - n\widehat{\boldsymbol{\Xi}}'(\boldsymbol{\Lambda}_1(\widehat{\phi}_1) \otimes \boldsymbol{\Lambda}_2(\widehat{\phi}_2))^{-1}\widehat{\boldsymbol{\Xi}}.$$

The result of Lemma 3 can be rewritten in several ways. For example,

$$pqnr = \frac{1}{1+(p-1)\phi_1}\mathrm{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right] + \frac{1}{1-\phi_1}\sum_{i=2}^{p}\mathrm{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right], \tag{8}$$

or

$$pqnr = \frac{1}{1+(q-1)\phi_2}\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q)\mathbf{A}\right] + \frac{1}{1-\phi_2}\sum_{i=2}^{q}\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_i^q)\mathbf{A}\right]. \tag{9}$$

Putting (8) into (6) and after some calculations, we obtain

$$\frac{(p-1)\phi_1}{(1-\phi_1)(1+(p-1)\phi_1)}\left[\frac{1}{1+(p-1)\phi_1}\mathrm{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right] + \frac{1}{1-\phi_1}\sum_{i=2}^{p}\mathrm{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right]\right]$$
$$+\frac{(p-1)}{(1+(p-1)\phi_1)^2}\mathrm{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right] - \sum_{i=2}^{p}\frac{1}{(1-\phi_1)^2}\mathrm{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1})\mathbf{A}\right] = 0.$$

Multiplying the above equation by $(1+(p-1)\phi_1)^2(1-\phi_1)^2$ and then, some manipulations yield

$$\widehat{\phi}_1 = \frac{1}{p-1}\frac{(p-1)\mathrm{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right] - \sum_{i=2}^{p} \mathrm{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right]}{\mathrm{tr}\left[(\mathbf{I}_p \otimes [\boldsymbol{\Lambda}_2(\widehat{\phi}_2)]^{-1})\widehat{\mathbf{A}}\right]}.$$

Similarly, putting (9) into (7), it follows that

$$\widehat{\phi}_2 = \frac{1}{q-1} \frac{(q-1)\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{G}_1^q)\widehat{\mathbf{A}}\right] - \sum_{i=2}^q \mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{G}_i^q)\widehat{\mathbf{A}}\right]}{\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widehat{\phi}_1)]^{-1} \otimes \mathbf{I}_q)\widehat{\mathbf{A}}\right]}. \qquad \square$$

4.1. $H_0^1 : D[\mathbf{y_d}] = \boldsymbol{\Sigma} \otimes \mathbf{I_p} \otimes \boldsymbol{\Lambda}_\mathbf{2}(\boldsymbol{\phi_2})$

Consider the hypothesis that the measurements grouped by the "first" factor levels are not correlated, i.e., $H_0^1 : D[\mathbf{y}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\phi_2)$. The hypothesis is identical to the assumption $\phi_1 = 0$ and also means that the diagonal elements of matrix $\boldsymbol{\Lambda}_1(\phi_1)$ equal 1. Under the null hypothesis, the score vector is given by

$$\mathbf{s}_{\phi_1} = \left.\frac{\partial \ln L(\boldsymbol{\Xi}, \boldsymbol{\Sigma}, \phi_1, \phi_2)}{\partial \phi_1}\right|_{\boldsymbol{\Xi}=\widetilde{\boldsymbol{\Xi}}, \boldsymbol{\Sigma}=\widetilde{\boldsymbol{\Sigma}}, \phi_2=\widetilde{\phi}_2, \phi_1=0}, \tag{10}$$

where $\widetilde{\boldsymbol{\Xi}}, \widetilde{\boldsymbol{\Sigma}}, \widetilde{\phi}_2$ are maximum likelihood estimators under the restriction $\phi_1 = 0$. Utilizing Theorem 1, these estimators can be formulated as follows:

Corollary 1. (of Theorem 1) *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$, $d \in \{1, \ldots, n\}$, *with its likelihood given in Lemma 1. Moreover,* $\boldsymbol{\Lambda}_1(\phi_1) = \mathbf{I}_p$ *and* $\boldsymbol{\Lambda}_2(\phi_2)$ *is an unknown diagonal matrix with elements:* $\lambda_2[1, 1] = 1 + (q-1)\phi_2$, $\lambda_2[j, j] = 1 - \phi_2$, $j \in \{2, \ldots, q\}$. *Then, the maximum likelihood estimates of the parameters satisfy the following equations:*

$$\begin{aligned}
\widetilde{\boldsymbol{\Xi}} &= \tfrac{1}{n}\sum_{d=1}^{n} \mathbf{Y}_d, \\
pqn\widetilde{\boldsymbol{\Sigma}} &= \sum_{d=1}^{n} \mathbf{Y}_d'(\mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\widetilde{\phi}_2))^{-1}\mathbf{Y}_d - n\widetilde{\boldsymbol{\Xi}}'(\mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\widetilde{\phi}_2))^{-1}\widetilde{\boldsymbol{\Xi}}, \\
\widetilde{\phi}_2 &= \tfrac{1}{q-1} \frac{(q-1)\mathrm{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_1^q)\widetilde{\mathbf{A}}\right] - \sum_{i=2}^q \mathrm{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_i^q)\widetilde{\mathbf{A}}\right]}{\mathrm{tr}\widetilde{\mathbf{A}}},
\end{aligned}$$

where $\widetilde{\mathbf{A}} = \sum_{d=1}^n (\mathbf{Y}_d - \widetilde{\boldsymbol{\Xi}})\widetilde{\boldsymbol{\Sigma}}^{-1}(\mathbf{Y}_d - \widetilde{\boldsymbol{\Xi}})'$.

The information matrix for all parameters is given by $\mathcal{I} = -E\left(\frac{\partial^2 \ln L(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}^2}\right)$, where $\boldsymbol{\theta} = \{\boldsymbol{\Xi}, \boldsymbol{\Sigma}, \phi_1, \phi_2\}$ and $\mathcal{I} : (pqr + r^2 + 2) \times (pqr + r^2 + 2)$.

The first and second derivatives of the log likelihood function are presented in Appendix A. Moreover, the details involved in determining the information matrix are given in Appendix B. Under H_0^1 and with assumption $\{\widetilde{\boldsymbol{\Xi}}, \widetilde{\boldsymbol{\Sigma}}^{-1}, \phi_1 = 0, \widetilde{\phi}_2\}$, the information matrix for $\boldsymbol{\theta} = \{\boldsymbol{\Xi}, \boldsymbol{\Sigma}, \phi_1, \phi_2\}$ can be expressed as

$$\mathcal{I} = \begin{bmatrix} \mathbf{B} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{C} & \mathbf{0} & \mathbf{d} \\ \mathbf{0} & \mathbf{0} & e & 0 \\ \mathbf{0} & \mathbf{d}' & 0 & g \end{bmatrix},$$

where

$$
\begin{aligned}
\mathbf{B} &= -E[\frac{d^2 \ln L}{d\boldsymbol{\Xi}^2}] = n[\widetilde{\boldsymbol{\Sigma}}^{-1} \otimes (\mathbf{I}_p \otimes \widetilde{\boldsymbol{\Lambda}}_2)^{-1}],\\
\mathbf{C} &= -E[\frac{d^2 \ln L}{d[(\boldsymbol{\Sigma}^{-1})^{\triangle}]^2}] = \frac{pqn}{2}\mathbf{H}_r(\widetilde{\boldsymbol{\Sigma}} \otimes \widetilde{\boldsymbol{\Sigma}})\mathbf{H}_r,\\
\mathbf{d} &= -E[\frac{d^2 \ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle} d\phi_2}] = \tfrac{np(q-1)}{2}\left[\tfrac{1}{1+(q-1)\widetilde{\phi}_2} - \tfrac{1}{1-\widetilde{\phi}_2}\right]\mathbf{H}_r \operatorname{vec}\widetilde{\boldsymbol{\Sigma}},\\
e &= -E[\tfrac{d^2 \ln L}{d\phi_1{}^2}] = \frac{1}{2}qrn(p-1)p,\\
g &= -E[\tfrac{d^2 \ln L}{d\phi_2{}^2}] = \tfrac{prn(q-1)}{2}\left[\tfrac{1}{(1-\widetilde{\phi}_2)^2} + \tfrac{q-1}{(1+(q-1)\widetilde{\phi}_2)^2}\right].
\end{aligned}
\tag{11}
$$

Thus, Rao's score test statistic for testing $H_0^1 : D[\mathbf{y}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\phi_2)$ equals

$$
W_s = s_{\phi_1}^2 \mathcal{I}_{1.2}^{-1}, \tag{12}
$$

where $\mathcal{I}_{1.2}^{-1}$ is the inverse of the partial information matrix for ϕ_1, i.e.,

$$
\mathcal{I}_{1.2}^{-1} = 1/e,
$$

and the score $s_{\phi_1}^2$ is presented in (10). Rao's score test statistic for testing the relationship between observations for the "first" factor follows asymptotically a Chi-square distribution with 1 degree of freedom.

In the next theorem, Rao's score test statistic for testing $H_0^1 : D[\mathbf{y}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\phi_2)$ is formulated.

Theorem 2. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$*, with its likelihood given in Lemma 1. Then, Rao's score test statistic for testing the hypothesis* $H_0^1 : D[\mathbf{y_d}] = \boldsymbol{\Sigma} \otimes \mathbf{I_p} \otimes \boldsymbol{\Lambda_2}(\boldsymbol{\phi_2})$ *equals*

$$
W_s = \frac{\left\{(p-1)\operatorname{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\widetilde{\phi}_2)]^{-1})\widetilde{\mathbf{A}}\right] - \sum_{i=2}^p \operatorname{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\widetilde{\phi}_2)]^{-1})\widetilde{\mathbf{A}}\right]\right\}^2}{2pqrn(p-1)},
$$

where $\widetilde{\phi}_2$ *and* $\widetilde{\mathbf{A}}$ *are given in Corollary 1. The test statistic is asymptotically Chi-square distributed with* 1 *degree of freedom.*

Proof. The derivative $\frac{dlnL}{d\phi_1}$ in Lemma 2, under the hypothesis $H_0 : D[\mathbf{y}_d] = \boldsymbol{\Sigma} \otimes \mathbf{I}_p \otimes \boldsymbol{\Lambda}_2(\phi_2)$ with estimators given in Corollary 1, can be written

$$
\frac{dlnL}{d\phi_1} = \tfrac{p-1}{2}\operatorname{tr}\left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\widetilde{\phi}_2)]^{-1})\widetilde{\mathbf{A}}\right] - \tfrac{1}{2}\sum_{i=2}^{p}\operatorname{tr}\left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\widetilde{\phi}_2)]^{-1})\widetilde{\mathbf{A}}\right].
$$

Using (11) and (12) and performing some calculations, the result is established. □

Note that based on the results obtained for testing the hypothesis H_0^1, it is easy to formulate the test statistic for $D[\mathbf{y}_d] = \boldsymbol{\Sigma} \otimes \boldsymbol{\Lambda}_1(\phi_1) \otimes \mathbf{I}_q$.

Corollary 2. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$*, with its likelihood given in Lemma 1. Then, Rao's score test statistic for testing the hypothesis* $H_0 : D[\mathbf{y_d}] = \boldsymbol{\Sigma} \otimes \boldsymbol{\Lambda_1}(\boldsymbol{\phi_1}) \otimes \mathbf{I_q}$ *equals*

$$W_s = \frac{\left\{(q-1)\mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widetilde{\phi}_1)]^{-1} \otimes \mathbf{G}_1^q)\widetilde{\mathbf{A}}\right] - \sum_{i=2}^q \mathrm{tr}\left[([\boldsymbol{\Lambda}_1(\widetilde{\phi}_1)]^{-1} \otimes \mathbf{G}_i^q)\widetilde{\mathbf{A}}\right]\right\}^2}{2pqrn(q-1)},$$

where

$$\widetilde{\boldsymbol{\Xi}} = \tfrac{1}{n}\sum_{d=1}^{n} \mathbf{Y}_d,$$

$$pqn\widetilde{\boldsymbol{\Sigma}} = \sum_{d=1}^{n} \mathbf{Y}_d'(\boldsymbol{\Lambda}_1(\widetilde{\phi}_1) \otimes \mathbf{I}_q)^{-1}\mathbf{Y}_d - n\widetilde{\boldsymbol{\Xi}}'(\boldsymbol{\Lambda}_1(\widetilde{\phi}_1) \otimes \mathbf{I}_q)^{-1}\widetilde{\boldsymbol{\Xi}},$$

$$\widetilde{\phi}_1 = \tfrac{1}{p-1}\frac{(p-1)\mathrm{tr}\left[(\mathbf{G}_1^p \otimes \mathbf{I}_q)\widetilde{\mathbf{A}}\right] - \sum_{i=2}^p \mathrm{tr}\left[(\mathbf{G}_i^p \otimes \mathbf{I}_q)\widetilde{\mathbf{A}}\right]}{\mathrm{tr}\widetilde{\mathbf{A}}},$$

where $\widetilde{\mathbf{A}} = \sum_{d=1}^n (\mathbf{Y}_d - \widetilde{\boldsymbol{\Xi}})\widetilde{\boldsymbol{\Sigma}}^{-1}(\mathbf{Y}_d - \widetilde{\boldsymbol{\Xi}})'$. *The test statistic is asymptotically Chi-square distributed with* 1 *degree of freedom.*

4.2. $H_0^2 : D[\mathbf{y_d}] = \boldsymbol{\Sigma} \otimes \mathbf{I_p} \otimes \mathbf{I_q}$

Now, a test statistic for testing correlation between observations grouped by levels of the first factor and the second factor is considered simultaneously. According to the null hypothesis, $\phi_1 = 0$ and $\phi_2 = 0$. In this case, the score vector $\mathbf{s}'_{\{\phi_1,\varphi_2\}} = \left[\frac{\partial lnL}{\partial\phi_1}, \frac{\partial lnL}{\partial\phi_2}\right]$ is determined for $\{\widetilde{\boldsymbol{\Xi}}, \widetilde{\boldsymbol{\Sigma}}^{-1} |_{\varphi_1=0,\phi_2=0}\}$, where $\widetilde{\boldsymbol{\Xi}}$ and $\widetilde{\boldsymbol{\Sigma}}^{-1}$ are maximum likelihood estimators under the hypothesis H_0^2. The estimators are presented in Corollary 3.

Corollary 3. (of Theorem 1) *Let* $\mathbf{Y}_d \sim N_{pq,r}(\boldsymbol{\Xi}, \boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2), \boldsymbol{\Sigma})$*,* $d \in \{1, \ldots, n\}$*, with its likelihood given in Lemma 1. Moreover,* $\boldsymbol{\Lambda}_1(\phi_1) = \mathbf{I}_p$ *and* $\boldsymbol{\Lambda}_2(\phi_2) = \mathbf{I}_q$. *Then, the maximum likelihood estimates of the parameters satisfy:*

$$\widetilde{\boldsymbol{\Xi}} = \tfrac{1}{n}\sum_{d=1}^{n} \mathbf{Y}_d,$$

$$pqn\widetilde{\boldsymbol{\Sigma}} = \sum_{d=1}^{n} \mathbf{Y}_d'\mathbf{Y}_d - n\widetilde{\boldsymbol{\Xi}}'\widetilde{\boldsymbol{\Xi}}.$$

It follows from Corollary 3 that maximum likelihood estimators are obtained explicitly. The information matrix for estimation of all parameters under the hypothesis H_0^2 can be written

$$\mathcal{I} = \begin{bmatrix} \mathbf{B} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{C} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & e & 0 \\ \mathbf{0} & \mathbf{0} & 0 & g \end{bmatrix},$$

where

$$\mathbf{B} = -E[\frac{d^2 \ln L}{d\mathbf{\Xi}^2}] = n[\widetilde{\mathbf{\Sigma}}^{-1} \otimes \mathbf{I}_{pq}],$$

$$\mathbf{C} = -E[\frac{d^2 \ln L}{d[(\mathbf{\Sigma}^{-1})^{\triangle}]^2}] = \frac{pqn}{2}\mathbf{H}_r(\widetilde{\mathbf{\Sigma}} \otimes \widetilde{\mathbf{\Sigma}})\mathbf{H}'_r,$$

$$e = -E[\frac{d^2 \ln L}{d\phi_1{}^2}] = \frac{qrn(p-1)p}{2}, \tag{13}$$

$$g = -E[\frac{d^2 \ln L}{d\phi_2{}^2}] = -E[\frac{d^2 \ln L}{d\phi_2{}^2}] = \frac{prn(q-1)q}{2}. \tag{14}$$

Rao's score test statistic equals

$$W_s = \mathbf{s}'_{\{\phi_1,\phi_2\}}\mathcal{I}_{1.2}^{-1}\mathbf{s}_{\{\phi_1,\phi_2\}}, \tag{15}$$

where $\mathcal{I}_{1.2}^{-1}$ is the inverse of the partial information matrix

$$\mathcal{I}_{1.2} = \begin{bmatrix} e & 0 \\ 0 & g \end{bmatrix}, \tag{16}$$

and the score vector is defined in (10).

In the next theorem, we formulate Rao's score test statistic for testing $H_0^2 : D[\mathbf{y}_d] = \mathbf{\Sigma} \otimes \mathbf{I}_p \otimes \mathbf{I}_q$:

Theorem 3. *Let* $\mathbf{Y}_d \sim N_{pq,r}(\mathbf{\Xi}, \mathbf{\Lambda}_1(\phi_1)\otimes\mathbf{\Lambda}_2(\phi_2), \mathbf{\Sigma})$, $d \in \{1,\ldots,n\}$, *be independent and identically distributed observations, where* $\mathbf{\Xi} : pq \times r$ *is the mean,* $\mathbf{\Sigma}$ *is an unknown dispersion matrix and* $\mathbf{\Lambda}_1(\phi_1)$ *and* $\mathbf{\Lambda}_2(\phi_2)$ *are unknown diagonal matrices with elements:* $\lambda_1[1,1] = 1 + (p-1)\phi_1$, $\lambda_1[i,i] = 1 - \phi_1$, $i \in \{2,\ldots,p\}$, $\lambda_2[1,1] = 1 + (q-1)\phi_2$, $\lambda_2[j,j] = 1 - \phi_2$, $j \in \{2,\ldots,q\}$. *Then, Rao's score test statistic for testing the hypothesis* $H_0^2 : D[\mathbf{y_d}] = \mathbf{\Sigma} \otimes \mathbf{I_p} \otimes \mathbf{I_q}$ *can be written*

$$W_s = \tfrac{1}{2(p-1)pqrn}\left[(p-1)\mathrm{tr}\left[(\mathbf{G}_1^p \otimes \mathbf{I}_q)\widetilde{\mathbf{A}}\right] - \sum_{i=2}^{p}\mathrm{tr}\left[(\mathbf{G}_i^p \otimes \mathbf{I}_q)\widetilde{\mathbf{A}}\right]\right]^2$$
$$+\tfrac{1}{2(q-1)pqrn}\left[(q-1)\mathrm{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_1^q)\widetilde{\mathbf{A}}\right] - \sum_{i=2}^{q}\mathrm{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_i^q)\widetilde{\mathbf{A}}\right]\right]^2,$$

where $\widetilde{\mathbf{A}} = \sum_{d=1}^n(\mathbf{Y}_d - \widetilde{\mathbf{\Xi}})\widetilde{\mathbf{\Sigma}}^{-1}(\mathbf{Y}_d - \widetilde{\mathbf{\Xi}})'$ *and estimators* $\tilde{\mathbf{\Xi}}, \tilde{\mathbf{\Sigma}}$ *are given in Corollary 3. The test statistic is asymptotically Chi-square distributed with* 2 *degrees of freedom.*

Proof. The derivatives $\frac{dlnL}{d\phi_1}$ and $\frac{dlnL}{d\phi_2}$ in Lemma 2, under the hypothesis $H_0^2 : D[\mathbf{y}_d] = \mathbf{\Sigma} \otimes \mathbf{I}_p \otimes \mathbf{I}_q$, equal

$$\frac{dlnL}{d\phi_1} = \tfrac{p-1}{2}\mathrm{tr}\left[(\mathbf{G}_1^p \otimes \mathbf{I}_q)\mathbf{A}\right] - \tfrac{1}{2}\sum_{i=2}^{p}\mathrm{tr}\left[(\mathbf{G}_i^p \otimes \mathbf{I}_q)\mathbf{A}\right],$$

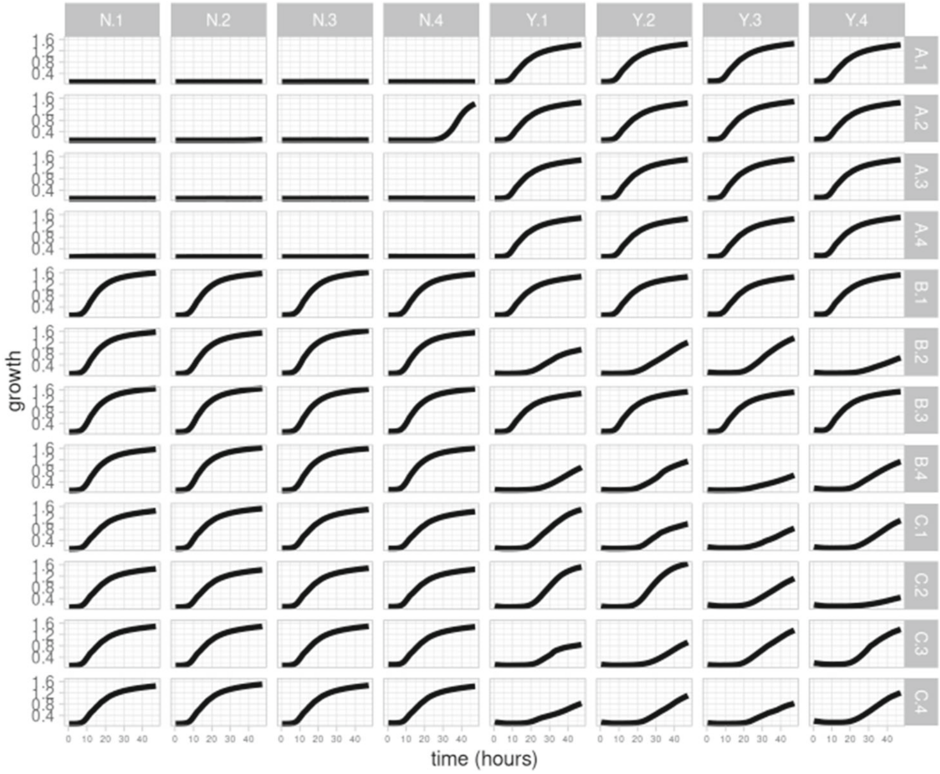

Figure 2. Growth curves obtained from the 96 wells. For each combination of yeast species (A,B,C), and supplement (Y for yes, N for no), 16 wells are presented .

$$\frac{d lnL}{d\phi_2} = \tfrac{q-1}{2}\text{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_1^q)\mathbf{A}\right] - \tfrac{1}{2}\sum_{j=2}^{q}\text{tr}\left[(\mathbf{I}_p \otimes \mathbf{G}_j^q)\mathbf{A}\right].$$

Using (13)–(16), and performing some calculations establish the result. □

5. EXPERIMENTAL RESULTS

Consider the experiment presented in the Introduction, where the mixture of apple juice is affected by two factors: three types of yeast, $p = 3$, and the supplementation by $K_2S_2O_5$ (yes/no), $q = 2$. The samples were poured manually on a multiwell with 96 wells. Each of the wells was filled by the apple juice with given types of yeast and with or without supplementation, the growth of yeast was observed, and measurements were taken every 20 min during 45 h. In Fig. 2, the growth curves of yeast from each well is shown.

From each of the growth curve, three characteristics ($r = 3$) were measured: the time point where the growing process started, the speed of growth, and the asymptote of the growth curve. The matrices $\mathbf{\Gamma}_1$ and $\mathbf{\Gamma}_2$ used to transform the data are given by

$$\mathbf{\Gamma}_1 = \begin{bmatrix} \frac{1}{\sqrt{3}} & 0 & -\frac{2}{\sqrt{6}} \\ \frac{1}{\sqrt{3}} & \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{6}} \\ \frac{1}{\sqrt{3}} & -\frac{1}{\sqrt{2}} & \frac{1}{\sqrt{6}} \end{bmatrix}, \quad \mathbf{\Gamma}_2 = \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 1 \\ 1 & -1 \end{bmatrix}.$$

Let us test the hypothesis $H_0^1 : D[\mathbf{y}_d] = \mathbf{\Sigma} \otimes \mathbf{I}_p \otimes \mathbf{\Lambda}_2(\phi_2)$ given in Sect. 4.1. Using the flip-flop algorithm, the estimators given in Corollary 1 equal

$$\tilde{\mathbf{\Xi}} = \begin{bmatrix} 4.2562 & 0.0738 & 0.5954 \\ -0.2851 & -0.0106 & -0.1667 \\ -0.0465 & 0.0018 & 0.0171 \\ 0.0149 & 0.0006 & 0.0015 \\ -0.0307 & 0.0185 & -0.0303 \\ 0.0148 & -0.0175 & 0.0361 \end{bmatrix},$$

$$\tilde{\mathbf{\Sigma}} = \begin{bmatrix} 4.45 \cdot 10^{-4} & 6.8 \cdot 10^{-5} & 2.75 \cdot 10^{-4} \\ 6.8 \cdot 10^{-5} & 8.7 \cdot 10^{-5} & 3.51 \cdot 10^{-4} \\ 2.75 \cdot 10^{-4} & 3.51 \cdot 10^{-4} & 4.35 \cdot 10^{-3} \end{bmatrix},$$

$$\tilde{\mathbf{\Lambda}}_2(\phi_2) = \begin{bmatrix} 1.2576 & 0 \\ 0 & 0.7423 \end{bmatrix}.$$

Rao's score test statistics given in Theorem 2 equals $W_S = 0.7098$ which is approximately Chi-square distributed with 1 degree of freedom. Assuming the significance level 0.05, there is not enough evidence to reject the null hypothesis (p-value$=$0.3995).
Testing correlation between the measurements grouped by second factor $H_0 : D[\mathbf{y}_d] = \mathbf{\Sigma} \otimes \mathbf{\Lambda}_1(\phi_1) \otimes \mathbf{I}_q$ (Corollary 2), the estimators are as follows:

$$\tilde{\mathbf{\Xi}} = \begin{bmatrix} 4.2562 & 0.0738 & 0.5954 \\ -0.2851 & -0.0106 & -0.1667 \\ -0.0465 & 0.0018 & 0.0171 \\ 0.0149 & 0.0006 & 0.0015 \\ -0.0307 & 0.0185 & -0.0303 \\ 0.0148 & -0.0175 & 0.0361 \end{bmatrix},$$

$$\tilde{\mathbf{\Sigma}} = \begin{bmatrix} 4.45 \cdot 10^{-4} & 6.11 \cdot 10^{-5} & 2.65 \cdot 10^{-4} \\ 6.11 \cdot 10^{-5} & 8.43 \cdot 10^{-5} & 3.57 \cdot 10^{-4} \\ 2.65 \cdot 10^{-4} & 3.57 \cdot 10^{-4} & 4.45 \cdot 10^{-3} \end{bmatrix},$$

$$\mathbf{\Lambda}_1(\phi_1) = \begin{bmatrix} 1.0859 & 0 & 0 \\ 0 & 0.9570 & 0 \\ 0 & 0 & 0.9570 \end{bmatrix}.$$

Rao's score test statistics given in Corollary 2 equals $W_S = 11.33$ which is approximately Chi-square distributed with 1 degree of freedom. Assuming the significance level 0.05, the null hypothesis rejected (p-value$=$0.0007). Thus, there is an effect of supplementation by $K_2S_2o_3$.

Now, consider the test given in Sect. 4.2 $H_0^2 : D[\mathbf{y}_d] = \mathbf{\Sigma} \otimes \mathbf{I}_p \otimes \mathbf{I}_q$. In this case, the explicit estimators given in Corollary 3 equal

$$\tilde{\mathbf{\Xi}} = \begin{bmatrix} 4.2562 & 0.0738 & 0.5954 \\ -0.2851 & -0.0106 & -0.1667 \\ -0.0465 & 0.0018 & 0.0171 \\ 0.0149 & 0.0006 & 0.0015 \\ -0.0307 & 0.0185 & -0.0303 \\ 0.0148 & -0.0175 & 0.0361 \end{bmatrix}$$

$$\tilde{\mathbf{\Sigma}} = \begin{bmatrix} 4.46 \cdot 10^{-4} & 5.93 \cdot 10^{-5} & 2.42 \cdot 10^{-4} \\ 5.93 \cdot 10^{-5} & 8.40 \cdot 10^{-5} & 3.63 \cdot 10^{-4} \\ 2.42 \cdot 10^{-4} & 3.63 \cdot 10^{-4} & 4.49 \cdot 10^{-3} \end{bmatrix}$$

and Rao's score statistic given in Theorem 3 takes the value $W_s = 7.409$ which is approximately Chi-square distributed with 2 degrees of freedom. Assuming the significance level 0.05 the null hypothesis is rejected (p-value$=$0.025).

The analysis was performed using R 4.2.2, and both data and code will be available as supplementary material.

6. CONCLUSIONS

In this paper, we use Rao's score to test the relationship between measurements in two-factor experiments. We have proposed a solution for testing the hypothesis that there is no correlation between observations grouped with respect to factors. We transform the original data as $\mathbf{x}_d \sim N_{pqr}(\boldsymbol{\mu}, \mathbf{\Sigma} \otimes \mathbf{\Psi}_1 \otimes \mathbf{\Psi}_2)$, $d \in \{1, \ldots, n\}$, where $\mathbf{\Sigma}$: $r \times r$ is an unstructured dispersion matrix for characteristics, and $\mathbf{\Psi}_1$: $p \times p$ and $\mathbf{\Psi}_2$: $q \times q$ are correlation matrices for the factors and have the compound symmetric structure to model $\mathbf{Y}_d \sim N_{pq,r}(\mathbf{\Xi}, \mathbf{\Lambda}_1(\phi_1) \otimes \mathbf{\Lambda}_2(\phi_2), \mathbf{\Sigma})$, $d \in \{1, \ldots, n\}$, where $\mathbf{\Xi} : pq \times r$ is the mean, $\mathbf{\Sigma}$ is unknown covariance matrix and $\mathbf{\Lambda}_1(\phi_1)$, $\mathbf{\Lambda}_2(\phi_2)$ are unknown diagonal matrices. The given test statistics are based on the transformed observations $\mathbf{Y}_d$. We have applied our results to a data set obtained from a fermentation process.

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APPENDIX A

In this paper, the derivative of the matrix $\mathbf{Y} : r \times s$ with respect to the matrix $\mathbf{X} : p \times q$ is defined as (see Kollo and von Rosen 2005, p. 127)

$$\frac{d\mathbf{Y}}{d\mathbf{X}} = \frac{\partial}{\mathrm{vec}\mathbf{X}}\mathrm{vec}'\mathbf{Y}$$

where

$$\frac{\partial}{vec\mathbf{X}} = \left(\frac{\partial}{\partial x_{11}}, \ldots, \frac{\partial}{\partial x_{p1}}, \frac{\partial}{\partial x_{12}}, \ldots, \frac{\partial}{\partial x_{p2}}, \ldots, \frac{\partial}{\partial x_{1q}}, \ldots, \frac{\partial}{\partial x_{pq}}\right)'$$

and vec$(\cdot)$ denotes the vec-operator from $R^{p\times q}$ to R^{pq}, putting columns underneath, starting with the first one. Moreover,

$$\frac{d^2\mathbf{Y}}{d\mathbf{X}^2} = \frac{\partial}{\mathrm{vec}\mathbf{X}}\mathrm{vec}'\frac{d\mathbf{Y}}{d\mathbf{X}}$$

(see Kollo and von Rosen 2005, p. 138). To determine the needed derivatives, the following lemma is used.

Lemma 4. Kollo and von Rosen (2005 p. 79,p. 99,pp. 128–133) *Let* $\mathbf{A}$ *and* $\mathbf{B}$ *be constants, and let* $\mathbf{X}^{\triangle}$ *denote the upper triangle of* $\mathbf{X}$. *Moreover, let* $\mathbf{H}_r = \mathbf{V}_r(\mathbf{I}_{r^2} + \mathbf{K}_{r,r} - (\mathbf{K}_{r,r})_d)$, *where* $\mathbf{V}_r : \frac{1}{2}r(r+1)\times r^2$ *is a block partitioned matrix,* $\mathbf{V}_r = ([\mathbf{V}_{11}], \ldots, [\mathbf{V}_{rr}])_{[d]}$, $\mathbf{V}_{ii} = (\mathbf{e}_1, \ldots, \mathbf{e}_i)'$, $i \in \{1, 2, \ldots, r\}$, $\mathbf{e}_i$ *is the ith unit basis vector,* $\mathbf{K}_{r,r}$ *is the commutation matrix, and* $(\mathbf{K}_{r,r})_d$ *is the diagonal matrix obtained from* $\mathbf{K}_{r,r}$. *Then,*

(i)

$$\frac{d\mathbf{X}}{d\mathbf{X}} = \mathbf{I}_p, \quad \textit{if} \quad \mathbf{X}:\ p\times q \textit{ is unstructured,}$$
$$\frac{d\mathbf{X}}{d\mathbf{X}^{\triangle}} = \mathbf{H}_p, \quad \textit{if} \quad \mathbf{X}:\ p\times p \textit{ is symmetric;}$$

(ii)

$$\frac{d\ln|\mathbf{X}|}{d\mathbf{X}^{\triangle}} = \mathbf{H}_p\mathrm{vec}(\mathbf{X}^{-1}) \ \textit{ if } \mathbf{X}\textit{: } p\times p\textit{, is symmetric;}$$

(iii)

$$\frac{d\mathrm{tr}(\mathbf{A}'\mathbf{X})}{d\mathbf{X}} = \mathrm{vec}\mathbf{A} \quad \textit{if} \quad \mathbf{X}:\ p\times q,\ \textit{is unstructured,}$$
$$\frac{d\mathrm{tr}(\mathbf{A}'\mathbf{X})}{d\mathbf{X}^{\triangle}} = \mathbf{H}_p\mathrm{vec}\mathbf{A} \quad \textit{if} \mathbf{X}:\ p\times p,\ \textit{is symmetric;}$$

(iv)

$$\frac{d\mathrm{tr}(\mathbf{X}'\mathbf{A}\mathbf{X}\mathbf{B})}{d\mathbf{X}} = \begin{cases} \mathrm{vec}(\mathbf{A}'\mathbf{X}\mathbf{B}') + \mathrm{vec}(\mathbf{A}\mathbf{X}\mathbf{B}), & \textit{if } \ \mathbf{X}: \ p \times q, \ \textit{is unstructured,} \\ \mathbf{H}_p[\mathrm{vec}(\mathbf{A}'\mathbf{X}\mathbf{B}') + \mathrm{vec}(\mathbf{A}\mathbf{X}\mathbf{B})], & \textit{if } \ \mathbf{X}: \ p \times p, \ \textit{is symmetric;} \end{cases}$$

(v)

$$\frac{d(\mathbf{A}'\mathrm{vec}\mathbf{X})}{d\mathbf{X}} = \frac{d(\mathrm{vec}'\mathbf{X}\mathbf{A})}{d\mathbf{X}} = \mathbf{A};$$

(vi)

$$\frac{d\mathbf{X}^{-1}}{d\mathbf{X}^{\triangle}} = -\mathbf{H}_r(\mathbf{X}^{-1} \otimes \mathbf{X}'^{-1}).$$

The first derivatives of the log likelihood function, $\ln(L(\boldsymbol{\Xi}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}_1(\phi_1), \boldsymbol{\Lambda}_2(\phi_2)))$ given in Lemma 1 equal:

$$\begin{aligned}
\frac{d\ln L}{d\boldsymbol{\Xi}} &= \mathrm{vec}[(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1} \sum_{d=1}^{n} \mathbf{Y}_d \boldsymbol{\Sigma}^{-1} - n(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1} \boldsymbol{\Xi} \boldsymbol{\Sigma}^{-1}], \\
\frac{d\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}} &= \tfrac{pqn}{2} \mathbf{H}_r \mathrm{vec}\boldsymbol{\Sigma} - \frac{1}{2} \mathbf{H}_r \mathrm{vec} \Bigg[\sum_{d=1}^{n} \mathbf{Y}'_d (\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1} \mathbf{Y}_d \\
&\quad -2 \sum_{d=1}^{n} \mathbf{Y}'_d (\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1} \boldsymbol{\Xi} + n \boldsymbol{\Xi}' (\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1} \boldsymbol{\Xi} \Bigg], \\
\frac{d\ln L}{d\phi_1} &= \tfrac{1}{2} qrn(p-1)(\tfrac{1}{1-\phi_1} - \tfrac{1}{1+(p-1)\phi_1}) \\
&\quad + \tfrac{1}{2} \tfrac{(p-1)}{(1+(p-1)\phi_1)^2} \mathrm{tr} \left[(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}) \mathbf{A} \right] \\
&\quad - \tfrac{1}{2} \sum_{i=2}^{p} \tfrac{1}{(1-\phi_1)^2} \mathrm{tr} \left[(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}) \mathbf{A} \right], \\
\frac{d\ln L}{d\phi_2} &= \tfrac{1}{2} prn(q-1)(\tfrac{1}{1-\phi_2} - \tfrac{1}{1+(q-1)\phi_2}) \\
&\quad + \tfrac{1}{2} \tfrac{(q-1)}{(1+(q-1)\phi_2)^2} \mathrm{tr} \left[([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q) \mathbf{A} \right] \\
&\quad - \tfrac{1}{2} \sum_{i=2}^{q} \tfrac{1}{(1-\phi_2)^2} \mathrm{tr} \left[([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_i^q) \mathbf{A} \right].
\end{aligned}$$

Now, using a property of the vec-operator and (v) of Lemma 4 we obtain

$$\frac{d^2 \ln L}{d\boldsymbol{\Xi}^2} = -n[\boldsymbol{\Sigma}^{-1} \otimes (\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}].$$

Using (v) from Lemma 4

$$\frac{d^2 \ln L}{d\boldsymbol{\Xi}\, d(\boldsymbol{\Sigma}^{-1})^{\triangle}} = \mathbf{H}_r\{\mathbf{I}_r \otimes [(\sum_{d=1}^{n} \mathbf{Y}_d' - n\boldsymbol{\Xi}')(\boldsymbol{\Lambda}_1(\phi_1) \otimes \boldsymbol{\Lambda}_2(\phi_2))^{-1}]\}.$$

From (iii) and (iv) of Lemma 4, and after some transformations,

$$\begin{aligned}\frac{d^2 \ln L}{d\boldsymbol{\Xi}\, d\phi_1} &= \tfrac{(p-1)}{(1+(p-1)\phi_1)^2} \mathrm{vec}\left[\left(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}\right)\left(n\boldsymbol{\Xi} - \sum_{d=1}^{n} \mathbf{Y}_d\right)\boldsymbol{\Sigma}^{-1}\right] \\ &\quad - \sum_{i=2}^{p} \tfrac{1}{(1-\phi_1)^2} \mathrm{vec}\left[\left(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}\right)\left(n\boldsymbol{\Xi} - \sum_{d=1}^{n} \mathbf{Y}_d\right)\boldsymbol{\Sigma}^{-1}\right],\end{aligned}$$

and

$$\begin{aligned}\frac{d^2 \ln L}{d\boldsymbol{\Xi}\, d\phi_2} &= \tfrac{(q-1)}{(1+(q-1)\phi_2)^2} \mathrm{vec}\left[\left([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q\right)\left(n\boldsymbol{\Xi} - \sum_{d=1}^{n} \mathbf{Y}_d\right)\boldsymbol{\Sigma}^{-1}\right] \\ &\quad - \sum_{i=2}^{q} \tfrac{1}{(1-\phi_2)^2} \mathrm{vec}\left[\left([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_i^q\right)\left(n\boldsymbol{\Xi} - \sum_{d=1}^{n} \mathbf{Y}_d\right)\boldsymbol{\Sigma}^{-1}\right].\end{aligned}$$

From (v) and (vi) of Lemma 4, it follows that

$$\frac{d^2 \ln L}{d[(\boldsymbol{\Sigma}^{-1})^{\triangle}]^2} = -\tfrac{pqn}{2}\mathbf{H}_r(\boldsymbol{\Sigma} \otimes \boldsymbol{\Sigma})\mathbf{H}'_r.$$

Using Lemma 4 (iii), and after some transformations,

$$\begin{aligned}&\frac{d^2 \ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle} d\phi_1} \\ &= \tfrac{1}{2}\frac{(p-1)}{(1+(p-1)\phi_1)^2}\mathbf{H}_r \mathrm{vec}\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \boldsymbol{\Xi})'\left(\mathbf{G}_1^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}\right)(\mathbf{Y}_d - \boldsymbol{\Xi})\right] \\ &\quad -\tfrac{1}{2}\mathbf{H}_r \sum_{i=2}^{p} \tfrac{1}{(1-\phi_1)^2} \mathrm{vec}\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \boldsymbol{\Xi})'\left(\mathbf{G}_i^p \otimes [\boldsymbol{\Lambda}_2(\phi_2)]^{-1}\right)(\mathbf{Y}_d - \boldsymbol{\Xi})\right],\end{aligned}$$

and

$$\begin{aligned}&\frac{d^2 \ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle} d\phi_2} \\ &= \tfrac{1}{2}\tfrac{(q-1)}{(1+(q-1)\phi_2)^2}\mathbf{H}_r \mathrm{vec}\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \boldsymbol{\Xi})'\left([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q\right)(\mathbf{Y}_d - \boldsymbol{\Xi})\right] \\ &\quad -\tfrac{1}{2}\sum_{i=2}^{q}\mathbf{H}_r \sum_{i=2}^{p} \tfrac{1}{(1-\phi_2)^2} \mathrm{vec}\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \boldsymbol{\Xi})'\left([\boldsymbol{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_i^q\right)(\mathbf{Y}_d - \boldsymbol{\Xi})\right].\end{aligned}$$

Moreover,

$$\begin{aligned}
\frac{d^2 \ln L}{d\phi_1^2} &= \tfrac{1}{2}qrn(p-1)\left[\tfrac{1}{(1-\phi_1)^2} + \tfrac{p-1}{(1+(p-1)\phi_1)^2}\right] \\
&\quad - \tfrac{(p-1)^2(1+(p-1)\phi_1)}{(1+(p-1)\phi_1)^4}\operatorname{tr}\left[\left(\mathbf{G}_1^p \otimes [\mathbf{\Lambda}_2(\phi_2)]^{-1}\right)\mathbf{A}\right] \\
&\quad - \sum_{i=2}^{p} \tfrac{(1-\phi_1)}{(1-\phi_1)^4}\operatorname{tr}\left[\left(\mathbf{G}_i^p \otimes [\mathbf{\Lambda}_2(\phi_2)]^{-1}\right)\mathbf{A}\right], \\
\frac{d^2 \ln L}{d\phi_1 d\phi_2} &= \tfrac{1}{2}\tfrac{(q-1)}{(1+(q-1)\phi_2)^2}\operatorname{tr}\left[\left(\mathbf{V} \otimes \mathbf{G}_1^q\right)\mathbf{A}\right] - \tfrac{1}{2}\sum_{i=2}^{q}\tfrac{1}{(1-\phi_2)^2}\operatorname{tr}\left[\left(\mathbf{V} \otimes \mathbf{G}_i^q\right)\mathbf{A}\right],
\end{aligned}$$

where

$$\begin{aligned}
\mathbf{V} &= \tfrac{-(p-1)}{(1+(p-1)\phi_1)^2}\mathbf{G}_1^p + \sum_{j=2}^{p}\tfrac{1}{(1-\phi_1)^2}\mathbf{G}_j^p, \\
\frac{d^2 \ln L}{d\phi_2^2} &= \frac{prn(q-1)}{2}\left(\tfrac{1}{(1-\phi_2)^2} + \tfrac{q-1}{(1+(q-1)\phi_2)^2}\right) \\
&\quad - \tfrac{(q-1)^2}{(1+(q-1)\phi_2)^3}\operatorname{tr}\left[([\mathbf{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q)\mathbf{A}\right] \\
&\quad - \tfrac{1}{(1-\phi_2)^3}\sum_{i=2}^{q}\operatorname{tr}\left[([\mathbf{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_i^q)\mathbf{A}\right].
\end{aligned}$$

APPENDIX B

To determine entries of the information matrix, the following well known lemma is used.

Lemma 5. *Let* $\mathbf{X} \sim N_{p,n}(\boldsymbol{\mu}, \mathbf{\Sigma}, \mathbf{\Psi})$. *Then,*

$$E[\mathbf{X}\mathbf{A}\mathbf{X}'] = \operatorname{tr}(\mathbf{\Psi}\mathbf{A})\mathbf{\Sigma} + \boldsymbol{\mu}\mathbf{A}\boldsymbol{\mu}'.$$

Assuming that $\mathbf{Y}_d \sim N_{pq,r}(\mathbf{\Xi}, \mathbf{\Lambda}_1(\phi_1) \otimes \mathbf{\Lambda}_2(\phi_2), \mathbf{\Sigma})$, $d \in \{1, \ldots, n\}$, using Lemma 5,

$$\begin{aligned}
&E\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})\mathbf{\Sigma}^{-1}(\mathbf{Y}_d - \mathbf{\Xi})'\right] = nr(\mathbf{\Lambda}_1(\phi_1) \otimes \mathbf{\Lambda}_2(\phi_2)), \\
&E\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})'(\mathbf{G}_1^p \otimes [\mathbf{\Lambda}_2(\phi_2)]^{-1})(\mathbf{Y}_d - \mathbf{\Xi})\right] = nq(1 + (p-1)\phi_1)\mathbf{\Sigma}, \\
&\sum_{i=2}^{p} E\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})'(\mathbf{G}_i^p \otimes [\mathbf{\Lambda}_2(\phi_2)]^{-1})(\mathbf{Y}_d - \mathbf{\Xi})\right] = nq(p-1)(1-\phi_1)\mathbf{\Sigma}, \\
&E\left[\sum_{d=1}^{n}(\mathbf{Y}_d - \mathbf{\Xi})'([\mathbf{\Lambda}_1(\phi_1)]^{-1} \otimes \mathbf{G}_1^q)(\mathbf{Y}_d - \mathbf{\Xi})\right] = np(1 + (q-1)\phi_2)\mathbf{\Sigma},
\end{aligned}$$

$$\sum_{i=2}^{q} E\left[\sum_{d=1}^{n}(\mathbf{Y}_d-\boldsymbol{\Xi})'([\boldsymbol{\Lambda}_1(\phi_1)]^{-1}\otimes\mathbf{G}_i^q)(\mathbf{Y}_d-\boldsymbol{\Xi})\right]=np(q-1)(1-\phi_2)\boldsymbol{\Sigma}.$$

The above formulas can be used to determine $E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_1}\right]$, $E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_2}\right]$, $E\left[\frac{d^2\ln L}{d\phi_1{}^2}\right]$, $E\left[\frac{d^2\ln L}{d\phi_2{}^2}\right]$ and $E\left[\frac{d^2\ln L}{d\phi_1 d\phi_2}\right]$.

The information matrix for the estimation $\{\boldsymbol{\Xi},\boldsymbol{\Sigma}^{-1},\phi_1,\phi_2\}$ equals

$$\mathcal{I}(\boldsymbol{\Xi},\boldsymbol{\Sigma}^{-1},\phi_1,\phi_2)=\begin{bmatrix} -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}^2}\right] & & & \\ -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d(\boldsymbol{\Sigma}^{-1})^{\triangle}}\right] & -E\left[\frac{d^2\ln L}{d((\boldsymbol{\Sigma}^{-1})^{\triangle})^2}\right] & & \\ -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d\phi_1}\right] & -E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_1}\right] & -E\left[\frac{d^2\ln L}{d\phi_1{}^2}\right] & \\ -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d\phi_2}\right] & -E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_2}\right] & -E\left[\frac{d^2\ln L}{d\phi_1 d\phi_2}\right] & -E\left[\frac{d^2\ln L}{d\phi_2{}^2}\right] \end{bmatrix},$$

where

$$-E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}^2}\right]=n\left[\boldsymbol{\Sigma}^{-1}\otimes(\boldsymbol{\Lambda}_1(\phi_1)\otimes\boldsymbol{\Lambda}_2(\phi_2))^{-1}\right],$$

$$-E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d(\boldsymbol{\Sigma}^{-1})^{\triangle}}\right]=\mathbf{0},\quad -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d\phi_1}\right]=\mathbf{0},\quad -E\left[\frac{d^2\ln L}{d\boldsymbol{\Xi}d\phi_2}\right]=\mathbf{0},$$

$$-E\left[\frac{d^2\ln L}{d\left((\boldsymbol{\Sigma}^{-1})^{\triangle}\right)^2}\right]=\tfrac{pqn}{2}\mathbf{H}_r(\boldsymbol{\Sigma}\otimes\boldsymbol{\Sigma})\mathbf{H}_r,$$

$$-E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_1}\right]=\tfrac{-nq(p-1)}{2}\left[\tfrac{1}{1+(p-1)\phi_1}-\tfrac{1}{1-\phi_1}\right]\mathbf{H}_r\operatorname{vec}\boldsymbol{\Sigma},$$

$$-E\left[\frac{d^2\ln L}{d(\boldsymbol{\Sigma}^{-1})^{\triangle}d\phi_2}\right]=\tfrac{-np(q-1)}{2}\left[\tfrac{1}{1+(q-1)\phi_2}-\tfrac{1}{1-\phi_2}\right]\mathbf{H}_r\operatorname{vec}\boldsymbol{\Sigma},$$

$$-E\left[\frac{d^2\ln L}{d\phi_1{}^2}\right]=\tfrac{1}{2}qrn(p-1)\left[\tfrac{1}{(1-\phi_1)^2}+\tfrac{p-1}{(1+(p-1)\phi_1)^2}\right],$$

$$-E\left[\frac{d^2\ln L}{d\phi_1 d\phi_2}\right]=-\tfrac{1}{2}nr(p-1)(q-1)\tfrac{-p\phi_1}{(1+(p-1)\phi_1)(1-\phi_1)}\tfrac{q\phi_2}{(1-\phi_2)(1+(q-1)\phi_2)},$$

$$-E\left[\frac{d^2\ln L}{d\phi_2{}^2}\right]=\tfrac{prn(q-1)}{2}\left[\tfrac{1}{(1-\phi_2)^2}+\tfrac{q-1}{(1+(q-1)\phi_2)^2}\right].$$

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