THE UNIVERSITY OF TEXAS AT SAN ANTONIO, COLLEGE OF BUSINESS

Working Paper SERIES

l

Date September 15, 2015 **Date September 15, 2015**

Score test for a separable covariance structure with the first component as compound symmetric correlation matrix

> Katarzyna Filipiak Department of Mathematical and Statistical Methods Poznan University of Life Sciences Wojska Polskiego 28, PL-60637 Poznan, Poland E-mail: kas_l@up.poznan.pl

Daniel Klein Institute of Mathematics, Faculty of Science P. J. Safarik University Jesenna 5, 040 01 Kosice, Slovakia daniel.klein@upjs.sk

Anuradha Roy _ Department of Management Science and Statistics The University of Texas at San Antonio One UTSA Circle, San Antonio, TX 78249 USA Email: aroy@utsa.edu Phone: +00-210-458-6343, Fax: +00-210-458-6350

Copyright © 2014, by the author(s). Please do not quote, cite, or reproduce without permission from the author(s).

ONE UTSA CIRCLE SAN ANTONIO, TEXAS 78249-0631 210 458-4317 | BUSINESS.UTSA.EDU

Score test for a separable covariance structure with the first component as compound symmetric correlation matrix

Katarzyna Filipiak Department of Mathematical and Statistical Methods Poznań University of Life Sciences Wojska Polskiego 28, PL-60637 Poznań, Poland E-mail: kasfil@up.poznan.pl

Daniel Klein Institute of Mathematics, Faculty of Science P. J. Safárik University Jesenná 5, 040 01 Košice, Slovakia daniel.klein@upjs.sk

Anuradha Roy [∗] Department of Management Science and Statistics The University of Texas at San Antonio One UTSA Circle, San Antonio, TX 78249 USA Email: aroy@utsa.edu Phone: +00-210-458-6343, Fax: +00-210-458-6350

Abstract

Likelihood ratio tests (LRTs) for separability of a covariance structure for doubly multivariate data are widely studied in the literature. There are three types of LRT: biased tests based on an asymptotic chi-square null distribution; unbiased/unmodified tests based on an empirical null distribution; and unbiased/modified tests with a test statistic modified to follow a theoretical chi-square null distribution. The Rao's score test (RST) statistic, an alternative for both biased and unbiased/unmodified versions of the corresponding LRT test statistics are derived for a common case. The separability of a covariance structure with the first component as a compound symmetric correlation matrix under the assumption of multivariate normality is tested. Simulation studies compare the biased LRT to biased RST, and unbiased/unmodified LRT to unbiased/unmodified RST. The RSTs outperform their corresponding LRTs in general. Three examples are presented. Since the RST does not require estimation of a general variance-covariance matrix (the alternative hypothesis), this test can be performed for small sample sizes, where the variance-covariance matrix could not be estimated for the corresponding LRT, making the LRT infeasible. In cases where both LRT and RST are feasible, the RST outperforms a comparable LRT.

Keywords: Empirical null distribution; Likelihood ratio test; Maximum likelihood estimates; Rao's score test; Separable covariance structure

2000 Mathematics Subject Classification: Primary 62H15; Secondary 62H12

[∗]Correspondence to: Anuradha Roy, Department of Management Science and Statistics, The University of Texas at San Antonio, One UTSA Circle, San Antonio, TX 78249, USA

1 Introduction

This article is concerned with a very important hypothesis testing problem of a 2−separable covariance structure (defined in Section 2) as found in two-level or doubly multivariate data. Modern experimental techniques allow to collect and store multi-level multivariate data (Leiva and Roy, 2011) in almost all fields such as agriculture, biology, biomedical, medical, environmental and engineering research, where the observations are collected on more than one response variable (q) at different locations (p) repeatedly over time (t) and at different depths (d) etc. These multi-level multivariate observations may have variances that differ across locations, time and depths, and developing efficient techniques for accounting these variations is of great importance for any statistical analysis.

In many practical problems, where the repeated measures occur, the covariance matrix of these repeated measures is found to have some structure. For measurements of the same type made in the same way it is usual to assume variance homogeneity too. Crowder and Hand (1990, p.60) say "While it is robust not to assume knowledge of the covariance structure, this can result in rather weak inference in the sense that too many degrees of freedom are used up in estimating the covariance parameters, leaving too few for the parameters of interest." The unstructured (UN) covariance matrix does not require stationarity, but is overparametrized since correlation should decay as the space or time points become more widely separated and estimating parameters which are close to zero only adds extra variability due to estimation of excessive parameters and thus losing degrees of freedom. Thus, for example, we assume stationarity as a consequence of the assumption of equicorrelated covariance structure - compound symmetry (CS) - which may be appropriate where the repeated measurements are all made at about the same time, as in the often used 'split-plots' set-up. The CS structure is also plausible where the measurements are made at unequally spaced times over a longer period. The advantages of using CS structure over repeated measures include flexibility in using the structured covariance matrices for the repeated measures and savings in degrees of freedom for testing of hypothesis. In other cases, there might be some strict temporal sequence where the covariance matrix has AR(1) structure, as often seen in medical data.

For doubly multivariate data, separable structure can additionally be used to model data without losing many degrees of freedom and still avoid an over-constrained model. Consider an example of a medical data set where the detection of a cancerous region from surrounding tissues (skeletonization) of patients suffering from breast cancer is the focus. Pinto Pereira et al. (2009) divided each breast image into 48 regions and then estimated the percent density (PD) for each one of its regions. However, they only used one marker, the PD, in their analysis. A better result with a high reliability

may be achieved if joint analysis of the PD and a measure of microcalcifications, which are often the only detectable sign of breast cancer, can be done together. These two measurements $(q = 2)$, the PD and a measure of microcalcifications, are not only correlated among themselves, but also exploit the strong regional covariance over the 48 regions $(p = 48)$. In this example equicorrelated covariance structure could be one of the plausible structures over 48 regions. Besides CS, a few other plausible correlation structures over repeated measures among many are autoregressive of order one $(AR(1)),$ circular and Toeplitz. Non-stationary unstructured (UN) and antedependent variance-covariance matrices are other possibilities. All structures on the repeated measures are tentative; so before any statistical analysis of doubly multivariate data one needs to perform tests for the most suitable separable structures with the first component (structure on repeated measurements) as one of the above plausible structures, i.e., (CS \otimes UN), or (AR(1) \otimes UN) or (UN \otimes UN) etc.

1.1 Existing Tests

The most common hypotheses testing procedures for large samples are the likelihood ratio (Wilks, 1938), the Wald (Wald, 1943), and the Rao's score (Rao, 1948) tests. These were all developed using one-level multivariate models. These tests have earned the status of default methods, with a neat and unified asymptotic theory. They are widely used in almost all areas from agriculture to engineering research among many others even for the smallest possible sample size (n) . The likelihood ratio test criterion Λ (Anderson, 1984) or a function of it, $\mathcal{L} = -2\text{ln}\Lambda$ (Wald, 1943), is the most commonly used test statistic. The quantity $\mathcal L$ under the null hypothesis is asymptotically distributed as a χ^2 under normality assumption and is used as the test statistic with large sample size. When the data are not large enough, χ^2 distribution is generally an inadequate approximation thus resulting in erroneous conclusions. When the sample size is small or moderate, Korin (1968) studied the accuracy of the approximation and expressed the null distribution of $\mathcal L$ in the form of an asymptotic series of central χ^2 distribution and then derived the distribution of $\mathcal L$ using this series.

All the above-mentioned tests have been established for traditional multivariate data (say with q response variables); in other words, just for 'one-level multivariate data' in a large sample setting. Hypothesis testing of a 2−separable covariance structure with both unstructured components has been widely studied by many authors Dutilleul, 1999; Roy and Khattree, 2003; Lu and Zimmerman, 2005; Roy, 2007; Srivastava et al., 2008; Werner et al., 2008). Roy and Khattree (2005a, b) have also studied this 2−separable covariance structure by assuming a compound symmetry (CS) or autoregressive of order one AR(1) correlation structures on the first component just to avoid the identifiability problem. Roy and Khattree (2007a) have shown that the choice of appropriate

covariance structure is crucial for two-level multivariate data in the context of classification, and it almost always affects the misclassification error rate, in a major way. Thus, it is vital to test the appropriate covariance structure on the multi-level multivariate observations before any statistical analysis. Roy and Leiva (2008) further studied the 2−separable covariance structure by assuming both the components as structured $(CS \text{ or } AR(1))$ which is useful for spatio-temporal repeated measurements. For example, for modeling the covariance of multivariate environmental monitoring data obtained repeatedly over time and space, or for modeling covariance structure of glucose measurement at 15 different regions $(p = 15)$ in both the hemispheres $(q = 2)$ of the brain (Worsley et al., 1991). All these authors used likelihood ratio test (LRT) statistic for testing various permutations of patterns of 2−separable covariance structures. Among these authors Lu and Zimmerman (2005) and Roy and Leiva (2008) have used unbiased/unmodified LRT, and simulations are used to build its sampling distribution and find quantiles. Others worked on biased LRT, based on the theoretical chi-square null distribution; in this case the rejection rate of null hypothesis is not equal to the nominal Type I error when the null hypothesis is true. It is worthwhile to mention here that using biased LRT, MIXED procedure of SAS Software (SAS Institute Inc., 2009) can test the hypotheses for 2−separable covariance structure with the first component as CS or AR(1) correlation or unstructured covariance structures. Therefore, we see that hypotheses tests for separable structures are a well developed area, and biased and unbiased/unmodified LRTs are available.

Several authors also proposed unbiased/modified LRT statistic in which the test statistic is modified in order to match the theoretical chi-square distribution to test the separability of variancecovariance structure. Mitchell et al. (2006) derived a modified LRT statistic to test the separability of a covariance matrix using the ratio of the mean of the LRT to the asymptotic mean to estimate the critical value of the distribution of the LRT statistic for two-level data. Simpson (2010) proposed an adjusted likelihood ratio test of separability for unbalanced two-level multivariate data using the technique proposed by Mitchell *et al.* (2006). He also suggested another less conservative and more straightforward adjustment in his paper. Simpson (2010) as well addressed the particular case where the within subject correlation decreases exponentially in both levels. Very recently Manceur and Dutilleul (2013) presented an unbiased/modified LRT, based on penalty-based homothetic transformation of the LRT statistic, for separability of a variance-covariance structure, by multiplying the test statistic by a constant. This constant is estimated by simulation so that the distribution of the test statistic approaches chi-square even for small samples. At the core of their work was the finding that a simple homothetic transformation based on an optimal penalty was sufficient to modify the biased LRT statistics for separability, so the distributions of LRT statistics thus modified

are χ^2 already for moderate sample sizes. Manceur and Dutilleul (2013) also calculated standardized empirical bias. However, since the estimation of unstructured Ω is necessary in all these modified tests, the sample size n bigger than pq is required.

The LRT statistic is reliable with very large samples. Nevertheless, in the real-life applications we have only finite samples; small sample sizes are the norm because of limited measurement opportunities. One way of overcoming the problem of the accuracy of the asymptotic approximation under the null distribution of the unmodifed LRT statistic for testing 2-separable covariance structure for small or moderate sample sizes is to exploit the empirical null distribution (END) of the LRT statistic. Lu and Zimmerman (2005) and Roy and Leiva (2008) derived ENDs of the LRT statistics for testing 2−separable covariance structure with both unstructured components and both structured components respectively. One can clearly see from these two articles that the ENDs of the LRT statistics are quite different from their limiting χ^2 distributions for small sample size with $n > pq$. Therefore, the LRT fails as a matter of practical use because its distribution is very different from its limiting χ^2 distribution for small samples; in addition, the LRT cannot be used for $n \leq pq$ for the general unstructured variance-covariance matrix as alternative hypothesis, a common problem for LRT. Nevertheless, researchers still use the theoretical chi square distribution even for small samples as exact tests are not available in such cases.

In many two-level multivariate data applications it is possible to model a dataset with $n \leq pq$ without testing for separability of the variance-covariance matrix by postulating the separability. For example, MIXED procedure of SAS can fit linear models, and Roy and Khattree's (2007a, b) classification rules can classify individuals with separable covariance structure when $n \leq pq$. It is commonly done in practice. However, before applying MIXED procedure of SAS, or Roy and Khattree's classification rules one must test whether the data have separable covariance structure. Unfortunately, all the above mentioned available unmodified LRT based tests or the modified LRT based tests need the assumption $n > pq$, which is often not possible in applied setting given the limitations on data collection. So, even if the methods are available for modeling data using separable structure when $n \leq pq$, the testing is not, which is the limiting factor of any statistical analysis for two-level data. However, Simpson et al. (2014) very recently provides a method in this context which avoids this limitation. We propose a different approach.

1.2 Proposed Tests

Rao's score test (RST) is an alternative or competitor to LRT; in this article we propose a new approach, an unmodified RST procedure, to test a 2−separable covariance structure with the first component as a CS correlation matrix, which essentially means that all measurements for any characteristic within the same subject are equicorrelated. The biggest advantage of RST is that it only exploits the null hypothesis, and thus does not need the assumption $n > pq$ as LRT does. We compare the performances of this new RST procedure with unmodifed LRT procedure. When both components of the 2−separable covariance structure are unstructured, the RST requires a sample size $n > \max(p, q)$, which can be large for many repeated measures (p) . However, when the first separable component is the CS correlation structure, RST only requires a sample size $n > q$, which is independent of the number of repeated measures. Given the increasing collection of multi-level data on which separability could be assessed, we develop a new method of testing separability of a covariance structure using RST when n is just greater than q , which is a substantial improvement over the LRT. This method will give the opportunity to many statistical practitioners and researchers to test the separability in small sample situation before applying the separability structure to their applications.

We perform simulation experiments to check the finite sample performance of both the RST and the LRT statistics, comparing a biased LRT to a biased RST, and an unbiased/unmodified LRT to an unbiased/unmodified RST. Both LRT and RST are equivalent to the first order of asymptotics, but differ to some extent in the second order properties; neither is uniformly superior to the other. Thus, empirical type I error is determined for both LRT and RST statistics to show that the biasedness of RST is much smaller than LRT for nominal significance level 0.01 as well as 0.05. Moreover, we derive the ENDs of the RST and LRT statistics, compare an unbiased/unmodified LRT to an unbiased/unmodified RST, and show that for small samples the END of the RST statistic gives much more reliable inference than the END of the LRT statistic. In other words, we show that the difference between the END of RST statistic and its limiting χ^2 distribution is much smaller than the difference between the END of LRT statistic and its limiting χ^2 distribution for any small or moderate sample size. We also derive ENDs of RST statistics for $q < n \le pq$, the computation of which is not even possible for LRT statistics. The simplicity of the standard χ^2 test is convenient, but comes at potentially considerable cost because it differs substantially from the END especially for large number of repeated measurements (p) . To show the performance of the ENDs for both RST and LRT statistics we perform simulation studies up to 15 repeated measurements with the number of variables as two and three.

This article is organized as follows. In Section 2 separability hypothesis of a covariance matrix for two-level data is introduced, and the formulation of the test statistics is presented. RST is defined in Section 3. Simulation studies are performed in Section 4 to calculate the observed Type I error rates, the ENDs of RST and LRT statistics and the power of the tests. Three real data examples to show the performance of our new proposed method, comparing the biased LRT to the biased RST and the unbiased/unmodified LRT to the unbiased/unmodified RST, are given in Section 5, and finally Section 6 summarizes with several comments along with the scope for the future research. Proofs of some basic results of matrix algebra which are needed in deriving the maximum likelihood estimates (MLEs) of the matrix parameters and the RST statistic in Section 3 are presented in A. Empirical percentiles of the null distributions of LRT and RST statistics for several combinations of p, q and n are presented in B.

2 Separability hypothesis of a covariance matrix

Let X_i for $i = 1, \ldots, n$ be the independent and identically distributed $(q \times p)$ −dimensional observation matrices, measurements on q characteristics at p time points on *i*th individual. We assume $\mathbf{X}_i \sim N_{q,p}(\mathbf{M},\mathbf{\Omega}),$ i.e., $\text{vec}\mathbf{X}_i \sim N_{pq}(\text{vec}\mathbf{M},\mathbf{\Omega}),$ where $\text{vec}\mathbf{M} \in \mathbb{R}^{pq}$, $\text{vec}(\cdot)$ is the operator stacking the columns of a $q \times p$ matrix into $pq \times 1$ dimensional vector, and Ω is assumed to be a $pq \times pq$ positive definite matrix. We denote $\text{vec}X_i = x_i$ and $\text{vec}M = \mu$. We define the vector of unknown parameters $\boldsymbol{\theta} = (\boldsymbol{\mu}', \text{vech}'\Omega)'$, where vech(·) is the operator stacking the columns of a $pq \times pq$ dimensional symmetric matrix into $\left(\frac{pq(pq+1)}{2}$ dimensional vector by eliminating all the supradiagonal elements. The number of unknown parameters to be estimated in Ω is $pq(pq + 1)/2$, which increases very rapidly with the increase of the dimension of either the number of characteristics q , or the number of time points p. Estimation of Ω is impossible when the sample size $n \leq pq$. So, researchers usually rely on structured covariance matrices which depend on a smaller set of unknown parameters. The problem, though, is knowing what the structure is. A form of the covariance matrix Ω suitable for doubly multivariate data or two-level data is a 2−separable variance-covariance structure as follows:

$$
\Omega_{pq} = \Psi \otimes \Sigma_{q \times q}, \qquad (1)
$$

where both Ψ and Σ are unstructured positive definite matrices and \otimes represents the Kronecker product. The $q \times q$ matrix Σ represents the variance-covariance matrix of the q response variables at any given time point. We assume Σ does not depend on time and it is the same for all time points. The $p \times p$ matrix Ψ represents the variance-covariance matrix of the repeated measurements on a given characteristic and it is assumed to be the same for all characteristics as well. The number of unknown parameters to be estimated in the separable structure (1) is only $p(p+1)/2+q(q+1)/2-1$ (with the first diagonal element of Ψ as one to circumvent the over-identifiability problem of Ψ and Σ in $\Psi \otimes \Sigma$, that is why the total number of parameters gets reduced by one) which is much

less than $pq(pq + 1)/2$ in an unstructured variance-covariance matrix Ω . Several authors, e.g., Boik (1991), Galecki (1994), Naik and Rao (2001), Chaganty and Naik (2002), and Roy and Khattree (2007a, b) have observed many advantages of using the separable covariance structure over the usual unstructured variance-covariance matrix for analyzing two-level multivariate data. In this article we consider CS correlation structure on Ψ , so that the number of unknown parameters to be estimated further reduces to $1 + q(q+1)/2$.

We consider the RST and LRT for testing the separability of the variance-covariance matrix Ω with half structured and half unstructured matrices, i.e.,

$$
H_0: \Omega = \Psi \otimes \Sigma, \Psi \text{ CS against } H_A: \Omega \text{ unstructured.} \tag{2}
$$

The matrices Ψ , Σ and Ω are positive definite matrices. The variance-covariance matrix Σ is assumed to be unstructured. Given that Ψ has a CS correlation structure, it can be written as $\Psi = (1 - \rho)I_p + \rho I_p I'_p$. Since Ψ is a positive definite matrix, we should have $-1/(p-1) < \rho < 1$. Note that Ψ is a CS correlation structure with only one unknown correlation parameter ρ . We choose Ψ a correlation matrix with all p diagonal elements as one, not a covariance matrix just to circumvent the identifiability problem of the $p \times p$ matrix Ψ and the $q \times q$ matrix Σ . Thus, the $(p \times p)$ −dimensional CS correlation matrix Ψ has only one parameter, and $(q \times q)$ −dimensional unstructured variance-covariance matrix Σ has $q(q+1)/2$ parameters. Recently, there has been a discussion by Dutilleul and Roy in Lee et al. (2010) on the definition of ML estimators and their identifiability for 2−separable variance-covariance structure. This problem is circumvented in this paper by choosing Ψ as a correlation matrix.

When the log-likelihood function is a smooth curve well approximated by a quadratic function, RST and LRT are identical under null hypothesis (see Lemma 1 in Engle (1984), p. 782). Rao (1984, p. 418; 2005) also mentioned that under the normality assumption RST and LRT statistics have the same asymptotic distribution χ^2_{ν} where the degrees of freedom (df) ν is equal to the number of parameters estimated under H_A minus the number of parameters estimated under H_0 . Thus, in our separable structure set up (2) we have

$$
\nu = \frac{pq(pq+1)}{2} - \frac{q(q+1)}{2} - 1.
$$
\n(3)

One may see the testing of the H_0 in (2) as a following sequence of two hypotheses:

$$
H_{01} : \mathbf{\Omega} = \mathbf{V} \otimes \mathbf{\Sigma}, \mathbf{V} \text{ UN against } H_{A1} : \mathbf{\Omega} \text{ unstructured}, \tag{4}
$$

assuming V as positive definite with df ν_1 as

$$
\nu_1 = \frac{pq(pq+1)}{2} - \frac{q(q+1)}{2} - \frac{p(p+1)}{2} + 1,
$$

and then, assuming the general separable structure H_{01} in (4) has been accepted, testing separability with one CS factor matrix against general separability as follows:

$$
H_{02} : \Omega = \Psi \otimes \Sigma, \Psi \text{ CS against } H_{A2} : V \otimes \Sigma, V \text{ UN},
$$
 (5)

with df ν_2 as

$$
\nu_2 = \frac{p(p+1)}{2} - 2.
$$

In other words, H_0 in (2), is equivalent to the test sequence

$$
H_0 \equiv H_{02} \circ H_{01},
$$

where '^o' means 'after'. Thus, we see that H_{01} is the null hypothesis corresponding to the test of general separability and H_{02} is the null hypothesis corresponding to the test of separability with the first component as CS correlation structure. Now, the minimum sample size required to test H_{01} in (4) using LRT is $n_1 = pq + 1$ and the same for H_{02} in (5) using LRT is $n_2 = \max(p, q) + 1$, whereas, using RST the minimum sample sizes required to test the H_{01} in (4) and H_{02} in (5) are $n_1 = \max(p, q) + 1$ and $n_2 = q + 1$ respectively. Therefore, the minimum sample size needed to test $H_{02} \circ H_{01}$ using LRT is $pq + 1$ and the minimum sample size needed to test $H_{02} \circ H_{01}$ using RST is $(\text{max}(p, q) + 1)$. Nevertheless, the minimum sample size needed to test H_0 using LRT is $pq + 1$ and the minimum sample size needed to test H_0 using RST is $q + 1$. Hence, instead of going straight to H_0 , if we test the sequence $H_{02} \circ H_{01}$, the required sample size for RST is $(\max(p, q) + 1)$. So, if the number of repeated measurements p is large as in the examples in the Introduction and $n < p$, then the sequence of $H_{02}^{\circ}H_{01}$ cannot be tested. However, if $n > p$, one can test the sequence of $H_{02} \circ H_{01}$ in those examples. So, when the sample size is small, testing the sequence $H_{02} \circ H_{01}$ may not be possible. H_{02} in (5) is likely to be used in applications when it is known apriori that the data already has the general separable structure.

The proposed RST in this paper is for the Hypothesis (2), and not for the equivalent test sequence $H_{02} \circ H_{01}$. Testing the equivalent test sequence $H_{02} \circ H_{01}$ would need new theoretical calculations and simulations. Thus, we discuss only the testing of Hypothesis (2) in the following sections.

3 Rao's score test statistic

Let us assume that the log-likelihood function $\ln L(\mu, \Omega; X)$ with the data matrix X, where $X =$ $[x_1, x_2, \ldots, x_n] \in \mathbb{R}^{pq,n}$, is partially differentiable with respect to each coordinate of the parameter vector $(\mu', \text{vech}'\Omega)'$ for every data matrix X. Now we derive the expressions of the LRT and the RST statistics for testing the Hypothesis (2).

The LRT is based upon the difference between the maximum of the log-likelihood under the null and under the alternative hypotheses. The likelihood ratio Λ can be written as

$$
\Lambda = \frac{\max_{H_0} L}{\max_{H_A} L}.
$$

It is well known that, for large sample size and under normality assumption, the LRT statistic −2lnΛ is approximately distributed as χ^2_{ν} under H_0 . The degrees of freedom ν is given in (3). It is to be noted that if any of the covariance parameters fall on the boundary of their parameter space then the asymptotic distribution of $-2\text{ln}\Lambda$ becomes a mixture of χ^2 distributions as discussed in Self and Liang (1987). The Hypothesis (2) using LRT is discussed thoroughly in Roy and Khattree (2005a). In this paper we will derive and discuss the same Hypothesis (2) using RST.

Let $s(\theta) = (s_1(\theta)', s_2(\theta)')' = \left(\frac{\partial \text{ln}L}{\partial x'}\right)$ $\frac{\partial{\ln\!L}}{\partial{\bm{\mu}}'}, \frac{\partial{\ln\!L}}{\partial{\text{vech}}'}$ $\overline{\partial \text{vech}^{\prime} \Omega}$ \int_{0}^{∞} be the score vector. Then the Fisher information matrix can be defined as

$$
\mathcal{F}(\theta) = -E\left[\frac{\partial s(\theta)}{\partial \theta'}\right] \stackrel{df}{=} \begin{pmatrix} \mathcal{F}_{11} & \mathcal{F}_{12} \\ \mathcal{F}'_{12} & \mathcal{F}_{22} \end{pmatrix}, \tag{6}
$$

where \mathcal{F}_{11} , \mathcal{F}_{12} and \mathcal{F}_{22} are $pq \times pq$, $pq \times pq(pq + 1)/2$ and $pq(pq + 1)/2 \times pq(pq + 1)/2$ matrices respectively. Let the Fisher information matrix exist and be invertible. The Rao's score (RS)

$$
s(\widehat{\boldsymbol{\theta}})' \mathcal{F}^{-1}(\widehat{\boldsymbol{\theta}}) s(\widehat{\boldsymbol{\theta}}), \tag{7}
$$

where $\hat{\boldsymbol{\theta}} = (\hat{\boldsymbol{\mu}}', \text{vech}'(\hat{\boldsymbol{\Psi}} \otimes \hat{\boldsymbol{\Sigma}}))^{\prime}$ is the MLE of $\boldsymbol{\theta}$ under the null hypothesis H_0 , is defined as the RST statistic. This statistic is also approximately distributed as χ^2_{ν} with the same degrees of freedom ν given in (3). We now obtain the expression of the RST statistic to test the null hypothesis H_0 in the following section.

Let us define the centered form of the data matrix $\bm{Y}(\bm{\mu})$ as $\bm{Y}(\bm{\mu}) = \bm{X} - \bm{1}'_n \otimes \bm{\mu}$. Then

$$
\boldsymbol{Y}(\boldsymbol{\mu}) \sim N_{pq,n}(\boldsymbol{0},\boldsymbol{\Omega},\boldsymbol{I}_n),
$$

which means

$$
\text{vec}\boldsymbol{Y}(\boldsymbol{\mu})\sim N_{npq}(\boldsymbol{0},\boldsymbol{I}_n\otimes\boldsymbol{\Omega}).
$$

The log-likelihood function in terms of this centered data matrix $Y(\mu)$ can be written as

$$
\ln L(\boldsymbol{\mu}, \boldsymbol{\Omega}; \boldsymbol{X}) = -\frac{npq}{2}\ln(2\pi) - \frac{n}{2}\ln|\boldsymbol{\Omega}| - \frac{1}{2}\text{vec}'\boldsymbol{Y}(\boldsymbol{\mu}) (\boldsymbol{I}_n \otimes \boldsymbol{\Omega}^{-1})\text{vec}\boldsymbol{Y}(\boldsymbol{\mu}). \tag{8}
$$

In order to determine the score vector, we first differentiate the above log-likelihood function $\ln L$

with respect to μ . We get

$$
\frac{\partial \ln L}{\partial \mu'} = -\frac{1}{2} \cdot \frac{\partial \text{vec}' \mathbf{Y}(\mu)(\mathbf{I}_n \otimes \mathbf{\Omega}^{-1}) \text{vec} \mathbf{Y}(\mu)}{\partial \mu'}
$$
\n
$$
= -\frac{1}{2} \cdot \frac{\partial \text{vec}' \mathbf{Y}(\mu)(\mathbf{I}_n \otimes \mathbf{\Omega}^{-1}) \text{vec} \mathbf{Y}(\mu)}{\partial \text{vec}' \mathbf{Y}(\mu)} \cdot \frac{\partial \text{vec} \mathbf{Y}(\mu)}{\partial \mu'}
$$
\n
$$
= -\frac{1}{2} \cdot 2 \cdot \text{vec}' \mathbf{Y}(\mu)(\mathbf{I}_n \otimes \mathbf{\Omega}^{-1}) \cdot \left(-\frac{\partial \text{vec}(\mathbf{1}_n' \otimes \mu)}{\partial \mu'} \right)
$$
\n
$$
= \text{vec}' \mathbf{Y}(\mu)(\mathbf{1}_n \otimes \mathbf{\Omega}^{-1}), \tag{9}
$$

which is a pq-dimensional row vector. Now, we differentiate lnL given in (8) with respect to vech Ω . Using Proposition 3 (ii), Proposition 1 (iii) in A and the symmetricity of Ω we get

$$
\frac{\partial \ln L}{\partial \text{vech}'\Omega} = \frac{\partial \ln L}{\partial \text{vec}'\Omega} \cdot \frac{\partial \text{vec}'\Omega}{\partial \text{vech}'\Omega} = \frac{\partial \ln L}{\partial \text{vec}'\Omega} \cdot \mathbf{D}_{pq}
$$
\n
$$
= -\frac{n}{2} \frac{\partial \ln |\Omega|}{\partial |\Omega|} \cdot \frac{\partial |\Omega|}{\partial \text{vec}'\Omega} \cdot \mathbf{D}_{pq}
$$
\n
$$
- \frac{1}{2} \frac{\partial \text{vec}'Y(\mu)(I_n \otimes \Omega^{-1})\text{vec}Y(\mu)}{\partial \text{vec}'(I_n \otimes \Omega^{-1})} \cdot \frac{\partial \text{vec}(I_n \otimes \Omega^{-1})}{\partial \text{vec}'\Omega^{-1}} \cdot \frac{\partial \text{vec}\Omega^{-1}}{\partial \text{vec}'\Omega} \cdot \mathbf{D}_{pq}
$$
\n
$$
= -\frac{n}{2} \text{vec}'\Omega^{-1} \mathbf{D}_{pq}
$$
\n
$$
+ \frac{1}{2} (\text{vec}'Y(\mu) \otimes \text{vec}'Y(\mu))(I_n \otimes \mathbf{K}_{pq,n} \otimes I_{pq}) (\text{vec}I_n \otimes I_{p^2q^2})(\Omega^{-1} \otimes \Omega^{-1}) \mathbf{D}_{pq}
$$
\n
$$
= -\frac{n}{2} \text{vec}'\Omega^{-1} \mathbf{D}_{pq} + \frac{1}{2} \text{vec}'(Y(\mu)Y'(\mu))(\Omega^{-1} \otimes \Omega^{-1}) \mathbf{D}_{pq}, \tag{10}
$$

which is a $pq(pq + 1)/2$ -dimensional row vector. Now, the log-likelihood lnL is maximized at a value $\hat{\theta}$ when $\frac{\partial \text{ln}L}{\partial \theta'} = 0$. It is easy to see from (9) that the MLE of μ is

$$
\widehat{\boldsymbol{\mu}} = \frac{1}{n} \mathbf{X} \mathbf{1}_n.
$$

Now, substituting the value of $\widehat{\boldsymbol{\mu}}$ in $\boldsymbol{Y} (\boldsymbol{\mu})$ we get

$$
\begin{array}{rcl}\operatorname{vec} Y(\widehat{\mu}) & = & \operatorname{vec}\left(\boldsymbol{X}-\boldsymbol{1}_n'\otimes\frac{1}{n}\boldsymbol{X}\boldsymbol{1}_n\right) = \operatorname{vec}\boldsymbol{X} - \left(\boldsymbol{1}_n\otimes\left(\frac{1}{n}\boldsymbol{1}_n'\otimes\boldsymbol{I}_{pq}\right)\operatorname{vec}\boldsymbol{X}\right) \\
& = & (\boldsymbol{Q}_{\boldsymbol{1}_n}\otimes\boldsymbol{I}_{pq})\operatorname{vec}\boldsymbol{X} = \operatorname{vec}\left(\boldsymbol{X}\boldsymbol{Q}_{\boldsymbol{1}_n}\right).\n\end{array}
$$

We now derive the expression of the RST statistic for H_0 . We start with the calculations of the four

component matrices in the Fisher information matrix $\mathcal{F}(\theta)$ in (6). We have

$$
\mathcal{F}_{11} = -E \left[\frac{\partial}{\partial \mu'} \left(\frac{\partial \ln L}{\partial \mu'} \right) \right] = -E \left[\frac{\partial (\mathbf{1}_n' \otimes \mathbf{\Omega}^{-1}) \text{vec} \mathbf{Y}(\mu)}{\partial \mu'} \right]
$$
\n
$$
= -E \left[\frac{\partial (\mathbf{1}_n' \otimes \mathbf{\Omega}^{-1}) \text{vec} \mathbf{Y}(\mu)}{\partial \text{vec} \mathbf{Y}(\mu)} \cdot \frac{\partial \text{vec} \mathbf{Y}(\mu)}{\partial \mu'} \right]
$$
\n
$$
= -(\mathbf{1}_n' \otimes \mathbf{\Omega}^{-1}) E \left[\frac{\partial \text{vec}(\mathbf{X} - \mathbf{1}_n' \otimes \mu)}{\partial \mu'} \right]
$$
\n
$$
= (\mathbf{1}_n' \otimes \mathbf{\Omega}^{-1}) (\mathbf{I}_n \otimes \mathbf{K}_{1,1} \otimes \mathbf{I}_{pq}) (\mathbf{1}_n \otimes \mathbf{I}_{qp})
$$
\n
$$
= n\mathbf{\Omega}^{-1}, \tag{11}
$$

and
$$
\mathcal{F}_{12} = \mathcal{F}'_{12} = -E \left[\frac{\partial}{\partial \text{vech}' \Omega} \left(\frac{\partial \ln L}{\partial \mu'} \right) \right] = -E \left[\frac{\partial (\mathbf{1}'_n \otimes \Omega^{-1}) \text{vec} Y(\mu)}{\partial \text{vech}' \Omega} \right]
$$

\n
$$
= -E \left[\frac{\partial (\mathbf{1}'_n \otimes \Omega^{-1}) \text{vec} Y(\mu)}{\partial \text{vec}' (\mathbf{1}'_n \otimes \Omega^{-1})} \cdot \frac{\partial \text{vec} (\mathbf{1}'_n \otimes \Omega^{-1})}{\partial \text{vec}' \Omega^{-1}} \cdot \frac{\partial \text{vec} \Omega^{-1}}{\partial \text{vec}' \Omega} \cdot D_{pq} \right]
$$

\n
$$
= E \left[(\text{vec}' Y(\mu) \otimes I_{pq}) (I_n \otimes K_{pq,1} \otimes I_{pq}) (\mathbf{1}_n \otimes I_{p^2q^2}) (\Omega^{-1} \otimes \Omega^{-1}) \right] D_{pq}
$$

\n
$$
= 0.
$$
 (12)

Now by denoting $H = \text{vec}(Y(\mu)Y'(\mu))$ and then using the expression (6.5) of Ghazal and Neudecker (2000, p. 81): $\text{E}[\boldsymbol{Z}\boldsymbol{Z}'] = \text{tr}[\boldsymbol{V}]\boldsymbol{U} + \boldsymbol{M}\boldsymbol{M}'$ for vec $\boldsymbol{Z} \sim N_{kl}(\text{vec}\boldsymbol{M},\boldsymbol{V}\otimes\boldsymbol{U}),$ we get

$$
\mathrm{E}[\boldsymbol{H}] = (\mathrm{tr}[\boldsymbol{I}_n])(\mathrm{vec}\boldsymbol{\Omega}) = n(\mathrm{vec}\boldsymbol{\Omega}).
$$

Using this result, the Equation (10) and the Lemma 1 in A we can write

$$
\mathcal{F}_{22} = -E \left[\frac{\partial}{\partial \text{vech}' \Omega} \left(\frac{\partial \ln L}{\partial \text{vech}' \Omega} \right) \right]
$$
\n
$$
= \frac{n}{2} D'_{pq} \cdot \frac{\partial \text{vec} \Omega^{-1}}{\partial \text{vec}' \Omega} \cdot D_{pq} - \frac{1}{2} E \left[\frac{\partial D'_{pq} (\Omega^{-1} \otimes \Omega^{-1}) H}{\partial \text{vec}' \Omega} \right] D_{pq}
$$
\n
$$
= -\frac{n}{2} D'_{pq} (\Omega^{-1} \otimes \Omega^{-1}) D_{pq}
$$
\n
$$
+ \frac{1}{2} (E[H] \otimes D_{pq})' (I_{pq} \otimes K_{pq,pq} \otimes I_{pq}) (I_{p^2q^2} \otimes \text{vec}\Omega^{-1} + \text{vec}\Omega^{-1} \otimes I_{p^2q^2}) (\Omega^{-1} \otimes \Omega^{-1}) D_{pq}
$$
\n
$$
= \frac{n}{2} D'_{pq} (\Omega^{-1} \otimes \Omega^{-1}) D_{pq}.
$$
\n(13)

Now, substituting the values of \mathcal{F}_{11} , \mathcal{F}_{12} and \mathcal{F}_{22} from (11), (12) and (13) in (6) we get the Fisher information matrix as

$$
\boldsymbol{\mathcal{F}}(\boldsymbol{\theta}) = \begin{pmatrix} n\boldsymbol{\Omega}^{-1} & \boldsymbol{0} \\ \boldsymbol{0} & \frac{n}{2}\boldsymbol{D}_{qp}^\prime(\boldsymbol{\Omega}^{-1}\otimes\boldsymbol{\Omega}^{-1})\boldsymbol{D}_{qp} \end{pmatrix}\!.
$$

Then, applying the Proposition 1.3.3. of Kollo and von Rosen (2005) and the Proposition 1 (iv) in

A we get the inverse of the Fisher information matrix as follows:

$$
\mathcal{F}^{-1}(\theta) = \begin{pmatrix} n\Omega^{-1} & 0 \\ 0 & \frac{n}{2}D'_{qp}(\Omega^{-1}\otimes \Omega^{-1})D_{qp} \end{pmatrix}^{-1}
$$

$$
= \begin{pmatrix} \frac{1}{n}\Omega & 0 \\ 0 & \left(\frac{n}{2}D'_{qp}(\Omega^{-1}\otimes \Omega^{-1})D_{qp}\right)^{-1} \end{pmatrix}
$$

$$
= \begin{pmatrix} \frac{1}{n}\Omega & 0 \\ 0 & \frac{2}{n}D^{+}_{qp}(\Omega\otimes \Omega)D^{+'}_{qp} \end{pmatrix} .
$$
(14)

Since the hypothesis we are interested in this article involves only the variance-covariance matrix, we derive the RST statistic corresponding to vech Ω . Now, the component of the score vector corresponding to vech Ω is

$$
\begin{array}{rcl} s_2(\boldsymbol{\theta}) & = & -\dfrac{n}{2}\boldsymbol{D}'_{pq} \text{vec} \boldsymbol{\Omega}^{-1} + \dfrac{1}{2}\boldsymbol{D}'_{pq}(\boldsymbol{\Omega}^{-1} \otimes \boldsymbol{\Omega}^{-1}) \text{vec}(\boldsymbol{Y}(\boldsymbol{\mu}) \boldsymbol{Y}'(\boldsymbol{\mu})) \\ & \stackrel{df}{=} & s_{21}(\boldsymbol{\theta}) + s_{22}(\boldsymbol{\theta}), \end{array}
$$

where

$$
\begin{array}{rcl} s_{21}(\boldsymbol{\theta}) & = & -\dfrac{n}{2}\boldsymbol{D}'_{pq}({\rm vec}\boldsymbol{\Omega}^{-1}), \\[2mm] \text{and} & s_{22}(\boldsymbol{\theta}) & = & \dfrac{1}{2}\boldsymbol{D}'_{pq}(\boldsymbol{\Omega}^{-1}\otimes\boldsymbol{\Omega}^{-1}){\rm vec}(\boldsymbol{Y}(\boldsymbol{\mu})\boldsymbol{Y}'(\boldsymbol{\mu})). \end{array}
$$

Let $\hat{\mu}$, $\hat{\Psi}$ and $\hat{\Sigma}$ be the ML estimators under the null hypothesis. Therefore, the estimator $\hat{\theta}$ under the null hypothesis H_0 is

$$
\widehat{\boldsymbol{\theta}} = \begin{pmatrix} \widehat{\boldsymbol{\mu}} \\ \mathrm{vech}(\widehat{\boldsymbol{\Psi}} \otimes \widehat{\boldsymbol{\Sigma}}) \end{pmatrix}.
$$

For MLEs $\hat{\Sigma}$, and $\hat{\Psi}$ or $\hat{\rho}$ see Equations (3) and (6) in Roy and Khattree (2005a). These two equations in Roy and Khattree (2005a) are analytically intractable, and should be solved simultaneously and iteratively to get the MLEs $\hat{\Sigma}$ and $\hat{\Psi}$; see Roy and Khattree (2005a, p. 301) for the algorithm to solve the Equations (3) and (6) in their paper. The SAS code for the algorithm is available from Roy's website. Now substituting the expression $\mathcal{F}^{-1}(\theta)$ from (14) in (7) we write the RST statistic or Rao's score (RS) for the null hypothesis H_0 as the sum of four components due to $s_{21}(\hat{\theta}), s_{22}(\hat{\theta})$ and \mathcal{F}_{22}^{-1} as

$$
RS = \frac{2}{n} s_2'(\widehat{\boldsymbol{\theta}}) \boldsymbol{D}_{pq}^+(\widehat{\boldsymbol{\Omega}} \otimes \widehat{\boldsymbol{\Omega}}) \boldsymbol{D}_{pq}^{+\prime} s_2(\widehat{\boldsymbol{\theta}})
$$

= RS₁₁ + RS₁₂ + RS₂₁ + RS₂₂, (15)

where the notation $\hat{\Omega}$ is used to represent $\Psi \otimes \hat{\Sigma}$. Now, from the symmetry of the quadratic form we have $RS_{21} = RS_{12}$. We will now evaluate the components in (15) one by one using Proposition 2

in A to get an expression of RS in terms of $\hat{\Psi}$ and $\hat{\Sigma}$. We have

$$
RS_{11} = \frac{2}{n} s'_{21}(\hat{\boldsymbol{\theta}}) \boldsymbol{D}_{pq}^+(\hat{\boldsymbol{\Omega}} \otimes \hat{\boldsymbol{\Omega}}) \boldsymbol{D}_{pq}^{+'} s_{21}(\hat{\boldsymbol{\theta}})
$$

\n
$$
= \frac{n}{2} \text{vec}' \hat{\boldsymbol{\Omega}}^{-1} \boldsymbol{N}_{pq}(\hat{\boldsymbol{\Omega}} \otimes \hat{\boldsymbol{\Omega}}) \boldsymbol{N}_{pq}(\text{vec}\hat{\boldsymbol{\Omega}}^{-1})
$$

\n
$$
= \frac{n}{2} \text{vec}' \hat{\boldsymbol{\Omega}}^{-1}(\hat{\boldsymbol{\Omega}} \otimes \hat{\boldsymbol{\Omega}}) \text{vec}\hat{\boldsymbol{\Omega}}^{-1}
$$

\n
$$
= \frac{n_{pq}}{2}, \qquad (16)
$$

$$
RS_{12} = \frac{2}{n} s'_{21}(\hat{\theta}) D_{pq}^{+}(\hat{\Omega} \otimes \hat{\Omega}) D_{pq}^{+'} s_{22}(\hat{\theta})
$$

\n
$$
= -\frac{1}{2} \text{vec}' \hat{\Omega}^{-1} N_{pq}(\hat{\Omega} \otimes \hat{\Omega}) N_{pq}(\hat{\Omega}^{-1} \otimes \hat{\Omega}^{-1}) \text{vec}(Y(\hat{\mu}) Y'(\hat{\mu}))
$$

\n
$$
= -\frac{1}{2} \text{vec}' \hat{\Omega}^{-1} \text{vec}(X Q_{1_n} X')
$$

\n
$$
= -\frac{1}{2} \text{tr} \left[\hat{\Omega}^{-1} X Q_{1_n} X' \right]
$$

\n
$$
= -\frac{1}{2} \text{tr} \left[(\hat{\Psi}^{-1} \otimes \hat{\Sigma}^{-1}) X Q_{1_n} X' \right],
$$
 (17)

and

$$
RS_{22} = \frac{2}{n} s'_{22}(\hat{\boldsymbol{\theta}}) \mathbf{D}_{pq}^{+}(\hat{\boldsymbol{\Omega}} \otimes \hat{\boldsymbol{\Omega}}) \mathbf{D}_{pq}^{+'} s_{22}(\hat{\boldsymbol{\theta}})
$$

\n
$$
= \frac{1}{2n} \text{vec}'(\mathbf{Y}(\hat{\boldsymbol{\mu}}) \mathbf{Y}'(\hat{\boldsymbol{\mu}})) (\hat{\boldsymbol{\Omega}}^{-1} \otimes \hat{\boldsymbol{\Omega}}^{-1}) \mathbf{N}_{pq}(\hat{\boldsymbol{\Omega}} \otimes \hat{\boldsymbol{\Omega}}) \mathbf{N}_{pq}(\hat{\boldsymbol{\Omega}}^{-1} \otimes \hat{\boldsymbol{\Omega}}^{-1}) \text{vec}(\mathbf{Y}(\hat{\boldsymbol{\mu}}) \mathbf{Y}'(\hat{\boldsymbol{\mu}}))
$$

\n
$$
= \text{vec}'(\mathbf{X} \mathbf{Q}_{1n} \mathbf{X}') (\hat{\boldsymbol{\Omega}}^{-1} \otimes \hat{\boldsymbol{\Omega}}^{-1}) \text{vec}(\mathbf{X} \mathbf{Q}_{1n} \mathbf{X}')
$$

\n
$$
= \frac{1}{2n} \text{tr} \left[(\hat{\boldsymbol{\Psi}}^{-1} \otimes \hat{\boldsymbol{\Sigma}}^{-1}) \mathbf{X} \mathbf{Q}_{1n} \mathbf{X}' (\hat{\boldsymbol{\Psi}}^{-1} \otimes \hat{\boldsymbol{\Sigma}}^{-1}) \mathbf{X} \mathbf{Q}_{1n} \mathbf{X}' \right].
$$
 (18)

Now, after substituting the values of $RS_{11}, RS_{12}, RS_{21}$ and RS_{22} from (16), (17) and (18) in (15), we get the RST statistic or RS to test the null hypothesis H_0 as

$$
\begin{array}{lll} \mathrm{RS} & = & \displaystyle \frac{nqp}{2} - \mathrm{tr}\left[(\widehat{\Psi}^{-1} \otimes \widehat{\boldsymbol{\Sigma}}^{-1}) \boldsymbol{X} \boldsymbol{Q}_{1_n} \boldsymbol{X}' \right] + \\ & & \displaystyle + \frac{1}{2n} \mathrm{tr}\left[(\widehat{\Psi}^{-1} \otimes \widehat{\boldsymbol{\Sigma}}^{-1}) \boldsymbol{X} \boldsymbol{Q}_{1_n} \boldsymbol{X}' (\widehat{\Psi}^{-1} \otimes \widehat{\boldsymbol{\Sigma}}^{-1}) \boldsymbol{X} \boldsymbol{Q}_{1_n} \boldsymbol{X}' \right], \end{array}
$$

which has an asymptotic χ^2 distribution with ν degrees of freedom, where ν is given in (3).

Remark 1. Observe that the above RST statistic depends only on the data matrix X , the ML estimate of Ψ with an explicit expression in ρ , and the ML estimate of the $q \times q$ dimensional variancecovariance matrix Σ . The RST statistic does not need the ML estimate of the pq \times pq dimensional unstructured variance covariance matrix Ω , as does the LRT statistic. Thus, the minimum number of observations needed to calculate the RST statistic is only $q + 1$, a quantity independent of p, whereas the minimum number of observations needed to calculate the LRT statistic is $pq + 1$, as it

depends on the ML estimate of the pq \times pq dimensional unstructured variance-covariance matrix Ω , which can grow very fast with the increase in p. Thus, the RST is an huge improvement over the LRT: one can test the null hypothesis H_0 with only $q + 1$ observations using RST.

4 Simulation Study

We perform simulation studies to compare the LRT and RST for the biased and unbiased/unmodified approaches. These simulations use two-level multivariate data assuming the 2−separable covariance structure $\Psi \otimes \Sigma$ on each subject, where Ψ has a CS correlation structure with correlation coefficient ρ on the repeated measurements for each characteristic. First, to compare the biased LRT with biased RST, we compute the observed Type I error rates, $\hat{\alpha}$ to measure their biasedness. In other words, we would like to see for which n the observed $\hat{\alpha}$ approaches the nominal α level for different values of p, the number of repeated measurements, and for different values of ρ , when the nominal Type I error rate $\alpha = 0.01$. Second, we compare the unbiased/unmodified LRT and RST using empirical null distributions (ENDs). Suppose the RST to contrast the Hypothesis (2) has the rejection region $\{RST > \kappa_\alpha\}$, and κ_α is chosen so that the test has significance level $\alpha = 0.01$ or 0.05. The significance level (or Type I error) for the RST for Hypothesis (2) is defined as

$$
\alpha = P(\text{reject } H_0 \text{ when } H_0 \text{ is true}) = P_{\mathbf{\Psi} \otimes \mathbf{\Sigma}}(\text{RST statistic} > \kappa_\alpha),\tag{19}
$$

so, κ_{α} is the 100(1 – α)% quantile of the RST under null hypothesis. Note that the distribution of RST is not known either under H_0 or any model under H_A . But we can compute this test (i.e., compute κ_{α}) and its properties using Monte Carlo simulation (Rizzo, 2008). To reduce the Monte Carlo error one needs to increase the simulation size. Let $\hat{\kappa}_{\alpha}$ is an estimate of κ_{α} . We denote the observed Type I error rates for LRT and RST statistics as $\hat{\alpha}_{\text{LRT}}$ and $\hat{\alpha}_{\text{RST}}$ respectively, and calculate them when the nominal significance level $\alpha = 0.01$ as well as $\alpha = 0.05$, for different values of n, p and ρ in the following section.

4.1 Observed Type I error rates for biased LRT and RST statistics

Samples of various sizes from small to large, e.g., $n = 10, 15, 20, 25, 30, 50, 75$ and 100 are generated from a pq-variate normal population $N_{pq}(\mathbf{0}, \Psi \otimes \Sigma)$. The number of repeated measurements p is chosen as 3, 4, 5 and 7, and the number of characteristics q as 3. The (3×3) −dimensional variance-covariance matrix Σ is taken as

$$
\Sigma = \begin{pmatrix} 2 & 1 & 2 \\ 1 & 4 & 3 \\ 2 & 3 & 5 \end{pmatrix},
$$

and the correlation coefficient ρ of repeated measurements in the CS correlation structure Ψ is chosen as -0.4, -0.2, -0.1, 0.3, 0.5, 0.7 and 0.9 for each p such that $-\frac{1}{n-1}$ $\frac{1}{p-1} < \rho < 1$. We generate $50,000$ samples for each combination of the parameters under H_0 . Table 1 shows the empirical Type I error rates for both LRT and RST statistics, with all combinations of n , p and ρ for the nominal Type I error rate $\alpha = 0.01$ for 50,000 simulations. For $p = 3, 4, 5$ and 7 both LRT and RST statistics are approximately distributed as χ^2_{ν} under H_0 , with degrees of freedom $\nu = 38, 71, 113$ and 224 respectively using (3). The observed Type I error rates for all the statistics appear to increase with p for a fixed ρ , which is manifested by the uniformly larger Type I error rates for $p = 7$. We also notice that Type I errors do not substantially change with ρ for LRT as well as for RST statistics and it does not depend on Σ .

As expected the Type I error rates do decrease with the sample size n. Notice that RST performs much better for small and moderate n than its counterpart LRT. For $p = 4$ the Type I error rate 0.01 is achieved only for sample size 25 in the case of RST. For each combination of n, p and ρ we see that $\hat{\alpha}_{RST}$ is always much less than $\hat{\alpha}_{LRT}$. It is clear from Table 1 that $\hat{\alpha}_{RST}$ is approximately equal to the nominal significance level 0.01 for small and moderate sample sizes, which is not the case for $\hat{\alpha}_{\text{LRT}}$. A sample size of about 75 is required for $p = 5$ so that the empirical Type I error rate is approximately equal to the nominal significance level 0.01 in the case of RST, but a sample size of about 200 is required for $p = 5$ in the case of LRT for the same scenario. For $p = 7$, the empirical significance level decreases very slowly and even at $n = 200$ it is not close to the nominal significance level $\alpha = 0.01$ in the case of LRT; see Roy and Khattree (2005a) for detail. This suggests that LRT may not perform well when p is large, even for the large sample sizes. In contrast, a sample size of about 100 is required for $p = 7$, so that the empirical Type I error rate is approximately equal to the nominal significance level 0.01 in the case of RST. Thus, we see that RST performs much better than LRT in the small to moderate sample cases.

Since Type I errors do not substantially change with ρ for LRT as well as for RST statistics as noticed in Table 1, we also calculate $\hat{\alpha}_{\text{LRT}}$ and $\hat{\alpha}_{\text{RST}}$ when the nominal significance level $\alpha = 0.05$, for $\rho = 0.05$ and for various values of n and p for 50,000 simulations. The results are presented in Table 2.

| | $p \rightarrow$ | | 3 | | $\overline{4}$ | $\bf 5$ | | $\overline{7}$ | |
|------------------|-------------------|------------------------------|---------------------------------|--|---|--|--|--|--|
| \boldsymbol{n} | $\rho \downarrow$ | $\widehat{\alpha}_{\rm LRT}$ | $\widehat{\alpha}_{\text{RST}}$ | $\overline{\hat{\alpha}}_{\text{LRT}}$ | $\overline{\widehat{\alpha}_{\rm RST}}$ | $\overline{\hat{\alpha}}_{\text{LRT}}$ | $\overline{\hat{\alpha}}_{\text{RST}}$ | $\overline{\hat{\alpha}}_{\text{LRT}}$ | $\overline{\hat{\alpha}}_{\text{RST}}$ |
| 10 | -0.4 | 0.913 | 0.021 | | | | | | |
| | -0.2 | 0.914 | 0.021 | | | | | | |
| | -0.1 | 0.914 | 0.021 | | | | | | |
| | 0.1 | 0.913 | 0.021 | | | | | | |
| | 0.3 | 0.913 | 0.021 | | | | | | |
| | 0.5 | 0.913 | 0.021 | | | | | | |
| | 0.7 | 0.913 | 0.021 | | | | | | |
| | 0.9 | 0.913 | 0.021 | | | | | | |
| 15 | -0.4 | 0.365 | 0.016 | | | $\overline{}$ | $\overline{}$ | $\frac{1}{2}$ | |
| | -0.2 | 0.365 | 0.016 | 0.876 | 0.023 | | | | |
| | -0.1 | 0.364 | 0.016 | 0.876 | 0.023 | | | | |
| | 0.1 | 0.364 | 0.016 | 0.876 | 0.023 | | | | |
| | $\rm 0.3$ | 0.365 | 0.016 | 0.876 | 0.023 | | | | |
| | 0.5 | 0.365 | 0.016 | 0.876 | 0.023 | | | | |
| | 0.7 | 0.365 | 0.016 | 0.876 | 0.023 | | | | |
| | 0.9 | 0.364 | $\,0.015\,$ | 0.876 | 0.023 | | | | |
| 20 | -0.4 | 0.174 | 0.014 | | | | | $\overline{}$ | |
| | -0.2 | 0.174 | $\,0.014\,$ | 0.500 | 0.018 | 0.902 | 0.024 | | |
| | -0.1 | 0.174 | 0.014 | 0.500 | 0.018 | 0.901 | 0.024 | | |
| | $0.1\,$ | 0.174 | 0.014 | 0.500 | 0.018 | 0.901 | 0.025 | | |
| | 0.3 | 0.174 | 0.014 | 0.500 | 0.018 | 0.901 | 0.024 | | |
| | 0.5 | 0.174 | 0.014 | 0.500 | 0.018 | 0.901 | 0.024 | | |
| | 0.7 | 0.174 | 0.014 | 0.500 | 0.018 | 0.901 | 0.024 | | |
| | 0.9 | 0.174 | 0.014 | 0.500 | 0.019 | 0.901 | 0.024 | | |
| 25 | -0.4 | 0.104 | 0.014 | | | | | | |
| | -0.2 | 0.104 | 0.014 | 0.283 | 0.018 | 0.634 | 0.021 | | |
| | -0.1 | 0.105 | 0.014 | 0.283 | 0.018 | 0.634 | 0.021 | 0.999 | 0.029 |
| | 0.1 | 0.104 | 0.014 | 0.284 | 0.018 | 0.633 | 0.021 | 0.999 | 0.029 |
| | 0.3 | 0.104 | 0.014 | 0.284 | 0.018 | 0.633 | 0.021 | 0.999 | 0.029 |
| | 0.5 | 0.104 | 0.014 | 0.284 | 0.017 | 0.634 | 0.021 | 0.999 | 0.029 |
| | 0.7 | 0.105 | 0.014 | 0.283 | 0.017 | 0.634 | 0.021 | 0.999 | 0.029 |
| | 0.9 | 0.105 | 0.014 | 0.283 | 0.017 | 0.634 | 0.021 | 0.999 | 0.029 |

Table 1: Observed Type I error rates $\hat{\alpha}_{\rm LRT}$ and $\hat{\alpha}_{\rm RST}$ when the nominal significance level $\alpha=0.01$ for different values of $n,\,p,$ and ρ based on 50,000 simulations

It is to be noted that the standard error of a statistic is important in evaluating the accuracy of an estimate. Since the empirical Type I error rate, which is a proportion, estimates the nominal significance level α , the standard error of an empirical Type I error rate is $\sqrt{(\alpha(1-\alpha))/50000}$. So,

Table 2: Observed Type I error rates $\hat{\alpha}_{\text{LRT}}$ and $\hat{\alpha}_{\text{RST}}$ when the nominal significance level $\alpha = 0.05$ for different values of n, p, with $\rho = 0.5$ based on 50,000 simulations

| $p \rightarrow$ | 3 | | | 4 | | 5 | | 7 |
|------------------|------------------------------|--|-------------------------|-------------------------|--|---------------------------------|--|---------------------------------|
| \boldsymbol{n} | $\widehat{\alpha}_{\rm LRT}$ | $\overline{\hat{\alpha}}_{\text{RST}}$ | ∼ $\alpha_{\rm LRT}$ | ∼ $\alpha_{\rm RST}$ | $\overline{\hat{\alpha}}_{\text{LRT}}$ | $\widehat{\alpha}_{\text{RST}}$ | $\overline{\hat{\alpha}}_{\text{LRT}}$ | $\widehat{\alpha}_{\text{RST}}$ |
| 10 | 0.965 | 0.083 | | | | | | |
| 15 | 0.593 | 0.068 | 0.952 | 0.088 | | | | |
| 20 | 0.372 | 0.062 | 0.719 | 0.076 | 0.967 | 0.090 | | |
| 25 | 0.269 | 0.061 | 0.519 | 0.073 | 0.826 | 0.081 | 1.000 | 0.103 |
| 30 | 0.208 | 0.060 | 0.389 | 0.067 | 0.658 | 0.076 | 0.992 | 0.093 |
| 50 | 0.122 | 0.054 | 0.192 | 0.057 | 0.308 | 0.065 | 0.689 | 0.071 |
| 75 | 0.093 | 0.054 | 0.127 | 0.056 | 0.184 | 0.060 | 0.386 | 0.065 |
| 100 | 0.078 | 0.052 | 0.100 | 0.054 | 0.135 | 0.057 | 0.258 | 0.063 |

in case of nominal significance level 0.01, the standard error of an empirical Type I error rate is 4.45×10^{-4} and in case of nominal significance level 0.05, the standard error of an empirical Type I error rate is 9.75×10^{-4} . The maximum standard errors for $\hat{\alpha}_{LRT}$ and $\hat{\alpha}_{RST}$ for each p of the simulated type I rates are presented in Table 3. These results give a better sense of how different the simulated type I error distributions are between the LRT and the RST.

Table 3: Maximal empirical standard errors of $\hat{\alpha}_{\text{LRT}}$ and $\hat{\alpha}_{\text{RST}}$ when the nominal significance level $\alpha = 0.05$ for different values of p, with $\rho = 0.5$ based on 50,000 simulations

| $\alpha_{\rm LRT}$ | $\alpha_{\rm RST}$ | |
|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--|
| 0.00064 0.00215 | | 0.00224 | 0.00067 | | 0.00221 0.00068 | | 0.00222 0.00075 | |

Therefore, we see that when the number of repeated measurements (p) is not small, our proposed test may have little power for small samples, especially when the repeated measures are correlated, however performance of RST is much better than LRT. This simulation study allows us to assess the relative performance of these two testing procedures by comparing the empirical Type I error rate under various settings. We see that when the number of repeated measurements increases, both the tests lose power for having higher degrees of freedom. Also, as mentioned before, the empirical significance level decreases very slowly with the increased sample size (n) to the nominal significance level, for both $\alpha = 0.01$ and $\alpha = 0.05$ for a fixed p.

Plots of the Type I error rate as a function of the sample size for RST and LRT statistics for several repeated measures p, $q = 3$, $\rho = 0.5$ and $\alpha = 0.01$ are given in Figure 1. Clearly, as the number of repeated measures, p, increases, empirical Type I error increases. Also, Type I error rate decreases as the sample size (n) increases for each combination of p, $q = 3$, and $\rho = 0.5$ for LRT, however, Type I error rate is always very low, almost equal to $\alpha = 0.01$ for all sample sizes for RST. This finding motivated us to compute the empirical percentiles of the null distribution of RST as well as LRT statistics for various values of n, p, q and $\rho = 0.5$ in the following section as we have only finite samples in real data applications. We use these empirical percentiles tables to conduct power analysis in Section 4.3.

Figure 1: Plots of the Type I error rate as a function of the sample size for RST and LRT statistics for several repeated measures p, $q = 3$, $\rho = 0.5$ and for $\alpha = 0.01$. Plot lines: Dashed – LRT; Solid – RST.

4.2 Empirical 90th, 95th and 99th percentiles of the null distribution of unbiased/unmodified LRT and RST statistics

In this section we conduct some simulation experiments to study the finite sample performance by estimating the percentiles of the END of RST as well as LRT statistics. The number of repeated measurements p is chosen as 2, 3, 4, 5, 7, 10 and 15, and the number of characteristic q is taken as 2 and 3. Samples of various sizes are drawn from $N_{pq}(\mathbf{0}, \Psi \otimes \Sigma)$. We assume Ψ has CS correlation structure with $\rho = 0.5$ only (since previous results showed little sensitivity to ρ). The (3×3) –dimensional variance-covariance matrix Σ is taken as in the previous section. Tables 4 – 6 and Tables 11 – 16 present the estimates of the empirical $90th$, $95th$ and $99th$ percentiles of the END of LRT along with the END of RST statistics based on 50,000 simulations for various values of n, p and q. We have compared simulations for $10,000$, $50,000$ and $100,000$ runs for various choices of p and q , and we have found that simulated results are stable for 50,000. After some preliminary

studies we decided to use 50,000 runs.

The empirical percentiles allow us to assess the relative performance of the two testing procedures LRT and RST in small to moderate sample size set-up by comparing the percentiles of the END with that of its limiting χ^2 distribution under various settings of n, p and q. We also see in our simulation studies that with different correlation coefficients ρ in the CS correlation structure Ψ , the percentiles of the ENDs of both LRT and RST statistics change minutely with ρ for various values of n, p and q. Thus, it appears that the empirical percentiles of the null distributions in Tables $4-6$ and Tables 11 – 16 will work reasonably well in practice for approximating the limiting χ^2 in small to moderate sample size set-up. It is to be noted that the computation of ENDs is time consuming; for example, a medium category computer takes about 17 hours to compute the results presented in Table 4, while it takes about 55 hours for the Table 16.

We see from Tables $4-6$ and Tables $11-16$ that after certain n the empirical percentiles converge very slowly to χ^2 percentiles. It is clear that the bias from the limiting χ^2 percentile decreases as sample size increases. It appears that the percentiles of RST statistic provide better approximation and work well for approximating the limiting χ^2 distribution than that of the LRT statistic. We observe that, when n is small, both the ENDs of LRT and RST statistics are to some extent different from the limiting χ^2 distribution. From Figure 2 we see that just for $n = 4$ and $n = 9$ ENDs of RST statistics are very close to its limiting χ^2 distribution for $p = q = 3$. We also see from Figure 2 that for $n = 4$ ENDs of RST statistics is not close to its limiting χ^2 distribution for $p = 5$ and $q = 3$, however for $n = 15$ it is fairly close to its limiting χ^2 distribution. Note that computations of the ENDs of LRT statistics are not even possible for $n = 4$ and $n = 9$ for $p = q = 3$; also computations of the ENDs of LRT statistics are not even possible for $n = 4$ and $n = 15$ for $p = 5$ and $q = 3$. From Figures 3 it is clear that just for $n = 20$ ENDs of the RST statistics are very close to its limiting χ^2 distribution for $p = 5$ and $q = 3$, whereas for its counterpart LRT statistics it is not the case.

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{\rm RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{\rm RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| 3 | | | | 30.227 | 33.030 | 38.047 |
| 4 | | | | 28.321 | 31.408 | 37.331 |
| 5 | | | | 27.336 | 30.322 | 36.940 |
| 6 | | | | 26.766 | 29.598 | 36.149 |
| 7 | 68.933 | 79.094 | 101.535 | 26.342 | 29.319 | 36.053 |
| 8 | 51.331 | 58.133 | 72.047 | 26.202 | 29.064 | 35.482 |
| 9 | 44.399 | 50.033 | 61.456 | 25.831 | 28.680 | 35.196 |
| 10 | 40.748 | 45.725 | 55.948 | 25.680 | 28.529 | 34.688 |
| 15 | 32.903 | 36.515 | 44.132 | 25.427 | 28.155 | 34.164 |
| 20 | 30.421 | 33.822 | 40.883 | 25.263 | 28.060 | 33.840 |
| 25 | 29.022 | 32.338 | 39.168 | 25.075 | 28.055 | 33.853 |
| 27 | 28.798 | 31.995 | 38.568 | 25.161 | 27.905 | 34.214 |
| 30 | 28.181 | 31.277 | 37.733 | 25.039 | 27.743 | 33.630 |
| 40 | 27.232 | 30.456 | 36.949 | 25.020 | 27.902 | 33.815 |
| 50 | 26.750 | 29.747 | 35.892 | 24.925 | 27.709 | 33.557 |
| 75 | 26.134 | 28.939 | 35.040 | 24.982 | 27.750 | 33.582 |
| 100 | 25.599 | 28.543 | 34.368 | 24.789 | 27.585 | 33.340 |
| 125 | 25.523 | 28.465 | 34.350 | 24.837 | 27.687 | 33.493 |
| 150 | 25.378 | 28.191 | 34.253 | 24.814 | 27.504 | 33.324 |
| 200 | 25.161 | 27.978 | 33.891 | 24.750 | 27.481 | 33.449 |
| ∞ | 24.769 | 27.587 | 33.409 | 24.769 | 27.587 | 33.409 |

Table 4: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p = 3$, $q = 2$ and different values of n

From the results of the simulation studies we see that the ENDs of RST statistics present significant set of nice features. They not only have a good asymptotic behavior for increasing sample sizes, but also have very good performance for very small sample sizes, e.g., for sample sizes exceeding only by one or two the number of variables q . We see that there is an associated error when we use percentile of RST statistic instead of true χ^2 percentile. For example, we see that 90th percentile of the RST statistic is 21.112 for $p = 2, q = 3$ and $n = 100$, whereas the true χ^2 percentile is 21.064. Therefore, the relative error is $(21.112 - 21.064)/21.064 = 0.226\%$. This shows that END introduces some error, however it is acceptable when p is not too large and n is not too small. Table 7 presents the relative errors between the RST statistics and their ENDs for 90th percentile for different values of n and p, along with $q = 3$. The same for the LRT statistics for 90th percentile are also given in Table 7 in the second row in both *italics* and parenthesis for each combination of n and p . We see that the percent errors between the LRT statistics and their ENDs are much more higher than that of the RST statistics. Also, note that for small sample size n , LRT fails to calculate the percentiles under H_0 . The errors associated with ENDs for both RST and LRT statistics increase with p, which is expected though, for a fixed sample size n. Also, the errors decrease with n for a fixed p, as large n means more information and thus the errors get reduced. The same pattern of behavior is observed for 95th as well as for 99th percentiles (results are not shown here). All these characteristics add up

to make the ENDs of the RST statistics the best choice for practical applications of the test studied for small as well as for moderate sample sizes. We thus have the following remark.

Remark 2. From Table 7, as well as from Figures 2 and 3 we observe that for small and moderate sample sizes the END of the RST statistic converges to the limiting χ^2 distribution much faster than the corresponding END of the LRT statistic. Thus, we conclude that the END of RST statistic performs much better than the END of LRT statistic for both small and moderate sample studies, and it is then prudent to use the END of RST statistic as opposed to the END of LRT statistic for any real-life applications assuming a stationary model for one of the two matrices.

Figure 2: Plots of the empirical histogram and the limiting χ^2 distribution for RST statistics for sample sizes 4 and 9 for $p = 3$ (up). The same for sample sizes 4 and 15 for $p = 5$ (down).

Figure 3: Plots of the empirical histogram and the limiting χ^2 distribution for LRT and RST statistics for sample sizes 20 and 100 for $p = 5$.

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{RST}(90)$ | $Q_{RST}(95)$ | $Q_{\rm RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|---------------|---------------|-------------------|
| 4 | | | | 22.344 | 23.458 | 25.425 |
| 5 | | | | 22.592 | 24.206 | 27.077 |
| 6 | | | | 22.522 | 24.407 | 27.954 |
| 7 | 64.211 | 74.505 | 97.059 | 22.321 | 24.491 | 28.501 |
| 8 | 47.083 | 53.649 | 67.636 | 22.216 | 24.465 | 28.768 |
| 9 | 40.000 | 45.297 | 56.885 | 21.885 | 24.180 | 29.010 |
| 10 | 36.430 | 41.250 | 51.250 | 22.006 | 24.275 | 29.115 |
| 15 | 28.772 | 32.388 | 39.738 | 21.593 | 24.023 | 28.885 |
| 20 | 26.366 | 29.695 | 36.434 | 21.477 | 23.981 | 28.958 |
| 25 | 25.072 | 28.210 | 34.654 | 21.410 | 23.928 | 29.121 |
| 27 | 24.846 | 27.897 | 34.381 | 21.402 | 23.941 | 29.005 |
| 30 | 24.218 | 27.174 | 33.295 | 21.238 | 23.669 | 29.016 |
| 40 | 23.419 | 26.358 | 32.381 | 21.253 | 23.854 | 28.960 |
| 50 | 22.885 | 25.746 | 31.678 | 21.194 | 23.787 | 29.220 |
| 75 | 22.252 | 24.967 | 30.469 | 21.208 | 23.728 | 29.191 |
| 100 | 21.922 | 24.509 | 30.232 | 21.112 | 23.595 | 28.870 |
| 125 | 21.744 | 24.409 | 30.202 | 21.095 | 23.669 | 29.213 |
| 150 | 21.612 | 24.273 | 29.812 | 21.084 | 23.655 | 29.002 |
| 200 | 21.465 | 24.188 | 29.782 | 21.097 | 23.667 | 29.201 |
| ∞ | 21.064 | 23.685 | 29.141 | 21.064 | 23.685 | 29.141 |

Table 5: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p=2,\,q=3$ and different values of n

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{\rm RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{\rm RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| 4 | | | | 58.318 | 62.261 | 72.774 |
| 5 | | | | 56.072 | 60.108 | 69.189 |
| 6 | | | | 54.589 | 58.741 | 67.418 |
| $\overline{7}$ | | | | 53.957 | 58.087 | 67.135 |
| 8 | | | | 53.314 | 57.342 | 66.195 |
| 9 | | | | 52.568 | 56.538 | 65.284 |
| 10 | 130.348 | 145.199 | 178.340 | 52.306 | 56.270 | 65.028 |
| 15 | 75.239 | 81.388 | 93.834 | 51.238 | 55.108 | 63.240 |
| 20 | 66.025 | 71.293 | 82.013 | 50.694 | 54.552 | 62.882 |
| 25 | 61.507 | 66.411 | 76.058 | 50.549 | 54.501 | 62.657 |
| 27 | 60.521 | 65.215 | 74.874 | 50.482 | 54.331 | 62.389 |
| 30 | 59.103 | 63.834 | 73.027 | 50.370 | 54.332 | 62.294 |
| 40 | 56.291 | 60.628 | 69.513 | 50.193 | 54.037 | 61.810 |
| 50 | 54.679 | 59.157 | 67.366 | 49.927 | 53.776 | 61.636 |
| 75 | 52.975 | 57.117 | 65.265 | 49.926 | 53.844 | 61.660 |
| 100 | 51.833 | 55.932 | 64.165 | 49.614 | 53.553 | 61.496 |
| 125 | 51.358 | 55.326 | 63.733 | 49.619 | 53.454 | 61.776 |
| 150 | 51.212 | 55.040 | 63.079 | 49.755 | 53.490 | 61.361 |
| 200 | 50.647 | 54.494 | 62.158 | 49.596 | 53.395 | 60.849 |
| ∞ | 49.513 | 53.384 | 61.162 | 49.513 | 53.384 | 61.162 |

Table 6: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p=3,\,q=3$ and different values of n

Table 7: Relative error between the RST statistics and their ENDs for 90th percentile for various values of p and n .

| $p \rightarrow$ | $\mathcal{D}_{\mathcal{L}}$ | 3 | $\overline{4}$ | 5 | 7 | 10 | 15 |
|-----------------|-----------------------------|---|----------------|-----------------|--------|----------|----------|
| $n\downarrow$ | | | | | | | |
| $\overline{4}$ | 6.076 | 17.784 | 21.657 | 23.889 | 27.246 | 29.662 | 31.157 |
| | | | | | | | |
| 6 | 6.922 | 10.253 | 13.076 | 14.971 | 16.863 | 18.065 | 19.022 |
| | | | | | | | |
| 8 | 5.466 | 7.677 | 9.716 | 10.707 | 12.167 | 13.091 | 13.625 |
| | (123.522) | | | | | | |
| 10 | 4.474 | 5.642 | 7.170 | 8.191 | 9.461 | 10.173 | 10.621 |
| | | (72.949) (163.263) | | | | | |
| 20 | 1.958 | 2.385 | 3.400 | 3.885 | 4.455 | 4.851 | 5.073 |
| | | (25.168) (33.350) (45.282) (63.792) | | | | | |
| 30 | 0.824 | 1.732 | 2.310 | 2.583 | 2.902 | 3.228 | 3.300 |
| | | (14.971) (19.370) (24.541) (31.212) (49.192) | | | | | |
| 40 | 0.895 | 1.374 | 1.625 | 1.861 | 2.086 | 2.321 | 2.458 |
| | | (11.180) (13.691) (16.691) (20.799) (30.286) (52.174) | | | | | |
| 50 | 0.615 | 0.836 | 1.121 | 1.560 | 1.642 | 1.901 | 1.947 |
| | | (8.645) (10.434) (12.737) (15.827) (22.031) | | | | (34.860) | (76.922) |
| 75 | 0.683 | 0.834 | 0.815 | 1.071 | 1.200 | 1.266 | 1.289 |
| | | (5.638) (6.993) (8.127) (9.903) (13.192) (19.492) | | | | | (33.036) |
| 100 | 0.226 | 0.205 | 0.637 | 0.703 1.023 | | 0.947 | 0.980 |
| | (4.074) | (4.686) (5.804) (7.072) (9.563) (13.603) | | | | | (21.648) |

Note: the values in the parenthesis and italics are the relative error between the LRT statistics and their ENDs for 90th percentile for various values of p and n .

Computations for calculating the END for fixed n, p, q, ρ and Σ are carried out by the algorithm presented below. The Mathematica code to compute END are available from the authors on request. Algorithm Outline:

- Step 1 Fix n, p, q, ρ and Σ . Calculate $\Psi = (1 \rho)I_p + \rho J_p$.
- Step 2 Set the seed to 123213789.
- Step 3 Generate the observation matrix X from the matrix normal distribution $N_{pq,n}(\mathbf{0}, \Psi)$ Σ, I_n).
- Step 4 Get the pooled sample variance-covariance matrix for repeated measures, say G.
- **Step 5** Obtain an initial estimate of ρ as $\hat{\rho}_0 = (\mathbf{1}_p'\mathbf{G} \mathbf{1}_p \text{tr}(\mathbf{G}))/p(p-1)$. Take $\hat{\Psi}_0 = (1-\hat{\rho}_0)\mathbf{I}_p +$ $\hat{\rho}_0 J_p$ as an initial estimate of Ψ .
- **Step 6** Compute $\widehat{\mathbf{\Sigma}} = \frac{1}{n p}$ $\frac{1}{np}\sum_{i=1}^p (e_i\otimes I_q)'(\widehat{\Psi}\ \otimes I_q) \mathbf{X}\ \bm{Q_1}_n \bm{X}'(\bm{e}_i\otimes I_q),$ where \bm{e}_i is p-th column of I_p .

Step 7 Compute $k_0 = nqp(p-1)$, $a = \text{tr}((\boldsymbol{I}_p \otimes \widehat{\boldsymbol{\Sigma}}) \mathbf{X} \ \boldsymbol{Q}_{1_n} \boldsymbol{X}'),$ and $b = \text{tr}((\boldsymbol{J}_p \otimes \widehat{\boldsymbol{\Sigma}}) \mathbf{X} \ \boldsymbol{Q}_{1_n} \boldsymbol{X}').$

- **Step 8** Compute the value of $\hat{\rho}$ by solving the cubic equation $k_0(p-1)\hat{\rho}^3 + (k_0 k_0(p-1) + (p-1)\hat{\rho}^3)$ $(1)^{2}a - (p-1)b\hat{\rho}^{2} + (2(p-1)a - k_{0})\hat{\rho} + a - b = 0$. Ensure that $-1/(p-1) < \hat{\rho} < 1$. Truncate $\hat{\rho}$ to $-1/(p-1)$ or 1, if it is outside this range.
- Step 9 Compute the revised estimate of $\hat{\Psi}$ from $\hat{\rho}$.
- **Step 10** Compute the revised estimate of $\hat{\Sigma}$ using $\hat{\Psi}$ obtained in Step 9.
- Step 11 Repeat Steps 7, 8, 9 and 10 until convergence is attained. This is ensured by verifying that the maximum of the absolute difference between two successive values of $\hat{\rho}$ and the absolute difference between two successive values of $tr(\hat{\Sigma})$ is less than a pre-determine number $\varepsilon (= 10^{-6},$ say).

Step 12 Calculate the Rao's score test statistic $RS = nqp/2 - \text{tr}(\mathbf{Z}) + (1/2n)\text{tr}(\mathbf{Z}^2)$, where

$$
\mathbf{Z} = (\widehat{\mathbf{\Psi}} \otimes \widehat{\mathbf{\Sigma}}) \mathbf{X} \, \mathbf{Q}_{1_n} \mathbf{X}'.
$$

Step 13 Repeat Steps 3-12 50,000 times.

4.3 Power Simulations

Power analysis is very important for applications to real data. Thus, we carry out some power simulations to study the finite sample performance of the tests comparing the LRT and the RST approaches. The power of a statistical test (Lehmann and Romano, 2005), e.g., for RST, is a function and is defined as

$$
\beta(\mathbf{\Omega}) = P_{\mathbf{\Omega}}(\text{reject } H_0 \text{ when using RST given } H_0 \text{ is false}) = P_{\mathbf{\Omega}}(RST > \hat{\kappa}_{\alpha}),
$$

where κ_{α} is defined in (19), and $\hat{\kappa}_{\alpha}$ is an estimate of κ_{α} This function cannot be computed exactly, but can be approximated using Monte Carlo technique (Rizzo, 2008). Now, both RST and LRT statistics depend on n, p and q. So, both RST and LRT statistics are functions of n, p and q as shown in Tables 8 and 9. It seems RST is more powerful than the LRT for the alternative in our study.

Like observed Type I error rates $\hat{\alpha}_{\text{LRT}}$ and $\hat{\alpha}_{\text{RST}}$ here also samples of various sizes from small to large, e.g., $n = 4, 6, 8, 10, 15, 20, 25, 30, 50, 75$ and 100 are generated from a pq-variate normal population $N_{pq}(\mathbf{0}, \mathbf{\Omega})$, where $\mathbf{\Omega}$ is an unstructured positive definite matrix. The number of repeated measurements p is chosen as 3, 4, 5 and 7, and the number of characteristics q as 3. We generate 50,000 samples for each combination of parameters p, q and n. The empirical powers of LRT and RST for $p = 3, 4, 5$ and $p = 7$ and for different values of n are given in Tables 8 and 9 for $\alpha = 0.01$ and 0.05 respectively.

| $p \rightarrow$ | | 3 | | 4 | | 5 | 7 | |
|------------------|--------------------------------|----------------------|--------------|------------|-------|------------|---|------------|
| \boldsymbol{n} | LRT | RST | $_{\rm LRT}$ | RST | LRT | RST | LRT | RST |
| 4 | | 0.022 | | 0.021 | | 0.018 | | 0.014 |
| 6 | $\qquad \qquad \longleftarrow$ | 0.044 | | 0.034 | | 0.028 | $\qquad \qquad \overbrace{\qquad \qquad }^{}$ | 0.021 |
| 8 | $\overline{}$ | 0.067 | | 0.053 | | 0.037 | $\qquad \qquad -$ | 0.027 |
| 10 | 0.020 | 0.097 | | 0.078 | | 0.055 | $\overbrace{\hspace{15em}}$ | 0.037 |
| 15 | 0.134 | 0.229 | 0.058 | 0.174 | | 0.117 | $\qquad \qquad \overbrace{\qquad \qquad }^{}$ | 0.070 |
| 20 | 0.316 | 0.397 | 0.205 | 0.330 | 0.099 | 0.228 | $\qquad \qquad$ | 0.130 |
| 25 | 0.536 | 0.583 | 0.372 | 0.479 | 0.226 | 0.346 | 0.073 | 0.209 |
| 30 | 0.713 | 0.750 | 0.580 | 0.662 | 0.391 | 0.504 | 0.158 | 0.295 |
| 50 | 0.985 | 0.989 | 0.961 | 0.976 | 0.887 | 0.927 | 0.682 | 0.773 |
| 75 | 1.000 | 1.000 | 1.000 | 1.000 | 0.997 | 0.999 | 0.973 | 0.986 |
| 100 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.999 | 1.000 |

Table 8: Empirical powers of LRT and RST for different values of n and p for $\alpha = 0.01$ based on 50,000 simulations

While there is some correspondence between Type I error and power in these tests, it is not a strong linkage. This is because neither the null nor alternative hypotheses are point hypotheses; both describe sets of covariance structures. This makes the concept of a statistical distance between

hypotheses very difficult to measure. The measure of discrepancy between hypotheses is based on Genton (2007). It is to be noted that this measure is used in nearest Kronecker product for a space time covariance matrix problem, and it is not sufficient to measure the distance between our structured covariance matrix and the alternative. For our studies we assumed nonseparable covariance matrix as true hypothesis. The results presented in the tables are for large distances from separability. For determining empirical power of the LRT and the RST we use the corresponding empirical null distributions.

Table 9: Empirical powers of LRT and RST for different values of n and p for $\alpha = 0.05$ based on 50,000 simulations

| $p \rightarrow$ | 3 | | 4 | | | 5 | | 7 |
|------------------|-------|----------------------|---|----------------------|---------------------------------|----------------------|-------------------|----------------------|
| \boldsymbol{n} | LRT | RST | $_{\rm LRT}$ | RST | LRT | RST | LRT | RST |
| 4 | | 0.092 | $\overline{}$ | 0.086 | | 0.073 | | 0.065 |
| 6 | | 0.142 | | 0.125 | | 0.102 | | 0.084 |
| 8 | | 0.199 | $\qquad \qquad \overbrace{\qquad \qquad }^{}$ | 0.166 | $\hspace{0.1mm}-\hspace{0.1mm}$ | 0.137 | $\qquad \qquad$ | 0.107 |
| 10 | 0.094 | 0.269 | $\qquad \qquad -$ | 0.233 | $\hspace{0.05cm}$ | 0.176 | $\qquad \qquad -$ | 0.132 |
| 15 | 0.350 | 0.469 | 0.202 | 0.391 | | 0.304 | | 0.216 |
| 20 | 0.583 | 0.672 | 0.441 | 0.591 | 0.275 | 0.469 | | 0.327 |
| 25 | 0.773 | 0.817 | 0.642 | 0.743 | 0.474 | 0.624 | 0.231 | 0.448 |
| 30 | 0.882 | 0.909 | 0.798 | 0.863 | 0.645 | 0.758 | 0.391 | 0.583 |
| 50 | 0.997 | 0.998 | 0.992 | 0.995 | 0.967 | 0.983 | 0.875 | 0.926 |
| 75 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 0.995 | 0.998 |
| 100 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |

As expected, empirical power increases steadily with n for a fixed p , as increase in n provides more information. We observe this phenomenon for both $\alpha = 0.01$ and 0.05 for LRT as well as for RST. Now, since the number of parameters in the $(pq \times pq)$ –dimensional unstructured variance-covariance matrix Ω is $pq(pq+1)/2$, increase in p for a fixed n means more parameters to estimate. So, too many degrees of freedom are used up in estimating too many parameters in the $(pq \times pq)$ −dimensional covariance matrix Ω , and consequently power decreases with the increase of p for LRT as well as for RST. The most important factor to be noticed from Tables 8 and 9 is that the power of LRT is always smaller than the power of RST, especially for small samples for both $\alpha = 0.01$ and 0.05. If we compare Tables 8 and 9, as expected we see that the increase in the Type I error (α) , increases the power of a test. We notice that as the number of repeated measures, p , increases empirical power decreases. It is to be noted, that a bigger power study is needed, since our study is only for one unstructured Ω as the alternative hypothesis.

5 Three real data examples

To illustrate our proposed testing method, in this section we test the Hypothesis (2) on three data sets. The first one is of relatively smaller in size, and the second and third ones are of moderately larger sizes. We use the biased along with the unbiased and unmodified RST in these examples to see the performance of our new method and evaluate the performance in comparison to the biased along with the unbiased and unmodified LRT method.

Example 1 (*Dental Data*). The data set is from Timm (1980, Table 7.2). The data were originally collected by T. Zullo of the School of Dental Medicine at the University of Pittsburgh. There are nine subjects in the data set. Measurements at three different time points $(p = 3)$ were made on each of $q = 3$ characteristics. Note that the null hypothesis cannot be tested using the LRT as the number of subjects $n = 9$ is not greater than $pq = 9$. Therefore, if we take all three measurements LRT cannot be performed, nonetheless RST can be performed as it only requires $n > q$. The calculated value of RST statistic is 54.8215 (see Table 10) with 38 df $(\frac{9 \cdot 10}{2} - \frac{3 \cdot 4}{2} - 1 = 38)$. Now, $\chi^{2}_{38,0.05} = 53.384$ and $\chi_{38,0.01}^2 = 61.162$. Therefore, we reject the null hypothesis at 5% level of significance and fail to reject it at 1% level of significance. From Table 6 we notice that our calculated RST statistic is less than the corresponding critical values, the empirical 95th percentiles for $n = 9$: $END_{9,0.1}^{RST} = 52.568$ and $END_{9,0.05}^{RST} = 56.538$. So, we reject the null hypothesis at 10% level of significance for RST (p−value < 0.1). Nevertheless, we fail to reject the null hypothesis at 5% level of significance for RST (p–value > 0.05). Thus, we draw a little different conclusion when we use END of RST statistic in place of the limiting χ^2 distribution.

For the purpose of comparison of the LRT and the RST, we now consider only two measurements $(q = 2)$. The test statistics values are given in Table 10. We will first consider measurements 1 and 2. The calculated value of the LRT statistic with 17 df is 27.0035. Now, $\chi^2_{17,0.1} = 24.769$ and $\chi^2_{17,0.05} = 27.587$. Therefore, we fail to reject the null hypothesis marginally at 5% level of significance, but reject it at 10% level of significance. However, RS= 22.1995 with the same 17 df. Therefore, in this case we fail to reject the null hypothesis at 10% level of significance (p–value > 0.1). Nevertheless, these inferences are not accurate or correct, as from Table 4 we notice that both our calculated LRT and RST statistics are less than the corresponding empirical 90th percentiles for $n = 9$: END^{IRT}_{9,0.1} = 44.399 and END^{RST}_{9,0.1} = 25.831. So, we fail to reject the null hypothesis at 10% level of significance for both LRT and RST (p -value > 0.1).

| Data | n p | | | | ν LRT (END p-value) RST (END p-value) | | LRT $(\chi^2_{\nu} p$ -value) RST $(\chi^2_{\nu} p$ -value) | |
|---------|---------|-------------|-------|-----|---|----------------------------|---|-------------------|
| | | | | | | | | |
| Dental | | 9 3 | 1,2,3 | -38 | $\hspace{0.1mm}-\hspace{0.1mm}$ | $54.8215 (> 0.05 \< 0.10)$ | $\overline{}$ | $(>0.01 \< 0.05)$ |
| Dental | | 9 3 | 1.2 | -17 | 27.0035 (> 0.1) | 22.1995 (>0.1) | $(>0.05 \< 0.10)$ | > 0.1 |
| Dental | | $9 \quad 3$ | 1.3 | 17 | 40.4858 (> 0.1) | 23.3546 (> 0.1) | < 0.01 | > 0.1 |
| AIDS | 27 3 | | 1,2,3 | -38 | $134.8540 \leq 0.01$ | 114.6980 (< 0.01) | < 0.01 | < 0.01 |
| AIDS | 27 3 | | 1,2 | -17 | $80.4133 \ (< 0.01$ | 61.9511 (< 0.01) | < 0.01 | < 0.01 |
| Mineral | 25 2 | | 1,2,3 | -14 | 22.7675 (> 0.1) | 17.7937 (> 0.1) | $(>0.05 \< 0.10)$ | > 0.1 |

Table 10: Calculated values of LRT, RST statistics and their p−values along with the p−values of the limiting χ^2_{ν} distribution for different data sets

We further consider this data set with measurements 1 and 3. In this case the calculated values of LRT and RST are 40.4858 and 23.3546 respectively with 17 df. Since again $\chi^2_{17,0.1} = 24.769$ and $\chi^2_{17,0.01} = 33.409$, we reject the null hypothesis with p-value < 0.01 using LRT, but fail to reject the null hypothesis with p −value > 0.1 using RST. So, we see very different conclusions for both the tests. However, when we consider empirical null distributions, we see from Table 4 that again our calculated LRT and RST statistics are less than the respective 90th percentile values, and therefore we fail to reject the null hypothesis at 10% level of significance for both LRT and RST $(p$ -values > 0.1).

Thus, we draw very different conclusions on the null Hypothesis (2) when we use ENDs in place of the limiting χ^2 distributions. Nonetheless, the conclusions using LRT and RST are the same if we use the respective empirical distributions when $n > pq$.

Example 2 (Aids Data). The data set taken from Thompson (1991) corresponds to a sample of 27 patients involved in a pilot study for a new treatment for AIDS. Three different variables: TMHR scores, Karofsky scores, and T-4 cell counts, were measured at three time points at an interval of 90 days during the study. Thus, for this data set $p = 3$ and $q = 3$. The test statistics values are also given in Table 10. We will first consider all three variables. The calculated test statistic values for LRT and RST methods are equal to 134.85402 and 114.698 respectively with 38 df. Now, $\chi_{38,0.01}^2 = 61.162$. Therefore, we reject the null hypothesis at 1% level of significance $(p-\text{value} < 0.01)$ for both LRT and RST. Now, from Table 6 we see that the critical values, the empirical 99th percentiles for $n = 27$ are $END_{27,0.01}^{LRT} = 74.874$ and $END_{27,0.01}^{RST} = 62.389$. Thus, if we consider END we also reject the null hypothesis at 1% level of significance (p–value < 0.01) for LRT as well as for RST.

We further consider this data set with the 1st and the 2nd variables, i.e., with TMHR scores and Karofsky scores. In this case calculated test statistic values for LRT and RST methods are equal to

80.413 and 61.951 respectively with 17 df. Since $\chi_{17,0.01}^2 = 33.409$, we reject the null hypothesis at 1% level of significance (p−value < 0.01) for both LRT and RST. However, from Table 4 we see that the empirical 99th percentiles for $n = 27$ are $END_{27,0.01}^{LRT} = 38.568$ and $END_{27,0.01}^{RST} = 34.214$. Thus, if we consider END we also reject the null hypothesis at 1% level of significance (p–value < 0.01) for both LRT and RST.

From this example we see that if we use ENDs, we come to the same conclusions for both LRT and RST. Moreover, if we use limiting χ^2 distribution we reach the same conclusion as that of the ENDs.

Example 3 (Mineral Data). This data set is taken from Johnson and Wichern (2007, p. 43). An investigator measured the mineral content of bones (radius, humerus and ulna) by photon absorptiometry to examine whether dietary supplements would slow bone loss in 25 older women. Measurements were recorded for three bones on the dominant and non-dominant sides. Clearly, for this data set we have $p = 2$ and $q = 3$. The calculated test statistics values for LRT and RST are 22.7675 and 17.7937 respectively with 14 df and are given in Table 10. Observe that $\chi_{14,0.1}^2 = 21.064$ and $\chi^2_{14,0.05} = 23.685$. Therefore, basing on LRT, we reject the null hypothesis at 10% level of significance $(p-\text{value} < 0.1)$, but fail to reject the null hypothesis at 5% level of significance $(p-\text{value} > 0.05)$. In case of RST we fail to reject the null hypothesis at 10% level of significance (p-values > 0.1). Now, from Table 5 we see that the empirical 90th percentiles for $n = 25$ are $END_{25,0.1}^{LRT} = 25.072$ and $END_{25,0.1}^{RST} = 21.410$. Thus, if we consider ENDs we fail to reject the null hypothesis at 10% level of significance (p -value > 0.1) for LRT as well as for RST.

From this example we see that if we use ENDs, we come to the same conclusions for both the tests, whereas if we use limiting χ^2 distribution we reach different conclusions.

From the above examples we have the following suggestions for the researchers and statistical practitioners.

Remark 3. From the above examples we see that the inference changes most of the time if we use END as opposed to the limiting χ^2 distribution which is very conservative, especially if the test statistic value lies in the close neighborhood of the critical value of the χ^2 distribution. However, the conclusions remain the same for LRT and RST if we use END, which is more desirable. But most importantly, we see that the conclusions drawn from END using RST and the limiting χ^2 distribution are the same all but one time (in a marginal case with too small sample size) in a small sample example above. These observations suggest us to use RST instead of LRT for testing separability of the variance-covariance matrix with first component as CS correlation matrix for small and moderate sample sizes, and especially in small sample sizes. From these studies it can be seen that for precise conclusion it is always better to use END of RST if available instead of χ^2 . However, the above examples show that if END of RST is not available, the decision based on the limiting χ^2 distribution would not differ much. Remark 2 also reinforces Remark 3.

6 Summary and scope for the future

Two-level or doubly multivariate data are thriving in all disciplines in the 21st century, so this topic is of wide interest to many researchers and statistical practitioners in many industries. Here we develop a new hypothesis testing procedure to test the separability of a covariance matrix for two-level multivariate data using RST, which is no longer just an alternative or competitor to LRT, but is much superior to LRT in small and in moderate-sized data sets. A first advantage of the RST over the LRT is that it does not require an estimate of the information matrix under the alternative hypothesis. A second advantage of the RST over the LRT is that it converges to a Chi-square distribution much faster according to our simulation study. From the theoretical point of view the drawback of the RST is that at the beginning the RST needs more calculations connected with the Fisher information matrix $\mathcal F$, requiring second derivatives of likelihood functions and the inverse of the Fisher information matrix $\mathcal F$. However, it is enough to calculate it one time to obtain a simple form of the RST statistic. So, from computational point of view, RST is faster to obtain, because it does not need to find MLE's under H_A , which are more time-consuming. We see from Remark 1 that one may increase p for more information, and still can get stable estimate of the RST statistic with permissible minimum sample size $q + 1$, a quantity independent of p. Nevertheless, the condition $n > pq$ has some advantages, by providing smaller bias and higher precision to ML estimates that help for the behavior of both LRT and RST statistics and the characterization of their distributions - compared to when $n \leq pq$ and n is equal to or just about the permissible minimum sample size.

In this article we have taken the correlation matrix Ψ as CS. First, it is well known (see Naik and Rao, 2001; Jones, 1993) that the correlation matrix Ψ of the repeated measures usually has a simpler structure such as CS, AR(1), circular or Toeplitz as opposed to a general structure. In our formulation, it is easier to accommodate different structures for the correlation matrix of repeated measures (via Ψ). Thus, it may be worthwhile to develop tests of the null hypothesis H_0 with Ψ as AR(1), circular or Toeplitz for various types of two-level multivariate data sets. Likewise, if one prefers a non-stationary covariance structure, one can develop an RST statistic with Ψ as an

unstructured or antedependent covariance matrix. All these studies would surely help in providing an improved statistical analysis for two-level multivariate data.

The modeling of the mean may have an effect on the performance of separability tests for variancecovariance structures. Since the hypothesis we are interested in this article involves only the variancecovariance matrix, we derive the RST statistic corresponding to vech Ω by calculating the component of the score vector corresponding to vech Ω . If one wants to see the effect of the mean vector one needs to derive the RST statistic corresponding to μ too, i.e., derive the RST statistic corresponding to the score vector $s(\theta)$. We would like to solve this problem in near future and publish it in a future correspondence.

A relatively new criterion for testing hypothesis, referred to as the gradient test, has been proposed by Terrell (2002). Its statistic shares the same first order asymptotic properties with the three classical tests, the likelihood ratio, the Wald and the Rao's score statistics, and is very simple when compared with the same three classical tests. We will explore Terrell's method to develop a test statistic for the null hypothesis H_0 in near future, and will report it in a future correspondence.

Acknowledgement

The authors thank Professor Dietrich von Rosen at the Swedish University of Agricultural Sciences, Sweden, for the idea and inspiration of the method in the paper. The authors also thank Mr. Michael Anderson at the University of Texas at San Antonio for the careful reading of this paper. This research is partially supported by Ministry of Science and Higher Education in Iuventus Plus programme, grant No. 0.0123 /IP3/2011/71 (Katarzyna Filipiak) and by grant VEGA MS SR 1/0832/12 (Daniel Klein). The authors would like to thank the associate editor for his thoughtful comments, and the three reviewers for their constructive comments of an earlier version of this article, and for providing valuable recommendations that led to the substantially improved version of the article.

A Some algebraic definitions and results

Following Magnus and Neudecker (1986) let N_m be the symmetric idempotent $m^2 \times m^2$ matrix defined as $\mathbf{N}_m = \frac{1}{2}$ $\frac{1}{2}(\mathbf{I}_{m^2} + \mathbf{K}_{m,m})$, where $m^2 \times m^2$ matrices \mathbf{I}_{m^2} and $\mathbf{K}_{m,m}$ represent the identity matrix and the commutation matrix (c.f. Kollo and von Rosen, 2005) respectively. Then a unique $m^2 \times m(m+1)/2$ –dimensional transformation matrix \mathbf{D}_m is called a duplication matrix if

$$
\boldsymbol{D}_{m}\mathrm{vech}\boldsymbol{A}=\mathrm{vec}\boldsymbol{A};
$$

see Magnus and Neudecker (1986). Using the above definitions we have the following propositions.

Proposition 1. The following equalities hold:

$$
{\rm (i)} \ \ (I_n\otimes K_{n,n}) (K_{n,n}\otimes I_n) = K_{n^2,n};
$$

- (ii) $K_{m,k}(A \otimes B)K_{l,n} = B \otimes A$ for any $k \times l$ matrix A and $m \times n$ matrix B;
- (iii) $\text{vec}(A \otimes B) = (I_l \otimes K_{n,k} \otimes I_m)(\text{vec}A \otimes \text{vec}B)$ for any $k \times l$ matrix A and $m \times n$ matrix B;
- $({\bf iv})\ \left({\bm D}'_m({\bm A}^{-1}\otimes{\bm A}^{-1}){\bm D}_m\right)^{-1}={\bm D}_m^+({\bm A}\otimes{\bm A}){\bm D}_m^{+\prime}$ for any $m\times m$ nonsingular matrix ${\bm A},$ where ${\bm D}_m^+$ is a Moore-Penrose inverse of \mathbf{D}_m .

Proposition 2. For any $m \times m$ symmetric matrix **A** the following equalities hold:

- (i) N_m vec $A = \text{vec}A;$
- (ii) $K_{m,m}D_m = D_m;$
- (iii) $N_m(A \otimes A)N_m = N_m(A \otimes A) = (A \otimes A)N_m;$

$$
\textbf{(iv)}\;\; \boldsymbol{D}_m \boldsymbol{D}_m^+ = \boldsymbol{N}_m.
$$

The statements in the above propositions can be found in Magnus and Neudecker (1986) or Ghazal and Neudecker (2000).

Proposition 3. Let $F(Z)$ be a $k \times l$ matrix function of Z.

- (i) If Z is an $m \times n$ matrix, then $\frac{\partial \text{vec} F(Z)}{\partial \text{vec}' Z}$ is a kl \times mn matrix such that its (i, j) th element is the derivative of the ith element of $\text{vec}F(Z)$ with respect to the jth element of $\text{vec}Z$.
- (ii) If Z is an $m \times m$ symmetric matrix then

$$
\frac{\partial \text{vec} F(\boldsymbol{Z})}{\partial \text{vec}' \boldsymbol{Z}} = \frac{\partial \text{vec} F(\boldsymbol{Z})}{\partial \text{vec}' \boldsymbol{Z}} \cdot \frac{\partial \text{vec} \boldsymbol{Z}}{\partial \text{vec} \text{h}' \boldsymbol{Z}} = \frac{\partial \text{vec} F(\boldsymbol{Z})}{\partial \text{vec}' \boldsymbol{Z}} \cdot \boldsymbol{D}_n,
$$

where the derivative of the first term in the multiplicaton is calculated treating Z as non-symmetric. Proposition 3 (ii) follows from the chain rule as described in Magnus and Neudecker (1986). Using the above propositions we now have the following lemma.

Lemma 1. For any $m \times m$ symmetric matrix \boldsymbol{A}

(i) $(\text{vec}'A \otimes I_m)(I_m \otimes \text{vec}A^{-1}) = I_m;$

- (ii) $(\text{vec}A \otimes D_m)'(\boldsymbol{I}_m \otimes \boldsymbol{K}_{m,m} \otimes \boldsymbol{I}_m)(\boldsymbol{I}_{m^2} \otimes \text{vec}A^{-1}) = D'_m;$
- (iii) $(\text{vec}A \otimes D_m)'(\mathbf{I}_m \otimes \mathbf{K}_{m,m} \otimes \mathbf{I}_m)(\text{vec}A^{-1} \otimes \mathbf{I}_{m^2}) = D'_m;$

Proof. (i) Let $A_{i\bullet}$ denote the *i*-th row and $A_{\bullet j}$ denote the *j*-th column of matrix A. Then clearly

$$
\boldsymbol{A}_{i\bullet}\boldsymbol{A}_{\bullet j}^{-1} = \left\{ \begin{array}{ll} 1 & \text{if } i = j, \\ 0 & \text{if } i \neq j. \end{array} \right.
$$

Since

$$
(\mathrm{vec}'\boldsymbol{A}\otimes\boldsymbol{I}_n)(\boldsymbol{I}_n\otimes\mathrm{vec}\boldsymbol{A}^{-1})=\left\{\boldsymbol{A}_{i\bullet}\boldsymbol{A}_{\bullet j}^{-1}\right\}_{ij},
$$

we obtain (i).

(ii) From Proposition 2 (ii) and Proposition 1 (i), (iii) and Lemma 1 (i) we can write

$$
(\text{vec}A \otimes D_m)'(\boldsymbol{I}_m \otimes \boldsymbol{K}_{m,m} \otimes \boldsymbol{I}_m)(\boldsymbol{I}_{m^2} \otimes \text{vec}\boldsymbol{A}^{-1})
$$

\n
$$
= D'_m(\text{vec}\boldsymbol{A} \otimes \boldsymbol{I}_{m^2})'(\boldsymbol{I}_{m^2} \otimes \boldsymbol{K}_{m,m})(\boldsymbol{I}_m \otimes \boldsymbol{K}_{m,m} \otimes \boldsymbol{I}_m)(\boldsymbol{I}_{m^2} \otimes \text{vec}\boldsymbol{A}^{-1})
$$

\n
$$
= D'_m(\text{vec}\boldsymbol{A} \otimes \boldsymbol{I}_{m^2})'(\boldsymbol{I}_m \otimes \boldsymbol{K}_{m^2,m})(\boldsymbol{I}_{m^2} \otimes \text{vec}\boldsymbol{A}^{-1})
$$

\n
$$
= D'_m(\text{vec}\boldsymbol{A} \otimes \boldsymbol{I}_{m^2})'(\boldsymbol{I}_m \otimes \boldsymbol{K}_{m^2,m}(\boldsymbol{I}_m \otimes \text{vec}\boldsymbol{A}^{-1}))
$$

\n
$$
= D'_m((\text{vec}'\boldsymbol{A} \otimes \boldsymbol{I}_m)(\boldsymbol{I}_m \otimes \text{vec}\boldsymbol{A}^{-1}) \otimes \boldsymbol{I}_m)
$$

\n
$$
= D'_m.
$$

(iii) We have

$$
(\text{vec}A \otimes D_m)'(I_m \otimes K_{m,m} \otimes I_m)(\text{vec}A^{-1} \otimes I_{m^2})
$$

\n
$$
= D'_m \sum_{i=1}^m \sum_{j=1}^m (\text{vec}A \otimes I_{m^2})'(I_m \otimes E_{ij} \otimes E'_{ij} \otimes I_m)(\text{vec}A^{-1} \otimes I_{m^2})
$$

\n
$$
= D'_m \sum_{i=1}^m \sum_{j=1}^m (\text{vec}A \otimes I_{m^2})'(\text{vec}(E_{ij}A^{-1}) \otimes I_{m^2})
$$

\n
$$
= D'_m \sum_{i=1}^m \sum_{j=1}^m \text{tr}\left[AE_{ij}A^{-1}\right](E'_{ij} \otimes I_m)
$$

\n
$$
= D'_m \sum_{i=1}^m (E_{ii} \otimes I_m)
$$

\n
$$
= D'_m,
$$

where $\boldsymbol{E}_{ij} = \boldsymbol{e}_i \boldsymbol{e}'_j$ and \boldsymbol{e}_i is the *i*-th column of \boldsymbol{I}_m .

 \Box

B Empirical percentiles of the null distribution of LRT and RST statistics for several combinations of p , q and n

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{\rm RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{\rm RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| 3 | | | | 14.870 | 16.124 | 17.446 |
| $\overline{4}$ | | | | 13.239 | 15.367 | 19.063 |
| 5 | 34.557 | 41.986 | 57.578 | 12.239 | 14.435 | 18.953 |
| 6 | 23.919 | 28.418 | 38.353 | 11.804 | 13.940 | 18.422 |
| $\overline{7}$ | 20.071 | 23.857 | 32.368 | 11.553 | 13.524 | 18.301 |
| 8 | 17.985 | 21.262 | 28.342 | 11.402 | 13.349 | 17.797 |
| 9 | 16.586 | 19.552 | 26.262 | 11.209 | 13.065 | 17.590 |
| 10 | 15.735 | 18.695 | 25.160 | 11.224 | 13.155 | 17.607 |
| 15 | 13.522 | 15.915 | 21.253 | 11.013 | 12.829 | 17.068 |
| 20 | 12.746 | 15.049 | 20.063 | 10.995 | 12.800 | 16.712 |
| 25 | 12.216 | 14.431 | 19.282 | 10.889 | 12.716 | 17.028 |
| 27 | 12.090 | 14.266 | 19.097 | 10.879 | 12.734 | 16.839 |
| 30 | 11.923 | 14.184 | 18.703 | 10.828 | 12.697 | 16.722 |
| 40 | 11.477 | 13.621 | 18.099 | 10.743 | 12.616 | 16.770 |
| 50 | 11.323 | 13.368 | 17.951 | 10.730 | 12.635 | 16.792 |
| 75 | 11.167 | 13.194 | 17.497 | 10.740 | 12.642 | 16.705 |
| 100 | 10.998 | 12.969 | 17.315 | 10.691 | 12.568 | 16.948 |
| 125 | 10.825 | 12.832 | 17.102 | 10.613 | 12.528 | 16.627 |
| 150 | 10.811 | 12.791 | 17.222 | 10.628 | 12.543 | 16.763 |
| 200 | 10.784 | 12.757 | 16.923 | 10.672 | 12.558 | 16.644 |
| ∞ | 10.645 | 12.592 | 16.812 | 10.645 | 12.592 | 16.812 |

Table 11: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p = 2$, $q = 2$ and different values of n

Table 12: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p = 4$, $q = 3$ and different values of n

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|---------------|-------------------|---------------|
| $\overline{4}$ | | | | 105.398 | 111.562 | 125.228 |
| 5 | | | | 100.983 | 106.867 | 120.120 |
| 6 | | | | 97.964 | 103.873 | 116.879 |
| 8 | | | | 95.053 | 100.818 | 112.848 |
| 10 | | | | 92.847 | 98.290 | 110.686 |
| 12 | | | | 91.950 | 97.500 | 108.948 |
| 15 | 158.181 | 168.873 | 190.700 | 90.590 | 96.112 | 107.197 |
| 20 | 125.865 | 133.295 | 147.892 | 89.581 | 94.622 | 105.384 |
| 25 | 114.058 | 121.070 | 134.729 | 89.054 | 94.413 | 105.428 |
| 30 | 107.897 | 114.259 | 126.383 | 88.637 | 93.804 | 104.401 |
| 35 | 103.882 | 109.989 | 122.271 | 88.254 | 93.508 | 103.897 |
| 40 | 101.096 | 106.988 | 118.456 | 88.043 | 92.927 | 103.237 |
| 50 | 97.670 | 103.604 | 115.208 | 87.607 | 92.746 | 103.319 |
| 75 | 93.676 | 99.072 | 110.081 | 87.342 | 92.456 | 102.729 |
| 100 | 91.664 | 97.054 | 107.680 | 87.187 | 92.232 | 102.469 |
| 125 | 90.823 | 96.117 | 106.665 | 87.116 | 92.223 | 102.523 |
| 150 | 90.148 | 95.518 | 105.823 | 87.138 | 92.390 | 102.466 |
| 200 | 89.178 | 94.445 | 104.764 | 86.967 | 92.131 | 102.391 |
| ∞ | 86.635 | 91.670 | 101.621 | 86.635 | 91.670 | 101.621 |

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{\rm RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|---------------|-------------------|-------------------|
| $\overline{4}$ | | | | 164.330 | 173.128 | 191.403 |
| 5 | | | | 156.797 | 164.600 | 182.030 |
| 6 | | | | 152.502 | 160.348 | 176.634 |
| 8 | | | | 146.845 | 154.184 | 170.504 |
| 10 | | | | 143.508 | 150.908 | 166.040 |
| 12 | | | | 141.755 | 148.932 | 163.625 |
| 15 | | | | 139.811 | 146.810 | 161.214 |
| 20 | 217.259 | 228.517 | 249.515 | 137.797 | 144.415 | 157.764 |
| 25 | 187.491 | 196.404 | 213.762 | 136.733 | 143.274 | 157.020 |
| 30 | 174.044 | 182.113 | 197.796 | 136.070 | 142.630 | 155.900 |
| 35 | 165.742 | 173.532 | 188.688 | 135.731 | 142.095 | 155.404 |
| 40 | 160.232 | 167.613 | 181.731 | 135.112 | 141.327 | 154.295 |
| 50 | 153.637 | 161.152 | 175.388 | 134.712 | 141.223 | 153.951 |
| 75 | 145.779 | 152.569 | 165.676 | 134.064 | 140.456 | 152.839 |
| 100 | 142.024 | 148.673 | 161.851 | 133.576 | 140.000 | 152.877 |
| 125 | 140.005 | 146.360 | 159.271 | 133.635 | 139.788 | 151.979 |
| 150 | 138.671 | 145.233 | 158.134 | 133.442 | 139.624 | 152.296 |
| 200 | 137.180 | 143.617 | 156.191 | 133.175 | 139.508 | 152.130 |
| ∞ | 132.643 | 138.811 | 150.882 | 132.643 | 138.811 | 150.882 |

Table 13: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p=5,\,q=3$ and different values of n

Table 14: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p=7,\,q=3$ and different values of n

| \boldsymbol{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{\rm RST}(90)$ | $Q_{RST}(95)$ | $Q_{RST}(99)$ |
|------------------|-------------------|-------------------|-------------------|-------------------|---------------|---------------|
| 4 | | | | 320.045 | 333.168 | 361.732 |
| 5 | | | | 303.298 | 315.493 | 342.473 |
| 6 | | | | 293.932 | 305.697 | 330.462 |
| 8 | | | | 282.119 | 292.984 | 316.203 |
| 10 | | | | 275.313 | 285.590 | 307.403 |
| 12 | | | | 270.973 | 280.887 | 302.721 |
| 15 | | | | 266.898 | 276.713 | 296.705 |
| 20 | | | | 262.723 | 271.876 | 290.728 |
| 25 | 439.586 | 456.694 | 489.763 | 260.331 | 269.477 | 287.586 |
| 30 | 375.245 | 388.996 | 415.646 | 258.815 | 267.726 | 287.194 |
| 35 | 345.770 | 357.629 | 380.706 | 257.898 | 267.085 | 284.771 |
| 40 | 327.691 | 338.589 | 360.184 | 256.763 | 265.778 | 283.790 |
| 50 | 306.928 | 317.389 | 337.764 | 255.648 | 264.475 | 282.015 |
| 75 | 284.697 | 294.300 | 312.812 | 254.536 | 263.070 | 279.643 |
| 100 | 275.569 | 284.881 | 302.935 | 254.091 | 262.666 | 279.355 |
| 125 | 270.313 | 279.169 | 296.581 | 253.392 | 261.914 | 278.743 |
| 150 | 266.792 | 275.679 | 292.738 | 253.124 | 261.774 | 277.989 |
| 200 | 262.866 | 271.316 | 288.614 | 252.587 | 260.956 | 277.771 |
| ∞ | 251.517 | 259.914 | 276.159 | 251.517 | 259.914 | 276.159 |

| \it{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{\rm RST}(90)$ | $Q_{\rm RST}(95)$ | $Q_{\rm RST}(99)$ |
|----------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| $\overline{4}$ | | | | 644.667 | 664.529 | 707.946 |
| 5 | | | | 608.276 | 626.401 | 665.933 |
| 6 | | | | 587.009 | 604.763 | 640.058 |
| 8 | | | | 562.278 | 577.856 | 612.186 |
| 10 | | | | 547.768 | 562.611 | 594.212 |
| 12 | | | | 538.109 | 552.198 | 582.809 |
| 15 | | | | 529.319 | 543.350 | 572.790 |
| 20 | | | | 521.311 | 534.671 | 561.423 |
| 25 | | | | 516.178 | 529.025 | 554.500 |
| 30 | | | | 513.238 | 525.937 | 551.812 |
| 35 | 854.716 | 877.584 | 923.150 | 510.528 | 523.092 | 548.606 |
| 40 | 756.593 | 774.862 | 811.536 | 508.731 | 521.305 | 545.550 |
| 50 | 670.511 | 86.437 | 717.042 | 506.644 | 519.276 | 542.509 |
| 75 | 594.103 | 607.839 | 635.022 | 503.483 | 516.007 | 539.454 |
| 100 | 564.821 | 578.598 | 604.252 | 501.898 | 514.261 | 537.148 |
| 125 | 548.963 | 562.197 | 587.149 | 501.093 | 512.856 | 536.589 |
| 150 | 539.778 | 552.828 | 576.845 | 501.004 | 512.910 | 535.901 |
| 200 | 528.065 | 540.549 | 563.514 | 499.988 | 512.262 | 534.177 |
| ∞ | 497.190 | 508.893 | 531.335 | 497.190 | 508.893 | 531.335 |

Table 15: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p = 10$, $q = 3$ and different values of n

Table 16: Empirical 90th, 95th and 99th percentiles of the null distribution of LRT and RST statistics based on 50,000 simulations for $p = 15$, $q = 3$ and different values of n

| \it{n} | $Q_{\rm LRT}(90)$ | $Q_{\rm LRT}(95)$ | $Q_{\rm LRT}(99)$ | $Q_{RST}(90)$ | $Q_{RST}(95)$ | $Q_{RST}(99)$ |
|----------|-------------------|-------------------|--------------------------|---------------|---------------|---------------|
| 4 | | | | 1425.043 | 1457.008 | 1524.644 |
| $\bf 5$ | | | | 1343.057 | 1370.775 | 1433.269 |
| 6 | | | | 1293.202 | 1319.587 | 1378.464 |
| 8 | | | | 1234.561 | 1258.438 | 1309.237 |
| 10 | | | | 1201.916 | 1224.987 | 1272.263 |
| 12 | | | | 1181.405 | 1202.980 | 1248.336 |
| 15 | | | | 1160.459 | 1180.732 | 1223.385 |
| 20 | | | | 1141.643 | 1161.045 | 1199.219 |
| 25 | | | | 1129.622 | 1149.006 | 1186.455 |
| 30 | | | $\overline{}$ | 1122.381 | 1141.361 | 1180.518 |
| 35 | | | | 1117.097 | 1135.311 | 1172.995 |
| 40 | | | | 1113.225 | 1130.898 | 1167.173 |
| 50 | 1922.299 | 1957.103 | 2026.640 | 1107.674 | 1125.905 | 1161.561 |
| 75 | 1445.463 | 1468.783 | 1514.400 | 1100.529 | 1118.660 | 1152.947 |
| 100 | 1321.733 | 1342.645 | 1383.925 | 1097.170 | 1115.496 | 1148.483 |
| 125 | 1262.594 | 1282.593 | 1319.962 | 1095.268 | 1112.801 | 1146.797 |
| 150 | 1227.295 | 1246.608 | 1283.002 | 1093.888 | 1111.188 | 1143.588 |
| 200 | 1186.980 | 1205.457 | 1242.884 | 1091.553 | 1109.649 | 1143.251 |
| ∞ | 1086.521 | 1103.702 | 1136.416 | 1086.521 | 1103.702 | 1136.416 |

References

[1] Anderson, T.W., 2003. An Introduction to Multivariate Statistical Analysis (3rd Ed.). New Jersey: Wiley.

- [2] Boik, J.B., 1991. Scheffe's mixed model for multivariate repeated measures: A relative efficiency evaluation. Comm. Statist. Theory Methods 20, 1233–1255.
- [3] Chaganty, N.R., Naik, D.N., 2002. Analysis of multivariate longitudinal data using quasi-least squares. J. Statist. Plann. Inference 103, 421–436.
- [4] Crowder, M.J., Hand, D.J., 1990. Analysis of Repeated Measures (Monographs on Statistics & Applied Probability). Boca Raton, Florida: Chapman & Hall/CRC.
- [5] Dutilleul, P., 1999. The MLE algorithm for the matrix normal distribution. J. Stat. Comput. Simul. 64, 105–123.
- [6] Engle, R., 1984. Wald, likelihood ratio, and Lagrange multiplier tests in econometrics. In: Engle, R. and Intriligator, M.D. (Eds.), *Handbook of Econometrics*, Vol. II. North Holland, Amsterdam.
- [7] Galecki, A.T., 1994. General class of covariance structures for two or more repeated factors in longitudinal data analysis. Comm. Statist. Theory Methods 22, 3105–3120.
- [8] Genton, M.G., 2007. Separable approximations of space-time covariance matrices, Environmetrics 18, 681–695.
- [9] Ghazal, A.G., Neudecker, H., 2000. On second-order and fourth-order moments of jointly distributed random matrices: a survey. Linear Algebra Appl. 321, 61–93.
- [10] Johnson, R.A., Wichern, D.W., 2007. Applied Multivariate Statistical Analysis (6th Ed.). New Jersey: Pearson Prentice Hall.
- [11] Jones, R.H. 1993. Longitudinal Data with Serial Correlation: A State-Space Approach. London: Chapman Hall.
- [12] Kollo, T., von Rosen, D., 2005. Advanced Multivariate Statistics with Matrices. Dordrecht: Springer.
- [13] Korin, B.P., 1968. On the distribution of a statistics used for testing a covariance matrix. Biometrika 55, 171–178.
- [14] Lee, C.H., Dutilleul, P., Roy, A., 2010. Comment on "Models with a Kronecker product covariance structure: estimation and testing" by M. S. Srivastava, T. von Rosen and D. von Rosen. Math. Methods of Statist. 19, 88–90.
- [15] Lehmann, E.L., Romano, J.P., 2005. Testing Statistical Hypotheses (3rd Ed.). New York, USA: Springer.
- [16] Leiva, R., Roy, A., 2011. Linear discrimination for multi-level multivariate data with separable means and jointly equicorrelated covariance structure. J. Statist. Plann. Inference 141, 1910– 1924.
- [17] Lu, N., Zimmerman, D., 2005. The likelihood ratio test for a separable covariance matrix. Statist. Probab. Lett. 73, 449–457.
- [18] Magnus, J., Neudecker, H., 1986. Symmetry, 0-1 matrices and Jacobians, a review. Econom. Theory 2, 157–190.
- [19] Manceur, A.M., and Dutilleul, P., 2013. Unbiased modified likelihood ratio tests for simple and double separability of a variance-covariance structure. *Statist. Probab. Lett.* 83, 631–636.
- [20] Mitchell, M., Genton, M., Gumpertz, M., 2006. A likelihood ratio test for separability of covariances. J. Multivariate Anal. 97, 1025–1043.
- [21] Naik, D.N., Rao, S.S., 2001. Analysis of multivariate repeated measures data with a Kronecker product structured covariance matrix. J. Appl. Stat. 28, 91–105.
- [22] Pinto Pereira, S.M., McCormack, V.A., Moss, S.M., dos Santos, S.I. 2009. The spatial distribution of radiodense breast tissue: a longitudinal study. Breast Cancer Res. 11:R33R44.
- [23] Rao, C.R., 1948. Large sample tests of statistical hypotheses concerning several parameters with applications to problems of estimation. *Math. Proc. Cambridge Philos. Soc.* 44, 50–57.
- [24] Rao, C.R., 1984. Linear Statistical Inference and its Applications (2nd Ed.). New Delhi: Wiley Easrtern Ltd.
- [25] Rao, C.R., 2005. Score test: Historical review and recent developments. Advances in Ranking and Selection, Multiple Comparisons, and Reliability, 3–20.
- [26] Rizzo, M., 2008. Statistical Computing With R. Chapman & Hall/CRC.
- [27] Roy, A., Khattree, R., 2003. Tests for mean and covariance structures relevant in repeated measures based discriminant analysis. J. Appl. Statist. Sci. 12, 91–104.
- [28] Roy, A., Khattree, R., 2005a. On implementation of a test for Kronecker product covariance structure for multivariate repeated measures data. Stat. Methodol. 2, 297–306.
- [29] Roy, A., Khattree, R., 2005b. Testing the hypothesis of a Kroneckar product covariance matrix in multivariate repeated measures data. Proceedings of the 30th Annual SAS Users Group International Conference (SUGI 30), Philadelphia.
- [30] Roy, A., Khattree, R., 2007a. Classification of multivariate repeated measures data with temporal autocorrelation. J. Appl. Statist. Sci. 15, 283–294.
- [31] Roy, A., Khattree, R., 2007b. Classification rules for repeated measures data from biomedical research. In: Khattree, R. and Naik, D. N. (Eds.), Computational Methods in Biomedical Research, 323–370.
- [32] Roy, A., 2007. A note on testing of Kronecker product covariance structures for doubly multivariate data. Proc. Amer. Statist. Assoc., Statistical Computing Section, 2157–2162.
- [33] Roy, A., Leiva, R., 2008. Likelihood ratio tests for triply multivariate data with structured correlation on spatial repeated measurements. Statist. Probab. Lett. 78, 1971–1980.
- [34] SAS Institute Inc. 2009. SAS/STAT User's Guide Version 9.3, Cary, NC: SAS Institute Inc.
- [35] Self, S.G., Liang, K., 1987. Asymptotic properties of maximum likelihood estimators and likelihood ratio tests under nonstandard conditions. J. Amer. Statist. Assoc. 82, 605–610.
- [36] Simpson, S.L., 2010. An adjusted likelihood ratio test for separability in unbalanced multivariate repeated measures data. Stat. Methodol. 7, 511–519.
- [37] Simpson, S.L., Edwards, L.J., Muller, K.E., Styner, M.A., 2014. Separability Tests for High-Dimensional, Low Sample Size Multivariate Repeated Measures Data. Journal of Applied Stat. DOI: 10.1080/02664763.2014.919251.
- [38] Srivastava, M., von Rosen, T., von Rosen, D., 2008. Models with a Kronecker product covariance structure: Estimation and testing. Math. Methods of Statist. 17, 357–370.
- [39] Terrell, G.R., 2002. The gradient statistic. Computing Science and Statistics 34, 206–215.
- [40] Thompson, G.L., 1991. A unified approach to rank tests for multivariate and repeated measures designs. J. Amer. Statist. Assoc. 86, 410–419.
- [41] Timm, N.H., 1980. Multivariate analysis of variance of repeated measurements. In: Krishnaiah, P. R. (Ed.), Handbook of Statistics, Vol. 1, North-Holland, 41–87.
- [42] Wald, A., 1943. Tests of statistical hypotheses concerning several parameters when the number of observations is large. Trans. Amer. Math. Soc. 5, 426–482.
- [43] Werner, K., Jansson, M., Stoica, P., 2008. On estimation of covariance matrices with Kronecker product structure. IEEE Trans. Signal Process. 56, 478–491.
- [44] Wilks, S., 1938. The large sample distribution of the likelihood ratio for testing composite hypotheses. Ann. Math. Statist. 9, 60–62.
- [45] Worsley, K.J., Evans, A.C., Strother, S.C., Tyler, J.L., 1991. A linear spatial correlation model, with applications to positron emission tomography. Journal of the American Statistical Association 86 (413), 55-67.