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Estimating common vector parameters in interlaboratory studies

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Abstract

The primary goal of this work is to extend two methods of random effects models to multiparameter situation. These methods comprise the DerSimonian–Laird estimator, stemming from meta-analysis, and the Mandel–Paule algorithm widely used in interlaboratory studies. The maximum likelihood estimators are also discussed. Two methods of assessing the uncertainty of these estimators are given.

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1. Introduction and summary

Statistical modeling and analysis of collaborative studies pose several fundamental questions about determination of the consensus (reference) value and its associated uncertainty. An appropriate choice of stochastic model can be especially difficult especially when measurements are made across a range of values of a physical characteristic, i.e. the reference value is a curve or a multivariate vector. Hedges and Olkin\cite{7} discuss several methods for combining data from several experiments which form the heart of the meta-analysis. In particular, in Chapter 10 these

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authors discuss multivariate models for effect size when observations from experimental and control group are available.

Multivariate data sets occur increasingly often in applications in interlaboratory metrological studies known as Key Comparisons when one has to determine the key comparison reference value (KCRV), i.e. the consensus vector mean. In this paper, statistical procedures are derived for consensus vector evaluation (a discretized version of possibly irregular underlying curve) along with estimates of the uncertainty of this value. An approach in spirit of meta-analysis for interlaboratory data is proposed when participating laboratories exhibit different accuracy. This model for Gaussian distributions leads to a class of matrix-weighted vector statistics to estimate the common vector mean and to a method of assessing the uncertainty of these estimates. In Section 2, maximum likelihood estimators are reviewed including the restricted maximum likelihood estimator. Since these estimators do not admit explicit form, and the likelihood equations may have several roots, we suggest to employ in practical situations simpler procedures, scalar versions of which are widely used in biological and physical applications and which deserve more attention from statistical community. These scalar procedures are the DerSimonian–Laird estimator and the Mandel–Paule algorithm. Their method of moments origin and their relationship to the maximum likelihood estimator and to the restricted maximum likelihood estimator are discussed in Section 3.

We investigate the estimation problem of the covariance matrix of these procedures in Section 4 where approximate confidence ellipsoids are constructed. Section 5 contains results of Monte-Carlo simulation study and answers for motivating examples for this study. One of these examples is the Key Comparisons of accelerometers (CCAUV V-K1) [11] which was organized to compare measurements of sinusoidal linear accelerometers over the range of frequencies from 40 Hz to 5 kHz. It was the first such study in the field of vibration and shock with the task of measuring the charge sensitivity of two accelerometers standards (we report results only for single-ended design accelerometer). Each of the 12 participating National Metrology Institutes measured charge sensitivity at the specified frequencies by employing two transfer standard accelerometers under agreed physical conditions. The common charge sensitivity and its uncertainty was one of the goals of the study. The participating institutes reported their means and the sample covariance matrices for the frequencies in this range. We suggest two methods for estimating the reference value for charge sensitivity as a function of frequency and give confidence ellipsoids. In the original study this value is found separately for each type of accelerometer and for each specified frequency.

Another example is the study of Pyroceram 9606, a glass ceramic material especially suited for high temperature applications. This material is being used for performance evaluation of instruments measuring thermal properties such as thermal conductivity, thermal diffusivity, and specific heat (heat capacity). All these characteristics are temperature dependent, so the reference value must be a function of temperature. Twenty-eight thermal conductivity experiments in different countries have been performed on this material, and a consensus value for diffusivity and heat was needed. We have used unpublished data (participating laboratories results were of widely differing quality) kindly provided by J. Filliben and R. Zarr (National Institute of Standards and Technology).

2. The matrix formulation of the model and likelihood equations

In accordance with the goals discussed in Section 1 we formulate the following mathematical model in the situation where multiple (correlated) $q$-dimensional measurements are made by each of $p$ laboratories. In our model, the $i$th laboratory repeats its vector measurements $n_i (> q)$ times,
and the vector data $X_{ij}$ for $i = 1, \ldots, p$ and $j = 1, \ldots, n_i$ follow a one-way random effects MANOVA model, which may be both unbalanced and heteroscedastic, i.e.

$$X_{ij} = \theta + \ell_i + \epsilon_{ij}, \quad (1)$$

with mutually independent $\ell_i \sim N_q(0, \Xi)$ and $\epsilon_{ij} \sim N_q(0, \Delta_i)$, $j = 1, \ldots, n_i$. The vector $\theta$ plays the role of the common mean or the reference value, $\ell_i$ is the between-laboratories effect, and the $\epsilon$’s are the measurement errors. The unknown $q \times q$ matrix $\Xi$ may have rank smaller than $q$; $\theta$ represents an unknown $q$-dimensional parameter common to all laboratories. The goal is to estimate the structural parametric vector $\theta$, and to provide a standard error for this estimate. The covariance matrices $\Delta_i$ and $\Xi$ are nuisance parameters.

In matrix notation this model can be written as a particular case of the general linear model

$$y = T\theta + \ell + e.$$ 

Here $y$ is the total data vector of dimension $n = q(n_1 + \cdots + n_p)$; $T$ is a matrix of size $n \times q$ formed by $q \times q$ identity matrices written as a column; and $n$-dimensional vector $\ell$ is formed by stacked $n_i$ copies of $\ell_i$, $i = 1, \ldots, p$. Thus $\theta$ is the unknown parameter (fixed effects) vector, and $(\ell_1, \ldots, \ell_p)^T$ is random effect vector uncorrelated with the errors vector $e$.

The usual estimators of the laboratory means and of their covariance matrices are $X_i = \bar{X}_i = \frac{\sum_j X_{ij}}{n_i}$, and $S_i = \sum_j (X_{ij} - \bar{X}_i)(X_{ij} - \bar{X}_i)^T / [v_i n_i], v_i = n_i - 1$, with $X_i$, $S_i$, $i = 1, \ldots, p$, being (incomplete) sufficient statistics. Reduction by sufficiency to the sample means $\bar{X}_i$ and the sample covariance matrices $S_i$ makes this problem more specific. The model (1) leads to the following model for $X_i$,

$$X_i = \theta + \ell_i + \epsilon_i. \quad (2)$$

Under the above assumptions, $\ell_i \sim N(0, \Xi)$, $\epsilon_i \sim N(0, \Sigma_i = \Delta_i / n_i)$, with $\ell_i$ and $\epsilon_i$ being independent. Then, clearly,

$$\text{Var}(X_i) = \Xi + \Sigma_i.$$ 

The multiples of the sample covariance matrices, $v_i S_i$, are known to have a Wishart distribution $W_q(v_i, \Sigma_i)$.

2.1. The maximum likelihood estimators

The loglikelihood function $\ell$ for $X_i$ and $S_i$ can be written as

$$-2\ell = \sum_i \left[ (X_i - \theta)^T (\Sigma_i + \Xi)^{-1} (X_i - \theta) + \log |\Sigma_i + \Xi| \right]$$

$$+ \sum_i v_i [\text{tr}(S_i \Sigma_i^{-1}) + \log |\Sigma_i|].$$

The maximum likelihood estimator of $\theta$ has the form

$$\hat{\theta} = \sum_{i=1}^p \hat{\omega}_i X_i,$$

where the matrix weights have the form

$$\hat{\omega}_i = \left[ \sum_j (\hat{\Sigma}_j + \hat{\Xi})^{-1} \right]^{-1} (\hat{\Sigma}_i + \hat{\Xi})^{-1},$$

and $\hat{\Sigma}_i$ and $\hat{\Xi}$ are found as maximizers of $\ell$. When $q = 1$, this estimator was studied in [1,13,15].
The likelihood equations for $\Sigma_i$ and $\Xi$ are

$$
(\hat{\Sigma}_i + \hat{\Xi})^{-1} \left[ \mathbf{I} - (X_i - \hat{\theta})(X_i - \hat{\theta})^T (\hat{\Sigma}_i + \hat{\Xi})^{-1} \right] + v_i \hat{\Sigma}_i^{-1} \left( \mathbf{I} - S_i \hat{\Sigma}_i^{-1} \right) = 0
$$

(3)

and

$$
\sum_i \left[ (\hat{\Sigma}_i + \hat{\Xi})^{-1} (X_i - \theta)(X_i - \theta)^T (\hat{\Sigma}_i + \hat{\Xi})^{-1} - (\hat{\Sigma}_i + \hat{\Xi})^{-1} \right] = 0.
$$

(4)

Here and further $\mathbf{I}$ denotes the identity matrix whose dimension is clear from the context.

It follows that

$$
\sum_i v_i \hat{\Sigma}_i^{-1} \left( \mathbf{I} - S_i \hat{\Sigma}_i^{-1} \right) = 0.
$$

It is practical to determine the maximum likelihood estimators of $\theta$, $\Sigma_i$’s for fixed $\Xi = \mathbf{Y}$. Thus, if for non-negative definite matrix $\mathbf{Y}$

$$
F(\mathbf{Y}) = \min_{\theta, (\Sigma_i)} \sum_i \left[ (X_i - \theta)^T (\Sigma_i + \mathbf{Y})^{-1} (X_i - \theta) + \log |\Sigma_i + \mathbf{Y}| \right.
$$

$$
+ \left. v_i (\text{tr}(S_i \Sigma_i^{-1}) + \log |\Sigma_i|) \right],
$$

then the maximum likelihood estimator of $\Xi$ is $\arg \min F(\mathbf{Y})$.

The minimizers $\hat{\theta}(\mathbf{Y})$ and $\hat{\Sigma}_i(\mathbf{Y})$ can be determined from (3). An iterative scheme for solving (3) for fixed $i$ and $\hat{\theta}$,

$$
\Sigma_i^{(k+1)} = [v_i \mathbf{I} + B_k]^{-1} [v_i S_i + B_k (X_i - \hat{\theta})(X_i - \hat{\theta})^T B_k^T], \quad k = 0, 1, \ldots
$$

with $B_k = \Sigma_i^{(k)} \left[ \mathbf{I} + \Sigma_i^{(k)} \right]^{-1}$, converges fast. Eq. (4) shows that

$$
F'(\mathbf{Y}) = \sum_i v_i \left[ \hat{\Sigma}_i^{-1}(\mathbf{Y}) S_i \hat{\Sigma}_i^{-1}(\mathbf{Y}) - \hat{\Sigma}_i^{-1}(\mathbf{Y}) \right],
$$

so that for any non-negative definite matrix $\mathbf{Y}_0$,

$$
F(\mathbf{Y}) = F(\mathbf{Y}_0) + \text{tr}(F'(\mathbf{Y}_0)(\mathbf{Y} - \mathbf{Y}_0)) + O(\|\mathbf{Y} - \mathbf{Y}_0\|^2).
$$

The Hessian of $F$ can be found from (3), but it has a complicated form. The constrained optimization problem (the matrix $\mathbf{Y}$ must be non-negative definite) is rather awkward. For these reasons, it is much more convenient to solve unconstrained optimization problems in $q \times r$-dimensional matrix $\mathbf{Z}$, $r = 1, \ldots, q$ of rank $r$ with $\mathbf{Y} = Z^T Z$.

If $\mathbf{Y} - \mathbf{Y}_0 = V^T \mathbf{V}$, then

$$
(\hat{\Sigma}_i + \mathbf{Y})^{-1} = (\hat{\Sigma}_i + \mathbf{Y}_0)^{-1} - (\hat{\Sigma}_i + \mathbf{Y}_0)^{-1} V \left[ \mathbf{I} + V^T (\hat{\Sigma}_i + \mathbf{Y}_0)^{-1} V \right]^{-1} V^T (\hat{\Sigma}_i + \mathbf{Y}_0)^{-1},
$$

and

$$
|\hat{\Sigma}_i + \mathbf{Y}| = |\hat{\Sigma}_i + \mathbf{Y}_0| \times |\mathbf{I} + V^T (\hat{\Sigma}_i + \mathbf{Y}_0)^{-1} V|.
$$
Therefore,

\[ F(Y) \leq F(Y_0) - \sum_i \left[ (X_i - \hat{\theta})^T (\hat{\Sigma}_i + Y_0)^{-1} V \left[ I + V^T (\hat{\Sigma}_i + Y_0)^{-1} V \right]^{-1} \right. \]
\[ \times \left. V^T (\hat{\Sigma}_i + Y_0)^{-1} (X_i - \hat{\theta}) - \log |I + V^T (\hat{\Sigma}_i + Y_0)^{-1} V| \right], \]

where \( \hat{\Sigma}_i = \hat{\Sigma}_i(Y_0) \), and \( \hat{\theta} = \hat{\theta}(Y_0) \). Therefore, one can construct a recursive sequence \( Z_{k+1} = Z_k + t_k P_k, k = 0, 1, \ldots \) for \( Y_k = Z_k^T Z_k \), in which the search directions \( U_k \) are taken to be the eigenvectors of \( F'(Y_k) \) corresponding to negative eigenvalues and positive step sizes \( t_k \) are chosen as to minimize

\[ \sum_i \left[ \log |I + t^2 U_k^T (\hat{\Sigma}_i + Y_0)^{-1} U_k| - t^2 (X_i - \hat{\theta})^T (\hat{\Sigma}_i + Y_0)^{-1} \right. \]
\[ \times \left. U_k [I + t^2 U_k^T (\hat{\Sigma}_i + Y_0)^{-1} U_k]^{-1} U_k^T (\hat{\Sigma}_i + Y_0)^{-1} (X_i - \hat{\theta}) \right]. \]

Then, provided this minimum is attained at a positive \( t_k \), \( F(Z_{k+1}^T Z_{k+1}) \leq F(Z_k^T Z_k) = F(Y_k) \).

The estimator of \( \text{Var}(\hat{\theta}) \) is usually obtained from the inverse of the observed Fisher information,

\[ \hat{\text{Var}}(\hat{\theta}) = \left[ \sum_j (\hat{\Sigma}_j + \hat{\Xi}) \right]^{-1}. \] (5)

Sometimes the likelihood equations are solved via the EM-Algorithm in which the \( \ell_i \) are interpreted as missing observations (see [14, Chapter 8]). This method works well when \( \Sigma_i \) do not depend on \( i \), but for different \( \Sigma_i \)'s leads to fairly cumbersome equations even when \( q = 1 \). Besides the recursive sequence obtained by this method is guaranteed to converge only to one of local maximums. The likelihood function may not be unimodal, i.e. can have several local extrema, so that all iterative algorithms are sensitive to the initial value. The estimator of \( Y \) discussed in Section 3.1 provides a good choice for this value.

In variance component problems the restricted maximum loglikelihood estimator is commonly recommended. To obtain the form of the restricted function, one can use the expression obtained in [5, p. 325]. It is based on the matrix formulation of the model (1) given in Section 2. The covariance matrix \( V \) of \( \ell + e \) is block-diagonal with \( n_i q \times n_i q \) blocks formed by sums of diagonal blocks determined by the matrix \( \Delta_i \) and blocks formed by \( \Xi \). Therefore, \( V_i^{-1} \) has a similar form with the diagonal blocks \( \Delta_i^{-1} \) and the off-diagonal entries \( -\Delta_i^{-1} \Xi (I + n_i \Delta_i^{-1}) \Xi \Delta_i^{-1} \). Also \( |V| = \prod_{i=1}^p |\Sigma_i|^{(n_i-1)|n_i \Xi + \Delta_i|} \).

Thus the restricted loglikelihood function \( \ell_R \) in the variance parameters \( \Sigma_i \) and \( \Xi \) is to within an additive constant,

\[-2 \ell_R = \sum_i \left[ (X_i - \hat{\theta})^T (\Sigma_i + \Xi)^{-1} (X_i - \hat{\theta}) + \log |\Sigma_i + \Xi| \right] \]
\[+ \log \left| \sum_i (\Sigma_i + \Xi)^{-1} \right| + \sum_i \nu_i \left[ \text{tr}(S_i \Sigma_i^{-1}) + \log |\Sigma_i| \right]. \] (6)

We will use (6) later in Section 3.2.
3. Weighted means statistics

Because of complicated nature of the maximum likelihood estimator, simpler procedures are desired. Even without normality assumption when the within-trials and between-trials covariance matrices \( \Sigma_i \) and \( \Xi \) are known, the least-squares estimator of the parameter \( \theta \) in the model (1) is a weighted means statistic \( \tilde{X} \). Let \( W_i = [\text{Var}(X_i)]^{-1} = (\Sigma_i + \Xi)^{-1} \) and \( W = \sum_{i=1}^{p} W_i \). Then \( \tilde{X} \) is found from the following equation,

\[
W \tilde{X} = \sum_{i=1}^{p} W_i X_i.
\]  

(7)

It makes sense to employ the available statistics \( S_i \) to approximate the within-trials covariance matrices \( \Sigma_i \). In other terms we restrict the class of estimators (7) to those with matrix weights of the form

\[
W_i = W_i(Y) = (S_i + Y)^{-1}
\]

for some non-negative definite matrix \( Y \). If \( W^- = [\sum_{i=1}^{p} W_i(Y)]^- \), denotes a generalized inverse of \( \sum_{i=1}^{p} W_i \), then an estimator \( \tilde{X} \) of \( \theta \) from this class has the following representation,

\[
\tilde{X} = \tilde{X}Y = W^- \sum_{i=1}^{p} W_i X_i = \sum_{i=1}^{p} \omega_i X_i.
\]  

(9)

Estimators of the form (9) are of interest. They include the analog of one of the traditional estimators of the common vector mean suggested by Graybill and Deal [4] in the case \( q = 1 \),

\[
\tilde{X}_0 = \left[ \sum_{i=1}^{p} S_i^{-1} \right]^{-1} \sum_{i=1}^{p} S_i^{-1} X_i,
\]  

(10)

and the sample mean,

\[
\tilde{X}_\infty = \frac{1}{p} \sum_{i=1}^{p} X_i.
\]

Sometimes the within-laboratories variances \( \Sigma_i \) can be assumed to be known (in practice they are taken to be \( S_i \)). The maximum likelihood estimator \( \tilde{X}_{\text{SM}} \) of \( \theta \) also is a weighted means statistic (9) with the weights of the form (8), where \( Y = Y_{\text{SM}} \) is the minimizer in \( Y \) of the negative loglikelihood function,

\[
\sum_{i=1}^{p} \left[ (X_i - \tilde{X})^T (Y + S_i)^{-1} (X_i - \tilde{X}) + \log |Y + S_i| \right].
\]  

(11)

The resulting likelihood equation,

\[
\sum_{i=1}^{p} \left[ (Y + S_i)^{-1} (X_i - \tilde{X})(X_i - \tilde{X})^T (Y + S_i)^{-1} - (Y + S_i)^{-1} \right] = 0,
\]

can be solved iteratively.

In the sequel we give two simpler methods of choosing the matrix \( Y \).
3.1. DerSimonian–Laird procedure

If the matrix weights \( W_i \) are arbitrary, but the matrix \( W \) is non-singular, then for \( \tilde{X} \) defined by (7),

\[
\sum_i W_i^{1/2} E(X_i - \tilde{X})(X_i - \tilde{X})^T W_i^{1/2} = \sum_{i=1}^{p} W_i^{1/2} \left( I - W^{-1} W_i \right) \text{Var}(X_i) \left( I - W^{-1} W_i \right)^T W_i^{1/2} + \sum_{i=1}^{p} W_i^{1/2} W^{-1} \left( \sum_{k,k\neq i} W_k \text{Var}(X_k) W_k \right) W^{-1} W_i^{1/2}.
\]

In particular, when \( W_i = \Sigma_i^{-1} \), \( \text{Var}(X_i) = \Sigma_i + \Xi \),

\[
\sum_i \Sigma_i^{-1/2} \left( I - W^{-1} \Sigma_i^{-1} \right) \Xi \left( I - W^{-1} \Sigma_i^{-1} \right)^T \Sigma_i^{-1/2} + \sum_i \Sigma_i^{-1/2} W^{-1} \left( \sum_{k,k\neq i} \Sigma_k^{-1}\Xi \Sigma_k^{-1} \right) W^{-1} \Sigma_i^{-1/2} = \sum_i \Sigma_i^{-1/2} E(X_i - \tilde{X})(X_i - \tilde{X})^T \Sigma_i^{-1/2} - pI + \sum_i \Sigma_i^{-1/2} W^{-1} \Sigma_i^{-1/2}.
\]

We suggest to use (13) as an estimating equation for the parameters \( \theta \) and \( \Xi \) in the following way (provided that \( \Sigma_i \) are replaced by \( S_i \)). Let \( \tilde{X}_0 \) be the Graybill–Deal estimator (10). Put

\[
\mathbf{B} = \sum_i S_i^{-1/2} (X_i - \tilde{X}_0)(X_i - \tilde{X}_0)^T S_i^{-1/2} - pI + \sum_i S_i^{-1/2} \left( \sum_k S_k^{-1} \right)^{-1} S_i^{-1/2},
\]

so that (symmetric) \( \mathbf{B} \) estimates the right-hand side of (13). With \( \tilde{\omega}_i = [\sum_{j=1}^{p} S_j^{-1}]^{-1} S_i^{-1} \), determine a symmetric matrix \( Y \) from the equation

\[
\sum_i S_i^{-1/2} (I - \tilde{\omega}_i) Y (I - \tilde{\omega}_i)^T S_i^{-1/2} + \sum_i S_i^{-1/2} \left( \sum_{j:j\neq i} \tilde{\omega}_j Y \tilde{\omega}_j^T \right) S_i^{-1/2} = \mathbf{B}.
\]

Take \( Y_{DL} = Y_+ \) to be the positive part of \( Y \), i.e. let \( Y_{DL} \) have the same spectral decomposition as \( Y \), with eigenvalues being positive parts of these of \( Y \). The matrix weights of the estimator \( \tilde{X}_{DL} \) then are

\[
W_i = (Y_{DL} + S_i)^{-1}.
\]

Eq. (14) extends the procedure suggested by DerSimonian and Laird [3] when \( q = 1 \), which is an immensely popular method in biostatistics especially in analysis of multicenter clinical trials. In fact, the number of references to the paper by DerSimonian and Laird exceeds 1500. This popularity is due mainly to the fact that this is a simple non-iterative procedure, which admits an approximate formula for the variance of the resulting estimator.

To solve (14), denote by \( \text{Vec}(A) \) the \( q^2 \times 1 \) vector formed by stacking the columns of the \( q \times q \) matrix \( A \) under each other, and by \( A \bigotimes B \) the tensor (Kronecker) product of matrices \( A \) and \( B \).
Then, according to Lemma 16.1.2 and Theorem 16.2.1 in [6]
\[
\text{Vec} \left( S_i^{-1/2} (I - \tilde{\omega}_i) Y (I - \tilde{\omega}_i) \right) = \left[ S_i^{-1/2} (I - \tilde{\omega}_i) \bigotimes S_i^{-1/2} (I - \tilde{\omega}_i) \right] \text{Vec}(Y),
\]
and
\[
\text{Vec} \left( \sum_i S_i^{-1/2} \left( \sum_{j: j \neq i} \tilde{\omega}_j Y \tilde{\omega}_j^T \right) S_i^{-1/2} \right) = \left( \sum_{i \neq j} S_i^{-1/2} \tilde{\omega}_j \bigotimes S_i^{-1/2} \tilde{\omega}_j \right) \text{Vec}(Y).
\]
Thus, the vectorized version of (14) holds when
\[
\left[ \sum_i S_i^{-1/2} (I - \tilde{\omega}_i) \bigotimes S_i^{-1/2} (I - \tilde{\omega}_i) + \sum_{i \neq j} S_i^{-1/2} \tilde{\omega}_j \bigotimes S_i^{-1/2} \tilde{\omega}_j \right] \text{Vec}(Y) = \text{Vec}(B).
\]
Assuming that the needed matrix is invertible, one obtains the formula for \( Y \),
\[
\text{Vec}(Y) = \left[ \sum_{i,j} S_i^{-1/2} \tilde{\omega}_j \bigotimes S_i^{-1/2} \tilde{\omega}_j + \sum_i S_i^{-1/2} \bigotimes S_i^{-1/2} - \sum_i S_i^{-1/2} \bigotimes S_i^{-1/2} \right]^{-1} \text{Vec}(B).
\]
Eq. (14) can be solved by using matrices of smaller size. Denote by \( \text{Vech}(A) \) the \( q(q + 1)/2 \times 1 \) vector formed by stacking the subdiagonal elements of a \( q \times q \) matrix \( A \) under each other, \( \text{Vech}(A) = (a_{11}, a_{21}, \ldots, a_{q1}, a_{22}, \ldots, a_{q2}, \ldots, a_{qq})^T \). Then for every symmetric matrix \( A \), \( \text{Vec}(A) = G_q \text{Vech}(A) \), with the duplicating matrix \( G_q \) of size \( q^2 \times q(q + 1)/2 \) (see [5, Section 16.4] or [9, Section 3.8]). If \( H_q \) is a left inverse of \( G_q \), (14) means that
\[
H_q \left[ \sum_i S_i^{-1/2} (I - \tilde{\omega}_i) \bigotimes S_i^{-1/2} (I - \tilde{\omega}_i) + \sum_{i \neq j} S_i^{-1/2} \tilde{\omega}_j \bigotimes S_i^{-1/2} \tilde{\omega}_j \right] = \text{Vech}(B),
\]
and \( \text{Vech}(Y) \) can be obtained from this equation.

3.2. The Mandel–Paule procedure

When \( q = 1 \), an easily implementable method for estimating the common mean was suggested by Mandel and Paule [10]. The goal here is to extend this algorithm to the vector situation.

Even without the normality assumption, (12) implies that for the optimal weights, \( W_i = [\text{Var}(X_i)]^{-1} \),
\[
E \sum_i [\text{Var}(X_i)]^{-1/2} (X_i - \bar{X})(X_i - \bar{X})^T [\text{Var}(X_i)]^{-1/2} = pI - \sum_i [\text{Var}(X_i)]^{-1/2} W^{-1} [\text{Var}(X_i)]^{-1/2}.
\]

(17)
As in Section 3.1, the identity (17) can be used as the estimating equation for \( \theta \) and \( \Xi \), provided that \( \Sigma_i \) are estimated by \( S_i \). The suggestion here is to choose \( Y \), which is designed to estimate \( \Xi \), as an (approximate) solution of the matrix equation,

\[
\sum_i (S_i + Y)^{-1/2}(X_i - \bar{X})(X_i - \bar{X})^T (S_i + Y)^{-1/2} + \sum_i (S_i + Y)^{-1/2} \left[ \sum_k (S_k + Y)^{-1} \right]^{-1} (S_i + Y)^{-1/2} = pI. \tag{18}
\]

Notice that (18) implies that

\[
\text{tr} \left( \sum_i (X_i - \bar{X})^T (S_i + Y)^{-1}(X_i - \bar{X}) \right) = (p - 1)q,
\]

and for \( q = 1 \) the second sum in the left-hand side of (18) reduces to 1. In this case the original Mandel–Paule algorithm recommends weights of the from (8) such that

\[
\sum_{i} \frac{(X_i - \bar{X})^2}{S_i + Y} = p - 1.
\]

Eq. (18) can be interpreted as a simplified version of the restricted maximum likelihood equation. Indeed it follows from (6) that

\[
(\hat{\Sigma}_i + Y)^{-1} = (\hat{\Sigma}_i + Y)^{-1} \left[ (X_i - \hat{\theta})(X_i - \hat{\theta})^T + \left( \sum_k (\hat{\Sigma}_k + Y)^{-1} \right)^{-1} \right] (\hat{\Sigma}_i + Y)^{-1}
\]

\[
+ y_i \hat{\Sigma}_i^{-1} (I - S_i \hat{\Sigma}_i^{-1}).
\]

If \( \hat{\Sigma}_k = S_k \), then

\[
\sum_i (S_i + Y)^{-1/2}(X_i - \hat{\theta})(X_i - \hat{\theta})^T (S_i + Y)^{-1/2} = pI - \sum_i (S_i + Y)^{-1/2} \left[ \sum_k (S_k + Y)^{-1} \right]^{-1} (S_i + Y)^{-1/2},
\]

so that, if the estimates \( S_i \) from the individual studies are close to the REML estimators, then the REML estimator of \( \Xi \) must be close to the solution \( Y \) of (18). When \( q = 1 \), a similar result was derived in [12]. Asymptotic properties of the scalar version of the Mandel–Paule rule are investigated in [13].

To find an approximate solution, we look for solutions close to \( Y_{DL} \) and put \( Y_{MP} = Y_{DL} + y \) with a “small” symmetric matrix \( y \). Matrix differentiation [9, Section 8.1] shows that with

\[
W_{DL} = \sum_k (S_k + Y_{DL})^{-1},
\]

\[
L = \frac{1}{2} \sum_i (S_i + Y_{DL})^{-1/2} [(X_i - \bar{X}_{DL})(X_i - \bar{X}_{DL})^T + W_{DL}^{-1}]
\]

\[
\times (S_i + Y_{DL})^{-1/2} \otimes (S_i + Y_{DL})^{-1} + \frac{1}{2} \sum_i (S_i + Y_{DL})^{-1} \otimes (S_i + Y_{DL})^{-1/2}
\]
As in Section 3.1, (19) can be replaced by

\[ y = \sum_{i,j} (S_i + Y_{DL})^{-1/2} \omega_j \bigotimes (S_i + Y_{DL})^{-1/2} \omega_j \]

the vectorized version of (18) for the “correction” term \( y \) has the form,

\[ \mathbf{L} \text{Vec}(y) = \text{Vec}(\mathbf{R}). \]

If the matrix \( \mathbf{L} \) is non-singular,

\[ \text{Vec}(y) = \mathbf{L}^{-1} \text{Vec}(\mathbf{R}). \]  \hspace{1cm} (19)

As in Section 3.1, (19) can be replaced by

\[ \text{Vech}(y) = [H_y \mathbf{L} G_y]^{-1} \text{Vech}(\mathbf{R}). \]

The simulations show that the solution obtained from the following simplified version \( \mathbf{L}_{\text{sim}} \) of the matrix \( \mathbf{L} \) leads to a good numerical approximation to \( \text{Vech}(y) \),

\[
\mathbf{L}_{\text{sim}} = \frac{1}{2} \sum_i (S_i + Y_{DL})^{-1/2} [(X_i - \bar{X}_{DL})(X_i - \bar{X}_{DL})^T + W_{DL}^{-1}]
\times (S_i + Y_{DL})^{-1/2} \bigotimes (S_i + Y_{DL})^{-1} + \frac{1}{2} \sum_i (S_i + Y_{DL})^{-1} \bigotimes (S_i + Y_{DL})^{-1/2}
\times [(X_i - \bar{X}_{DL})(X_i - \bar{X}_{DL})^T + W_{DL}^{-1}](S_i + Y_{DL})^{-1/2}
\times \sum_{i,j} (S_i + Y_{DL})^{-1/2} \omega_j \bigotimes (S_i + Y_{DL})^{-1/2} \omega_j.
\]

After \( y \) has been determined, one can take \( Y_{MP} = [Y_{DL} + y]_+ \) (so that \( Y_{MP} \) has the same spectral decomposition as \( Y_{DL} + y \), with the eigenvalues being positive parts of these of \( Y_{DL} + y \)).

Thus, the Mandel–Paule rule is the weighted means statistic (7) whose matrix weights have the form,

\[ W_i = (Y_{MP} + S_i)^{-1}. \]  \hspace{1cm} (20)
As the DerSimonian–Laird estimator, this extension of the Mandel–Paule rule provides the estimate $\tilde{X}$ of the common parameter $\theta$ along with the estimate $Y_{MP}$ of $\Sigma$.

We formulate our main results.

**Proposition 3.1.** The DerSimonian–Laird estimator of the common vector mean $\theta$ is the weighted mean statistic (9) with the matrix weights (8) where $Y = Y_{DL}$ solves (14). The vectorized form of this matrix satisfies (16). The Mandel–Paule rule is determined by the weights of the form (8) with $Y$ found from (18). If the REML estimators of $\Sigma_i$ are $S_i$, then the Mandel–Paule estimator is the REML estimator of $Y$. Its approximate version is given by $Y_{MP} = Y_{DL} + y$, where $y$ satisfies (19).

Now we turn to estimation of the covariance matrix of the weighted means statistics (7), as this estimator is needed for confidence ellipsoids.

### 4. Covariance matrix estimation

Here we discuss two estimators of the covariance matrix of the weighted means statistics (7) for arbitrary, but fixed, symmetric non-negative definite matrix weights $W_i$ assuming that $W = \sum_{i=1}^p W_i$ is a non-singular matrix. Denote $\omega_i = W^{-1} W_i$, $i = 1, \ldots, p$. Then $\sum_{i=1}^p \omega_i = I$, and all eigenvalues of $\omega_i$ are real positive numbers, smaller than one, although these matrices do not have to commute or to be symmetric or positive definite.

#### 4.1. Unbiased quadratic procedures

We start with the search for a quadratic estimator in the residuals, $X_i - \tilde{X}$, of

$$\text{Var}(\tilde{X}) = \sum_{i=1}^p \omega_i \text{Var}(X_i) \omega_i^T.$$ 

In other terms the goal is to find $q \times q$ non-negative definite matrices $Q_i$, such that

$$\sum_{i=1}^p Q_i E(X_i - \tilde{X})(X_i - \tilde{X})^T Q_i^T = \sum_{i=1}^p \omega_i \text{Var}(X_i) \omega_i^T,$$

or

$$\sum_{i=1}^p Q_i (I - \omega_i) \text{Var}(X_i)(I - \omega_i)^T Q_i^T + \sum_{i \neq j} Q_j \omega_i \text{Var}(X_i) \omega_i^T Q_j^T$$

$$= \sum_{i=1}^p \omega_i \text{Var}(X_i) \omega_i^T.$$ 

It follows that for any $i = 1, \ldots, p$,

$$Q_i (I - \omega_i) \text{Var}(X_i)(I - \omega_i)^T Q_i^T + \sum_{k:k \neq i} Q_k \omega_i \text{Var}(X_i) \omega_i^T Q_k^T = \omega_i \text{Var}(X_i) \omega_i^T.$$
As in Section 3.1, these equations hold for all symmetric matrices \( \text{Var}(X_i) \) if and only if

\[
\begin{aligned}
H_q \left[ Q_i (I - \omega_i) \otimes Q_i (I - \omega_i) + \sum_{k \neq i} Q_k \omega_i \otimes Q_k \omega_i \right] G_q \\
= H_q \left( \omega_i \otimes \omega_i \right) G_q.
\end{aligned}
\]

The identity (21) shows that for \( i = 1, \ldots, p \),

\[
H_q \left( Q_i \otimes Q_i \right) \left[ (I - \omega_i) \otimes (I - \omega_i) - \omega_i \otimes \omega_i \right] G_q \\
+ H_q \sum_k \left( Q_k \otimes Q_k \right) \left( \omega_i \otimes \omega_i \right) G_q = H_q \left( \omega_i \otimes \omega_i \right) G_q.
\]

We rewrite these equalities in the form

\[
\begin{aligned}
H_q \left( Q_i \otimes Q_i \right) \left[ (I - \omega_i) \otimes (I - \omega_i) - \omega_i \otimes \omega_i \right] G_q H_q \\
= H_q \omega_i \otimes \omega_i G_q H_q - H_q \sum_k \left( Q_k \otimes Q_k \right) \left( \omega_i \otimes \omega_i \right) G_q H_q,
\end{aligned}
\]

and use the fact that for any \( q \times q \) matrix \( A, (A \otimes A)G_q H_q = G_q H_q (A \otimes A) \) [9, Section 3.8]. Assuming that matrices \( (I - \omega_i) \otimes (I - \omega_i) - \omega_i \otimes \omega_i = I \otimes I - \omega_i \otimes I - I \otimes \omega_i \) are invertible, one gets

\[
\begin{aligned}
H_q \left( Q_i \otimes Q_i \right) G_q H_q \\
= \left[ H_q \left( \omega_i \otimes \omega_i \right) G_q H_q - H_q \sum_k \left( Q_k \otimes Q_k \right) \left( \omega_i \otimes \omega_i \right) G_q H_q \right] \\
\quad \times \left[ (I - \omega_i) \otimes (I - \omega_i) - \omega_i \otimes \omega_i \right]^{-1}.
\end{aligned}
\]

Let

\[
\Omega_j = H_q \omega_j \otimes \omega_j \left[ I \otimes I - \omega_j \otimes I - I \otimes \omega_j \right]^{-1} G_q.
\]

Then multiplying by \( G_q \) from the left and summing up by \( i \) gives

\[
\sum_i H_q \left( Q_i \otimes Q_i \right) G_q \left[ I + \sum_j \Omega_j \right] = \sum_j \Omega_j, 
\]

so that for \( i = 1, \ldots, p \),

\[
H_q \left( Q_i \otimes Q_i \right) G_q = \Omega_i - \sum_j \Omega_j \left[ I + \sum_j \Omega_j \right]^{-1} \Omega_i = \left[ I + \sum_j \Omega_j \right]^{-1} \Omega_i.
\]

Thus, an unbiased quadratic estimator of \( \text{Var}(\tilde{X}) \) exists if and only if the weights \( \omega_i \) are such that the corresponding matrices (22) admit representation (23).
Notice that if \( \lambda_1^{(i)}, \ldots, \lambda_q^{(i)} \) are the eigenvalues of \( \omega_i \), then \( \Omega_i \) has eigenvalues \( \frac{\lambda_s^{(i)} \lambda_t^{(i)}}{1 - \lambda_s^{(i)} - \lambda_t^{(i)}} \), \( 1 \leq s \leq t \leq q \). For example, if all matrices \( \omega_i \) commute, then the eigenvalues \( H_q(Q_i \otimes Q_i)G_q \) must be proportional to those of \( \Omega_i \), i.e.

\[
\frac{\lambda_s^{(i)} \lambda_t^{(i)}}{1 - \lambda_s^{(i)} - \lambda_t^{(i)}} = C_s^{(i)} \mu_t^{(i)}
\]

for \( 1 \leq s \leq t \leq q \). This can hold if and only if \( \lambda_s^{(i)} \equiv \lambda_t^{(i)} \), i.e. if all \( \omega_i \) are scalar multiples of \( I \), \( \omega_i = \lambda^{(i)} I \), \( \sum_i \lambda^{(i)} = 1 \), in which case when \( \max_k \lambda^{(k)} < \frac{1}{2} \), \( \Omega_i = \frac{\lambda^{(i)}^2}{1 - 2\lambda^{(i)}} I \), and

\[
Q_i = \sqrt{\frac{\left(\lambda^{(i)}\right)^2}{1 - 2\lambda^{(i)}}} I.
\]

In the case when \( \lambda^{(i)} \equiv 1/p \), i.e. \( \bar{X} \) is the sample mean \( \bar{X}_\infty \), the unbiased quadratic estimator is the classical unbiased estimator,

\[
S = \frac{1}{p(p-1)} \sum_{i=1}^p (X_i - \bar{X})(X_i - \bar{X})^T.
\]

If (23) holds, an estimator of \( \mbox{Var}(\bar{X}) \) can be readily found. Indeed,

\[
\mbox{Vech} \left( \sum_{i=1}^p Q_i E(X_i - \bar{X})(X_i - \bar{X})^T Q_i^T \right)
\]

\[
= \sum_{i=1}^p H_q(Q_i \otimes Q_i) G_q \mbox{Vech}(E(X_i - \bar{X})(X_i - \bar{X})^T)
\]

\[
= \left[ I + \sum_j \Omega_j \right]^{-1} \left[ \sum_i \Omega_i \mbox{Vech}(E(X_i - \bar{X})(X_i - \bar{X})^T) \right].
\]

Thus, \( \mbox{Vech} \left( \sum_{i=1}^p \omega_i \mbox{Var}(X_i) \omega_i^T \right) \) could be estimated by the right-hand side of (24). The same formula is amenable to calculation of the unbiased estimator of \( \mbox{Vech}(\mbox{Var}(\bar{X})) \) when more general estimators of the form

\[
\sum_i C_i \mbox{Vech}((X_i - \bar{X})(X_i - \bar{X})^T)
\]

with \( q(q+1)/2 \times q(q+1)/2 \) matrices \( C_i \) (not necessarily of the form (23)) are allowed. Of course such an estimate may not produce a positive definite matrix in which case its positive part is taken.
When \( q = 1 \), one obtains the formula originally derived in [2],
\[
Q_i^2 = \frac{\omega_i^2}{1 - 2\omega_i} \left[ 1 + \sum_k \frac{\omega_k^2}{1 - 2\omega_k} \right]^{-1}.
\]

Obviously this is not a satisfactory solution if \( \max_i \omega_i \geq \frac{1}{2} \).

### 4.2. Almost unbiased estimators of a covariance matrix

As in the general case an unbiased quadratic estimator of \( \text{Var}(\tilde{X}) \) does not exist, we put forward a different estimator which can be justified in a more general setting of linear models (such as (1)).

As before, let \( \omega_i \) be fixed normalized matrix weights, \( \sum_i \omega_i = I \). To estimate the covariance matrix \( \text{Var}(\tilde{X}) \) of the (unbiased) weighted means statistic \( \tilde{X} \), one can use the almost unbiased estimate of \( \text{Var}(X_i) \) derived in [8] as follows. One has
\[
\text{Var}(X_i - \tilde{X}) = (I - \omega_i)\text{Var}(X_i)(I - \omega_i)^T + \sum_{k \neq i} \omega_k \text{Var}(X_k)\omega_k^T
\]
\[
= \sum_k \omega_k \text{Var}(X_k)\omega_k^T + \text{Var}(X_i) - \omega_i \text{Var}(X_i) - \text{Var}(X_i)\omega_i^T.
\]

Of course, when \( \omega_i = [\sum_{j=1}^p \text{Var}(X_j)^{-1}]^{-1} \text{Var}(X_i)^{-1} \), the first term in the right-hand side simplifies to
\[
\sum_k \omega_k \text{Var}(X_k)\omega_k^T = \left[ \sum_{i=1}^p \text{Var}(X_i)^{-1} \right]^{-1} = \frac{1}{2} \omega_i \text{Var}(X_i) + \frac{1}{2} \text{Var}(X_i)\omega_i^T,
\]
and by substituting this expression in the previous formula, one obtains
\[
\text{Var}(X_i - \tilde{X}) = \text{Var}(X_i) - \frac{1}{2} \omega_i \text{Var}(X_i) - \frac{1}{2} \text{Var}(X_i)\omega_i^T.
\]

Horn et al. [8, p. 382] argue that by continuity if the weights are only approximately correct, this is an approximate identity. Thus, an almost unbiased estimator of \( \text{Var}(X_i - \tilde{X}) \) is derived by solving (in \( V_i \)) the following equation
\[
(X_i - \tilde{X})(X_i - \tilde{X})^T = V_i - \frac{1}{2} \omega_i V_i - \frac{1}{2} V_i \omega_i^T.
\]

Here symmetric \( V_i \) serves as an estimate of \( \text{Var}(X_i) \). This solution can be found like one in (23). More precisely,
\[
\text{Vech}(\text{Var}(X_i)) = \left[ H_q \left( I - \frac{1}{2} \omega_i \bigotimes I - \frac{1}{2} I \bigotimes \omega_i \right) G_q \right]^{-1} \text{Vech}((X_i - \tilde{X})(X_i - \tilde{X})^T).
\]

The same agreement as in Sections 2 and 3.1 about taking the positive part of a non-positively defined symmetric matrix is applicable here too. Actually, as in our situation, \( \text{Var}(X_i) \geq \Sigma_i \) and an unbiased estimate \( S_i \) of \( \Sigma_i \) is available, it makes sense to use as the final estimator of \( \text{Var}(X_i) \),
\[
\max[\bar{\text{Var}}(X_i), S_i] = S_i + [\bar{\text{Var}}(X_i) - S_i]_+ \text{ with } \bar{\text{Var}}(X_i) \text{ determined from (25).}
\]
The resulting formula for $\text{Var}(\widetilde{X})$ estimator has the form,

$$
\text{Var}(\widetilde{X}) = \sum_i \omega_i \text{Var}(X_i) \omega_i^T,
$$

(26)

which can be recovered from its vectorized version via (25),

$$
\text{Vech}(\text{Var}(\widetilde{X})) = \sum_i G_q \left( \omega_i \otimes \omega_i \right) H_q
$$

$$
\times \left[ H_q \left( I - \frac{1}{2} \omega_i \otimes 1 - \frac{1}{2} 1 \otimes \omega_i \right) G_q \right]^{-1} \text{Vech}((X_i - \widetilde{X})(X_i - \widetilde{X})^T).
$$

(27)

Table 1
The covariance matrices of seven estimators when $q = 2; \ p = 3, 6, n = 9, 18$ and their estimates

<table>
<thead>
<tr>
<th>Estimator</th>
<th>$p = 3, n = 9$</th>
<th>$p = 3, n = 18$</th>
<th>$p = 6, n = 9$</th>
<th>$p = 6, n = 18$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\tilde{Y}$</td>
<td>0.68 0.07</td>
<td>0.67 0.05</td>
<td>0.35 0.04</td>
<td>0.33 0.02</td>
</tr>
<tr>
<td>$S$</td>
<td>0.50 0.05</td>
<td>0.24 0.02</td>
<td>1.23 0.13</td>
<td>0.58 0.06</td>
</tr>
<tr>
<td>$GD$</td>
<td>0.68 0.08</td>
<td>0.64 0.07</td>
<td>0.40 0.04</td>
<td>0.34 0.03</td>
</tr>
<tr>
<td>$p = 3, n = 18$</td>
<td>0.08 0.64</td>
<td>0.07 0.57</td>
<td>0.04 0.35</td>
<td>0.03 0.31</td>
</tr>
<tr>
<td>$(28)$</td>
<td>0.08 0.01</td>
<td>0.10 0.00</td>
<td>0.03 0.00</td>
<td>0.04 0.01</td>
</tr>
<tr>
<td>$DL$</td>
<td>0.54 0.06</td>
<td>0.53 0.07</td>
<td>0.26 0.03</td>
<td>0.25 0.02</td>
</tr>
<tr>
<td>$p = 6, n = 9$</td>
<td>0.06 0.46</td>
<td>0.07 0.46</td>
<td>0.03 0.23</td>
<td>0.02 0.21</td>
</tr>
<tr>
<td>$(26)$</td>
<td>0.54 0.06</td>
<td>0.53 0.05</td>
<td>0.26 0.03</td>
<td>0.25 0.02</td>
</tr>
<tr>
<td>$p = 6, n = 18$</td>
<td>0.06 0.48</td>
<td>0.05 0.48</td>
<td>0.03 0.23</td>
<td>0.02 0.22</td>
</tr>
<tr>
<td>$(28)$</td>
<td>0.59 0.07</td>
<td>0.58 0.05</td>
<td>0.31 0.03</td>
<td>0.29 0.03</td>
</tr>
<tr>
<td>$MP$</td>
<td>0.55 0.08</td>
<td>0.54 0.07</td>
<td>0.28 0.03</td>
<td>0.27 0.02</td>
</tr>
<tr>
<td>$p = 26$</td>
<td>0.08 0.49</td>
<td>0.07 0.47</td>
<td>0.03 0.24</td>
<td>0.02 0.23</td>
</tr>
<tr>
<td>$(26)$</td>
<td>0.59 0.05</td>
<td>0.57 0.06</td>
<td>0.31 0.03</td>
<td>0.29 0.03</td>
</tr>
<tr>
<td>$(28)$</td>
<td>0.59 0.05</td>
<td>0.57 0.06</td>
<td>0.31 0.03</td>
<td>0.29 0.03</td>
</tr>
<tr>
<td>$ML$</td>
<td>0.54 0.04</td>
<td>0.53 0.08</td>
<td>0.27 0.04</td>
<td>0.24 0.02</td>
</tr>
<tr>
<td>$(5)$</td>
<td>0.46 0.02</td>
<td>0.60 0.05</td>
<td>0.26 0.02</td>
<td>0.31 0.02</td>
</tr>
<tr>
<td>$R$</td>
<td>0.54 0.03</td>
<td>0.53 0.02</td>
<td>0.26 0.02</td>
<td>0.24 0.02</td>
</tr>
<tr>
<td>$(26)$</td>
<td>0.03 0.46</td>
<td>0.02 0.45</td>
<td>0.02 0.23</td>
<td>0.02 0.21</td>
</tr>
<tr>
<td>$(5)$</td>
<td>0.38 0.01</td>
<td>0.35 0.02</td>
<td>0.23 0.01</td>
<td>0.22 0.01</td>
</tr>
<tr>
<td>$SN$</td>
<td>0.25 0.00</td>
<td>0.31 0.02</td>
<td>0.15 0.01</td>
<td>0.20 0.01</td>
</tr>
<tr>
<td>$(26)$</td>
<td>0.00 0.23</td>
<td>0.02 0.29</td>
<td>0.01 0.14</td>
<td>0.01 0.18</td>
</tr>
<tr>
<td>$(5)$</td>
<td>0.55 0.03</td>
<td>0.52 0.06</td>
<td>0.28 0.03</td>
<td>0.27 0.02</td>
</tr>
<tr>
<td>$SN$</td>
<td>0.36 0.00</td>
<td>0.49 0.05</td>
<td>0.21 0.02</td>
<td>0.25 0.02</td>
</tr>
<tr>
<td>$(5)$</td>
<td>0.00 0.29</td>
<td>0.05 0.44</td>
<td>0.02 0.18</td>
<td>0.02 0.23</td>
</tr>
</tbody>
</table>
The statistic (26) gives an estimate of the covariance matrix of any weighted means statistic for fixed weights $\omega_i$. This estimate is uniquely defined when $I - \frac{1}{2}\omega_i \otimes I - \frac{1}{2}I \otimes \omega_i$ is invertible, which holds provided that $I - \omega_i$ is non-singular.

When $\omega_i \equiv p^{-1}I$, i.e. when $\bar{X}$ is the sample mean, this estimator coincides with the classical unbiased estimator $S$.

**Proposition 4.1.** An unbiased quadratic estimator, $\sum_{i=1}^{p} Q_i(X_i - \bar{X})(X_i - \bar{X})^T Q_i^T$, of the covariance matrix $\sum_{i=1}^{p} \omega_i \text{Var}(X_i)\omega_i^T$ for fixed weights $\omega_i$ is defined when the matrices $\Omega_i$ given by (22) admit representation (23), in which case its vectorized form is given by the right-hand side of (24). The almost unbiased estimator (26) of $\text{Var}(\bar{X})$ satisfies (25) and its vectorized version is given by (27).

An alternative estimator of $\text{Var}(\bar{X})$ is

$$\text{Var}(\bar{X}) = \left[ \sum_i \text{Var}(X_i)^{-1} \right]^{-1}. \quad (28)$$

In particular, this estimate is commonly used for the maximum likelihood estimator although it is known to underestimate the true variance. Exact theoretical comparison of (28) and (26) is difficult, but simulations reported in the next section suggest that (26) is a better estimate of this variance.

5. Example and simulation results

Here we report the results of a Monte-Carlo simulation study when $q = 2$ or $3$, $p = 3$ or 6. The distribution of $S_i$ was taken to be that of a Wishart random matrix with parameters $n_i - 1$ and $\Sigma_i$. The distribution of the within-laboratory covariance matrices, $\Sigma_i$, was the inverse Wishart distribution with parameters $q + 2$ and $I$, so that $E\Sigma_i = I$. We chose $\Xi = [1, 0.2; 0.2, 0.8]$ for $q = 2$ and $\Xi = [1.8, 0.2, 0.1; 0.2, 2.1, 0.4; 0.1, 0.4, 2.5]$ when $q = 3$. The sample sizes vector either had equal coordinates, $n_i \equiv n = 9$; $n = 18$, or $n$ was a permutation of integers $1, \ldots, p$ plus 5.

<table>
<thead>
<tr>
<th>p \times n, \text{ samples}</th>
<th>q = 2 when p = 3, 6; n = 9, 18</th>
</tr>
</thead>
<tbody>
<tr>
<td>$p = 3, n = 9$</td>
<td>$p = 3, n = 18$</td>
</tr>
<tr>
<td>$\hat{\Sigma}_{DL}$</td>
<td>1.23 0.19</td>
</tr>
<tr>
<td></td>
<td>0.19 1.05</td>
</tr>
<tr>
<td>$\hat{\Sigma}_{MP}$</td>
<td>0.91 0.14</td>
</tr>
<tr>
<td></td>
<td>0.14 0.80</td>
</tr>
<tr>
<td>$\hat{\Sigma}_{SN}$</td>
<td>0.56 0.03</td>
</tr>
<tr>
<td></td>
<td>0.03 0.38</td>
</tr>
<tr>
<td>$\hat{\Sigma}_{R}$</td>
<td>0.70 0.08</td>
</tr>
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Table 3
The estimators of $\Sigma = [1.0, 0.2, 0.1; 0.2, 1.2, 0.8; 0.1, 0.8, 1.6]$, $q = 3$ when $p = 3, 6$; $n$ is a permutation of $(1, \ldots, p)+5$

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Table 4
The covariance matrices of six estimators for $q$, $p$ and $n$ as in Table 3

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Table 1 contains the covariance matrices of the studied estimators. The DerSimonian–Laird method, and the Mandel–Paule algorithm (which behaved very similarly to the DerSimonian–Laird method) systematically were among the best procedures. They did remarkably well compared to the “golden standard” of maximum likelihood procedures which are more computationally intensive (Tables 2, 3). The Graybill–Deal estimator $GD$ has a variance matrix substantially exceeding that of all other estimators, and the sample mean was the second worst. For this reason we excluded these estimators in Table 4 which gives the simulated values of the covariance matrices of six estimators and their estimates via (26), (28) or (5) when $q = 3$ and the sample sizes of $p = 3, 6$ laboratories are chosen at random. Clearly, (26) gives a much better estimate of the covariance matrix of the weighted means procedures than (28). The latter is especially inadequate in the case of the Graybill–Deal estimator $GD$. Because of heterogeneity the sample covariance matrix $S$ turns out to be a rather poor estimator of the covariance matrix of the sample mean.

Tables 2 and 3 contain the estimators of the between-laboratory effect $\Xi$ for these values of $q$, $p$ and $n$. They show that the likelihood estimators systematically underestimate $\Xi$ while the Mandel–Paule procedure, $Y_{MP}$, and the DerSimonian–Laird method, $Y_{DL}$, gave better answers. However, since the DerSimonian–Laird rule is computationally simpler than the Mandel–Paule algorithm, we can recommend it in the multivariate case (and it does not need any recommendations in the scalar case being the tool-of-choice for meta-analysis.)

Our simulations also demonstrated that the distribution of the pivotal ratio, $(\hat{\theta} - \theta)^T [\hat{\text{Var}}(\hat{\theta})]^{-1} (\hat{\theta} - \theta)$ can be well approximated by a multiple of $F$-distribution with $q$ and $p - q$ degrees of freedom (Fig. 1).

![Fig. 1. The plot of the estimated density of $[\hat{\text{Var}}(\hat{\theta})]^{-1/2}(\hat{\theta} - \theta)$ for the maximum likelihood estimator when $q = 2$, $p = 7$, and $\Xi = [1, 0.2; 0.2, 0.8]$.](image-url)
Fig. 2. Confidence ellipsoid for the charge sensitivity in the Key Comparisons of accelerometers, $q = 3$, $p = 14$, $Y_{DL}$ is the zero matrix.

Fig. 3. Confidence ellipse for the diffusivity and thermal heat in the thermal diffusivity example, $q = 2$, $p = 28$, and $Y_{DL} = [0.084, -0.277; -0.277, 0.914]$.

To illustrate techniques of Section 3 we implemented them in the accelerometers key comparisons study [11] mentioned in Section 1 and in interlaboratory study of thermal diffusivity and conductivity. Only the results for the frequencies 40, 50 and 63 Hz are given here (Fig. 2).
The Mandel–Paule procedure and the DerSimonian–Laird method gave virtually the same answer for \( \hat{\theta}^T = [0.12678, 0.12667, 0.12672] \), with the zero matrix \( \hat{\Xi} \) and the estimated covariance matrix \( \hat{\text{Var}}(\hat{\theta}) = 1.0e - 07 \times [0.3982, 0.0222, -0.0206; 0.0222, 0.3849, 0.0075; -0.0206, 0.0075, 0.3856] \).

This matrix leads to an approximate confidence ellipsoid for \( \hat{\theta} \) on the basis of \( F \)-distribution with \( q = 3 \) and \( p - q = 11 \) degrees of freedom. This ellipsoid provides useful information about the joint behavior of the charge sensitivities for these frequencies. Notice that the maximum likelihood estimators were slightly different: \([0.12675, 0.12671, 0.12667]\) (Fig. 3).

References