An Empirical Bayes Approach to Shrinkage Estimation on the Manifold of Symmetric Positive-Definite Matrices

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ABSTRACT

The James–Stein estimator is an estimator of the multivariate normal mean and dominates the maximum likelihood estimator (MLE) under squared error loss. The original work inspired great interest in developing shrinkage estimators for a variety of problems. Nonetheless, research on shrinkage estimation for manifold-valued data is scarce. In this article, we propose shrinkage estimators for the parameters of the Log-Normal distribution defined on the manifold of \(N \times N\) symmetric positive-definite matrices. For this manifold, we choose the Log-Euclidean metric as its Riemannian metric since it is easy to compute and has been widely used in a variety of applications. By using the Log-Euclidean distance in the loss function, we derive a shrinkage estimator in an analytic form and show that it is asymptotically optimal within a large class of estimators that includes the MLE, which is the sample Fréchet mean of the data. We demonstrate the performance of the proposed shrinkage estimator via several simulated data experiments. Additionally, we apply the shrinkage estimator to perform statistical inference in both diffusion and functional magnetic resonance imaging problems. Supplementary materials for this article are available online.

1. Introduction

Symmetric positive-definite (SPD) matrices are common in applications of science and engineering. In computer vision problems, they are encountered in the form of covariance matrices, for example, region covariance descriptors (Tuzel, Porikli, and Meer 2006), and in diffusion magnetic resonance imaging, for example, region covariance descriptors (Tuzel, Porikli, and Meer 2006), and in diffusion magnetic resonance imaging, etc. If \(X_i\) is a random sample from the multivariate normal distribution on \(\mathbb{R}^p\). The sample mean \(\bar{X} = \frac{1}{n} \sum_{i=1}^{n} X_i\) is the maximum likelihood estimator (MLE) for the mean of the underlying normal distribution, and the James–Stein (shrinkage) estimator (James and Stein 1961) was shown to be better (under squared error loss) than the MLE when \(p > 2\) and the covariance matrix of the underlying normal distribution is assumed to be known. Inspired by this result, the goal of this article is to develop shrinkage estimators for data residing in \(P_M\), the space of \(N \times N\) SPD matrices.

Then, the above optimization problem can be solved by Riemannian gradient descent algorithms (Gabay 1982; Groisser 2004; Moakher 2005; Pennec 2006; Afshari 2011; Udriste 2013). However, Riemannian gradient descent algorithms are usually computationally expensive, and efficient recursive algorithms for computing the sample FM have been presented in the literature for various Riemannian manifolds by Sturm (2003), Ho et al. (2013), Salehian et al. (2015), Chakraborty and Vemuri (2015), Lim and Pálfia (2014), and Chakraborty and Vemuri (2019).

In \(\mathbb{R}^p\) with the Euclidean metric, the sample FM is just the ordinary sample mean. Suppose that \(X_1,\ldots,X_n\) are a random sample from the multivariate normal distribution on \(\mathbb{R}^p\). For the model \(X_i \sim N(\mu, \sigma^2)\), where \(\mu\) and \(\sigma^2\) are known, the MLE of \(\mu\) is \(\hat{\mu}_{\text{MLE}} = \frac{1}{n} \sum_{i=1}^{n} X_i\), which is an unbiased estimate; the Fréchet mean; Stein's unbiased risk estimate; Tweedie's estimator.
the MLE. Subsequently, James and Stein (1961) proposed the estimator

$$X = \left(1 - \frac{(p-2)\sigma^2}{\|X\|^2}\right)X$$

where $X = [X_1, \ldots, X_p]^T$, which is now referred to as the James–Stein (shrinkage) estimator.

Ever since the work reported in James and Stein (1961), shrinkage estimators have been developed for the parameters of other distributions, such as the Poisson and Gamma (Clevenson and Zidek 1975; Berger 1980). In order to understand shrinkage estimation fully, one must understand why the process of shrinkage improves estimation. In this context, Efron and Morris presented a series of works to provide an empirical Bayes interpretation by modifying the original James–Stein estimator to suit different problems (Efron and Morris 1973a, 1973b). The empirical Bayes approach to designing a shrinkage estimator can be described as follows. First, reformulate the model as a Bayesian model, that is, place a prior on the parameters. Then, the hyperparameters of the prior are estimated from the data. Efron and Morris (1973b) presented several examples of different shrinkage estimators developed within this empirical Bayes framework.

In all the works cited above, the domain of the data has invariably been a vector space and, as mentioned earlier, many applications naturally encounter data residing in non-Euclidean spaces. Hence, generalizing shrinkage estimation to non-Euclidean spaces is a worthwhile pursuit. In this article, we focus on shrinkage estimation for the Riemannian manifold $PN$. We assume that the observed SPD matrices are drawn from a Log-Normal distribution defined on $PN$ (Schwartzman 2016) and we are interested in estimating the mean and the covariance matrix of this distribution. We point out that a simple method to derive a shrinkage estimator in this case is to apply James–Stein shrinkage to the log-transformed SPD matrices. However, this does not lead to an optimal shrinkage estimator. Hence, we derive shrinkage estimators for the parameters of the Log-Normal distribution using an empirical Bayes framework, which is described in detail subsequently, and show that the proposed estimator is asymptotically optimal within a class of estimators including the MLE. We discuss this issue in more detail in Section 3.2.

We present simulated data experiments which demonstrate that the proposed shrinkage estimator of the mean of the Log-Normal distribution is better (in terms of risk) than the sample mean estimator. We discuss this issue in more detail in Section 3.2.

Besides estimation of the mean of different distributions, estimation of the covariance matrix (or the precision matrix) of a multivariate normal distribution is an important problem in statistics, finance, engineering and many other fields. The usual estimator, namely the sample covariance matrix, performs poorly in high-dimensional problems and many researchers have endeavored to improve covariance estimation by applying the concept of shrinkage in this context (Stein 1975; Daniels and Kass 2001; Ledoit and Wolf 2003; Donoho, Gavish, and Johnstone 2018). In this literature, it is assumed that for each $i = 1, \ldots, p$, we observe iid vectors $X_{i1}, \ldots, X_{i,n_i} \in \mathbb{R}^N$ where for each $j = 1, \ldots, n_i$, the covariance matrix of $X_{ij}$ is $\Sigma_j \in P_N$. This framework is distinct from our setup, where we assume that our observations are estimates $\bar{X}_1, \ldots, \bar{X}_p \in P_N$.

The rest of this article is organized as follows. In Section 2, we present relevant material on the Riemannian geometry of $PN$ and shrinkage estimation. The main theoretical results are stated in Section 3, with the proofs of the theorems relegated to the supplementary materials. In Section 4, we demonstrate how the proposed shrinkage estimators perform via several synthetic data examples and present applications to (real data) diffusion tensor imaging (DTI), a clinically popular version of dMRI, and rs-fMRI. Specifically, we apply the proposed shrinkage estimator to (i) estimation of the brain atlases (templates) of patients with Parkinson’s disease and a control group, (ii) identification of the regions of the brain where the two groups differ significantly, and (iii) estimation of connectivity networks from rs-fMRI. Finally, in Section 5 we discuss our contributions and present some future research directions.

2. Preliminaries

In this section, we briefly review the commonly used Log-Euclidean metric for $PN$ proposed by Arsigny et al. (2007) and the concept of Stein’s unbiased risk estimate, which will form the framework for deriving the shrinkage estimators.

2.1. Riemannian Geometry of $PN$

In this work, we endow the manifold $PN$ with the Log-Euclidean metric. We note that there is another commonly used Riemannian metric on $PN$, called the affine-invariant metric (see Terras (2016, Chap. 1) for its introduction and Lenglet et al. (2006) and Moakher (2005) for its applications). The affine-invariant metric is computationally more expensive; however, because in some applications it provides results that are indistinguishable from those obtained under the Log-Euclidean metric, as demonstrated in Arsigny et al. (2007) and Schwartzman (2016), we choose to work with the Log-Euclidean metric. For other metrics on $PN$ used in a variety of applications, we refer the reader to the recent survey by Feragen and Fuster (2017).

The Log-Euclidean metric is a bi-invariant Riemannian metric on the abelian Lie group $(PN, \odot)$ where $X \odot Y = \exp(\log X + \log Y)$. The intrinsic distance $d_{LE} : P_N \times P_N \to \mathbb{R}$ induced by the Log-Euclidean metric has a very simple form, namely $d_{LE}(X, Y) = \|\log X - \log Y\|$, where $\|\cdot\|$ is the Frobenius norm. Let $Sym(N)$ be the vector space of $N \times N$ symmetric matrices. Consider the map $\text{vec} : Sym(N) \to \mathbb{R}^{N(N+1)/2}$ given by
vec(Y) = \left[ y_{11}, \ldots, y_{nn}, \sqrt{2}(y_{ij})_{i,j} \right]^T \text{ (Schwartzman 2016)}. This map is actually an isomorphism between Sym(N) and \( \mathbb{R}^{N(N+1)/2} \). To make the notation more concise, for \( X \in P_N \), we denote \( \tilde{X} = \text{vec}(\log X) \in \mathbb{R}^{N(N+1)/2} \). From the definition of vec, we see that \( d_E(X, Y) = \| \tilde{X} - \tilde{Y} \| \).

Given \( X_1, \ldots, X_n \in P_N \), we denote the sample FM with respect to the Log-Euclidean distance given above by \( \tilde{X} = \arg \min_{M \in P_N} n^{-1} \sum_{i=1}^{n} \tilde{d}_{LE}(X_i, M) = \exp \left( n^{-1} \sum_{i=1}^{n} \log X_i \right) \).

### 2.2. The Log-Normal Distribution on \( P_N \)

In this work, we assume that the observed SPD matrices follow the Log-Normal distribution introduced by Schwartzman (2016), which can be viewed as a generalization of the Log-Normal distribution on \( \mathbb{R}^+ \) to \( P_N \). The definition is as follows.

**Definition 1.** Let \( X \) be a \( P_N \)-valued random variable. We say \( X \) follows a Log-Normal distribution with mean \( M \in P_N \) and covariance matrix \( \Sigma \in P_{N(N+1)/2} \), or \( X \sim LN(M, \Sigma) \), if \( \tilde{X} \sim N(\tilde{M}, \tilde{\Sigma}) \).

From the definition, it is easy to see that \( E \log X = \log M \) and \( E\|\log X - \log M\|^2 = E\|\tilde{X} - \tilde{M}\|^2 = \text{tr}(\Sigma) \). Some important results regarding this distribution were obtained in Schwartzman (2016). The following proposition, proved in Schwartzman (2016), for the MLEs of the parameters will be useful subsequently.

**Proposition 1.** Let \( X_1, \ldots, X_n \overset{\text{iid}}{\sim} LN(M, \Sigma) \). Then, the MLEs of \( M \) and \( \Sigma \) are \( \hat{M}_{\text{MLE}} = \tilde{X} \) and \( \hat{\Sigma}_{\text{MLE}} = n^{-1} \sum_{i=1}^{n} (\tilde{X}_i - \tilde{M}_{\text{MLE}})(\tilde{X}_i - \tilde{M}_{\text{MLE}})^T \). The MLE of \( M \) is the sample FM under the Log-Euclidean metric.

### 2.3. Bayesian Formulation of Shrinkage Estimation in \( \mathbb{R}^P \)

As discussed earlier, the James–Stein estimator originated from the problem of simultaneous estimation of multiple means of (univariate) normal distributions. The derivation relied heavily on properties of the univariate normal distribution. Later, Efron and Morris (1973b) gave an empirical Bayes interpretation for the James–Stein estimator, which is presented by considering the hierarchical model

\[
X_i | \theta_i \sim N(\theta_i, A), \quad i = 1, \ldots, p, \\
\theta_i \sim N(\mu, \lambda),
\]

where \( A \) is known and \( \mu \) and \( \lambda \) are unknown. The posterior mean for \( \theta_i \) is

\[
\hat{\theta}_i^{\mu, \lambda} = \frac{\lambda}{\lambda + A} X_i + \frac{A}{\lambda + A} \mu. \tag{2}
\]

The parametric empirical Bayes method for estimating the \( \theta_i \)'s consists of first estimating the prior parameters \( \lambda \) and \( \mu \) and then substituting them into (2). The prior parameters \( \lambda \) and \( \mu \) can be estimated by the MLE. For the special case of \( \mu = 0 \), this method produces an estimator similar to the James–Stein estimator (1). Although this estimator is derived in an (empirical) Bayesian framework, it is of interest to determine whether it has good frequentist properties. For example, if we specify a loss function \( L \) and consider the induced risk function \( R \), one would like to determine whether the estimator has uniformly smallest risk within a reasonable class of estimators. For (2), the optimal choice of \( \lambda \) and \( \mu \) is

\[
(\hat{\lambda}^{opt}, \hat{\mu}^{opt}) = \arg \min_{\lambda, \mu} R(\lambda^{\mu, \lambda}, \theta),
\]

where \( \theta = [\theta_1, \ldots, \theta_p]^T \) and \( \hat{\theta}_i^{\mu, \lambda} = [\hat{\theta}_1^{\mu, \lambda}, \ldots, \hat{\theta}_p^{\mu, \lambda}]^T \). The definition is as follows.

**Definition 2.** Let \( Y \) be an \( N \)-valued random variable. We say \( Y \) follows a Log-Normal distribution with mean \( \bar{Y} \) and covariance matrix \( \Sigma \), or \( Y \sim LN(\bar{Y}, \Sigma) \), if \( \tilde{Y} \sim N(\tilde{\bar{Y}}, \tilde{\Sigma}) \). The challenge part of this endeavor is to derive SURE, which depends heavily on the risk function and the underlying distribution of the data. This approach has been used to derive estimators for many models. For example, Xie, Kou, and Brown (2012) derived the (asymptotically) optimal shrinkage estimator for a heteroscedastic hierarchical model, and their result is further generalized in Jing et al. (2016) and Kong et al. (2017).

### 3. An Empirical Bayes Shrinkage Estimator for Log-Normal Distributions

In this section, we consider the model

\[
X_{ij} \overset{\text{iid}}{\sim} LN(M_i, \Sigma_i), \quad i = 1, \ldots, p, \quad j = 1, \ldots, n,
\]

and develop shrinkage estimators for the vector of means \( M = [M_1, \ldots, M_p] \) and the array of covariance matrices \( \Sigma = [\Sigma_1, \ldots, \Sigma_p] \). The motivation for this model is that for the applications of DTI, we have \( n \) DT images and each DT image contains \( p \) voxels. The diffusive behavior of water molecules in each voxel is characterized by a \( 3 \times 3 \) SPD matrix. The \( X_{ij} \)'s are \( P_N \)-valued random matrices. For completeness, we first briefly review the shrinkage estimator of \( M \) proposed by Yang and Vemuri (2019), who assumed \( \Sigma_i = A I \), where the \( A_i \)'s are known positive numbers and \( I \) is the identity matrix. The assumption on \( \Sigma \) is useful when \( n \) is small since for small sample sizes the MLE for \( \Sigma \) is very unstable. Next, we present estimators for both \( M \) and \( \Sigma \). Besides presenting these estimators, we establish asymptotic optimality results for the proposed estimators. To be more precise, we show that the proposed estimators are asymptotically optimal within a large class of estimators that contains the MLE.

Another related interesting problem often encountered in practice involves group testing and estimating the “difference” between two given groups. Consider the model

\[
X_{ij} \overset{\text{iid}}{\sim} LN(M_i^{(1)}, \Sigma_i^{(1)}), \quad i = 1, \ldots, p, \quad j = 1, \ldots, n_x,
\]

\[
Y_{ij} \overset{\text{iid}}{\sim} LN(M_i^{(2)}, \Sigma_i^{(2)}), \quad i = 1, \ldots, p, \quad j = 1, \ldots, n_y,
\]
where the $X_{ij}$'s and $Y_{ij}$'s are independent. We want to estimate the differences between $M_i^{(1)}$ and $M_i^{(2)}$ for $i = 1, \ldots, p$ and select the $i$'s for which the differences are large. However, the selected estimates tend to overestimate the corresponding true differences. The bias introduced by the selection process is termed selection bias (Dawid 1994). Selection bias originates from the fact that there are two possible reasons for the selected differences to be large: (i) the true differences are large and (ii) the random errors contained in the estimates are large. Tweedie's formula (Efron 2011), which we discuss and briefly review in Section 3.3, deals with precisely this selection bias, in the context of the normal means problem. In this work, we apply an analogue of Tweedie's formula designed for the context of SPD matrices.

### 3.1. An Estimator of $M$ When $\Sigma$ is Known

For completeness, we briefly review the work of Yang and Vemuri (2019) where the authors presented the estimator for $M$ assuming that $\Sigma_i = A_i I$ and the $A_i$'s are known positive numbers. Under this assumption, they considered the class of estimators given by

$$\hat{M}^{\mu}_i = \exp \left( \frac{n\lambda}{n\lambda + A_i} \log \hat{X}_i + \frac{A_i}{n\lambda + A_i} \log \mu \right),$$

(3)

where $\mu \in P_N$, $\lambda > 0$, and $\hat{X}_i$ is the sample FM of $X_{i1}, \ldots, X_{in}$. Using the Log-Euclidean distance as the loss function $L(\hat{M}, M) = p^{-1} \sum_{i=1}^{p} d^2_{LE}(\hat{M}_i, M_i)$, they showed that the SURE for the corresponding risk function $R(\hat{M}, M) = EL(\hat{M}, M)$ is given by

$$\text{SURE}(\lambda, \mu) = \frac{1}{p} \sum_{i=1}^{p} A_i \left( \lambda \| \log \hat{X}_i - \log \mu \| ^2 + \frac{q(2\lambda^2 - A_i^2)}{n} \right),$$

where $q = N(N + 1)/2$. Hence, $\lambda$ and $\mu$ can be estimated by

$$(\hat{\lambda}^\text{SURE}, \hat{\mu}^\text{SURE}) = \arg \min_{\lambda, \mu} \text{SURE}(\lambda, \mu).$$

Their shrinkage estimator for $M_i$ is given by

$$\hat{M}_i^{\text{SURE}} = \exp \left( \frac{n\lambda^{\text{SURE}}}{n\lambda^\text{SURE} + A_i} \log \hat{X}_i + \frac{A_i}{n\lambda^\text{SURE} + A_i} \log \hat{\mu}^\text{SURE} \right).$$

(4)

They also presented the following two theorems showing the asymptotic optimality of the shrinkage estimator.

**Theorem 1.** Assume the following conditions:

(i) $\limsup_{p \to \infty} p^{-1} \sum_{i=1}^{p} A_i^2 < \infty$,

(ii) $\limsup_{p \to \infty} p^{-1} \sum_{i=1}^{p} \lambda \| \log M_i \| ^2 < \infty$,

(iii) $\limsup_{p \to \infty} p^{-1} \sum_{i=1}^{p} \| \log M_i \| ^{2+\delta} < \infty$ for some $\delta > 0$.

Then,

$$\sup_{\lambda > 0, \| \log \mu \| < \infty, \| \log \hat{X}_i \|} \left| \text{SURE}(\lambda, \mu) - L(\hat{M}^{\mu}_i, M) \right| \to 0 \text{ prob as } p \to \infty.$$

**Theorem 2.** If assumptions (i)–(iii) in Theorem 1 hold, then for every $\lambda > 0$ and $\mu \in P_N$,

$$\limsup_{p \to \infty} \left[ R(\hat{M}_i^{\text{SURE}}, M) - R(\hat{M}^{\mu}_i, M) \right] \leq 0.$$

### 3.2. Estimators for $M$ and $\Sigma$

In Yang and Vemuri (2019), the covariance matrices of the underlying distributions were assumed to be known, to simplify the derivation. In real applications however, the covariance matrices are rarely known, and in practice they must be estimated. In this article, we consider the general case of unknown covariance matrices, which is more challenging and pertinent in real applications. Let

$$X_{ij}|(M_i, \Sigma_i) \sim \text{LN}(M_i, \Sigma_i)$$

$$M_i|\Sigma_i \sim \text{LN}(\mu, \lambda^{-1}\Sigma_i)$$

$$\Sigma_i \sim \text{Inv-Wishart}(\Psi, v),$$

(5)

for $i = 1, \ldots, p$ and $j = 1, \ldots, n$. The prior for $(M_i, \Sigma_i)$ is called the Log-Normal-Inverse-Wishart (LNIW) prior, and it is motivated by the normal-inverse-Wishart prior in the Euclidean space setting. We emphasize that the main reason for choosing the LNIW prior over others is the property of conjugacy which leads to a closed-form expression for our estimators. Let

$$\tilde{X}_i = \exp \left( n^{-1} \sum_{j=1}^{n} \log X_{ij} \right) \text{ and}$$

$$S_i = \sum_{j=1}^{n} (\tilde{X}_{ij} - \tilde{X}_i) (\tilde{X}_{ij} - \tilde{X}_i)^T.$$

Then the posterior distributions of $M_i$ and $\Sigma_i$ are given by

$$M_i|(X_{ij}|i, j, \Sigma_i)_{i,j=1}^{p} \sim \text{LN} \left( \frac{n\log \tilde{X}_i + \lambda \log \mu}{\lambda + n}, \frac{\lambda + n^{-1}\Sigma_i}{v + n - 1} \right),$$

$$\Sigma_i|S_i \sim \text{Inv-Wishart}(\Psi + S_i, v + n - 1),$$

and the posterior means for $M_i$ and $\Sigma_i$ are given by

$$\hat{M}_i = \frac{n\tilde{X}_i + \lambda \log \mu}{\lambda + n}$$

and

$$\hat{\Sigma}_i = \frac{\Psi + S_i}{v + n - q - 2}.$$

(7)

Consider the loss function

$$L((\hat{M}, \hat{\Sigma}), (M, \Sigma)) = p^{-1} \sum_{i=1}^{p} d^2_{LE}(\hat{M}_i, M_i) + p^{-1} \sum_{i=1}^{p} \| \hat{\Sigma}_i - \Sigma_i \|^2$$

$$= L_1(\hat{M}, M) + L_2(\hat{\Sigma}, \Sigma).$$

Its induced risk function is

$$R((\hat{M}, \hat{\Sigma}), (M, \Sigma))$$

$$= p^{-1} \sum_{i=1}^{p} \left[ E d^2_{LE}(\hat{M}_i, M_i) + E \| \hat{\Sigma}_i - \Sigma_i \|^2 \right]$$

$$= p^{-1}(\lambda + n)^{-1} \sum_{i=1}^{p} \left[ ntr\Sigma_i + \lambda^2 d^2_{LE}(\mu, M_i) \right]$$

$$+ p^{-1} \sum_{i=1}^{p} (v + n - q - 2)^{-1} \left[ (n - 1 + (v - q - 1)^2)tr(\Sigma_i^2) \right].$$
\[-2(n - 1)(\text{tr}(\Psi_S^2))/n + (n - 1)(\text{tr}(\psi^2))^2 + \text{tr}(\Psi^2)\],

with the detailed derivation given in the supplementary materials. The SURE for this risk function is

\[
\text{SURE}(\lambda, \Psi, v, \mu) = p^{-1}\left\{\frac{1}{n} - \frac{\mathbf{1}^T S_i}{\mathbf{1}^T S_i + \lambda^2 d_{LE}^2(\tilde{\mathbf{X}}_i, \mu)} + \frac{(v + n - 1)^2}{(n - 1)(n + 1)(n - 2)}\text{tr}(S_i^2)
\right. \\
+ \left. \frac{(n - 1)^2 - (v - q - 1)^2}{n - 1}\text{tr}(S_i^2) + 2\frac{v - q - 1}{n - 1}\text{tr}(\Psi S_i) + \text{tr}(\psi^2)\right\},
\]

with the detailed derivation given in the supplementary materials.

**Remark.** Note that instead of the LNIW prior, one may also consider a prior that captures the correlation structure (if there is any) among both the $M_i$’s and the $\Sigma_i$’s, which may be a more appropriate prior for some applications encountered in image analysis. However, such a prior will make the ensuing mathematical analysis much more complicated than it already is. Hence, we stay with the LNIW prior, and in Section 4 we take a more practical and effective approach (invoking smoothing) to deal with the aforementioned correlation structure.

The hyperparameter vector $(\lambda, \Psi, v, \mu)$ is estimated by minimizing the risk estimate $\text{SURE}(\lambda, \Psi, v, \mu)$, and the resulting shrinkage estimators of $M_i$ and $\Sigma_i$ are obtained by plugging in the minimizing vector into (7). This optimization step allows us to determine the shrinkage from the data. So, unlike the original James–Stein estimator which shrinks the estimate toward a fixed target, we are able to obtain nearly optimal estimates. Note that this is a non-convex optimization problem, and for such problems convergence relies heavily on the choice of the initialization. We suggest the following initialization, which is discussed in the supplementary materials:

$$
\mu_0 = \exp\left(p^{-1}\sum_{i=1}^{p} \log \tilde{X}_i\right),
$$

$$
\lambda_0 = \frac{np^{-1}\sum_{i=1}^{p} d_{LE}^2(\tilde{X}_i, \mu_0)}{p(n-1) - \sum_{i=1}^{p} \text{tr}S_i - p^{-1}\sum_{i=1}^{p} d_{LE}^2(\tilde{X}_i, \mu_0)},
$$

$$
\nu_0 = \frac{n - q - 2}{p(n - 1) - \sum_{i=1}^{p} \text{tr}(S_i)} + q + 1,
$$

$$
\Psi_0 = \frac{\nu_0 - q - 1}{p(n - 1) - \sum_{i=1}^{p} S_i}.
$$

In all our experiments, the algorithm converged in fewer than 20 iterations with this initialization. This concludes the description of our estimators of the unknown means and covariance matrices. Theorem 3 states that $\text{SURE}(\lambda, \Psi, v, \mu)$ approximates the true loss $L(\hat{M}^{\lambda, \mu}, \hat{\Sigma}^{\Psi, \nu}, (M, \Sigma))$ well in the sense that the difference between the two random variables converges to 0 in probability as $p \to \infty$. Additionally, Theorem 4 shows that the estimators of $M$ and $\Sigma$ obtained by minimizing $\text{SURE}(\lambda, \Psi, v, \mu)$ are asymptotically optimal in the class of estimators of the form (7).

**Theorem 3.** Assume the following conditions:

(i) $\limsup_{p \to \infty} \frac{p^2}{(n-1)(n+2)} \sum_{i=1}^{p} \text{tr}S_i < \infty$;

(ii) $\limsup_{p \to \infty} \frac{p^2}{(n-1)(n+2)} \sum_{i=1}^{p} d_{LE}^2(\tilde{X}_i, \mu_0) < \infty$;

(iii) $\limsup_{p \to \infty} \frac{p^2}{(n-1)(n+2)} \sum_{i=1}^{p} \text{tr}(\Psi S_i) + \text{tr}(\psi^2) < \infty$.

Then

$$
\sup_{\lambda > 0, \Psi > 0, L, M, \mu} \left| \text{SURE}(\lambda, \Psi, v, \mu) - L(\hat{M}^{\lambda, \mu}, \hat{\Sigma}^{\Psi, \nu}, (M, \Sigma)) \right| \overset{\text{prob}}{\to} 0 \quad \text{as} \quad p \to \infty.
$$

Note that the optimization has some constraints. However, in practice, with proper initialization as suggested earlier, the constraints on $\Psi$ and $\mu$ can be safely ignored. The reason is that, for $\Psi$ and $\mu$ far from $S_i$’s and $\tilde{X}_i$, respectively, the value of SURE will be large. The constraints on $\lambda$ and $\nu$ can easily be handled by standard constrained optimization algorithms, for example, L-BFGS-B (Byrd et al. 1995).

**Theorem 4.** If assumptions (i)–(iii) in Theorem 3 hold, then

$$
\limsup_{p \to \infty} \left| \text{SURE}(\lambda, \Psi, v, \mu) - L(\hat{M}^{\lambda, \mu}, \hat{\Sigma}^{\Psi, \nu}, (M, \Sigma)) \right| \overset{\text{prob}}{\to} 0 \quad \text{as} \quad p \to \infty.
$$

Note that in all the theorems above, we consider the asymptotic regime $p \to \infty$ while the size of the SPD matrix $N$ is held fixed. The main reason for fixing the size of the SPD matrix is that in our first application, namely the DTI analysis, the size of the diffusion tensors is always $3 \times 3$, because diffusion magnetic resonance images are three-dimensional images. However, the number of voxels $p$ can increase, as they are determined by the resolution of the acquired image, which can increase due to advances in medical imaging technology. This is different from the usual high-dimensional covariance matrix estimation problem in which the size of the covariance matrix is allowed to grow.

**Remark.** The proofs of Theorems 1 and 2 in Yang and Vemuri (2019) use arguments similar to those that already exist in the literature, and in that sense they are not very difficult. In contrast, the proofs of our Theorems 3 and 4 do not proceed along familiar lines. Indeed, they are rather complicated, the difficulty being that bounding the moments of Wishart matrices or the moments of the trace of Wishart matrices is nontrivial when the orders of the required moments are higher than two. We present these proofs in the supplementary materials.

**Remark.** SURE. Full-FM estimates the covariance matrices $\Sigma_i$’s, and this results in performance that is worse than if the covariance matrices were known. On the other hand, FM.LE and SURE-FM assume that the covariance matrices are known, and since this is not the case, we need to estimate them. So we're
not really comparing SURE.Full-FM with FM.LE and SURE-FM, but rather with versions of FM.LE and SURE-FM in which the covariance matrices are estimated. In SURE.Full-FM they are estimated jointly via shrinkage, whereas in FM.LE/SURE-FM they are estimated separately.

### 3.3. Tweedie’s Formula for F Statistics

One of the motivations for the development of our approach for estimating $M$ and $\Sigma$ is a problem in neuroimaging involving detection of differences between a patient group and a control group. The problem can be stated as follows. There are $n_x$ patients in a disease group and $n_y$ normal subjects in a control group. We consider a region of the brain image consisting of $p$ voxels. As explained in Section 4.2, the local diffusional property of water molecules in the human brain is of clinical importance, and it is common to capture this diffusional property at each voxel in diffusion magnetic resonance imaging (dMRI) via a zero-mean Gaussian with a $3 \times 3$ covariance matrix. Using any of the existing state-of-the-art dMRI analysis techniques, it is possible to estimate, from each patient image, the diffusion tensor $M_i$ corresponding to voxel $i$, for $i = 1, \ldots, p$. Let $M_i^{(1)}$ and $M_i^{(2)}$ denote the diffusion tensors corresponding to voxel $i$ for the disease and control groups, respectively. The goal is to identify the indices $i$ for which the difference between $M_i^{(1)}$ and $M_i^{(2)}$ is large. The model we consider is

$$
X_{ij} \overset{\text{iid}}{\sim} \text{LN}(\lambda_i, \Sigma_i), \quad i = 1, \ldots, p, \ j = 1, \ldots, n_x,
$$

$$
Y_{ij} \overset{\text{iid}}{\sim} \text{LN}(\lambda_i, \Sigma_i), \quad i = 1, \ldots, p, \ j = 1, \ldots, n_y.
$$

In this work, we use the Hotelling $T^2$ statistic for each $i = 1, \ldots, p$ as a measure of the difference between $M_i^{(1)}$ and $M_i^{(2)}$. The Hotelling $T^2$ statistic for SPD matrices has been proposed by Schwambach, Dougherty, and Taylor (2010), and is given by

$$
t^2 = (\bar{X}_i - \bar{Y}_i)^T \left[ \left( \frac{1}{n_x} + \frac{1}{n_y} \right) S_i \right]^{-1} (\bar{X}_i - \bar{Y}_i),
$$

where $\bar{X}_i$ and $\bar{Y}_i$ are the means of $\{X_{ij}\}$ and $\{Y_{ij}\}$, and $S_i = (n_x + n_y - 2)^{-1} (S_i^{(1)} + S_i^{(2)})$ is the pooled estimate of $\Sigma_i$ where $S_i^{(1)}$ and $S_i^{(2)}$ are computed using (6). Since the $X_{ij}$’s and $Y_{ij}$’s are Lognormally distributed, one can easily verify that the distribution of $t_i^2$ is given by

$$
t_i = \frac{\nu - q - 1}{\nu q} t_i^2 \overset{\text{iid}}{\sim} F_{q, \nu q - q - 1, \lambda_i},
$$

where $\nu = n_x + n_y - 2$ is a degrees of freedom parameter (recall that $q = N(N+1)/2$). Note that we make the assumption that the covariance matrices for the two groups are equal, that is, $\Sigma_i^{(1)} = \Sigma_i^{(2)} = \Sigma_i$. Similar results can be obtained for the unequal covariance case, but with more complicated expressions for the $T^2$ statistics and the degrees of freedom parameters.

The $\lambda_i$’s are the noncentrality parameters for the noncentral $F$ distribution and are given by

$$
\lambda_i = \left( \frac{1}{n_x} + \frac{1}{n_y} \right)^{-1} (M_i^{(1)} - M_i^{(2)})^T \Sigma_i^{-1} (M_i^{(1)} - M_i^{(2)}).
$$

These noncentrality parameters can be interpreted as the (squared) differences between $M_i^{(1)}$ and $M_i^{(2)}$, and they are the parameters we would like to estimate using the statistics (9) computed from the data. Then, based on estimates $\hat{\lambda}_i$, we select those $i$’s with large estimates, say the largest $1\%$ of all $\hat{\lambda}_i$. However, the process of selection from the computed estimates introduces selection bias. The bias comes from the fact that it is possible to select some indices $i$ for which the actual $\lambda_i$’s are not large but the random errors are large, so that the estimates $\hat{\lambda}_i$ are pushed away from the true parameters $\lambda_i$. There are several ways to correct for this bias, and Efron (2011) proposed to use Tweedie’s formula for such a purpose.

Tweedie’s formula was first proposed by Robbins (1956), and we review this formula here in the context of the classical normal means problem, which is stated as follows. We observe $Z_i \overset{\text{iid}}{\sim} N(\mu_i, \sigma^2)$, $i = 1, \ldots, p$, where the $\mu_i$’s are unknown and $\sigma^2$ is known, and the goal is to estimate the $\mu_i$’s. In the empirical Bayes approach to this problem we assume that the $\mu_i$’s are iid according to some distribution $G$. The marginal density of the $Z_i$’s is then $f(z) = \int \phi_0(z - \mu) dG(\mu)$, where $\phi_0$ is the density of the $N(0, \sigma^2)$ distribution. With this notation, if $G$ is known (so that $f$ is known), the best estimator of $\mu_i$ (under squared error loss) is the so-called Tweedie estimator given by

$$
\hat{\mu}_i = Z_i + \sigma^2((\nu - 1)/\nu)\hat{f}((\nu - 1)/\nu,\mu_i).$$

A feature of this estimator is that it depends on $G$ only through $f$ and this is desirable because it is fairly easy to estimate $f$ from the $Z_i$’s (so we don’t need to specify $G$). Another interesting observation about this estimator is that $\hat{\mu}_i$ is shrinking the MLE $\hat{\mu}_i^{MLE} = Z_i$ and can be viewed as a generalization of the James-Stein estimator which assumes $\mu_i \overset{\text{iid}}{\sim} N(0, \lambda)$ with unknown $\lambda$. The Tweedie estimator can be generalized to exponential families. Suppose that $Z_i \overset{\text{iid}}{\sim} \phi_0(Z_i)$, and the prior for $\phi$ is $G$. Then the Tweedie estimator for $\eta_i = \int f(z) dG(\eta)$, where $l(z) = \log \int f(z) dG(\eta)$ is the log of the marginal likelihood of the $Z_i$’s and $b_i(z) = \log f_i(z)$.

Although this formula is elegant and useful, it applies only to exponential families. Recently, Du and Hu (2020) derived a Tweedie-type formula for noncentral $\chi^2$ statistics, for situations where one is interested in estimating the noncentrality parameters. Suppose $Z_i \overset{\text{iid}}{\sim} \chi^2_{\lambda_i}$ and $\lambda_i \overset{\text{iid}}{\sim} G$. Then,

$$E(\lambda_i|Z_i) = \left[ (Z_i - v + 4) + 2Z_i \left( \frac{2\nu_i'(Z_i)}{1 + 2\nu_i'(Z_i)} + \nu_i'(Z_i) \right) \right] (1 + 2\nu_i(Z_i)),
$$

where $\lambda_i(\cdot)$ is the marginal log-likelihood of the $Z_i$’s (see Theorem 1 in Du and Hu 2020).

For our situation, if we define $Z_i = (\nu - q - 1)/\nu q t_i^2$, then $Z_i \overset{\text{iid}}{\sim} F_{q, \nu q - q - 1, \lambda_i}$ (recall that $\nu = n_x + n_y - 2$, see (9) and (10)). Assume that the $\lambda_i$’s are iid according to some distribution $G$. We now address the problem of how to obtain empirical Bayes estimates of the $\lambda_i$’s. Let $\Phi_{v_1,v_2,\lambda}$ be the cumulative distribution function (cdf) of the noncentral $F$ distribution, $F_{v_1,v_2,\lambda}$, and let $\tilde{\Phi}_{\nu} = \text{cdf of the noncentral } \chi^2 \text{ distribution, } \chi^2_{\lambda,\mu}$. Then the transformed variable $Y_i = \tilde{\Phi}^{-1}_{v_1,v_2,\lambda_i}(\Phi_{v_1,v_2,\lambda_i}(Z_i))$ follows a noncentral $\chi^2$ distribution with degrees of freedom parameter $v_1$ and noncentrality parameter $\lambda$, and we note that when $v_2$ is large, $\Phi_{v_1,v_2,\lambda}$ and $\tilde{\Phi}_{\nu}$ are nearly equal, so that this quantile
transformation is nearly the identity. However, the transformation depends on \( \lambda_i \), which is the parameter to be estimated, so we propose the following iterative algorithm for estimating \( \hat{E}(\lambda_i | Z_i) \). Let \( \hat{\lambda}_i^{(t)} \) be the estimate of \( \lambda_i \) at the \( t \)th iteration. Then our iterative update of \( \hat{\lambda}_i \) is given by

\[
\hat{\lambda}_i^{(t+1)} = \left[ (Y_i^{(t)} - v_1 + 4) + 2Y_i^{(t)} \left( \frac{2\nu_1 Y_i^{(t)}}{1 + 2\nu_1 Y_i^{(t)}} + l'_{v_1}(Y_i^{(t)}) \right) \right] \\
(1 + 2\nu_1 Y_i^{(t)}),
\]

where \( Y_i^{(t)} = \Phi^{-1}_{v_1,\nu_1,\lambda_i^{(t)}(Z_i)} \), \( v_1 = q \), and \( v_2 = v - q - 1 \).

Now the marginal log-likelihood \( l_0(y) \) is not available since the prior \( G \) for \( \lambda_i \) is unknown. There are several ways to estimate the marginal density of the \( Y_i^{(t)} \)'s. One of these is through kernel density estimation. However, the iterative formula involves the first and second derivatives of the marginal log-likelihood, and estimates of the derivatives of a density produced through kernel methods are notoriously unstable. There exist different approaches for dealing with this problem (see Sasaki et al. 2016; Shen and Ghosal 2017). Here we follow Efron (2011) and postulate that \( l_0(y) \) is well approximated by a polynomial of degree \( K \), and write \( l_0(y) = \sum_{k=0}^{K} \beta_k Y^k \). The coefficients \( \beta_k \), \( k = 1, \ldots, K \), can be estimated via Lindsey's method (Efron and Tibshirani 1996), which is a Poisson regression technique for (parametric) density estimation; the coefficient \( \beta_0 \) is determined by the requirement that \( f_0(y) = \exp(l_0(y)) \) integrates to 1.

The advantage of Lindsey's method over methods that use kernel density estimation is that it does not require us to estimate the derivatives separately, since \( l'_{v_1}(y) = \sum_{k=1}^{K} k \beta_k Y^{k-1} \) and \( l''_{v_1}(y) = \sum_{k=2}^{K} k(k - 1) \beta_k Y^{k-2} \). In our experience, with \( l'_{v_1} \) and \( l''_{v_1} \) estimated in this way, if we initialize the scheme by setting \( \hat{\lambda}_i^{(0)} \) to be the estimate of \( \lambda_i \) given by the Du and Hu (2020) procedure, then the algorithm converges in fewer than 10 iterations.

4. Experimental Results

Here we describe the performance of our methods on three synthetic datasets and three sets of real data from diffusion and functional magnetic resonance imaging. Details on these datasets will be given subsequently. For the synthetic data experiments, we show the following.

(i) The proposed shrinkage estimator for the FM (SURE.Full-FM, with simultaneous estimation of the covariance matrices) outperforms the sample FM (FM.LE) and the shrinkage estimator proposed by Yang and Vemuri (2019) (SURE.FM, with fixed covariance matrices); see Section 4.1.1.

(ii) Our estimator outperforms its competitors for different (increasing) values of \( N \), the size of the SPD matrices; see Section 4.1.2.

(iii) The shrinkage estimates of the group differences capture the regions that are significantly distinct between two groups of SPD matrix-valued images; see Section 4.1.3.

For the real data experiments, we demonstrate the following.

(iv) The SURE.Full-FM provides improvement over the two competing estimators (FM.LE and SURE.FM) for (a) computing an atlas (template) of diffusion tensor images acquired from human brains (Section 4.2.1) and (b) computing the mean connectivity networks from resting state functional MRI (fMRI) measurements (Section 4.2.2). The former experiment tests the framework for the accuracy by varying the spatial dimension, \( p \), of the images (i.e., the number of voxels), and the latter tests the accuracy under varying size, \( N \), of the SPD matrices.

(v) The proposed shrinkage estimator for detecting group differences is able to identify the regions that are significantly distinct between patients with Parkinson’s disease and control subjects; see Section 4.2.3.

Details of these experiments are presented in the following paragraphs.

4.1. Synthetic Data Experiments

We present three synthetic data experiments here to show that the proposed shrinkage estimator, SURE.Full-FM, outperforms the sample FM and SURE-FM under varying sample sizes and sizes of SPD matrices and that the shrinkage estimates of the group differences can accurately localize the regions that are significantly different between the two groups.

4.1.1. Comparison Between SURE.Full-FM and Competing Estimators

Using generated noisy SPD fields (\( P_i \)) as data, we now present performance comparisons of three estimators of \( M \): (a) SURE.Full-FM, which is the proposed shrinkage estimator, (b) SURE-FM, proposed by Yang and Vemuri (2019) which assumes that the covariance matrices are known and (c) the MLE, which is denoted by FM.LE (since by Proposition 1 it is the FM based on the Log-Euclidean metric). The synthetic data are generated according to (5). Specifically, we set \( \mu = I_3 \), \( \Psi = I_6 \), and \( n = 10 \), and we vary the variance \( \lambda_0 \) and the degrees of freedom parameter \( \nu \) of the prior distribution as follows: \( \lambda_0 = 10, 50, \) and \( \nu = 15, 30 \). Figure 1 shows the relationship between the average loss (averaged over \( m = 1000 \) repetitions) and the spatial dimension \( p \) under varying conditions for the three estimators. Note that, since the covariance matrices \( \Sigma_i \)'s are unknown in our synthetic data experiment and \( (n-1)^{-1} S_i \) is an unbiased estimate for \( \Sigma_i \), the \( A_i \)'s in (4) can be unbiasedly estimated by \( [(n-1)q]^{-1} tr S_i \). As is evident from Figure 1, for large \( \lambda \) the gains from using SURE.Full-FM are greater. This observation is in accordance with our intuition, which is that for large \( \lambda \), the \( M_i \)'s are clustered, and it is beneficial to shrink the MLEs of the \( M_i \)'s toward a common value. The main difference between SURE-FM and SURE.Full-FM is that the former requires knowledge of the \( \Sigma_i \)'s and in general such information is not available, and estimates for the \( \Sigma_i \)'s are needed to compute the SURE-FM. Hence, the performance of SURE-FM depends heavily on how good the estimates for the \( \Sigma_i \)'s are. In our synthetic data experiment, we consider the unbiased estimate \( \tilde{A}_i = [(n-1)q]^{-1} tr S_i \) for SURE.FM. In this case, the prior mean for \( \Sigma_i \) is \( E(\Sigma_i) = (\nu - q - 1)^{-1} \tilde{S}_i \), for which the assumption \( \Sigma_i = A_i I \)
seems reasonable. For large \( \nu \), the generated \( \Sigma_i \)'s are far from being identity matrices, which violates the assumption (this can be observed in Figure 1, where we see that SURE-FM is almost identical to FM.LE for \( \nu = 30 \)).

On the other hand, we can fix \( \lambda \) and \( \nu \) to see how different choices of \( \mu \) and \( \Psi \) affect the performance of our shrinkage estimator SURE.Full-FM. To do this, we fix \( n = 10, \lambda = 10 \), and \( \nu = 15 \) (so that we can compare with the top-left panel of Figure 1). We consider \( \mu = \text{diag}(2, 0.5, 0.5) \) and \( \Psi = \text{I} \). The results are shown in Figure 2. The top-left panel of Figure 1 shows that when \( \mu = \text{I} \) and \( \Psi = \text{I} \), there is no difference between SURE-FM and SURE.Full-FM, but Figure 2 shows that when one of \( \mu \) and \( \Psi \) is not the identity, our shrinkage estimator outperforms SURE-FM. For different choices of \( \lambda \) and \( \nu \), the improvement is more significant, following the trend we observed in Figure 1. Note that the chosen hyperparameters here, \( \lambda = 10, 50, 15, 30 \), are extreme. What we aim to show with this particular choice in the simulation is that the SURE-FM can perform either as well as the SURE.Full-FM or as poorly as the MLE. That is, the performance of SURE.Full-FM is the best possible performance that SURE-FM can achieve.

### 4.1.2. Performance Comparisons as Matrix Size Varies

In this section, we present some experiments to assess the improvement when we vary the size of the matrices. In particular, we consider the size \( N \) of the SPD matrices increasing from 10 to 100, and we fix \( p = 10, n = 5, \mu = I_3 \), and \( \Psi = I_q = \text{I}_N(N+1)/2 \) throughout the experiments. The results are shown in Figure 3. As we can see from the figure, although the average loss increases with increasing size (of the SPD matrices), the improvement of our estimator over the competitors is more significant for large \( N \).

### 4.1.3. Differences Between Two Groups of SPD-Valued Images

In this section, we demonstrate the method proposed in Section 3.3 for evaluating the difference between two groups of SPD-valued images. For this synthetic data experiment, we use \( P_2 \), the manifold of \( 2 \times 2 \) SPD matrices, since it is easy to visualize these matrices. For the visualization, we represent each \( 2 \times 2 \) SPD matrix of the SPD-valued image by an ellipse with the two eigenvectors as the axes of the ellipse and the two eigenvalues as the width and height along the corresponding axes. The data are created as follows. Given \( n, M^{(k)}_i \), \( \sigma_i^2 \), \( k = 1, 2, i = 1, \ldots, p \), generate

\[
X_{ij} \overset{\text{iid}}{\sim} \text{LN}(M^{(1)}_i, \sigma_i^2 I), \quad j = 1, \ldots, n_1,
\]

\[
Y_{ij} \overset{\text{iid}}{\sim} \text{LN}(M^{(2)}_i, \sigma_i^2 I), \quad j = 1, \ldots, n_2.
\]

We generate \( n_1 = n_2 = 30 \) \( P_2 \)-valued images for the two groups, and the size of each \( P_2 \)-valued image is \( 20 \times 20 \), which gives \( p = 20 \times 20 = 400 \). For the variances \( \sigma_i^2 \), we consider a low-variance scenario \( \sigma_i^2 \overset{\text{iid}}{\sim} U(0.1, 0.3) \) and a high-variance scenario \( \sigma_i^2 \overset{\text{iid}}{\sim} U(0.3, 0.8) \). The means \( M^{(k)}_i \) are depicted visually in Figure 4 (in the form of images with ellipses instead of gray values at each pixel), and the region in which the means are different is the top-right corner, containing a quarter of the pixels; this is the “ground truth” data.
As described in Section 3.3, we first compute the Hotelling $T^2$ statistic from $\{X_{ij}\}_{j=1}^{n_1}$ and $\{Y_{ij}\}_{j=1}^{n_2}$ for each $i$ and transform each of them to an $F$ statistic. We then have $p$ noncentral $F$ statistics, $f_i \sim F_{\nu_1, \nu_2, \lambda_i}$, $i = 1, \ldots, p$, where $\nu_1 = q = 3$, and $\nu_2 = n_1 + n_2 - 2 - q - 1 = n_1 + n_2 - 6$. With the resulting $F$ statistics, we can apply the algorithm described in Section 3.3 to estimate the noncentrality parameters (at each location), and for the estimation of the marginal log likelihood, we adopt Lindsey’s method and fit a polynomial of degree $K = 5$ to the log-likelihood $l_{\nu_1}$. We have experimented using different values of $K$, and we found that the results are robust to changes in $K$, at least for relatively small $K$. In our experiments, we set $n_1 = n_2 = 30$. As we can see from Figure 4, we expect the method to yield large values on the top-right corner of the image and small values for the rest of the matrix-valued image (field). We compare the proposed estimator $\lambda_{i,Tweedie}'$ to the estimator $\lambda_{i,MOM}' = \max \left( \frac{n_1 - 1}{n_2}, f_i - \nu_1, 0 \right)$, which is obtained by the method of moments (MOM) and truncated at 0, and also compare them for different $\sigma^2$’s. We compare with the MOM estimator instead of the MLE for two reasons: (i) the MLE for the noncentrality parameter of the noncentral $F$ distribution is expensive to compute, and (ii) the MOM is commonly used as a standard for comparison, see for example Kubokawa, Robert, and Saleh (1993). Figure 5 gives the results. As we can see, the density of the Tweedie-adjusted estimates concentrates in a smaller region when compared to that of the MOM estimates. This shows that the Tweedie-adjusted estimator allows us to capture the true region of difference better than does the MOM estimator, especially for small $\sigma^2$’s. This is due to the shrinkage effect in Tweedie’s formula.

4.2. Real Data Experiments

In this section, we present three real data experiments involving dMRI and rs-fMRI datasets. The dMRI data we use are publicly available via https://pdbp.ninds.nih.gov/our-data. dMRI is a diagnostic imaging technique that allows one to non-invasively probe the axonal fiber connectivity in the body by making the magnetic resonance signal sensitive to water diffusion through the tissue being imaged. In dMRI, the water diffusion is fully characterized by the probability density function of the displacement of water molecules, called the ensemble average propagator (EAP) (Callaghan 1993). A simple model that has been widely used to describe the displacement of water molecules is a zero mean Gaussian; its covariance matrix defines the diffusion tensor and characterizes the diffusivity function locally. The diffusion tensors are $3 \times 3$ SPD matrices and hence have 6 unique entries that need to be determined. Thus, the diffusion imaging
technique employed in this case involves the application of at least 6 diffusion sensitizing magnetic gradients for acquisition of full 3D MR images (Basser, Mattiello, and LeBihan 1994). This dMRI technique is called diffusion tensor imaging (DTI). Some practical techniques for estimating the diffusion tensors and the population mean of diffusion tensors have been reported in Wang and Vemuri (2004), Chefd’Hoteletal. (2004), Fletcher and Joshi (2004), Alexander (2005), Zhou et al. (2008), Lenglet, Rousson, and Deriche (2006), and Dryden, Koloydenko, and Zhou (2009).

DTI has been the de facto noninvasive dMRI diagnostic imaging technique of choice in the clinic for a variety of neurological ailments. After fitting/estimating the diffusion tensors at each voxel, scalar-valued or vector-valued measures are derived from the diffusion tensors for further analysis. For instance, fractional anisotropy (FA) is a scalar-valued function of the eigenvalues of the diffusion tensor and it was found that FA was reduced in the neuro-anatomical structure called the Substantia Nigra in patients with Parkinson’s disease compared to control subjects (Vaillancourt et al. 2009). In Schwartzman, Dougherty, and Taylor (2010) the authors used the full tensor information, and we adopt the same strategy here since the full tensor captures both the eigenvalues and eigenvectors, which can prove to be much more useful (compared to FA or other scalar measures) in order to assess the changes caused by pathologies to the underlying tissue micro-architecture revealed by dMRI.

### 4.2.1. Estimation of the Motor Sensory Tracts of Patients with Parkinson’s Disease

In this section, we demonstrate the performance of SURE.Full-FM on the dMRI scans of human brain data acquired from 50 patients with Parkinson’s disease and 44 control (normal) subjects. The dMRI acquisition parameters were as follows: repetition time \( T_{re} = 7748 \) ms, echo time \( T_{me} = 86 \) ms, flip angle \( = 90^\circ \), number of diffusion gradients \( = 64 \), field of view \( = 224 \times 224 \) mm, in-plane resolution \( = 2 \) mm isotropic, slice-thickness \( = 2 \) mm, and SENSE factor \( = 2 \). All the dMRI data were pre-registered into a common coordinate frame prior to any further data processing.

The motor sensory area fiber tracts (M1 fiber tracts) are extracted from each patient of the two groups using the template described in Archer, Vaillancourt, and Coombes (2017), which is freely available from http://lnlab.org. The size (length) of each tract is 33 voxels for the left hemisphere tract and 34 voxels for the right hemisphere tract. Diffusion tensors are then fit to each of the voxels along each of the tracts to obtain \( p = 3 \times 3 \) SPD matrices. We then compute the Log-Euclidean FM tract for each group over the patients, that is, the FM tract here also has 33 (34) diffusion tensors along the tract. We will use these FMs computed from the full population for each group as the “ground truth”; thus, the underlying distribution in this experiment is the empirical distribution formed by the observed data, that is, the 33 (34) SPD matrices. Then, we randomly draw a subsample of size \( n = 10, 20, 50, 100 \), with replacement, from each group and compute the SURE.Full-FM (our proposed estimator) and the two competing estimators (FM.LE and SURE-FM, respectively) for each group and for each subsample size \( n \). An explanation of why sampling is done with replacement is given in Section 5 of the supplementary materials. We compare the performance of the different estimators by the Log-Euclidean distance between the estimator and the “ground truth” FMs. The entire procedure is repeated for \( m = 100 \) random draws of subsamples and the average distances are reported in Table 1. Since our proposed shrinkage estimator jointly estimates the FM and the covariance matrices, we also compare our covariance estimates, denoted SURE.Full-Cov, with the MLE of the covariance matrices, that is, the sample covariance matrices. The results are shown in Table 2.
As is evident from Table 1, the SURE.Full-FM outperforms the competing estimators under varying size of subsamples. Also note that, as the sample size increases, the improvement is less significant, which is consistent with the observations on the synthetic data experiments in Section 4.1. Recall that in Section 4.1.1, the SURE.FM and the SURE.Full-FM perform equally well when the assumption $\Sigma_i = A_i I$ is not violated severely. For real data, it is impossible to check this assumption and it is unlikely to be true. Hence, in this real data experiment, SURE.Full-FM outperforms SURE.FM by a large margin. The improvement of the proposed shrinkage estimator for the covariance matrices over the MLEs is evident from Table 2. Another important issue is that for real data the independence assumption is unrealistic. For this reason we have described a simple simulation study to see how the dependence affects the performance of our estimator; see Section 6.2 of the supplementary materials.

### 4.2.2. Simultaneous Estimation of Resting State Functional MRI Connectivity Networks

In this section, we present an experiment on simultaneous estimation of connectivity networks from resting state functional MRI (rs-fMRI). Briefly, rs-fMRI is an MRI technique to measure human brain activity in the resting state, and a (functional) connectivity network computed from rs-fMRI measurements describes how different regions of the human brain are correlated functionally. Van Den Heuvel and Pol (2010) give a nice review on connectivity network analysis for rs-fMRI and its applications. There is a large literature on the relationship between disruption in functional connectivity (disconnectivity) and neurologic and psychiatric brain disorders, including Alzheimer’s disease, depression, and attention deficit hyperactivity disorder (ADHD) (Van Den Heuvel and Pol 2010, p. 529). Hence, functional connectivity networks have served as an important tool in such studies.

A functional connectivity matrix is constructed as follows. At each region of the brain, the blood oxygenation level dependent (BOLD) signal, which is a scalar measure of the neuronal activity in the region, can be detected by an MR scanner. Over the course of time, we obtain a time sequence of BOLD signals $b = [b_1, \ldots, b_n]$, where $n$ is the number of time points, at each region of the brain. To describe the connectivity between two regions, we compute the correlation between the two time sequences of BOLD signals from the two regions. In other words, the connectivity between the two regions measures how in-sync or out-of-sync the two regions are in terms of the BOLD signals. For $N$ regions, the connectivity matrix stores the pairwise connectivity (correlation) of each pair of regions. Hence, a connectivity network is essentially a correlation matrix. To apply the results discussed in Section 3, we consider the problem of simultaneous estimation of the connectivity networks from different rs-fMRI studies. We use the pre-processed networks from the USC Multimodal Connectivity Database (http://umcd.humanconnectomeproject.org/) (Brown et al. 2012). The datasets we used are ADHD200_CC200, PRURIM, and UCSF_MAC_PSP. There are in total seven groups emanating from these three datasets (ADHD200_CC200: Typically Developing, ADHD-Combined, and ADHD-Inattentive; PRURIM: Healthy and Psoriasis; UCSF_MAC_PSP: Control and Progressive Supranuclear Palsy), so here $p = 7$. (Because 7 is not large, our asymptotic optimality results do not apply; however, it is reasonable to expect that shrinkage gives an improvement here in the same way that shrinkage gives an improvement in the normal means problem when $p > 2$.)

Since the networks are from different studies targeting different disorders, the sizes of the connectivity networks and the sizes of the studies are all different. The sizes of the connectivity networks in these three datasets are $190 \times 190$ (ADHD200_CC200), $116 \times 116$ (PRURIM), and $27 \times 27$ (UCSF_MAC_PSP). Thus, we extract an $N \times N$ (where $N$ is fixed across all networks from different datasets) highly correlated sub-network from each network using a hierarchical clustering algorithm (Rokach and Maimon 2005) and the experiments are based on these sub-networks rather than on the original networks. As in the procedure in the previous section, we treat these (sub-)networks as the population and randomly draw subsamples (with replacement) from each group. Then we compute the average loss for the three estimators. The entire procedure is repeated $m = 1000$ times and the results are presented in Table 3. As was seen in Section 4.1.2, the improvement of our estimator over the competitors is more significant for large sub-network sizes. Note that in contrast to our experiment with synthetic data in Section 4.1.2, here we cannot keep increasing $N$: the maximum value is 27 because the connectivity network for the UCSF_MAC_PSP dataset is $27 \times 27$. This experiment demonstrates versatility of our shrinkage estimator to application domains beyond the analysis of dMRI datasets.

### 4.2.3. Tweedie-Adjusted Estimator as an Imaging Biomarker

Finally, we apply the shrinkage estimator proposed in Section 3.3 to identify the regions that are significantly distinct in diffusional properties (as captured via diffusion tensors) between patients with Parkinson’s disease and control subjects. In this experiment, the dataset consists of DTI scans of 46 patients with Parkinson’s disease and 24 control subjects. To identify the differences between the two groups, we use the DTI of the whole brain, which contains $p = 112 \times 112 \times 60$ voxels, without pre-selecting any region of interest. The diffusion tensors are fit at each voxel across the whole brain volume. The goal of this experiment is to see if we are able to automatically identify the regions capturing the large differences between the Parkinson’s disease group and control groups and qualitatively validate our findings against what is expected by expert neurologists. In this context, Prodoehl et al. (2013) observed that the region most affected by Parkinson’s disease is the Substantia Nigra, which is contained in the Basal Ganglia region of the human brain.

After computing both the Tweedie-adjusted estimates and the MOM estimates of the noncentrality parameters, we select

| $N$ | 3 | 5 | 7 | 10 |
|-----|---|---|---|----|
| FMLE | 0.409 (0.01) | 0.738 (0.01) | 1.387 (0.012) | 1.969 (0.016) |
| SURE-FM | 0.296 (0.005) | 0.641 (0.007) | 1.238 (0.009) | 1.854 (0.015) |
| SURE.Full-FM | 0.246 (0.006) | 0.534 (0.006) | 0.977 (0.006) | 1.581 (0.012) |

Bold values indicate the best results among the reported methods in the table.
Figure 6. Differences between scans of Parkinson’s disease group and those of the control group are superimposed on a dMRI scan of a randomly chosen Parkinson’s disease patient and indicated in red.

the voxels with the largest 1% estimates of the non-centrality parameters and mark those voxels in bright red. (There are other ways to determine the threshold for the selection, for example by using the false discovery rate (FDR) in hypothesis testing problems. However, this is beyond the scope of this article and we refer the reader to Schwartzman (2008) and Schwartzman, Dougherty, and Taylor (2010) for interesting work on FDR analysis for DTI datasets.) These voxels are where the large differences between Parkinson’s disease and control groups are observed. The results are shown in Figure 6. For better visualization, we threshold the estimates by the top 1%. To take into account the spatial structure, we apply a $4 \times 4 \times 4$ average mask to smooth the results. This smoothing may also be achieved by incorporating a spatial regularization term in the expression for SURE (8); however, the ensuing analysis becomes much more complicated and will be addressed in future work.

From the results, we can see that the shrinkage effect of our Tweedie-adjusted estimate successfully corrects selection bias and produces a more accurate identification of the affected regions. Our method is able to capture the Substantia Nigra, which is the region known to be affected by Parkinson’s disease. Notably, our method did not point to the apparently spurious and isolated regions selected by the MOM estimator (the tiny red spots in Figure 6(a)). We also mention that past research using FA-based analysis did not report the Internal Capsule as a region affected by Parkinson’s disease. We suspect that this discrepancy is due to the fact that FA discards the directional information of the diffusion tensors while we use the full diffusion tensor which contains the directional information. We plan to conduct a large-scale experiment in our future work to see if this observation continues to hold.

5. Discussion and Conclusions

In this work, we have presented shrinkage estimators for the mean and covariance of the Log-Normal distribution defined on the manifold $P_N$ of $N \times N$ SPD matrices. We also showed that the proposed shrinkage estimators are asymptotically optimal in a large class of estimators including the MLE. The proposed shrinkage estimators are in closed form and resemble (in form) the James–Stein estimator in Euclidean space $\mathbb{R}^p$. We demonstrated that the proposed shrinkage estimators outperform the MLE via several synthetic data examples and real data experiments using diffusion tensor MRI and rs-fMRI datasets. The improvements of the proposed shrinkage estimators are significant especially in the small sample size scenarios, which is very pertinent to medical imaging applications. Further, we also empirically demonstrated that the improvement in the distribution parameter estimates is achieved with increasing size of the SPD matrices as well.

Our work reported here is however based on the Log-Euclidean metric, and one of the drawbacks of this metric is that it is not invariant under affine transformations, which may be a desirable property in some applications. Unfortunately, the derivation of the shrinkage estimators under the affine-invariant metric is challenging due to the fact that there is no closed-form expression for some elementary quantities such as the sample FM, which makes it almost impossible to derive the corresponding closed form for the SURE. Our future research efforts will focus on developing a general framework for designing shrinkage estimators that are applicable to general Riemannian manifolds.

For applications in localizing the regions of the brain where two groups differ, our approach already works well, but it can potentially be improved if we take into account the fact that some features of neighboring voxels within a region are close. For instance, $M_i^{(k)}$ and $M_j^{(k)}$ should be close if voxels $i$ and $j$ are close. Currently, our approach is to apply a spatial smoother to the Tweedie-adjusted estimates. Instead, the improvement can be achieved by imposing regularization constraints, for example, a spatial process prior, in the proposed framework. However, the ensuing analysis becomes rather complicated and will be the focus of our future efforts.

Supplementary Materials

The supplementary materials include the proofs of Theorem 3 and 4, the detailed descriptions of the datasets used in Section 4.2, and additional simulation studies.

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JOURNAL OF THE AMERICAN STATISTICAL ASSOCIATION
271

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