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Large p Small n : Inference for the Mean

Piercesare Secchi, Aymeric Stamm, Simone Vantini

Abstract We present a new result that enables inference for the mean vector of a multivariate normal random variable when the number p of its components is far larger than the number n of sample units and the covariance structure is completely unknown. The result turns out to be a useful tool for the inferential analysis (e.i. confidence region and hypothesis testing) of data up to now mostly studied only within an explorative perspective, like functional data. To this purpose, an application to the analysis of brain vascular vessel geometry is developed and shown.

Key words: Functional data analysis, Testing statistical hypotheses.

1 Introduction

The advent and development of high precision data acquisition technologies in active fields of research (e.g., medicine, engineering, climatology, economics), that are able to capture real-time and/or spatially-referenced measures, have provided the scientific community with large amount of data that challenge the classical approach to data analysis.

Modern data sets (large p small n data sets, i.e. data sets characterized by a number of random variables that is much larger than the number of sample units) contrast traditional data sets (small p large n data sets, i.e. data sets characterized by a number of sample units that is much larger than the number of random variables)

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that drove the evolution of statistics and data analysis during the last century. This makes all classical inferential tools nearly useless in many fields at the forefront of scientific research and raises the demand for new modern inferential tools that suit this new kind of data. The aim of this paper is to provide statistical tools for the inferential analysis of large p small n data sets.

An active area of statistical research moving in this direction is functional data analysis (FDA). Indeed, in FDA each sample unit is represented by means of a function (e.g. Ramsay and Silverman, 2005; Ferraty and Vieu, 2006). Nowadays, the typical inferential approach of FDA is the projection of the n functions under investigation - virtually belonging to an ∞ -dimensional functional space - onto a finite p -dimensional functional subspace with p smaller than n . Roughly speaking, the original FDA is replaced by a classical multivariate analysis that is expected to well approximate the former one. Technically, performing this replacement means implicitly assuming that the image of the random function under investigation (i.e. the space which the realizations of the random function under analysis belong to) coincides with a specific finite p -dimensional functional subspace. This paper is a first attempt to provide inferential tools for the analysis of large p small n data (e.g. functional data) in a basis-free framework (for functional data this means that there are no assumptions on the spaces which the mean function and the auto-covariance function belong to).

The work of Srivastava (2007) moves in the same direction. In this work, some inferential results non depending on strong assumptions on the covariance structure are presented. Unfortunately, these results are asymptotic in both p and n (i.e. large p large n data). This makes them non suitable to perform inferential statistical analysis of large p small n data.

For clarity of exposition, in Section 2 we recall a few well known results about inference for the mean of a multivariate normal random variable; in Section 3, our new results about inference for the mean when the number p of random variables is far larger than the number n of sample units are presented, while in Section 4 an application of the previous results to the inferential analysis of the local radius of the internal carotid artery is reported.

2 Inference for the Mean: State of the Art

The classical approach to inference for the mean μ_p of a p -variate normal random variable with unknown covariance matrix Σ_p relies on a famous corollary of the Hotelling's Theorem that holds when the number n of sample units is larger than the number p of random variables.

Theorem 1 (Hotelling's Theorem). *Assume that (i) $\mathbf{X} \sim N_p(\mu_p, \Sigma_p)$, (ii) $W \sim \text{Wishart}_p(\frac{1}{m}\Sigma_p, m)$, (iii) \mathbf{X} and W are independent, then for $m \geq p$:*

$$\frac{m-p+1}{mp} (\mathbf{X} - \mu_p)' W^{-1} (\mathbf{X} - \mu_p) \sim F(p, m-p+1) .$$

Corollary 1 (Hotelling's Corollary). Assume that (i') $\{\mathbf{X}_i\}_{i=1,\dots,n} \sim iid N_p(\mu_p, \Sigma_p)$, then, for $n > p$:

$$\frac{(n-p)n}{(n-1)p} (\bar{\mathbf{X}} - \mu_p)' S^{-1} (\bar{\mathbf{X}} - \mu_p) \sim F(p, n-p),$$

where $\bar{\mathbf{X}}$ and S^{-1} are the sample mean and the inverse of the sample covariance matrix, respectively.

Corollary 1 makes possible the development of inferential tools for the estimate of the mean value of a p -variate normal random variable (e.g. confidence ellipsoidal regions or hypothesis testing) when the number n of sample units is larger than the number p of random variables; there are no assumptions on the covariance matrix Σ_p that is only required to be positively definite. Proofs of the previous results can be found, for instance, in Anderson (2003).

In more and more applications, the number p of random variables is far larger than the number n of sample units and the covariance matrix is unknown. Thus, Corollary 1 cannot be used to make inference for the mean in these cases. In the following section we provide a theorem and a corollary that can be used to make inference for the mean when n is finite, p goes to infinity, and the covariance matrix is unknown.

3 Inference for the Mean of Large p Small n Data

Given a real positively semi-definite $p \times p$ matrix A with $\{\lambda_i\}_{i=1,\dots,p}$ and $\{\mathbf{e}_i\}_{i=1,\dots,p}$ being its eigenvalues and eigenvectors respectively, $A^+ = \sum_{i:\lambda_i \neq 0} \frac{1}{\lambda_i} \mathbf{e}_i \mathbf{e}_i'$ is called the Moore-Penrose inverse of A (e.g Rao and Mitra, 1971). Moreover, we indicate with $\chi^2_{1-\alpha}(m)$ the $(1 - \alpha)$ -quantile of a random variable with distribution $\chi^2(m)$.

Theorem 2 (Generalized Hotelling's Theorem). Assume that:

- (i) $\mathbf{X} \sim N_p(\mu_p, \Sigma_p)$;
- (ii) $W \sim Wishart_p(\Sigma_p, m)$;
- (iii) \mathbf{X} and W are independent;

then, for $m \geq 1$:

$$\lim_{p \rightarrow +\infty} P \left[\frac{(tr \Sigma_p)^2}{tr \Sigma_p^2} (\mathbf{X} - \mu_p)' W^+ (\mathbf{X} - \mu_p) \leq \chi^2_{1-\alpha}(m) \right] = 1 - \alpha.$$

Corollary 2 (Generalized Hotelling's Corollary). *Assume that:*

$$(i') \quad \{\mathbf{X}_i\}_{i=1,\dots,n} \sim iid N_p(\boldsymbol{\mu}_p, \boldsymbol{\Sigma}_p);$$

then, for $n \geq 2$:

$$\lim_{p \rightarrow +\infty} P \left[\frac{n(\text{tr}\boldsymbol{\Sigma}_p)^2}{(n-1) \text{tr}\boldsymbol{\Sigma}_p^2} (\bar{\mathbf{X}} - \boldsymbol{\mu}_p)' S^+ (\bar{\mathbf{X}} - \boldsymbol{\mu}_p) \leq \chi_{1-\alpha}^2(n-1) \right] = 1 - \alpha ,$$

where $\bar{\mathbf{X}}$ and S^+ are the sample mean and the Moore-Penrose inverse of the sample covariance matrix, respectively.

The proof of Theorem 2 and of Corollary 2 can be found in Secchi et al. (2010). This proof is quite technical and - at the moment - it requires some specific regularity assumptions about the asymptotic behavior of $\boldsymbol{\Sigma}_p$.

Note that Corollary 2 is based on the univariate statistics $n(\bar{\mathbf{X}} - \boldsymbol{\mu}_p)' S^+ (\bar{\mathbf{X}} - \boldsymbol{\mu}_p)$. We named this statistics Generalized Hotelling's T^2 since it can be proven (Secchi et al., 2010) that it generalizes Hotelling's $T^2 = n(\bar{\mathbf{X}} - \boldsymbol{\mu}_p)' S^{-1} (\bar{\mathbf{X}} - \boldsymbol{\mu}_p)$ that appears in Corollary 1. Indeed, Hotelling's T^2 is defined only for $n > p \geq 1$ while the Generalized Hotelling's T^2 is defined for any n and p such that $n \geq 2$ and $p \geq 1$, and it coincides with the former when $n > p$. Strong connections with the univariate t statistic are discussed in Secchi et al. (2010).

Corollary 2 turns out to be a useful tool for the construction of confidence regions and hypothesis tests for the mean in all practical situations where the number p of random variables is far larger than the number n of sample units (e.g. genetics) or even virtually infinite (e.g. functional data).

A Confidence Region for the mean $\boldsymbol{\mu}_p$ can be defined as follows:

$$CR_\gamma(\boldsymbol{\mu}_p) := \left\{ \mathbf{m}_p : \frac{n(\text{tr}\boldsymbol{\Sigma}_p)^2}{(n-1) \text{tr}\boldsymbol{\Sigma}_p^2} (\mathbf{m}_p - \bar{\mathbf{X}})' S^+ (\mathbf{m}_p - \bar{\mathbf{X}}) \leq \chi_\gamma^2(n-1) \right\}, \quad (1)$$

with γ being the asymptotic confidence level.

Equivalently, an **Hypothesis Test** for $H_0 : \boldsymbol{\mu}_p = \boldsymbol{\mu}_{0p}$ versus $H_1 : \boldsymbol{\mu}_p \neq \boldsymbol{\mu}_{0p}$ with asymptotic significance level α has the following rejection region:

$$\begin{aligned} & \text{Reject } H_0 \text{ in favor of } H_1 \text{ if:} \\ & \frac{n(\text{tr}\boldsymbol{\Sigma}_p)^2}{(n-1) \text{tr}\boldsymbol{\Sigma}_p^2} (\bar{\mathbf{X}} - \boldsymbol{\mu}_{0p})' S^+ (\bar{\mathbf{X}} - \boldsymbol{\mu}_{0p}) > \chi_{1-\alpha}^2(n-1) . \end{aligned} \quad (2)$$

In practice, the use of Corollary 2, requires the computation of the coefficient $(tr\Sigma_p)^2/tr\Sigma_p^2$. Two different scenarios may occur:

- The coefficient $(tr\Sigma_p)^2/tr\Sigma_p^2$ is known even if Σ_p is not completely known. This occurs, for instance, in any situation where Σ_p is known up to a multiplying constant (e.g. if $\Sigma_p = \sigma^2\mathbf{I}_p$ with unknown σ^2 , $(tr\Sigma_p)^2/tr\Sigma_p^2$ turns out to be equal to p , or if $[\Sigma_p]_{ij} = \sigma^2 \min(i, j)$ with unknown σ^2 , i.e. a discrete time brownian motion, $(tr\Sigma_p)^2/tr\Sigma_p^2$ turns out to be equal to $3/2$).
- The coefficient $(tr\Sigma_p)^2/tr\Sigma_p^2$ is unknown. In this case we proceed by replacing it with an estimate while the confidence level in (1) and the significance level in (2) become approximate; for instance, in Section 4 the estimator $\frac{(n-2)(n+1)}{(n-1)^2} \frac{(trS)^2}{trS^2 - \frac{1}{n-1}(trS)^2}$ suggested in Secchi et al. (2010) is used.

The case $\Sigma_p = \sigma^2\mathbf{I}_p$ with unknown σ^2 is widely discussed in Srivastava (2007); in that work the distribution of the statistic $\frac{(p-n+2)n}{n-1}(\bar{\mathbf{X}} - \mu_p)'S^+(\bar{\mathbf{X}} - \mu_p)$ is detected for any $p > n$ under the assumption $\Sigma_p = \sigma^2\mathbf{I}_p$. The results presented in Srivastava (2007) are consistent with Corollary 2. Indeed, when $\Sigma_p = \sigma^2\mathbf{I}_p$, for $p \rightarrow +\infty$, the difference between the statistic $\frac{(p-n+2)n}{n-1}(\bar{\mathbf{X}} - \mu_p)'S^+(\bar{\mathbf{X}} - \mu_p)$ and the statistic $\frac{n(tr\Sigma_p)^2}{(n-1)tr\Sigma_p^2}(\bar{\mathbf{X}} - \mu_p)'S^+(\bar{\mathbf{X}} - \mu_p)$ converges a.s. to 0, and the limit distribution of the former statistic is a $\chi^2(n-1)$, as expected by Corollary 2.

Before showing an application of our results within the context of functional data analysis (e.g. the analysis of the local radius of 65 Internal Carotid Arteries), we want to point out some peculiar features of confidence region (1) and of test (2).

Because S^+ is positive semi-definite, the confidence region $CR_\gamma(\mu_p)$ - which for $n > p$ is a p -dimensional ellipsoid in a p -dimensional space - turns out to be a cylinder belonging to a p -dimensional space generated by an $n-1$ -dimensional ellipsoid. Its graphical visualization is of course non trivial. Nevertheless, knowing if a given vector \mathbf{m}_p of interest belongs to $CR_\gamma(\mu_p)$ is always trivial. Moreover it can be shown that $CR_\gamma(\mu_p)$ is bounded in all directions belonging to the random space $Im(S)$ and thus all projections onto these directions can be used to partially visualize $CR_\gamma(\mu_p)$. For instance, one may use the $n-1$ sample principal components (PCs) as natural directions onto which project and visualize $CR_\gamma(\mu_p)$.

Due to the non-null dimension of the random space $ker(S)$ and to the orthogonality between $ker(S)$ and $Im(S)$, we have that the statistics $\frac{n(tr\Sigma_p)^2}{(n-1)tr\Sigma_p^2}(\bar{\mathbf{X}} - \mu_{0p})'S^+(\bar{\mathbf{X}} - \mu_{0p})$ in the hypothesis test (2) does not change if μ_{0p} is replaced by $\mu_{0p} + \mu_{ker(S)}$ with $\mu_{ker(S)}$ being any vector belonging to $ker(S)$. This means that it might happen that H_0 is not rejected even for values of the sample mean $\bar{\mathbf{X}}$ that are “really very far” from μ_{0p} in some direction within $ker(S)$. This is not surprising, because the use of S^+ implies an exclusive focus on the space $Im(S)$, neglecting all $p-n+1$ directions associated to $ker(S)$.

4 An Application to the Radius of Brain Vascular Vessels

We present here an application of the results introduced in Section 3 to the analysis of a functional data set: the local radius of 65 internal carotid arteries (ICA). Details about the origin and elicitation of these data can be found in Sangalli et al. (2009a) and Sangalli et al. (2009b). The 65 patients are divided into two groups according to the presence and location of a cerebral aneurysm in their brain vascular system: the Lower group (made of 32 patients having an aneurysm along the ICA or healthy) and the Upper group (made of 33 patients having an aneurysm downstream of the ICA). For both groups, a 95% confidence region for the mean radius function and a test for the constancy of the mean radius function are computed.

From a numerical point of view, functional data have been discretized on a sufficiently fine grid and the values of the 65 functions in correspondence of the grid points have been used as realizations of the random variables. The grid size (in this case made of 258 points) has been chosen large enough to make the value of the terms on the left of inequalities (1) and (2) stabilize towards their limit values. In practice, we are dealing with two data sets characterized by $n = 32$ and $p = 258$, and $n = 33$ and $p = 258$, respectively, and the p -asymptotic approximation is going to be used.

In Figure 1, for the two data sets (first row of Figure 1), projections of the radius functions (colored curves) and of the 95% confidence region for the mean function (black dotted curves) along the 1st and 2nd PCs are reported (second and third row of Figure 1, respectively); in the language of multivariate statistics, we would refer to these bounds as the extremities of the T^2 -simultaneous confidence intervals along the direction indicated by the 1st and 2nd PCs. Similarly to the multivariate case, this representation is not exhaustive, indeed an infinite number of other directions can be explored by means of similar graphics to help the visualization of the confidence region. Note that the fact that a given function lies within the confidence bounds shown in Figure 1 does not imply that this function belongs to the confidence region (the correct procedure to know if a given function belongs to the confidence region remains using equation (1) directly).

Moreover, note that the bounds in Figure 1 appear to be extremely large compared to the variability presented by the data; this is not surprising in a framework where $p \gg n$. To this purpose, in the fourth row of Figure 1, the projection of the 95% confidence region (black dotted ellipse) onto the subspace generated by the 1st and 2nd PCs is compared with the confidence ellipse based on the classical Hotelling's T^2 with $p = 2$ (black full ellipse); this is the confidence region that one would have used if he had projected functional data onto the subspace generated by the 1st and 2nd PCs and had performed - therein - a classical bi-variate statistical analysis neglecting the randomness of the bi-dimensional space onto which the data are projected (i.e. assuming it as deterministically chosen instead of data dependent). It is evident that in the framework $p \gg n$, ignoring this randomness can make the actual confidence (or test significance) drift away from its nominal value.

Finally, we perform for the two populations a test for checking the constancy of the mean radius, i.e. $H_0 : E[R(s)] = \text{constant}$ versus $H_1 : E[R(s)] \neq \text{constant}$. This

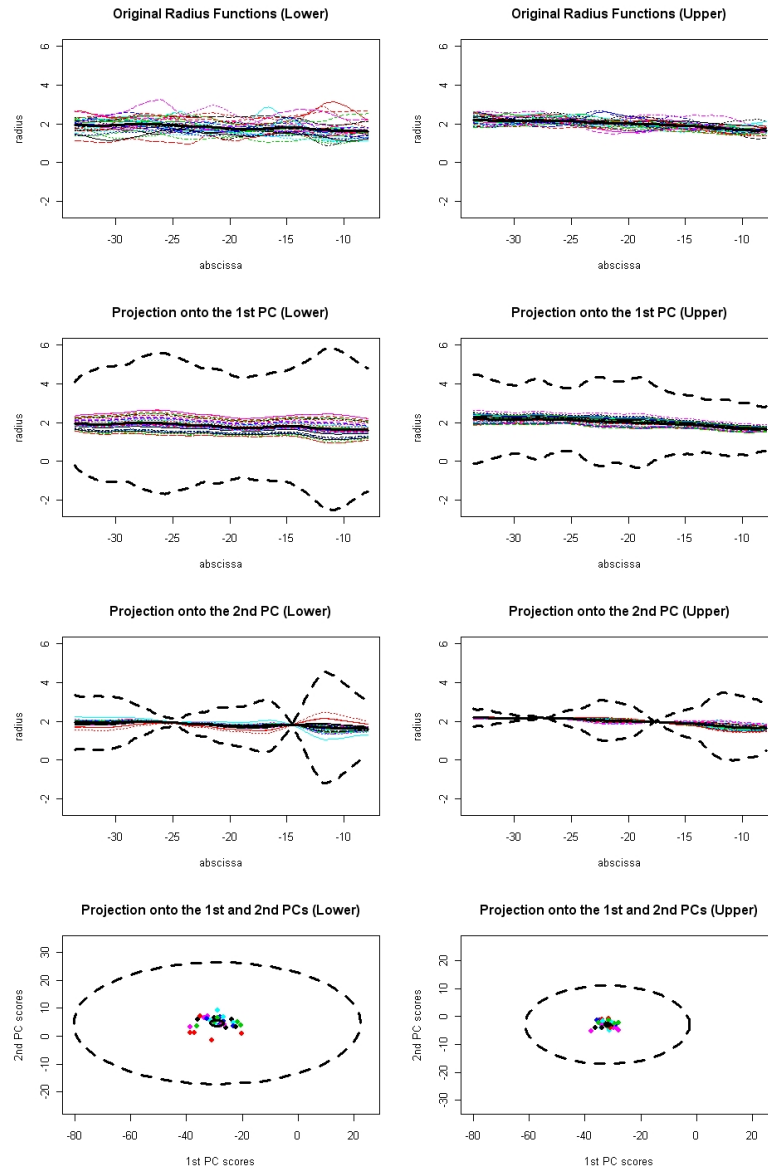


Fig. 1 First row: radius functions (colored curves). Second and third rows: projections of the radius functions (colored curves) and of the 95% confidence region (black dotted curves) along the 1st and 2nd principal components respectively. Fourth row: projections (by means of PC scores) onto the subspace generated by the 1st and 2nd principal components of the radius functions (colored points) and of the 95% confidence region (black dotted ellipse); for comparison the confidence ellipse based on the classical Hotelling's T^2 with $p = 2$ is reported (black full ellipse). Lower group on the left and Upper group on the right.

test is equivalent to the test $H_0 : E[R'(s)] = 0$ versus $H_1 : E[R'(s)] \neq 0$ that can be performed by applying test (2) to the first derivatives of the radius functions. In particular, the 65 first derivatives have been estimated by means of free-knot regression splines (Sangalli et al., 2009b) and the same grid used to build the confidence regions for the radius functions have been used to perform the test. At the significance level 5%, the null hypothesis of constancy of the mean radius is rejected for the Upper group (p -value < 0.001) and it is not for the Lower group (p -value $= 0.076$). Thus, a strong statistical evidence for the non-constancy of the mean radius within the last 30 mm of the ICA of patients with an aneurysm downstream of the ICA is found. This conclusion is coherent with the results illustrated in Sangalli et al. (2009a). But - differently from the latter work, where this conclusion is heuristically derived by means of subjective interpretations of functional principal components - in the present work the same conclusion is reached from an inferential perspective where the hypotheses of constancy and non-constancy of radius are formally defined and quantified by means of an hypothesis test procedure.

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