Parametric and Nonparametric Bootstrap Methods for General MANOVA

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Overview

- Multivariate data
  - Models
  - Limitations
- General MANOVA
  - Asymptotic tests
  - Resampling versions
- Summary
- References
Multivariate Data

- Occur frequently in practice
- More than one variable is observed per patient / subject
- Usual assumptions
  - Multivariate normality
  - Equal covariance matrices across the groups
  - Multivariate normality is quasi impossible to justify
- Multivariate data occur in factorial models
  - One-way layouts ($a = 4$ treatment groups, $p = 3$ endpoints)
  - Two-way factorial models (one-way layout with gender stratification)
  - ...
- Basically the same as ANOVA, but always one dimension more...
Data Layout

- Crossed designs
  - Example: Factor A with $a = 2$ levels, factor B with $b = 3$
  - Each vector $\mathbf{X}$ has $p$ components (endpoints)

<table>
<thead>
<tr>
<th>Factor B ($j = 1, 2, 3$)</th>
<th>$j = 1$</th>
<th>$j = 2$</th>
<th>$j = 3$</th>
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<td>...</td>
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<td>Factor A ($i = 1, 2$)</td>
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<td>$\mathbf{X}<em>{21n</em>{21}}$</td>
<td>$\mathbf{X}<em>{22n</em>{22}}$</td>
<td>$\mathbf{X}<em>{23n</em>{23}}$</td>
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</table>
Factorial Designs

- \( X_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ij} + \epsilon_{ijk} \)
  - \( i = 1, \ldots, a; j = 1, \ldots, b; k = 1, \ldots, n_{ij} \)
  - \( E(\epsilon_{ijk}) = 0, \ Var(\epsilon_{ijk}) = \Sigma_{ij} \)
  - Example: \( i = m,f; j = 0, 1, 2, 3, 4 \)

- Hypotheses
  - No main effect A: \( \alpha_i = 0 \)
  - No main effect B: \( \beta_j = 0 \)
  - No interaction AB: \( \gamma_{ij} = 0 \)

- Simplification
  - \( \mu = (\mu_{11}, \ldots, \mu_{ab})' \)
  - \( H_0(A) : C_A \mu = 0; H_0(B) : C_B \mu = 0; H_0(AB) : C_{AB} \mu = 0 \)
  - Adequate matrices
Statistical Model

- Random vectors
  \[ \mathbf{X}_{ik} = \boldsymbol{\mu}_i + \epsilon_{ik}, i = 1, \ldots, a; k = 1, \ldots, n_i. \]

- Error terms
  \[
  \begin{align*}
  E(\epsilon_{ik}) &= 0, \ i = 1, \ldots, a, \ k = 1, \ldots, n_i, \\
  \text{Cov}(\epsilon_{ik}) &= \Sigma_i > 0, \ i = 1, \ldots, a, \ k = 1, \ldots, n_i, \\
  E(\|\epsilon_{ik}\|^4) &< \infty, \ i = 1, \ldots, a, \ k = 1, \ldots, n_i.
  \end{align*}
  \]

- Asymptotics: \( N \to \infty : \ N/n_i \to \kappa_i < \infty \)
Statistical Model - General MANOVA

- Re-arrangements

\[ X = (X'_{11}, \ldots, X'_{an_a})' \]
\[ \mu = (\mu'_1, \ldots, \mu'_d)' \]
\[ \mu_i = (\mu_{i}^{(1)}, \ldots, \mu_{i}^{(p)})', \quad i = 1, \ldots, a, \]
\[ \epsilon = (\epsilon'_{11}, \ldots, \epsilon'_{an_a})'. \]
General MANOVA: Hypotheses

- $H_0 : H\mu = 0$
  - Generalized Multivariate Behrens-Fisher problem: $H_0 : T\mu = 0$, $T = P_2 \otimes I_p$
  - Multivariate one-way layout: $H_0 : T\mu = 0$, $T = P_a \otimes I_p$
  - Crossed multivariate two-way layout with interactions: $H_0 : T\mu = 0$, $T = P_a \otimes \frac{1}{b} J_b \otimes I_p$
  - Hierarchically nested two-way design: $H_0 : T\mu = 0$, $T$ appropriate
Estimators

- **Point Estimates**
  - Sample means: \( \bar{X}_i. = \frac{1}{n_i} \sum_{k=1}^{n_i} X_{ik} \)
  - Mean vector: \( \bar{X}. = (\bar{X}_1., \ldots, \bar{X}_d.)' \)
  - Asymptotic distribution

\[
V_N = \text{Cov}(\sqrt{N} \; \bar{X}. ) = \text{diag}\left(\frac{N}{n_i} \Sigma_i : 1 \leq i \leq a \right).
\]

- Multivariate normal distribution

- Estimation of the covariance matrix

\[
\hat{V}_N = \text{diag}\left(\frac{N}{n_i} \hat{\Sigma}_i : 1 \leq i \leq a \right),
\]

\[
\hat{\Sigma}_i = \frac{1}{n_i - 1} \sum_{k=1}^{n_i} (X_{ik} - \bar{X}_i.)(X_{ik} - \bar{X}_i.)'.
\]
Test Statistics

- Wald-type statistic

\[ Q_N(T) = N \cdot \bar{X}' (T\hat{\nu}_N T)^+ T\bar{X} \sim \chi^2_{\text{rank}(T)}, N \to \infty. \]

- Statistic is not numerically intensive
- "easy" to compute with standard software
- Can be used to test general hypotheses in general MANOVA
- However, very large sample sizes are needed

- Idea: Explore resampling techniques as an approximation for small samples
Nonparametric Bootstrap Test

- Idea: estimate $\chi^2_{1-\alpha}(\text{rank}(T))$ via resampling
- Data: $X = (X'_{11}, \ldots, X'_{ana})'$
  - Draw with replacement from all data: $X^* = (X'^*_{11}, \ldots, X'^*_{ana})'$
  - $X'_{11}, \ldots, X'_{1n1}$: group 1
  - $X'_{21}, \ldots, X'_{2n2}$: group 2
  - ...
- Means: $\overline{X}^*_i = \frac{1}{n_i} \sum_{k=1}^{n_i} X'^*_ik \Rightarrow \overline{X}^* = (\overline{X}'^*_{1}, \ldots, \overline{X}'^*_{a})'$
- Estimated covariance matrix
  \[ \hat{V}^*_N = \text{diag}\left(\frac{N}{n_i} \hat{\Sigma}^*_i : 1 \leq i \leq a\right), \]
  \[ \hat{\Sigma}^*_i = \frac{1}{n_i - 1} \sum_{k=1}^{n_i} (X'^*_ik - \overline{X}^*_i)(X'^*_ik - \overline{X}^*_i)' . \]
- $Q_N^*(T) = N \cdot (\overline{X}^*')' T (T \hat{V}^*_N T)' + T \overline{X}^*.$
- Repeat these steps $nboot$-times
Why do Bootstrap Tests work?

- Data \( \mathbf{X} = (\mathbf{X}_1', \ldots, \mathbf{X}_{1n_1}', \mathbf{X}_{21}', \ldots, \mathbf{X}_{2n_2}')' \sim F_1 \sim F_2 

- Resampling \( \mathbf{X}^* = (\mathbf{X}_1', \ldots, \mathbf{X}_{1n_1}', \mathbf{X}_{21}', \ldots, \mathbf{X}_{2n_2}')' \sim \kappa_1 F_1 + \kappa_2 F_2 

  - \( E(\mathbb{E}(\overline{X}_1^* - \overline{X}_2^*|\mathbf{X})) = 0 \)
  - \( \text{Var}(\sqrt{N}(\overline{X}_1^* - \overline{X}_2^*|\mathbf{X})) \to \tilde{\sigma}^2 = \sum_{i=1}^{2} \kappa_i \sigma_i^2 + \sum_{i=1}^{2} \kappa_i (\mu_i - \sum_{\ell=1}^{2} \kappa_{i\ell} \mu_{\ell})^2 \)
  - Variance of resampled means depends on \( \sigma_i^2 \) and \( \mu_i \)

- Studentization
  - Consistent estimator of \( \tilde{\sigma}^2 \)!
When do Bootstrap Tests Work?

- Distribution of $Q^*_N(T)$ given $X$
  - Expectation of resampled mean difference: 0
  - Variance of studentized mean: 1
  - $Q^*_N(T)$ is conditionally $\chi^2_{\text{rank}(T)}$ (in probability)

**Bootstrap test works iff** $Q_N(T) \xrightarrow{D} \chi^2_{\text{rank}(T)}$

- In words
  - Resampling dist. mimicks the distribution of $Q_N(T)$ under $H_0$
  - The dist. of $Q_N(T)$ departs from the resampling dist. under $H_1$

- References
  - Konietschke and Pauly (2012 a, b), Konietschke et al. (2015)
Parametric Bootstrap Test

- **Data:** $\mathbf{X} = (\mathbf{X}'_{11}, \ldots, \mathbf{X}'_{an_a})'$
  - **Obtain:** $\hat{\Sigma}_i$
  - $\mathbf{X}'_{11}, \ldots, \mathbf{X}'_{1n_1} \sim N(\mathbf{0}, \hat{\Sigma}_1)$: group 1
  - $\mathbf{X}'_{21}, \ldots, \mathbf{X}'_{2n_2} \sim N(\mathbf{0}, \hat{\Sigma}_2)$: group 2
  - ...
- **Means:** $\overline{\mathbf{X}}^*_{i.} = \frac{1}{n_i} \sum_{k=1}^{n_i} \mathbf{X}^*_{ik} \Rightarrow \overline{\mathbf{X}}^* = (\overline{\mathbf{X}}'^*_{1.}, \ldots, \overline{\mathbf{X}}'^*_{a.})'$
- **Estimated covariance matrix**
  \[
  \hat{\mathbf{V}}^*_N = \text{diag} \left( \frac{N}{n_i} \hat{\Sigma}^*_i : 1 \leq i \leq a \right),
  \]
  \[
  \hat{\Sigma}^*_i = \frac{1}{n_i - 1} \sum_{k=1}^{n_i} (\mathbf{X}^*_{ik} - \overline{\mathbf{X}}^*_{i.})(\mathbf{X}^*_{ik} - \overline{\mathbf{X}}^*_{i.})'.
  \]
- $Q^*_N(\mathbf{T}) = N \cdot (\overline{\mathbf{X}}^*)' \mathbf{T} (\hat{\mathbf{V}}^*_N \mathbf{T})^+ \mathbf{T} \overline{\mathbf{X}}^*.$
- Repeat these steps $n_{boot}$-times
Simulation Settings - I

- \(a = 2, p = 4, \ nsim = nboot = 10,000\)

Setting 1: \(\Sigma_1 = I_4 + 0.5(J_4 - I_4) = \Sigma_2\)

Setting 2: \(\Sigma_1 = [\sigma_{rs}] = (0.6)^{|r-s|} = \Sigma_2\)

Setting 3: \(\Sigma_1 = I_4 + 0.5(J_4 - I_4)\) and \(\Sigma_2 = I_4 \cdot 3 + 0.5(J_4 - I_4)\)

Setting 4: \(\Sigma_1 = [\sigma_{rs}] = (0.6)^{|r-s|}\) and \(\Sigma_2 = (0.6)^{|r-s|} + I_4 \cdot 2\)
## Simulation Results - 1

<table>
<thead>
<tr>
<th>Dist (n₁, n₂)</th>
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<th>Setting 2</th>
<th>Setting 3</th>
<th>Setting 4</th>
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Simulation Settings - II

- $a = 4$, $p = 4$, $nsim = nboot = 10,000$

Setting 5: $\Sigma_i = \mathbf{I}_4 + 0.5(\mathbf{J}_4 - \mathbf{I}_4)$, $i = 1, \ldots, 4$, 

Setting 6: $\Sigma_i = [\sigma_{i,rs}] = (0.6)^{|r-s|}$, $i = 1, \ldots, 4$, 

Setting 7: $\Sigma_i = \mathbf{I}_4 \cdot i + 0.5(\mathbf{J}_4 - \mathbf{I}_4)$, $i = 1, \ldots, 4$, 

Setting 8: $\Sigma_i = [\sigma_{i,rs}] = (0.6)^{|r-s|} + \mathbf{I}_4 \cdot i$, $i = 1, \ldots, 4$, 

## Simulation Results - II

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Simulation Results

- Procedures seem to be “robust” against non-normality
- Depends on the amount of skewness
- Severe settings: Positive and negative pairings
- Parametric bootstrap is the most accurate procedure
- ... but not always accurate...
Summary

- Resampling methods for General MANOVA
  - Conditional CLT for studentized resampling tests
  - Resampling distributions are invariant under main effects
  - Asymptotic tests

- Repeated measures designs
  - \( X_k = (X_{1k}, X_{2k})' \), \( k = 1, \ldots, n \), \( E(X_1) = \mu \) and \( \text{Cov}(X_1) = \Sigma \)
  - Permutation tests für \( H_0 : \mu_1 = \mu_2 \)
    - Permuting all data \( X = (X_{11}, \ldots, X_{2n})' \) (K. and Pauly 2012)
  - \( X_k = (X_{1k}, X_{2k}, \ldots, X_{dk})' \), \( k = 1, \ldots, n \)
  - \( E(X_1) = \mu \) and \( \text{Cov}(X_1) = \Sigma \)
  - Permutation tests for low- and high-dimensional data
  - Multiple comparisons
References I


References II


References III
