Paired Mean Vector Test and Repeated Measures

ST 558: Multivariate Analytics

Module 3

Lecture 4

Paired Multivariate Comparisons

Suppose now that the data represent *pairs* of observations:

- p = 2: (Body temperature, heart rate) before and after 30 minutes of exercise for each of n = 10 subjects
- p = 3: (Salary, years of education, age) for n = 100 husband-wife pairs
- p = 14: Comprehensive metabolic panel (glucose, calcium, albumin, total protein, sodium, potassium, etc.) for n = 50 samples of blood which are split and measured by two different laboratories.

The same set of variables are measured under two different *conditions* (either on the same individual/unit at different times, or on different but **matched** units).

Typically the question of interest is to test whether the difference in mean vectors between the two conditions is zero.

Paired Multivariate Comparisons

The setting of paired comparisons is actually exactly the same as the one-sample case we have already explored:

- Let $\mathbf{X}_{k,i}$, $k = 1, 2$, $i = 1, \ldots, n$ represent the vector of measurements under condition k for unit (or matched pair) i
- Let $\boldsymbol{\mu}_k$ denote the population mean vector under condition k
- Define $\mathbf{D}_i = \mathbf{X}_{2,i} - \mathbf{X}_{1,i}$ to be the vector of differences between the measurements under the different conditions for unit (or matched pair) i.

Paired Multivariate Comparisons: Example

Example: Consider the example with Body Temperature and Heart Rate (Pulse) measured before and after 30 minutes of exercise for n = 10 subjects:

Subject	(Temp, Pulse) Before	(Temp, Pulse) After	(Temp, Pulse) Diff (After – Before)
1	$\mathbf{X}_{1,1} = (97.7, 73)$	$\mathbf{X}_{2,1} = (98.4, 85)$	$\mathbf{D}_1 = (0.7, 12)$
2	$\mathbf{X}_{1,2} = (99.2, 85)$	$\mathbf{X}_{2,2} = (100.0, 94)$	$\mathbf{D}_2 = (0.8, 9)$
3	$\mathbf{X}_{1,3} = (95.9, 76)$	$\mathbf{X}_{2,3} = (96.7, 86)$	$\mathbf{D}_3 = (0.8, 10)$
4	$\mathbf{X}_{1,4} = (98.0, 87)$	$\mathbf{X}_{2,4} = (98.8, 94)$	$\mathbf{D}_4 = (0.8, 7)$
5	$\mathbf{X}_{1,5} = (96.8, 76)$	$\mathbf{X}_{2,5} = (97.4, 84)$	$\mathbf{D}_5 = (0.6, 8)$
6	$\mathbf{X}_{1,6} = (96.6, 72)$	$\mathbf{X}_{2,6} = (97.2, 80)$	$\mathbf{D}_6 = (0.6, 8)$
7	$\mathbf{X}_{1,7} = (97.8, 71)$	$\mathbf{X}_{2,7} = (98.7, 81)$	$\mathbf{D}_7 = (0.9, 10)$
8	$\mathbf{X}_{1,8} = (97.7, 64)$	$\mathbf{X}_{2,8} = (99.3, 75)$	$\mathbf{D}_8 = (1.6, 11)$
9	$\mathbf{X}_{1,8} = (98.0, 63)$	$\mathbf{X}_{2,8} = (98.9, 68)$	$\mathbf{D}_9 = (0.9, 5)$
10	$\mathbf{X}_{1,10} = (97.3, 64)$	$\mathbf{X}_{2,10} = (98.2, 76)$	$\mathbf{D}_{10} = (0.9, 12)$

Paired Multivariate Comparisons

The goal is to test

$$H_0\colon \boldsymbol{\mu}_1 - \boldsymbol{\mu}_2 = \mathbf{0} \qquad \text{vs.} \qquad H_A\colon \boldsymbol{\mu}_1 - \boldsymbol{\mu}_2 \neq \mathbf{0}$$

or, equivalently, letting $\boldsymbol{\mu}_{\mathbf{D}} = \boldsymbol{\mu}_{\mathbf{1}} - \boldsymbol{\mu}_{\mathbf{2}}$,

$$H_0\colon \boldsymbol{\mu}_{\mathrm{D}} = \mathbf{0} \qquad \text{vs.} \qquad H_A\colon \boldsymbol{\mu}_{\mathbf{D}} \neq \mathbf{0}$$

Since the $\mathbf{D}_i$ are a multivariate sample from a population with mean $\boldsymbol{\mu}_{\mathrm{D}}$, we can just use the one-sample Hotelling's T^2 test to test the above hypotheses:

$$T^2(0) = n(\overline{\mathbf{D}})^T(\mathbf{S}_{\mathbf{D}})^{-1}(\overline{\mathbf{D}})$$

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$\mathbf{0}$ is the $(p\times 1)$ vector of zeros.

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or, equivalently, letting $\boldsymbol{\mu}_\mathbf{D} = \boldsymbol{\mu}_1 - \boldsymbol{\mu}_2$,

vs.

$\overline{\mathbf{D}}$ is the sample mean vector of the *difference vectors* $\mathbf{D}_i$

$\mathbf{S}_\mathbf{D}$ is the sample covariance matrix of the *difference vectors* $\mathbf{D}_i$

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$$T^2(0) = n(\overline{\mathbf{D}})^T(\mathbf{S}_\mathbf{D})^{-1}(\overline{\mathbf{D}})$$

Paired Multivariate Comparisons: Example

<u>Example:</u> Consider the example with Body Temperature and Heart Rate (Pulse) measured before and after 30 minutes of exercise for n = 10 subjects:

Subject	(Temp, P		(Temp, Pulse) Diff (After – Before)
1	$\mathbf{X}_{1,1} =$		$\mathbf{D}_1 = (0.7, 12)$
2	$\mathbf{X}_{1,2} =$		$\mathbf{D}_2 = (0.8, 9)$
3	$\mathbf{X}_{1,3} =$		$\mathbf{D}_3 = (0.8, 10)$
4	$\mathbf{X}_{1,4} =$		$\mathbf{D}_4 = (0.8, 7)$
5	$\mathbf{X}_{1,5} =$		$\mathbf{D}_5 = (0.6, 8)$
6	$\mathbf{X}_{1,6} = (96.6, 72)$	$\mathbf{X}_{2,6} = (97.2, 80)$	$\mathbf{D}_6 = (0.6, 8)$
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10	$\mathbf{X}_{1,10} = (97.3, 64)$	$\mathbf{X}_{2,10} = (98.2, 76)$	$\mathbf{D}_{10} = (0.9, 12)$

Perform the one-sample Hotelling's T^2 test on *this* multivariate data to test that the population mean vector of the *differences* is $[0, 0]^T$

Paired Multivariate Comparisons

Similarly, confidence regions for the mean difference vector $\boldsymbol{\mu}_{\mathbf{D}} = \boldsymbol{\mu}_{\mathbf{1}} - \boldsymbol{\mu}_{\mathbf{2}}$ may be constructed as

$$C = \left\{ \boldsymbol{\mu}_{\mathbf{D}0} : \frac{n-p}{(n-1)p} T^2(\boldsymbol{\mu}_{\mathbf{D}0}) \le F_{(p,n-p)}(\alpha) \right\}$$

$$= \left\{ \boldsymbol{\mu}_{\mathbf{D}0} : \frac{n-p}{(n-1)p} n(\overline{\mathbf{D}} - \boldsymbol{\mu}_{\mathbf{D}0})^T (\mathbf{S}_{\mathbf{D}})^{-1} (\overline{\mathbf{D}} - \boldsymbol{\mu}_{\mathbf{D}0}) \le F_{(p,n-p)}(\alpha) \right\}$$

Repeated Measures

Repeated measures data arise when the same *univariate* measurement is taken for each subject/unit under q different conditions (treatments, times).

- Adrenaline level measured for n = 30 subjects under the following q = 4 conditions: (Waking, jogging, watching scary movie, taking a test)
- Average yearly temperature measured at n = 5000 weather stations for q = 10 years (2000, 2001, 2002, …, 2009)
- Headache frequency recorded for n = 20 migraine sufferers taking each of q = 5 different medications in succession, randomly ordered and switching each month.

For repeated measures data, the question is typically to test whether the means of the measurements under all of the experimental conditions are equal.

Repeated Measures

- Let $\mathbf{X}_i = \left[X_{i1}, X_{i2}, \dots, X_{iq}\right]^T$ be the $(q\times 1)$ vector of measurements for subject/unit i under the q different conditions.
- Let $\boldsymbol{\mu} = \left[\,\mu_1, \mu_2, \dots, \mu_q\right]^T$ be the $(q\times 1)$ vector of population means under the q different conditions, so as we have seen before, $E\left(X_{ij}\right) = \mu_j$.
- The goal is to test

$$H_0\colon \mu_1 = \mu_2 = \ \dots = \mu_q \quad \text{vs.} \quad H_A\colon \text{Not all } \mu_j \text{ equal}$$

Repeated Measures

To test the repeated measures setting, we construct <u>*contrasts*</u>:

<u>Definition:</u> A <u>*contrast matrix*</u> $\mathbf{C}$ is a $((q-1)\times q)$ matrix with linearly independent rows, all of which are orthogonal to $\mathbf{1}_q$ (the $(q\times 1)$ vector of all ones).

Then for *any* such contrast matrix $\mathbf{C}$

$H_0: \mu_1 = \mu_2 = \ldots = \mu_q$ vs. H_A: Not all μ_j equal

is equivalent to testing $\mathbf{C}\boldsymbol{\mu} = \mathbf{0}_{q-1}$.

Repeated Measures

Example: Let

$$\mathbf{C}_1 = \begin{bmatrix} 1 & -1 & 0 & \cdots & 0 \\ 1 & 0 & -1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & 0 & 0 & \cdots & -1 \end{bmatrix}$$

Then $\mathbf{C}_1 \boldsymbol{\mu}$ is

$$\underset{((q-1)\times q)}{\begin{bmatrix} 1 & -1 & 0 & \cdots & 0 \\ 1 & 0 & -1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & 0 & 0 & \cdots & -1 \end{bmatrix}} \underset{(q\times 1)}{\begin{bmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_q \end{bmatrix}} = \underset{((q-1)\times 1)}{\begin{bmatrix} \mu_1 - \mu_2 \\ \mu_1 - \mu_3 \\ \vdots \\ \mu_1 - \mu_q \end{bmatrix}}$$

Repeated Measures

<u>Example:</u> Let

$$\mathbf{C}_2 = \begin{bmatrix} 1 & -1 & 0 & \cdots & 0 & 0 \\ 0 & 1 & -1 & \cdots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 & -1 \end{bmatrix}$$

Then $\mathbf{C}_2\boldsymbol{\mu}$ is

$$\underset{\big((q-1)\times q\big)}{\begin{bmatrix} 1 & -1 & 0 & \cdots & 0 & 0 \\ 0 & 1 & -1 & \cdots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & 1 & -1 \end{bmatrix}} \underset{(q\times 1)}{\begin{bmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_q \end{bmatrix}} = \underset{\big((q-1)\times 1\big)}{\begin{bmatrix} \mu_1 - \mu_2 \\ \mu_2 - \mu_3 \\ \vdots \\ \mu_{q-1} - \mu_q \end{bmatrix}}$$

Repeated Measures

From the original set of repeated measures random vectors $\mathbf{X}_i$, we can then create a new set of *contrast* vectors:

$$\underset{((q-1)\times 1)}{\boldsymbol{Y}_i} = \underset{((q-1)\times q)}{\mathbf{C}} \underset{(q\times 1)}{\mathbf{X}_i}$$

Then testing that

$$H_0\!: \mu_1 = \mu_2 = \ldots = \mu_q \quad \text{vs.} \quad H_A\!: \text{Not all } \mu_j \text{ equal}$$

may be done by using the new vectors $\boldsymbol{Y}_i$ and testing that $\boldsymbol{\mu}_{\mathbf{Y}} = \mathbf{0}_{q-1}$ using the one-sample Hotelling's T^2 test.

Repeated Measures

The test statistic is therefore

$$T^2(H_0) = n(\bar{\mathbf{Y}})^T(\mathbf{S}_{\mathbf{Y}})^{-1}(\bar{\mathbf{Y}})$$

with reference distribution $F_{q-1,n-q+1}$ since the dimension of the $\mathbf{Y}_i$ vectors is $p = q - 1$.

Therefore, we reject $H_0: \mu_1 = \mu_2 = \ldots = \mu_q$ at level α when $\frac{n-q+1}{(n-1)(q-1)} T^2(H_0) > F_{q-1,n-q+1}(\alpha)$.

Repeated Measures: Example

Example: Consider the example of measuring adrenaline (epinephrine) levels (pg/ml) for n = 10 subjects under q = 4 conditions: Waking, jogging, watching scary movie, taking a test

Subject	Adrenaline (Waking, Jogging, Movie, Test)
1	$\mathbf{X}_1 = [410\ \ 473\ \ 510\ \ 599]^T$
2	$\mathbf{X}_2 = [431\ \ 448\ \ 517\ \ 541]^T$
3	$\mathbf{X}_3 = [614\ \ 595\ \ 618\ \ 715]^T$
4	$\mathbf{X}_4 = [420\ \ 368\ \ 534\ \ 480]^T$
5	$\mathbf{X}_5 = [549\ \ 555\ \ 686\ \ 648]^T$
6	$\mathbf{X}_6 = [467\ \ 604\ \ 604\ \ 706]^T$
7	$\mathbf{X}_7 = [194\ \ 294\ \ 312\ \ 417]^T$
8	$\mathbf{X}_8 = [260\ \ 315\ \ 435\ \ 468]^T$
9	$\mathbf{X}_9 = [349\ \ 370\ \ 419\ \ 433]^T$
10	$\mathbf{X}_{10} = [450\ \ 499\ \ 610\ \ 691]^T$

$$\mathbf{C} = \begin{bmatrix} -1 & 1 & 0 & 0 \\ -1 & 0 & 1 & 0 \\ -1 & 0 & 0 & 1 \end{bmatrix}$$

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$$\mathbf{C} = \begin{bmatrix} -1 & 1 & 0 & 0 \\ -1 & 0 & 1 & 0 \\ -1 & 0 & 0 & 1 \end{bmatrix}$$

$$\mathbf{CX}_i = [X_2 - X_1, X_3 - X_1, X_4 - X_1]$$

Repeated Measures: Example

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Subject	Adrenaline (Waking, Jogging, Movie, Test)	Contrast Vector
1	$\mathbf{X}_1 = [410\ \ 473\ \ 510\ \ 599]^T$	$\mathbf{Y}_1 = \mathbf{CX}_1 = [63\ \ 100\ \ 189]^T$
2	$\mathbf{X}_2 = [431\ \ 448\ \ 517\ \ 541]^T$	$\mathbf{Y}_2 = \mathbf{CX}_2 = [17\ \ 86\ \ 110]^T$
3	$\mathbf{X}_3 = [614\ \ 595\ \ 618\ \ 715]^T$	$\mathbf{Y}_3 = \mathbf{CX}_3 = [-19\ \ 4\ \ 101]^T$
4	$\mathbf{X}_4 = [420\ \ 368\ \ 534\ \ 480]^T$	$\mathbf{Y}_4 = \mathbf{CX}_4 = [-52\ \ 114\ \ 60]^T$
5	$\mathbf{X}_5 = [549\ \ 555\ \ 686\ \ 648]^T$	$\mathbf{Y}_5 = \mathbf{CX}_5 = [6\ \ 137\ \ 99]^T$
6	$\mathbf{X}_6 = [467\ \ 604\ \ 604\ \ 706]^T$	$\mathbf{Y}_6 = \mathbf{CX}_6 = [137\ \ 137\ \ 239]^T$
7	$\mathbf{X}_7 = [194\ \ 294\ \ 312\ \ 417]^T$	$\mathbf{Y}_7 = \mathbf{CX}_7 = [100\ \ 118\ \ 223]^T$
8	$\mathbf{X}_8 = [260\ \ 315\ \ 435\ \ 468]^T$	$\mathbf{Y}_8 = \mathbf{CX}_8 = [55\ \ 175\ \ 208]^T$
9	$\mathbf{X}_9 = [349\ \ 370\ \ 419\ \ 433]^T$	$\mathbf{Y}_9 = \mathbf{CX}_9 = [21\ \ 70\ \ 84]^T$
10	$\mathbf{X}_{10} = [450\ \ 499\ \ 610\ \ 691]^T$	$\mathbf{Y}_{10} = \mathbf{CX}_{10} = [49\ \ 160\ \ 241]^T$

Repeated Measures: Example

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Subject	Adr[illegible]est)	Contrast Vector
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Perform the one-sample Hotelling's T^2 test on *this* multivariate data to test that the population mean vector of the *contrasts* is $[0, 0, 0]^T$

Repeated Measures

The choice of the contrast matrix **C** does not matter for the hypothesis test: <u>the exact same test statistic and decision will be obtained from any contrast matrix.</u>

However, the estimated contrasts and corresponding confidence intervals *will* differ depending on the contrast matrix chosen: therefore, choose a contrast matrix that is of interest.