Resampling Techniques and their Application

-Class 12-

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Example: Liver Weights of Wistar Rats

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x3 = c(3.71, 3.36, 3.38, 3.64, 3.41, 3.29, 3.61, 3.87)
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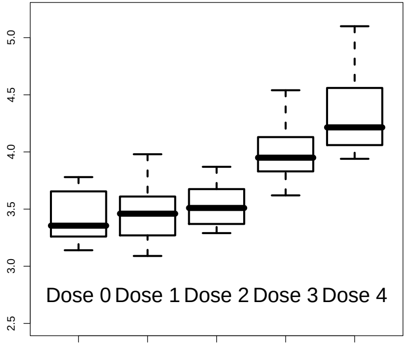
Example: Liver Weights of Wistar Rats

- Toxicity trial: 40 rats were randomized into 5 dose groups (Dose 0 - Dose 4)
- After treatment: relative liver weight of each animal
- Question: Which dose(s) differ from control? Trend?

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- **Multiple hypotheses**

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- In general

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- The contrast matrix **C** is nothing but the pattern of the alternative H_1
- In general, **C** is a $q \times a$ matrix. Each row vector is a contrast.

$$\boldsymbol{C} = \begin{pmatrix} \mathbf{c}_1' \\ \vdots \\ \mathbf{c}_q' \end{pmatrix} = \begin{array}{c} \begin{array}{cccc} \mu_1 & \mu_2 & \cdots & \mu_a \end{array} \\ \begin{pmatrix} c_{11} & c_{12} & \cdots & c_{1a} \\ c_{21} & c_{22} & \cdots & c_{2a} \\ \vdots & \vdots & \vdots & \vdots \\ c_{q1} & c_{q2} & \cdots & c_{qa} \end{pmatrix} \end{array} ; \sum_{i=1}^{a} c_{\ell i} = 0, \; \ell = 1, \ldots, q$$

General Contrasts

- Example 1: Many-to-one comparisons (Dunnett):

$$H_1 : \begin{cases} \mu_1 \neq \mu_2 \\ \mu_1 \neq \mu_3 \\ \vdots \\ \mu_1 \neq \mu_a \end{cases} \Leftrightarrow \boldsymbol{C} = \begin{pmatrix} -1 & 1 & 0 & \cdots & 0 \\ -1 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ -1 & 0 & \cdots & \cdots & -1 \end{pmatrix}$$

General Contrasts (II)

- Example 2: Trend (Williams)

$$H_1 : \begin{cases} \mu_1 \neq \mu_a \\ \mu_1 \neq \mu_{a-1} = \mu_a \\ \vdots \\ \mu_1 \neq \mu_2 = \ldots = \mu_a \end{cases} \Leftrightarrow \boldsymbol{C} = \begin{pmatrix} -1 & 0 & 0 & \cdots & 1 \\ -1 & 0 & 0 & \frac{n_{a-1}}{n_{a-1}+n_a} & \frac{n_a}{n_{a-1}+n_a} \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ -1 & \frac{n_2}{n_2+\ldots+n_a} & \cdots & \cdots & \frac{n_a}{n_2+\ldots+n_a} \end{pmatrix}$$

General Contrasts (III)

- Example 3: All-pairs (Tukey):

$$H_1 : \begin{cases} \mu_1 \neq \mu_2 \\ \mu_1 \neq \mu_3 \\ \vdots \\ \mu_1 \neq \mu_a \\ \mu_2 \neq \mu_3 \\ \vdots \\ \mu_{a-1} \neq \mu_a \end{cases} \Leftrightarrow \boldsymbol{C} = \begin{pmatrix} -1 & 1 & 0 & \cdots & 0 \\ -1 & 0 & 1 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & -1 & 1 \end{pmatrix}$$

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- And many more

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- And many more
- See *contrMat* function in *multcomp* package

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- Reject H_0, if any $H_0^{(\ell)}$ is rejected

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  - $\overline{\mathbf{X}}_{\cdot} = (\overline{X}_{1\cdot}, \ldots, \overline{X}_{a\cdot})'$ (vector of means)
- Variance of contrasts in means

$$
\begin{aligned}
\mathbf{S} &= Cov(\overline{\mathbf{X}}_{\cdot}) = diag\left(\frac{\sigma_1^2}{n_1}, \ldots, \frac{\sigma_a^2}{n_a}\right) \\
\mathbf{\Gamma} &= Cov(\boldsymbol{C}\overline{\mathbf{X}}_{\cdot}) = \boldsymbol{C}\mathbf{S}\boldsymbol{C}' = \boldsymbol{C}diag\left(\frac{\sigma_1^2}{n_1}, \ldots, \frac{\sigma_a^2}{n_a}\right)\boldsymbol{C}' \\
\sigma_\ell^2 &= Var(\boldsymbol{c}_\ell'\overline{\mathbf{X}}_{\cdot}) = \sum_{i=1}^{a} \sigma_i^2 \frac{c_{\ell i}^2}{n_i} = \mathbf{c}_\ell' \boldsymbol{S}\mathbf{c}_\ell
\end{aligned}
$$

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- Variance of a contrast

$$\begin{aligned}
\widehat{\mathbf{S}} &= diag\left(\frac{s_1^2}{n_1}, \ldots, \frac{s_a^2}{n_a}\right) \\
\widehat{\Gamma} &= \boldsymbol{C}\widehat{\mathbf{S}}\boldsymbol{C}' = \boldsymbol{C} diag\left(\frac{s_1^2}{n_1}, \ldots, \frac{s_a^2}{n_a}\right) \boldsymbol{C}' \\
\widehat{\sigma}_\ell^2 &= \mathbf{c}_\ell' \widehat{\mathbf{S}} \mathbf{c}_\ell
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\end{aligned}$$

```
library(multcomp)
C <-contrMat(rep(1,5),"Dunnett")
X<-c(x1,x2,x3,x4,x5)
n<-c(8,7,8,7,8)
N<-sum(n)
grp<-factor(c(rep(1:5,n)))
a<-5
Dat<-data.frame(X=X,grp=grp)
Xbar<-aggregate(X~grp,data=Dat,mean)[,2]
si2 <-aggregate(X~grp,data=Dat,var)[,2]

Shat <- diag(si2/n)
Gammahat<-C%*%Shat%*%t(C)
```

Multiple Comparisons

- For $H_0^{(\ell)} : \mathbf{c}_\ell' \boldsymbol{\mu} = 0$

$$T_\ell = \frac{\mathbf{c}_\ell' \overline{\mathbf{X}}_\cdot}{\sqrt{\widehat{\sigma}_\ell^2}}, \ell = 1, \ldots, q$$

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- Distribution of T_ℓ can be approximated by a t-distribution with

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```
diff <-C%*%Xbar
Tl<-diff/sqrt(c(diag(Gammahat)))

nul = sapply(1:nrow(C),function(arg){
c(t(C[arg,])%*%Shat%*%C[arg,])^2/
sum(C[arg,]^4*si2^2/(n^2*(n-1)))})

T0<-max(abs(Tl))
```

Multiple Contrast Test Procedures (MCTP)

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- Computation of c orrelation matrix$\boldsymbol{R}$:

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```
library(multcomp)

nu=round(min(nul))
Rhat<-cov2cor(Gammahat)
set.seed(1)
tmax=qmvt(0.95,tail="both",corr=Rhat,
df=nu)$quantile
T0>=tmax
$

pv<-sapply(1:4,function(j)
1-pmvt(-abs(Tl[j]),abs(Tl[j]),df=nu,
delta=rep(0,4),corr=Rhat)[1])
```

Properties

- Method is a multiple t-test
- In case of small samples, method might be liberal or conservative
- Resampling methods to improve the approximation /method
- Goal: Approximate the distribution of the maximum

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3. Reassign: $X_{11}^*, \ldots, X_{1n_1}^*$ are group 1, etc.

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8. Reject H_0, if the p-value

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A Parametric Bootstrap Approach

- Many different ways of generating $\mathbf{X}^*$ are possible

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