

STA305/1004 - Class 15

March 8, 2017

Today's Class

- ▶ Coding qualitative predictors in regression models
- ▶ Estimating treatment effects using least squares
- ▶ Multiple comparisons
- ▶ Sample size for ANOVA

Coding Qualitative Predictors in Regression Models

- ▶ A dummy or indicator variable in a regression takes on a finite number of values so that different categories of a nominal variable can be identified.
- ▶ The term dummy reflects the fact that the values taken on by such variables (e.g., 0, 1, -1) do not indicate meaningful measurements but rather categories of interest. (Kleinbaum et al., 1998)

Coding Qualitative Predictors in Regression Models

Consider a regression model: $y = \beta_0 + \beta_1 X_i + \epsilon$

Examples of dummy variables are:

$$X_1 = \begin{cases} 1 & \text{if treatment A} \\ 0 & \text{otherwise} \end{cases}$$

$$X_2 = \begin{cases} 1 & \text{if subject is male} \\ -1 & \text{if subject is female} \end{cases}$$

The variables X_1, X_2 are nominal variables describing treatment group and sex respectively.

Coding Qualitative Predictors in Regression Models

The following rule should be applied to avoid collinearity in defining a dummy variable for regression analysis:

if the nominal independent variable of interest has k categories then exactly $k - 1$ dummy variables should be defined to index the categories if the regression model contains an intercept term.

$$(X^T X)^{-1}$$

Dummy Coding

- ▶ Dummy coding compares each level to the reference level.
- ▶ The intercept is the mean of the reference group.
- ▶ Suppose that we would like to compare the mean number of candy colours in each box. The data from 3 smarties boxes are below.

```
count <- c(4,3,4,3,1,4,2,5,1,1,2,4)
colour <- as.factor(c(rep("Yellow",3),rep("Purple",3),
                      rep("Green",3),rep("Pink",3)))
```

colour	count
Yellow	4
Yellow	3
Yellow	4
Purple	3
Purple	1
Purple	4
Green	2
Green	5
Green	1
Pink	1
Pink	2
Pink	4

Dummy Coding

The average and sd of each colour is:

```
#Get means for each flavour  
sapply(split(count,colour),mean)
```

```
##      Green      Pink     Purple     Yellow  
## 2.666667 2.333333 2.666667 3.666667
```

```
#Get standard deviations for each flavour  
sapply(split(count,colour),sd)
```

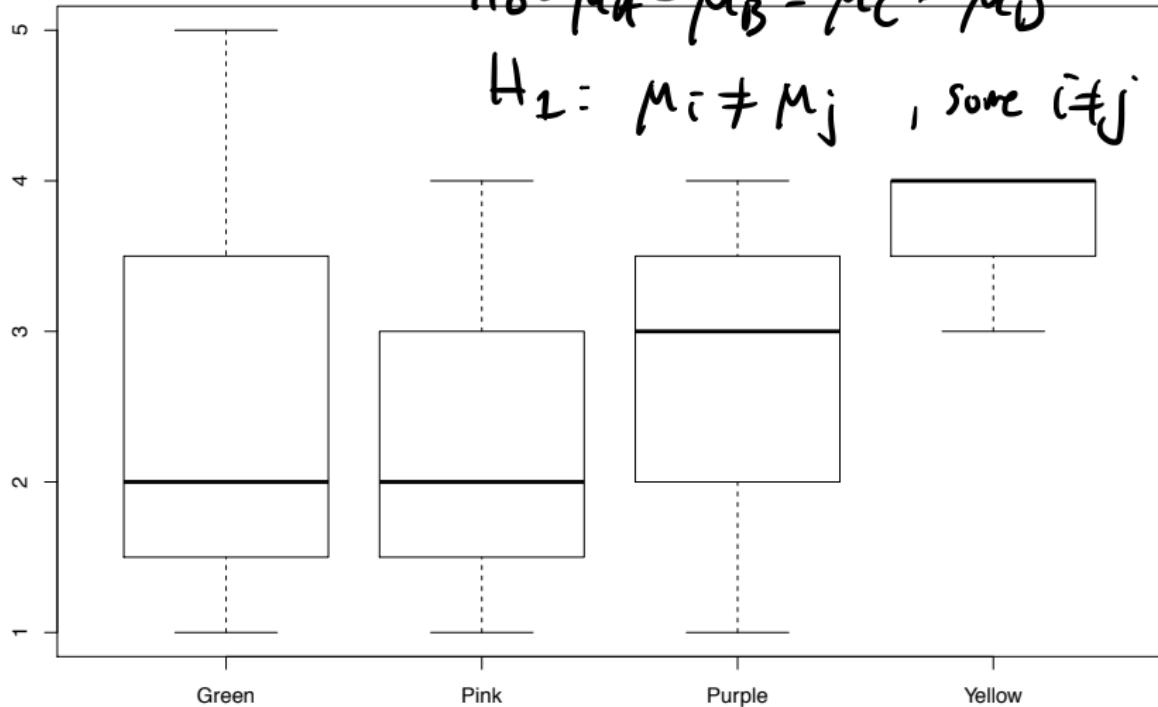
```
##      Green      Pink     Purple     Yellow  
## 2.0816660 1.5275252 1.5275252 0.5773503
```

Dummy Coding

```
boxplot(count~colour)
```

$$H_0: \mu_A = \mu_B = \mu_C = \mu_D$$

$$H_1: \mu_i \neq \mu_j \text{ , some } i \neq j$$



Dummy Coding

Dummy coding is the default in R and the most common coding scheme. It compares each level of the categorical variable to a fixed reference level.

```
contrasts(colour) <- contr.treatment(4)  
contrasts(colour) # print dummy coding - base is Green
```

```
##      2 3 4  
## Green 0 0 0  
## Pink  1 0 0  
## Purple 0 1 0  
## Yellow 0 0 1
```

$$X_1 = \begin{cases} 1 & \text{Pink} \\ 0 & \text{ow} \end{cases} \quad X_3 = \begin{cases} 1 & \text{Yellow} \\ 0 & \text{ow} \end{cases}$$
$$X_2 = \begin{cases} 1 & \text{Purple} \\ 0 & \text{ow} \end{cases}$$

Green is the reference category. The first column compares Pink to Green, the second column compares Purple to Green, and the third column compares Yellow to Green. The three columns define three dummy variables:

Dummy Coding

$$X_1 = \begin{cases} 1 & \text{if smartie is pink} \\ 0 & \text{otherwise} \end{cases}$$

$$X_2 = \begin{cases} 1 & \text{if smartie is purple} \\ 0 & \text{otherwise} \end{cases}$$

$$X_3 = \begin{cases} 1 & \text{if smartie is yellow} \\ 0 & \text{otherwise} \end{cases}$$

If $X_1 = X_2 = X_3 = 0$ then the colour of the smartie is green - the reference category.
This shows that we only require 3 dummy variables to define a nominal variable with 4 categories.

Dummy Coding

To change the reference level change the value of base in `contr.treatment()`.

```
contrasts(colour) <- contr.treatment(4,base = 2) # Now reference is pink  
contrasts(colour)
```

```
##      1 3 4  
## Green 1 0 0  
## Pink  0 0 0  
## Purple 0 1 0  
## Yellow 0 0 1
```

```
contrasts(colour) <- contr.treatment(4,base = 4) # Now reference is yellow  
contrasts(colour)
```

```
##      1 2 3  
## Green 1 0 0  
## Pink  0 1 0  
## Purple 0 0 1  
## Yellow 0 0 0
```

Deviation Coding

- ▶ This coding system compares the mean of the dependent variable for a given level to the overall mean of the dependent variable.

▶

$$X_1 = \begin{cases} 1 & \text{if smartie is green} \\ -1 & \text{if smartie is yellow} \\ 0 & \text{otherwise} \end{cases}$$

$$X_2 = \begin{cases} 1 & \text{if smartie is pink} \\ -1 & \text{if smartie is yellow} \\ 0 & \text{otherwise} \end{cases}$$

$$X_3 = \begin{cases} 1 & \text{if smartie is purple} \\ -1 & \text{if smartie is yellow} \\ 0 & \text{otherwise} \end{cases}$$

- ▶ 1 is used to compare a level to all other levels and -1 is assigned to yellow because it's the level that will never be compared to the other levels.
- ▶ In R the variables can be created using the `contr.sum()` function.
- ▶ The argument of 4 in `contr.sum(4)` indicates the number of levels of the factor.

Deviation Coding

```
contrasts(colour) <- contr.sum(4)
contrasts(colour)
```

```
##          [,1] [,2] [,3]
## Green      1    0    0
## Pink       0    1    0
## Purple     0    0    1
## Yellow    -1   -1   -1
```

Example - blood coagulation study

The table below gives coagulation times for blood samples drawn from 24 animals receiving four different diets A, B, C, and D.

	A	B	C	D
	60	65	71	62
	63	66	66	60
	59	67	68	61
	63	63	68	64
	62	64	67	63
	59	71	68	56
Treatment Average	61	66	68	61
Grand Average	64	64	64	64
Difference	-3	2	4	-3

Average of
all observations

$$\begin{array}{cccc} \text{“} & \text{“} & \text{”} & = \\ 61-64 & 66-64 & 68-64 & 61-64 \end{array}$$

Estimating treatment effects using least squares

y_{ij} is the j^{th} observation under the i^{th} treatment. Let μ be the overall mean. The model for diet $y_{ij} = \mu + \tau_i + \epsilon_{ij}$, $\epsilon_{ij} \sim N(0, \sigma^2)$ can be written in terms of the dummy variables X_1, X_2, X_3 as:

$$y_{ij} = \mu + \tau_1 X_{1j} + \tau_2 X_{2j} + \tau_3 X_{3j} + \epsilon_{ij},$$

where,

$$X_{1j} = \begin{cases} 1 & \text{if } j\text{th unit receives diet 2} \\ 0 & \text{otherwise} \end{cases}$$

$$X_{2j} = \begin{cases} 1 & \text{if } j\text{th unit receives diet 3} \\ 0 & \text{otherwise} \end{cases}$$

$$X_{3j} = \begin{cases} 1 & \text{if } j\text{th unit receives diet 4} \\ 0 & \text{otherwise} \end{cases}$$

diet 1

$$y_{ij} = \mu + \epsilon_{ij}$$

$$E(y_{ij}) = \mu$$

$$\therefore E(\epsilon_{ij}) = 0$$

diet 2

$$y_{ij} = \mu + \gamma_1 + \epsilon_{ij}$$

$$E(y_{ij}) = \mu + \gamma_1$$

Estimating treatment effects using least squares

It follows that $E(y_{Aj}) = \mu_A = \mu$ is the mean of diet A so

$$E(y_{Bj}) = \mu_B = \mu_A + \tau_1 \Rightarrow \tau_1 = \mu_B - \mu_A$$

$$E(y_{Cj}) = \mu_C = \mu_A + \tau_2 \Rightarrow \tau_2 = \mu_C - \mu_A$$

$$E(y_{Dj}) = \mu_D = \mu_A + \tau_3 \Rightarrow \tau_3 = \mu_D - \mu_A$$

The least squares estimates are:

$$\hat{\mu} = \bar{y}_{1..},$$

$$\hat{\tau}_1 = \bar{y}_{2..} - \bar{y}_{1..},$$

$$\hat{\tau}_2 = \bar{y}_{3..} - \bar{y}_{1..},$$

$$\hat{\tau}_3 = \bar{y}_{4..} - \bar{y}_{1..}.$$

Estimating treatment effects using least squares

- ▶ This model can also be written in matrix notation

$$y = X\beta + \epsilon$$

where $\beta = (\mu, \tau_1, \tau_2, \tau_3)$, $X = (\mathbf{1}, X_{i1}, X_{i2}, X_{i3})$, and $\epsilon = (\epsilon_{ij})$.

- ▶ X is an 24×4 design matrix with $\mathbf{1}$ is a 24×1 column vector of 1s, and ϵ is an 24×1 column vector.
- ▶ Note that τ_4 corresponding to the 4th treatment is implicitly set to 0. It is used as a constraint so that that $(X'X)^{-1}$ exists.

Example - blood coagulation study (treatment coding)

contrasts(tab0401\$diets) *defines +*

	B	C	D
A	0	0	0
B	1	0	0
C	0	1	0
D	0	0	1

```
lm.diets <- lm(y~diets, data=tab0401); round(summary(lm.diets)$coefficients, 2)
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	61	0.97	63.14	0
dietsB	5	1.37	3.66	0
dietsC	7	1.37	5.12	0
dietsD	0	1.37	0.00	1

$$\begin{aligned}H_0: \mu_A &= 0 \\H_0: \mu_B - \mu_A &= 0 \\H_0: \mu_C - \mu_A &= 0 \\H_0: \mu_D - \mu_A &= 0\end{aligned}$$

Diets B and C are significantly different from diet A

Example - blood coagulation study (treatment coding)

The averages for each of the four diets are in the table below.

Diet	A ($j = 1$)	B ($j = 2$)	C ($j = 3$)	D ($j = 4$)
Average ($\bar{y}_{j\cdot}$)	61	66	68	61

$$\bar{y}_{1\cdot} = 61,$$

$$\hat{\tau}_1 = \bar{y}_{2\cdot} - \bar{y}_{1\cdot} = 5$$

$$\hat{\tau}_2 = \bar{y}_{3\cdot} - \bar{y}_{1\cdot} = 7$$

$$\hat{\tau}_3 = \bar{y}_{3\cdot} - \bar{y}_{1\cdot} = -9.9 \times 10^{-15}.$$

Example - blood coagulation study (treatment coding)

The design matrix (first 12 observations) is

```
model.matrix(lm.diets)[1:12,]
```

```
##      (Intercept) dietsB dietsC dietsD
## 1              1     0     0     0
## 2              1     0     0     0
## 3              1     0     0     0
## 4              1     0     0     0
## 5              1     0     0     0
## 6              1     0     0     0
## 7              1     1     0     0
## 8              1     1     0     0
## 9              1     1     0     0
## 10             1     1     0     0
## 11             1     1     0     0
## 12             1     1     0     0
```

Example - blood coagulation study (treatment coding)

The design matrix (first 12 observations) with the observations y and treatment variable diets (first 12 observations) is

```
cbind(tab0401$y,tab0401$diets,model.matrix(lm.diets))[1:12,]
```

y_{ij} - observations

		(Intercept)	dietsB	dietsC	dietsD
##	1	62 1	1	0	0
##	2	60 1	1	0	0
##	3	63 1	1	0	0
##	4	59 1	1	0	0
##	5	63 1	1	0	0
##	6	59 1	1	0	0
<hr/>					
##	7	63 2	1	1	0
##	8	67 2	1	1	0
##	9	71 2	1	1	0
##	10	64 2	1	1	0
##	11	65 2	1	1	0
##	12	66 2	1	1	0

A

B

diets.

Example - blood coagulation study (deviation coding)

If deviation coding was used then the parameter estimates would represent different treatment effects. In the regression model the dummy variables would be defined as

$$X_1 = \begin{cases} 1 & \text{if diet is A} \\ -1 & \text{if diet is D} \\ 0 & \text{otherwise} \end{cases}$$

$$X_2 = \begin{cases} 1 & \text{if diet is B} \\ -1 & \text{if diet is D} \\ 0 & \text{otherwise} \end{cases}$$

$$X_3 = \begin{cases} 1 & \text{if diet is C} \\ -1 & \text{if diet is D} \\ 0 & \text{otherwise} \end{cases}$$

Example - blood coagulation study (deviation coding)

It follows that

$$y_{ij} = \gamma_0 + \gamma_1 x_{1i} + \gamma_2 x_{2i} + \gamma_3 x_{3i} + \varepsilon_{ij}$$

$$E(y_{Aj}) = \mu_A = \tau_0 + \tau_1$$

$$E(y_{Bj}) = \mu_B = \tau_0 + \tau_2$$

$$E(y_{Cj}) = \mu_C = \tau_0 + \tau_3$$

$$E(y_{Dj}) = \mu_D = \tau_0 - \tau_1 - \tau_2 - \tau_3$$

$$x_{1i} = \begin{cases} 1 & A \\ -1 & D \\ 0 & \text{o.w.} \end{cases}$$

$$x_{2i} = \begin{cases} 1 & B \\ -1 & D \\ 0 & \text{o.w.} \end{cases}$$

$$x_{3i} = \begin{cases} 1 & C \\ -1 & D \\ 0 & \text{o.w.} \end{cases}$$

If dict A

$$y_{\text{ref}} = \gamma_0 + \gamma_1 + \varepsilon_{ij}$$

$$\tau_0 = \frac{\mu_A + \mu_B + \mu_C + \mu_D}{4}$$

$$\tau_1 = \mu_A - \frac{\mu_A + \mu_B + \mu_C + \mu_D}{4}$$

$$\tau_2 = \mu_B - \frac{\mu_A + \mu_B + \mu_C + \mu_D}{4}$$

$$\tau_3 = \mu_C - \frac{\mu_A + \mu_B + \mu_C + \mu_D}{4}$$

Example - blood coagulation study (deviation coding)

```
attach(tab0401)
contrasts(tab0401$diets) <- contr.sum(4)
lm.diets <- lm(y~diets,data=tab0401)
round(summary(lm.diets)$coefficients,2)
```

define +

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	64	0.48	132.49	0.00
diets1	-3	0.84	-3.59	0.00
diets2	2	0.84	2.39	0.03
diets3	4	0.84	4.78	0.00

The mean Coagulation time for

- ▶ The estimate of the intercept $\hat{\tau}_0$ is the grand average.
- ▶ The slope estimates $\hat{\tau}_1, \hat{\tau}_2, \hat{\tau}_3$ are the differences between the treatment averages and grand average of diets A, B, and C.

→ diets 1, 2, 3 are significantly different from
the mean of all diets.
Coagulation time of

Compare A vs C

D vs B

Multiple Comparisons

Suppose that experimental units were randomly assigned to three treatment groups.
The hypothesis of interest is:

$$H_0 : \mu_1 = \mu_2 = \mu_3 \text{ vs. } H_1 : \mu_i \neq \mu_j.$$

Now, suppose that we reject H_0 at level α . Which pairs of means are significantly different from each other at level α ? There are $\binom{3}{2} = 3$ possibilities.

1. $\mu_1 \neq \mu_2$
2. $\mu_1 \neq \mu_3$
3. $\mu_2 \neq \mu_3$

Multiple Comparisons

Suppose that $k = 3$ separate (independent) hypothesis tests at level α tests are conducted:

$$P(A) + P(A^c) = 1$$

Why?

$$H_{0_k} : \mu_i = \mu_j \text{ vs. } H_{1_k} : \mu_i \neq \mu_j,$$

When H_0 is true, $P(\text{reject } H_0) = \alpha \Rightarrow 1 - P(\text{do not reject } H_0) = 1 - (1 - \alpha)$.

So, if H_0 is true then

why?

$$P(\text{reject at least one } H_{0_k}) = 1 - P(\text{do not reject any } H_{0_k})$$

This is the same as

$$1 - P(\text{do not reject } H_{0_1} \text{ and do not reject } H_{0_2} \text{ and do not reject } H_{0_3})$$

A₁

A₂

A₃

or since the hypotheses are independent

$$\underbrace{(1-\alpha)}_{=1-\alpha} = 1 - \alpha$$

$$1 - P(\text{do not reject } H_{0_1}) P(\text{do not reject } H_{0_2}) P(\text{do not reject } H_{0_3}) = 1 - (1 - \alpha)^3$$

If $\alpha = 0.05$ then the probability that at least one H_0 will be falsely rejected is $1 - (1 - .05)^3 = 0.14$, which is almost three times the type I error rate.

Suppose X_1, X_2, \dots, X_n are independent Bernoulli random variables with parameter p or $\text{Bern}(p)$

$$P(X_i=1) = p, \quad P(X_i=0) = 1-p \quad X_i = \begin{cases} 1 \\ 0 \end{cases}$$

$$P(\text{at least one } X_i = 1, i=1, \dots, n)$$

$$= P(X_1=1 \text{ or } X_2=1 \text{ or } \dots \text{ or } X_n=1)$$

$$= 1 - P(X_1=0 \text{ and } X_2=0 \text{ and } \dots \text{ and } X_n=0)$$

$$= 1 - P(X_1=0) P(X_2=0) \dots P(X_n=0)$$

$$= 1 - (1-p)(1-p) \dots (1-p) = (1-p)^n$$

$$X_i = \begin{cases} 1 & \text{reject } H_0 \text{ if } P(X_i=1)=\alpha \\ 0 & \text{do not reject } H_0 \end{cases}$$

Multiple Comparisons

A clinical trial comparing four treatment means using an ANOVA model at the 5% level found a significant F test. If all pairs of treatment means are compared then the probability of falsely declaring that at least one pair of treatment means is significantly different is:



Respond at PollEv.com/nathantaback



Text **NATHANTABACK** to 37607 once to join, then **A or B**

Type I error.

less than or equal to 0.05

A

11

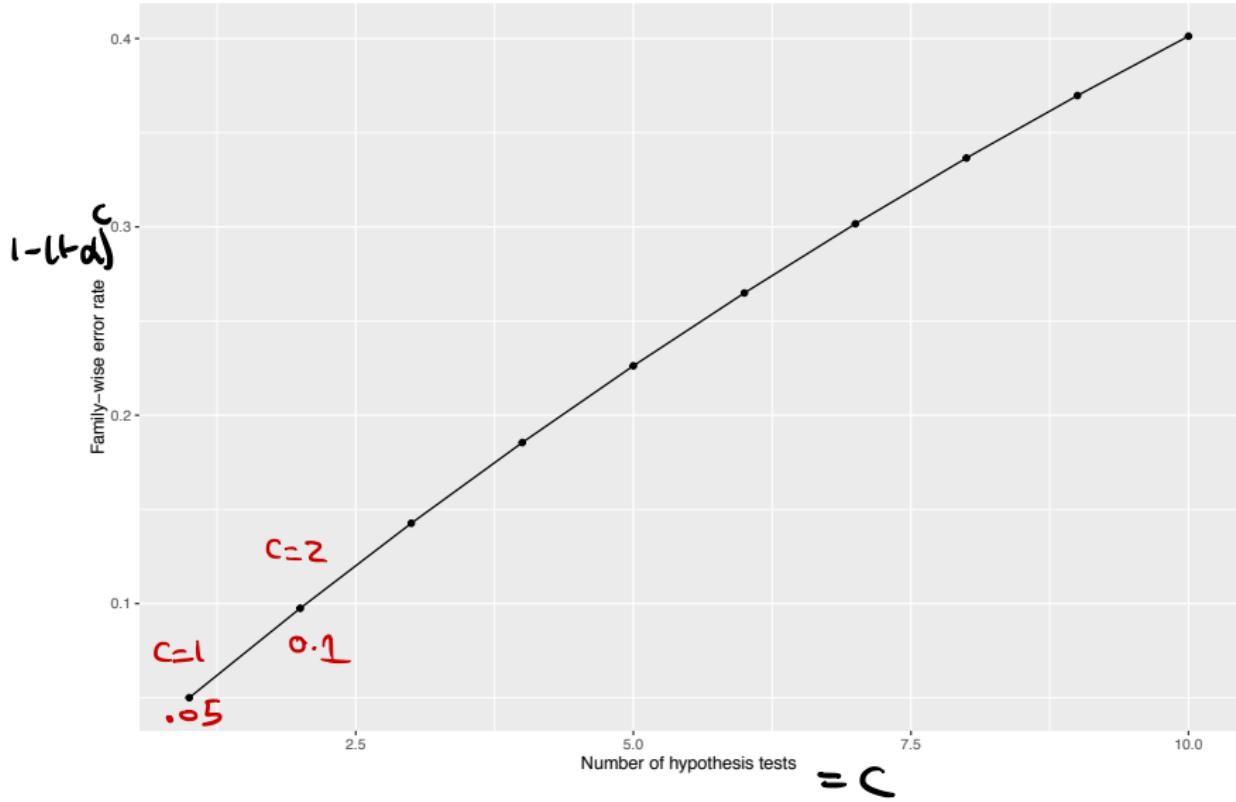
greater than 0.05

B 22

Figure 1:

Multiple Comparisons

Family-wise error rate $\alpha=0.05$



Multiple Comparisons

In general if

$$H_0 : \mu_1 = \mu_2 = \cdots = \mu_k \text{ vs. } H_1 : \mu_i \neq \mu_j.$$

If c independent hypotheses are conducted then the probability

$$P(\text{reject at least one } H_{0k}) = 1 - (1 - \alpha)^c$$

is called the **family-wise error rate**.

The **pairwise error rate** is $P(\text{reject } H_{0k}) = \alpha$ for any c .

The Multiple Comparisons Problem

- ▶ The multiple comparison problem is that multiple hypotheses are tested level α which increases the probability that at least one of the hypotheses will be falsely rejected (family-wise error rate).
- ▶ If treatment means are significantly different from the ANOVA F test then researchers will usually want to explore where the differences lie.
- ▶ Is it appropriate to test for differences looking at all pairwise comparisons?
- ▶ Testing all possible pairs increases the type I error rate.
- ▶ This means the chance that there is a higher probability, beyond the pre-stated type I error rate (e.g. 0.05), that a significant difference is detected when the truth is that no difference exists.



Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction

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INTRODUCTION

With the extreme dimensionality of functional neuroimaging data comes extreme risk for false positives. Across the 130,000 voxels in a typical fMRI volume the probability of a false positive is almost certain. Correction for multiple comparisons should be completed with these datasets, but is often ignored by investigators. To illustrate the magnitude of the problem we carried out a real experiment that demonstrates the danger of not correcting for chance properly.

METHODS

Subject. One mature Atlantic Salmon (*Salmo salar*) participated in the fMRI study. The salmon was approximately 18 inches long, weighed 3.8 lbs, and was not alive at the time of scanning.

Task. The task administered to the salmon involved completing an open-ended mentalizing task. The salmon was shown a series of photographs depicting human individuals in social situations with a specified emotional valence. The salmon was asked to determine what emotion the individual in the photo must have been experiencing.

Design. Stimuli were presented in a block design with each photo presented for 10 seconds followed by 12 seconds of rest. A total of 15 photos were displayed. Total scan time was 5.5 minutes.

Preprocessing. Image processing was completed using SPM2. Preprocessing steps for the functional imaging data included a 6-parameter rigid-body affine realignment of the fMRI timeseries, coregistration of the data to a T_1 -weighted anatomical image, and 8 mm full-width at half-maximum (FWHM) Gaussian smoothing.

Analysis. Voxelwise statistics on the salmon data were calculated through an ordinary least-squares estimation of the general linear model (GLM). Predictors of the hemodynamic response were modeled by a boxcar function convolved with a canonical hemodynamic response. A temporal high pass filter of 128 seconds was included to account for low frequency drift. No autocorrelation correction was applied.

Voxel Selection. Two methods were used for the correction of multiple comparisons in the fMRI results. The first method controlled the overall false discovery rate (FDR) and was based on a method defined by Benjamini and Hochberg (1995). The second method controlled the overall familywise error rate (FWER) through the use of Gaussian random field theory. This was done using algorithms originally devised by Friston et al. (1994).

DISCUSSION

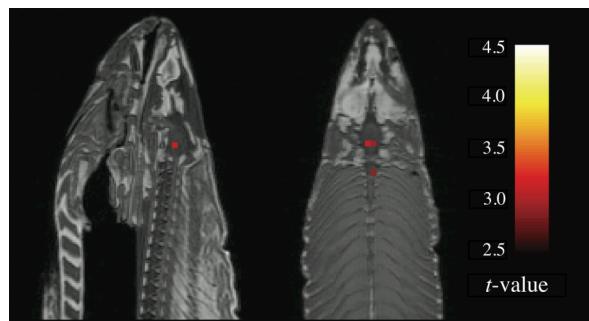
Can we conclude from this data that the salmon is engaging in the perspective-taking task? Certainly not. What we can determine is that random noise in the EPI timeseries may yield spurious results if multiple comparisons are not controlled for. Adaptive methods for controlling the FDR and FWER are excellent options and are widely available in all major fMRI analysis packages. We argue that relying on standard statistical thresholds ($p < 0.001$) and low minimum cluster sizes ($k > 8$) is an ineffective control for multiple comparisons. We further argue that the vast majority of fMRI studies should be utilizing multiple comparisons correction as standard practice in the computation of their statistics.

REFERENCES

Benjamini Y and Hochberg Y (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B*, 57:289-300.

Friston KJ, Worsley KJ, Frackowiak RSJ, Mazziotta JC, and Evans AC. (1994). Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping*, 1:214-220.

GLM RESULTS

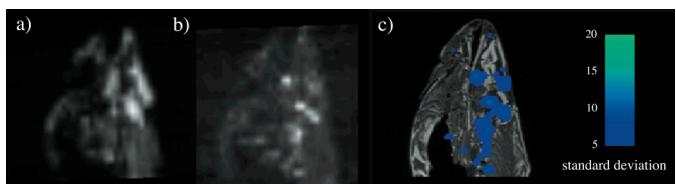


A t -contrast was used to test for regions with significant BOLD signal change during the photo condition compared to rest. The parameters for this comparison were $t(131) > 3.15$, $p(\text{uncorrected}) < 0.001$, 3 voxel extent threshold.

Several active voxels were discovered in a cluster located within the salmon's brain cavity (Figure 1, see above). The size of this cluster was 81 mm^3 with a cluster-level significance of $p = 0.001$. Due to the coarse resolution of the echo-planar image acquisition and the relatively small size of the salmon brain further discrimination between brain regions could not be completed. Out of a search volume of 8064 voxels a total of 16 voxels were significant.

Identical t -contrasts controlling the false discovery rate (FDR) and familywise error rate (FWER) were completed. These contrasts indicated no active voxels, even at relaxed statistical thresholds ($p = 0.25$).

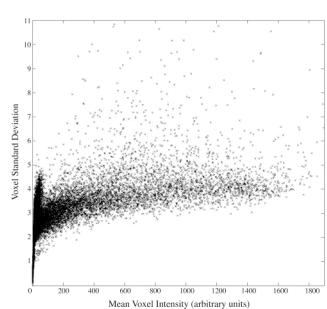
VOXELWISE VARIABILITY



To examine the spatial configuration of false positives we completed a variability analysis of the fMRI timeseries. On a voxel-by-voxel basis we calculated the standard deviation of signal values across all 140 volumes.

We observed clustering of highly variable voxels into groups near areas of high voxel signal intensity. Figure 2a shows the mean EPI image for all 140 image volumes. Figure 2b shows the standard deviation values of each voxel. Figure 2c shows thresholded standard deviation values overlaid onto a high-resolution T_1 -weighted image.

To investigate this effect in greater detail we conducted a Pearson correlation to examine the relationship between the signal in a voxel and its variability. There was a significant positive correlation between the mean voxel value and its variability over time ($r = 0.54$, $p < 0.001$). A scatterplot of mean voxel signal intensity against voxel standard deviation is presented to the right.



The Bonferroni Method

To test for the difference between the i th and j th treatments, it is common to use the two-sample t test. The two-sample t statistic is

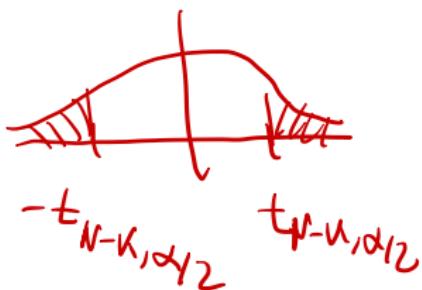
$$t_{ij} = \frac{\bar{y}_{j\cdot} - \bar{y}_{i\cdot}}{\hat{\sigma} \sqrt{1/n_j + 1/n_i}},$$

where $\bar{y}_{j\cdot}$ is the average of the n_j observations for treatment j and $\hat{\sigma}$ is $\sqrt{MS_E}$ from the ANOVA table.

Treatments i and j are declared significantly different at level α if

$$|t_{ij}| > t_{N-k, \alpha/2},$$

where $t_{N-k, \alpha/2}$ is the upper $\alpha/2$ percentile of a t_{N-k} .



The Bonferroni Method

The total number of pairs of treatment means that can be tested is

$$c = \binom{k}{2} = \frac{k(k-1)}{2}.$$

The Bonferroni method for testing $H_0 : \mu_i = \mu_j$ vs. $H_0 : \mu_i \neq \mu_j$ rejects H_0 at level α if

$$|t_{ij}| > t_{N-k, \alpha/2c},$$

where c denotes the number of pairs being tested.

Conducting each test at level α/c leads to a family wise error rate of α .

The Bonferroni Method

The unadjusted critical value
is $t_{20, .05/2} = 2.09$

In R the function pairwise.t.test() can be used to compute Bonferroni adjusted p-values.

This is illustrated below for the blood coagulation study.

```
pairwise.t.test(tab0401$y, tab0401$diets, p.adjust.method = "bonferroni")
```

```
##  
##  Pairwise comparisons using t tests with pooled SD  
##  
## data: tab0401$y and tab0401$diets  
##  
##    A      B      C  
## B 0.00934 - -  
## C 0.00031 0.95266 -  
## D 1.00000 0.00934 0.00031  
##  
## P value adjustment method: bonferroni
```

$$N=24, k=4$$

$$\alpha=0.05$$

$$C = 6 = \binom{4}{2}$$

$$t_{20, .05/2.6}$$

$$= t_{20, .05/12} = 2.95$$

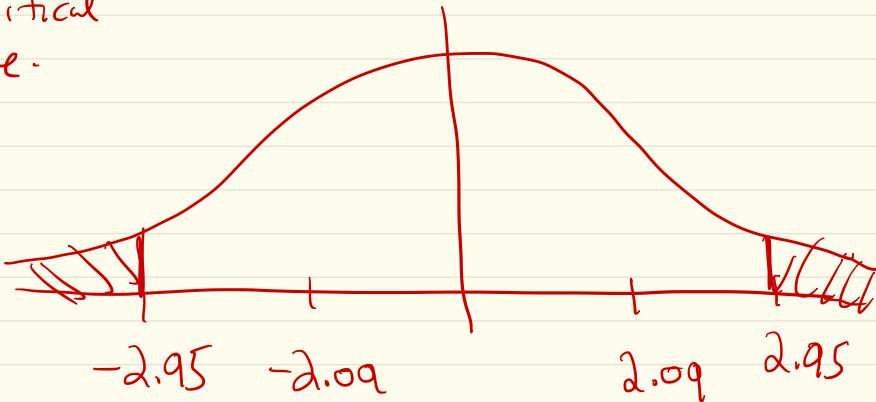
There are significant differences at the 5% level between diets A and B, A and C, B and D, and C and D using the Bonferroni method.

$$t_{20, 0.05/2} = 2.09 \quad t_{ij} = \frac{\bar{y}_i - \bar{y}_j}{\sqrt{\sigma^2(\frac{1}{n_i} + \frac{1}{n_j})}}$$

$$t_{20, 0.05/2} = 2.95$$

$|t_{ij}| > t_{\text{critical}}$
Value.

t_{20}



The Bonferroni Method

For comparison the unadjusted p-values are also calculated.

```
pairwise.t.test(tab0401$y,tab0401$diets,p.adjust.method = "none")
```

```
##  
##  Pairwise comparisons using t tests with pooled SD  
##  
## data: tab0401$y and tab0401$diets  
##  
##    A      B      C  
## B 0.0016  -     -  
## C 5.2e-05 0.1588 -  
## D 1.0000  0.0016 5.2e-05  
##  
## P value adjustment method: none
```

The significant differences are the same using the unadjusted p-values but the p-values are larger than the p-values adjusted using the Bonferroni method.

The Bonferroni Method

Each comparison is made at α/c so that the family-wise error rate is α .

A $100(1 - \alpha)\%$ simultaneous confidence interval for c pairs $\mu_i - \mu_j$ is

$$\bar{y}_{j\cdot} - \bar{y}_{i\cdot} \pm t_{N-k,\alpha/2c}\hat{\sigma}\sqrt{1/n_j + 1/n_i}$$

After identifying which pairs are different, the confidence interval quantifies the range of plausible values for the differences.

If the ^{Simultaneous} $100(1 - \alpha)\%$ CI ^{does not} contain 0
then the difference is significant at
level α .

family-wise.

The Bonferroni Method - coagulation study

The treatment means can be obtained from the table below.

	A	B	C	D
	60	65	71	62
	63	66	66	60
	59	67	68	61
	63	63	68	64
	62	64	67	63
	59	71	68	56
Treatment Average	61	66	68	61
Grand Average	64	64	64	64
Difference	-3	2	4	-3

The Bonferroni Method - coagulation study

$\hat{\sigma} = \sqrt{MS_E}$ can be obtained from the ANOVA table.

```
anova(lm(y~diets,data=tab0401))
```

```
## Analysis of Variance Table
##
## Response: y
##           Df Sum Sq Mean Sq F value    Pr(>F)
## diets      3   228    76.0  13.571 4.658e-05 ***
## Residuals 20   112     5.6
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The upper $.05/(2 \cdot 6) = 0.004$ percentile of the t_{24-4} can be obtained with the t quantile function in R `qt()`.

```
qt(p = 1-0.004,df = 20)
```

```
## [1] 2.945349
```

The Bonferroni Method - coagulation study

Plugging in these values to the confidence interval formula we can obtain a Bonferroni adjusted 95% confidence interval for $\mu_B - \mu_A$:

$$66 - 61 \pm 2.95\sqrt{5.6}\sqrt{1/6 + 1/6}$$

The lower and upper limits can be calculated in R.

```
66-61 - qt(p = 1-0.004,df = 20)*sqrt(5.6)*sqrt(1/6+1/6) # lower limit
```

```
## [1] 0.9758869
```

```
66-61 + qt(p = 1-0.004,df = 20)*sqrt(5.6)*sqrt(1/6+1/6) # upper limit
```

```
## [1] 9.024113
```

The 95% confidence interval for $\mu_B - \mu_A$ is (0.98, 9.02).

The Tukey Method

- ▶ The only difference between the Tukey and Bonferroni methods is in the choice of the critical value.
- ▶ Treatments i and j are declared significantly different at level α if

$$|t_{ij}| > \frac{1}{\sqrt{2}} q_{k, N-k, \alpha},$$

- ▶ t_{ij} is the observed value of the two-sample t-statistic
- ▶ $q_{k, N-k, \alpha}$ is the upper α percentile of the Studentized range distribution with parameters k and $N - k$ degrees of freedom.
- ▶ The CDF and inverse CDF of the Studentized Range Distribution is available in R via the functions `ptukey()` and `qtukey()` respectively.

The Tukey Method

A $100(1 - \alpha)\%$ simultaneous confidence interval for c pairs $\mu_i - \mu_j$ is

$$\bar{y}_{j\cdot} - \bar{y}_{i\cdot} \pm \frac{1}{\sqrt{2}} q_{k, N-k, \alpha} \hat{\sigma} \sqrt{1/n_j + 1/n_i}.$$

The Bonferroni method is more conservative than Tukey's method. In other words, the simultaneous confidence intervals based on the Tukey method are shorter.

The Tukey Method

- ▶ In the coagualtion study $N = 24$, $k = 4$ so the 5% critical value of the Studentized range distribution is obtained using the the inverse CDF function `qtukey()` for this distribution.
- ▶ The argument `lower.tail=FALSE` is used so we obtain the upper percentile of the distribution (i.e., the value of x such that $P(X > x) = 0.05$).

```
qtukey(p = .05, nmeans = 4, df = 20, lower.tail = FALSE)
```

```
## [1] 3.958293
```

The Tukey Method

- ▶ Let's obtain the Tukey p-value and confidence interval for $\mu_B - \mu_A$.
- ▶ The observed value of the test statistic is

$$q^{obs} = \sqrt{2}|t_{AB}|,$$

where

$$t_{AB} = \frac{\bar{y}_A - \bar{y}_B}{\hat{\sigma} \sqrt{1/n_A + 1/n_B}}.$$

```
(sqrt(2)*(66-61))/(sqrt(5.6)*sqrt(1/6+1/6))
```

```
## [1] 5.175492
```

The Tukey Method

The p-value

$$P(q_{4,20} > q^{obs})$$

is then obtained using the CDF of the Studentized range distribution

```
1-ptukey(q = sqrt(2)*5/sqrt(2*5.6/6),nmeans = 4,df = 20)
```

```
## [1] 0.007797788
```

The Tukey Method

The 95% limits of the Tukey confidence interval for $\mu_B - \mu_A$ is

```
tuk.crit <- qtukey(p=.05,nmeans=4,df=20,lower.tail=FALSE)
#lower limit
round(5-(1/sqrt(2))*tuk.crit*sqrt(5.6)*sqrt(1/6+1/6),2)
```

```
## [1] 1.18
```

```
#upper limit
round(5+(1/sqrt(2))*tuk.crit*sqrt(5.6)*sqrt(1/6+1/6),2)
```

```
## [1] 8.82
```

The Tukey Method

The width of the Tukey confidence interval for $\mu_B - \mu_A$ is

```
round((1/sqrt(2))*tuk.crit*sqrt(5.6)*sqrt(1/6+1/6),2)
```

```
## [1] 3.82
```

The width of Bonferroni $\mu_B - \mu_A$ is

```
round(qt(p = 1-0.004,df = 20)*sqrt(5.6)*sqrt(1/6+1/6),2)
```

```
## [1] 4.02
```

The Tukey Method

- ▶ This shows that the Tukey confidence interval is shorter than Bonferroni confidence intervals.
- ▶ The command `TukeyHSD()` can be used to obtain all the Tukey confidence intervals and p-values for an ANOVA.

The Tukey Method

```
TukeyHSD(aov(y~diets,data=tab0401))
```

```
round(TukeyHSD(aov(y~diets,data=tab0401))$diets,2)
```

	diff	lwr	upr	p	adj
## B-A	5	1.18	8.82	0.01	
## C-A	7	3.18	10.82	0.00	
## D-A	0	-3.82	3.82	1.00	
## C-B	2	-1.82	5.82	0.48	
## D-B	-5	-8.82	-1.18	0.01	
## D-C	-7	-10.82	-3.18	0.00	

does not contain 0

does contain 0 .

6 tests with family-wise error
rate of 0.05.

The Tukey Method

```
plot(TukeyHSD(aov(y~diets,data=tab0401)))
```

The CIs that do
contain the
vertical line at 0
are not significant!

