# **Powering Repeated Measure Tests**

Analysis of variance, or ANOVA, tests are designed to compare the means of multiple groups. Typically these groups include a control group and a number of treatment groups. Non-treatment factors such as sex may require multi-dimensional grouping of experimental subjects. In this document, we discuss the basic formulas for determining the power (and hence sample size requirements) of ANOVA tests.

#### The F-Distribution

ANOVA hypothesis tests rely on test statistics that have the F distribution. Under the null hypothesis, the statistics have the central F distribution. This distribution has two parameters, called numerator degrees of freedom and denomination degrees of freedom. When the null hypothesis is false, the statistics typically have the non-central F distribution, which has an additional parameter called the non-centrality parameter. We denote this distribution by  $F(x,df_1,df_2,\lambda) = \Pr[F \le x]$ . If  $\lambda=0$ , we omit the dependence on  $\lambda$  and refer to this notation as the central F distribution. Often it is required to invert this distribution in the first variable to find critical values, and we use the notation

$$x = F^{-1}(p, df_1, df_2, \lambda)$$
 (1)

to solve the equation  $p = \Pr[F \le x]$  for x when p has been specified.

In above, the definitions of notations are

- $df_1$  and  $df_2$  degree of freedom of *F*-Distribution, degree of freedom on numerator and denominator respectively;
- $\lambda$  is non-centrality parameter, sometime denoted by ncp.

The mean and variance of F-Distribution are

mean = 
$$\frac{d_{df}}{d_{df} - 2}$$
, if  $d_{df} > 2$   

$$Var = \frac{2d_{df}^2(n_{df} + d_{df} - 2)}{n(d - 2)^2(d - 4)}$$
, if  $d_{df} > 4$ 

### **Computing Power**

Computing power requires two steps. First we establish the critical region for the null hypothesis. Second we determine the probability that the test statistic lies outside the critical region when the null hypothesis is false. The latter computation requires an a priori estimate of "how false" the

null hypothesis is. The so-called "effect size" parameter is a measure of this discrepancy. The list of information we need to determine power is as follows:

- 1. Significance,  $\alpha$ , the probability of rejecting a true null, i.e. Type I error probability
- 2. Number of groups in the experimental design. This may be an array if the treatment regimen is multi-dimensional or if different non-treatment factors must be controlled for.
- 3. Minimum desired effect size, f.
- 4. Standard deviation of the measurements,  $\sigma$ .
- 5. Number of samples or replicates per group, n.

If the sample size is not known, one may alternatively specify the power  $1-\beta$  and determine the number of samples per group required to achieve this desired power. Here  $\beta$  is also referred as Type II error probability. The power  $(1-\beta)$  calculation typically looks like

$$F(F^{-1}(\alpha, df_1, df_2), df_1, df_2, \lambda) = \Pr[\text{non-central } F \leq \text{central } F \text{ specified critical value}].$$
 (2)

#### **R Functions**

- The inverse cumulative distribution function  $F_c = \mathbf{qf}(1 \alpha, df 1, df 2)$
- The cumulative distribution function  $pf(F_c, df 1, df 2, \lambda)$

#### Notation:

- $df_1$  and  $df_2$  degree of freedom of F-Distribution, degree of freedom on numerator and denominator respectively;
- $\lambda$  is non-centrality parameter, sometime denoted by ncp.

# One Way Anova: Power/Effect/Sample considerations

The one-way ANOVA model is given by

$$Y_{ik} = \mu_i + \varepsilon_{ik} = \mu + \eta_i + \varepsilon_{ik}, \quad 1 \le i \le a, 1 \le k \le n$$

in which:

- $\mu$  is the grand mean;
- $\eta_i$  are the main effects (and it is assumed  $\sum_{i=1}^a \eta_i = 0$ );
- $\varepsilon_{ik}$  are iid  $N(0, \sigma^2)$  random variables.
- *a* is number of treatments

This is a balanced design: all groups have the same number of samples, n, and the total sample size is na. To test hypotheses, we select a significance level  $\alpha$ , typically 0.05, but it may be less depending on the situation. The null hypothesis of interest is

•  $\eta_i = 0$  for all i.

To test this hypothesis, we compute the F distribution's critical value  $F_c = F^{-1}(1-\alpha,a-1,(n-1)a)$ . Under the null hypothesis, the F statistic has the central F distribution, with a-1numerator degrees of freedom and na-a denominator degrees of freedom. When the null hypothesis is false, the F statistic has a non-central F distribution. The noncentrality parameter  $\lambda$  is given by

$$\lambda = na \frac{f^2}{\sigma^2}$$

in which 
$$f = \sqrt{\frac{\sum_{i=1}^{a} (\mu_i - \overline{\mu})^2}{(a-1)}}$$
 is the "effect size," modeling with 1 simple numerical quantity

the distance from the "true" model to the null model of identical means. The null model requires all the  $\mu_i$  values to be the same, so f=0 under the null hypothesis. The power of the ANOVA test is then computed as  $1-\beta=F(F_c,a-1,(n-1)a,naf^2/\sigma^2)$ .

One issue with using R's "pwr" package is that the effect size used therein has a slightly different definition:

$$f' = \sqrt{\frac{\sum_{i=1}^{a} (\mu_i - \overline{\mu})^2}{\sigma^2 a}}$$

is the standardized effect size used in pwr (a usage derived from Cohen, 1988). To compensate for this discrepancy, in using pwr, we must convert

$$f' = \sqrt{\frac{\sum_{i=1}^{a} (\mu_i - \overline{\mu})^2}{\sigma^2 a}} = \frac{f}{\sigma} \sqrt{\frac{a-1}{a}}$$

# Two Way Anova: Power/Effect/Sample considerations

#### **Model**

The ANOVA model is given by

$$Y_{ijk} = \mu + \eta_i + \xi_j + \gamma_{ij} + \varepsilon_{ijk}, \quad 1 \le i \le a, 1 \le j \le b, 1 \le k \le n$$

in which:

- $\mu$  is the grand mean;
- $\eta_i$  are the main effects (and it is assumed  $\sum_{i=1}^a \eta_i = 0$ ), main independent mean;
- $\xi_i$  are the secondary effects (and it is assumed  $\sum_{i=1}^b \xi_i = 0$ ), secondary independent mean;
- $\gamma_{ij}$  are the interaction effects (and it is assumed  $\sum_{k=1}^{a} \gamma_{kj} = \sum_{l=1}^{b} \gamma_{il} = 0$  for each i, j);
- $\varepsilon_{ijk}$  are iid  $N(0, \sigma^2)$  random variables;
- a and b are number of levels in treatment 1 and 2 respectively.

This is a balanced design: all groups have the same number of samples, n, and the total sample size is nab. To test hypotheses, we select a significance level  $\alpha$ , typically 0.05, but it may be less depending on the situation. The three hypotheses of interest are

- $\eta_i = 0$  for all i.
- $\xi_i = 0$  for all j.
- $\gamma_{ij} = 0$  for all i,j.

Testing each hypothesis, we will need the critical F value for the test

$$F_c = F^{-1}(1-\alpha, a-1, (n-1)ab)$$

$$F_c = F^{-1}(1-\alpha, b-1, (n-1)ab)$$

3. 
$$F_c = F^{-1}(1-\alpha,(a-1)(b-1),(n-1)ab)$$

For each hypothesis, we have an effect size f. In each case, f denotes the discrepancy from null model:

$$f_M^2 = \frac{\sum_{i=1}^a (\eta_i - \overline{\eta})^2}{a - 1} \quad or \quad f_S^2 = \frac{\sum_{i=1}^b (\xi_i - \overline{\xi})^2}{b - 1} \quad or \quad f_I^2 = \frac{\sum_{j=1}^b \sum_{i=1}^a (\gamma_{ij} - \overline{\gamma})^2}{(a - 1)(b - 1)}$$

For each hypothesis, we compute the power using the formulae

$$1 - \beta = F(F_c, a-1, (n-1)ab, n(a-1)bf_M^2 / \sigma^2)$$

2. 
$$1-\beta = F(F_c, b-1, (n-1)ab, na(b-1)f_s^2 / \sigma^2)$$

3. 
$$1-\beta = F(F_c, (a-1)(b-1), (n-1)ab, n(a-1)(b-1)f_I^2/\sigma^2)$$

These relationships may also be used to determine the sample size per group, given the power 1- $\beta$  and the effect size f. Alternatively, one may determine the minimal detectable effect size f for a given power and sample size.

To treat the case of no interactions, the model becomes

$$Y_{ijk} = \mu + \eta_i + \xi_j + \varepsilon_{ijk}, \quad 1 \le i \le a, 1 \le j \le b, 1 \le k \le n$$

in which

- $\mu$  is the grand mean;
- $\eta_i$  are the main effects (and it is assumed  $\sum_{i=1}^a \eta_i = 0$ );
- $\xi_i$  are the secondary effects (and it is assumed  $\sum_{i=1}^b \xi_i = 0$ );
- $\varepsilon_{ijk}$  are iid  $N(0, \sigma^2)$  random variables.

Here we have only a+b-1 parameters instead of ab parameters. Only the first two hypotheses are of interest.

1 
$$F_c = F^{-1}(1-\alpha, a-1, nab - (a+b-1))$$

2. 
$$F_c = F^{-1}(1-\alpha, b-1, nab - (a+b-1))$$

The power/effect/sample computation is determined, for each test, by

1. 
$$1 - \beta = F(F_c, a-1, nab - (a+b-1), n(a-1)bf_M^2 / \sigma^2)$$

$$1 - \beta = F(F_c, b-1, nab - (a+b-1), na(b-1)f_s^2 / \sigma^2)$$

Generally speak, it is important to include interaction effects, and I would not recommend leaving them out *a priori*.

### Webapp notes

### **Input parameters**

Symbol	Description	Variable Name
α	Significance level (probability of rejecting a true null, i.e. Type I error probability)	sig
n	Number of subjects in each treatment / factor group (aka sample size per group) sample size per group)	
$\sigma$	Measured standard deviation	esSD_AOV
$f_M, f_S, f_I$	Effect size for Main, Secondary, and Interaction effects (assuming they are the same for now) esMean	
а	Number of <b>levels</b> in Factor 1 (or treatment 1) treatments[0].le	
b	Number of levels in Factor 2 (or treatment 2) treatments[1].level	

### **Two Way Anova Formula**

	Formula	Coding	
Main Tre			
$df_1 = df_M$	a-1	treatments[0].levels – 1	
$df_2$	(n-1)ab	(samplesize – 1)*treatments[0].levels*treatments[1].levels	
λ	$(a-1)b \cdot n(f_M / \sigma)^2$	(treatments[0].levels – 1) *treatments[1].levels * samplesize * (esMean / esSD_AOV) <sup>2</sup>	
Secondar	ry Treatment Effect		
$df_1 = df_S$	b-1	treatments[1].levels – 1	
$df_2$	(n-1)ab	(samplesize – 1) *treatments[1].levels	
λ	$a(b-1) n (f_S / \sigma)^2$	treatments[0].levels * (treatments[1].levels - 1) *samplesize * (esMean / esSD_AOV) <sup>2</sup>	
Interaction	Interaction Effect		
$df_1=df_1$	(a-1)(b-1)	(treatments[0].levels - 1) * (treatments[1].levels - 1)	
$df_2$	(n-1)ab	(samplesize – 1)*treatments[0].levels*treatments[1].levels	
λ	$(a-1)(b-1)n(f_I/\sigma)^2$	(treatments[0].levels – 1) * (treatments[1].levels – 1) * samplesize * (esMean / esSD_AOV) <sup>2</sup>	

Trt #	Math Notation for Power (1–β)	R Function Name	JS Computation
1	$F_c = F^{-1}(1-\alpha, a-1, (n-1)ab)$	quant = $qf(sig,dfM,df2)$ dfM = a - 1	<pre>dfM = treatments[0].levels-1 df2 = (samplesize-1)</pre>
		df2 = (n-1)ab	<pre>* treatments[0].levels</pre>
	$1-\beta = F(F_c, a-1, (n-1)ab, n(a-1)bf_M^2 / \sigma^2)$	pow = $pf(quant, dfM, df2, lambda1)$ lambda1= $n(a-1)bf_M^2/\sigma^2$	<pre>* treatments[1].levels lambda1 = samplesize * dfM      * treatments[1].levels      * (esMean/esSD_AOV)²</pre>
2	$F_c = F^{-1}(1-\alpha, b-1, (n-1)ab)$	quant = $qf(sig,dfS,df2)$ dfS = b-1	<pre>dfS = treatments[1].levels-1 lambda2 = samplesize * dfS</pre>
	$1 - \beta = F(F_c, b - 1, (n - 1)ab, na(b - 1)f_s^2 / \sigma^2)$	pow = $pf(quant, dfS, df2, lambda2)$ lambda2= $na(b-1)f_s^2/\sigma^2$	<pre>* treatments[0].levels * (esMean/esSD_AOV)²</pre>
3	$F_c = F^{-1}(1-\alpha,(a-1)(b-1),(n-1)ab)$	quant = $\mathbf{qf}(\text{sig,dfI,df2})$ $\mathbf{dfI} = (a-1)(b-1)$	<pre>dfI = (treatments[0].levels- 1)*(treatments[1].levels-1)</pre>
	$1 - \beta = F(F_c, (a-1)(b-1), (n-1)ab, \lambda_I)$ $\lambda_I = n(a-1)(b-1)f_I^2 / \sigma^2$	pow = $pf(quant, dfI, df2, lambda3)$ lambda3 = $\lambda_I$	lambda3 = samplesize * dfI * (esMean/esSD_AOV)²

### **Power for Three Way ANOVA**

#### **Model**

The 3-way ANOVA model with complete interaction modeling is given by

$$Y_{ijkm} = \mu + \eta_i + \xi_j + \zeta_k + \gamma_{ij} + \kappa_{jk} + \nu_{ik} + \tau_{ijk} + \varepsilon_{ijkm}, \quad 1 \le i \le a, 1 \le j \le b, 1 \le k \le c, 1 \le m \le n$$

in which:

- $\mu$  is the grand mean;
- $\eta_i$  are the main effects (and it is assumed  $\sum_{i=1}^a \eta_i = 0$ );
- $\xi_i$  are the secondary effects (and it is assumed  $\sum_{i=1}^b \xi_i = 0$ );
- $\zeta_i$  are the tertiary effects (and it is assumed  $\sum_{i=1}^{c} \zeta_i = 0$ );
- $\gamma_{ij}$  are the main-secondary interaction effects (and it is assumed  $\sum_{k=1}^{a} \gamma_{kj} = \sum_{l=1}^{b} \gamma_{il} = 0$  for each i, j);
- $\kappa_{ij}$  are the secondary-tertiary interaction effects (and it is assumed  $\sum_{l=1}^{b} \kappa_{lj} = \sum_{l=1}^{c} \kappa_{il} = 0$  for each i, j);
- $v_{ij}$  are the main-tertiary interaction effects (and it is assumed  $\sum_{l=1}^{a} v_{lj} = \sum_{l=1}^{c} v_{il} = 0$  for each i, j);
- $au_{ijk}$  are the three-way interaction effects with even more complicated constraints.
- $\varepsilon_{ijkm}$  are iid  $N(0, \sigma^2)$  random variables.

This is a balanced design: all groups have the same number of samples, n, and the total sample size is nab. To test hypotheses, we select a significance level  $\alpha$ , typically 0.05, but it may be less depending on the situation. There are seven hypotheses of interest:

- $\eta_i = 0$  for all i.
- $\xi_i = 0$  for all j.
- $\zeta_i = 0$  for all *i*.
- $\gamma_{ij} = 0$  for all i,j.
- $v_{ii} = 0$  for all I, j.
- $\kappa_{ij} = 0$  for all i,j.
- $\tau_{ijk} = 0$  for all i,j,k.

Testing each hypothesis, we will need the critical F value for the test

$$F_c = F^{-1}(1-\alpha, a-1, (n-1)abc)$$

$$F_c = F^{-1}(1-\alpha, b-1, (n-1)abc)$$

3 
$$F_c = F^{-1}(1-\alpha, c-1, (n-1)abc)$$

4 
$$F_c = F^{-1}(1-\alpha,(a-1)(b-1),(n-1)abc)$$

$$F_c = F^{-1}(1-\alpha,(a-1)(c-1),(n-1)abc)$$

6. 
$$F_c = F^{-1}(1-\alpha,(b-1)(c-1),(n-1)abc)$$

7. 
$$F_c = F^{-1}(1-\alpha,(a-1)(b-1)(c-1),(n-1)abc)$$

For each hypothesis, we have an effect size f. In each case, f denotes the distance from the null model:

$$f_M^2 = \frac{\sum_{i=1}^{a} (\eta_i - \overline{\eta})^2}{a - 1} \quad or \quad f_S^2 = \frac{\sum_{i=1}^{b} (\xi_i - \overline{\xi})^2}{b - 1} \quad or \quad f_T^2 = \frac{\sum_{i=1}^{c} (\zeta_i - \overline{\zeta})^2}{c - 1}$$

$$f_{MS}^{2} = \frac{\sum_{j=1}^{b} \sum_{i=1}^{a} (\gamma_{ij} - \bar{\gamma})^{2}}{(a-1)(b-1)} \quad or \quad f_{MT}^{2} = \frac{\sum_{j=1}^{c} \sum_{i=1}^{a} (\nu_{ij} - \bar{\nu})^{2}}{(a-1)(c-1)} \quad or \quad f_{ST}^{2} = \frac{\sum_{j=1}^{c} \sum_{i=1}^{b} (\kappa_{ij} - \hat{\kappa})^{2}}{(b-1)(c-1)}$$

$$f_{MST}^{2} = \frac{\sum_{k=1}^{c} \sum_{j=1}^{b} \sum_{i=1}^{a} (\tau_{ij} - \overline{\tau})^{2}}{(a-1)(b-1)(c-1)}$$

For each hypothesis, we compute the power using the formulae

1. 
$$1-\beta = F(F_c, a-1, (n-1)abc, n(a-1)bcf_M^2 / \sigma^2)$$

2. 
$$1 - \beta = F(F_c, b-1, (n-1)abc, na(b-1)cf_s^2 / \sigma^2)$$

3. 
$$1-\beta = F(F_c, c-1, (n-1)abc, nab(c-1)f_T^2/\sigma^2)$$

4. 
$$1 - \beta = F(F_c, (a-1)(b-1), (n-1)abc, n(a-1)(b-1)cf_{MS}^2 / \sigma^2)$$

5. 
$$1-\beta = F(F_c, (a-1)(c-1), (n-1)abc, n(a-1)b(c-1)f_{MT}^2/\sigma^2)$$

6. 
$$1-\beta = F(F_c, (b-1)(c-1), (n-1)abc, na(b-1)(c-1)f_{ST}^2/\sigma^2)$$

7. 
$$1-\beta = F(F_c,(a-1)(b-1)(c-1),(n-1)abc,n(a-1)(b-1)(c-1)f_{MST}^2/\sigma^2)$$

These relationships may also be used to determine the sample size per group, given the power  $1 - \beta$  and the effect size f. Alternatively, one may determine the minimal detectable effect size f for a given power and sample size.

### Webapp notes

### **Input parameters**

Symbol	Description	Variable Name
α	Significance level (probability of rejecting a true null, i.e.  Type I error probability)  sig	
n	Number of subjects in each treatment / factor group (aka sample size per group)  samplesize	
$\sigma$	Measured standard deviation	esSD_AOV
f	Effect size for Main, Secondary, Tertiary, and Interaction effects (assuming they are the same for now) esMean	
k	Number of Factors	
а	Number of <b>levels</b> in Factor 1 (or treatment 1)	treatments[0].levels
b	Number of levels in Factor 2 (or treatment 2)	treatments[1].levels
C	Number of levels in Factor 3 (or treatment 3)	treatments[2].levels

### **Three Way Anova Formula**

The df1 and  $\lambda$  are vectors length of n + 1 + nC2 + ... + nC(n-1). For Three Way Anova, the size of vectors are 3+1+3=7, in which 3C2=3.

Degree of freedom for denominator  $df2 = (n-1)abc = (\text{samplesize}-1) * \prod_{i=0}^{2} \text{treatments}[i].\text{levels}$ 

*df*1[i], for i = 1,2,...,7, degree of freedom for numerator:

Index	Effect	Formula	Code
1	1	(a-1)	treatments[0].levels – 1
2	2	(b-1)	treatments[0].levels – 1
3	3	(c-1)	treatments[0].levels – 1
4	1,2	(a-1)(b-1)	(treatments[0].levels - 1) (treatments[0].levels - 1)
5	1,3	(a-1)(c-1)	(treatments[0].levels - 1) (treatments[0].levels - 1)
6	2,3	(b-1)(c-1)	(treatments[0].levels - 1) $(treatments[0].levels - 1)$
7	1,2,3	(a-1)(b-1)(c-1)	$\prod_{i=0}^{2} (\text{treatments}[i].\text{levels - 1})$

$$\lambda[i]$$
, for  $i = 1, 2, ..., 7$ , and  $k = abc = \prod_{i=0}^{2} \text{treatments}[i]$ .levels, non-centrality parameter:

Index	Effect	Formula	Formula 2	Code
1	1	$n(a-1)bc(f/\sigma)^2$	$n*df1(1)*k/a*(f/\sigma)^2$	samplesize * df1(1)*k/ treatments[0].levels *
1	n(u-1)bc(f/O)	n(u-1)oc(y/0)	$n^{*}aj1(1)^{*}k/a^{*}(j/0)$	(esMean/esSD_AOV) <sup>2</sup>
2	2	$a = a(b - 1) = (f/a)^2$	$n*df1(2)*k/b*(f/\sigma)^2$	samplesize * df1(2)*k/ treatments[1].levels *
2	2	$n  a(b-1)c  (f/O)  \left[ n^* a f (2)^* k / b^*  (f/O) \right]$	(esMean/esSD_AOV) <sup>2</sup>	
2	2	1/( 1)/(// >2	* 101(2)*1 / * (C/ \( \)^2	samplesize * df1(3)*k/ treatments[2].levels *
3	3	$n ab(c-1) (f/\sigma)^2$	$n*df1(3)*k/c*(f/\sigma)^2$	(esMean/esSD_AOV) <sup>2</sup>

4	1,2	$n (a-1)(b-1)c(f/\sigma)^2$	$n*df1(4)*k/(ab)*(f/\sigma)^2$	samplesize * df1(4)*k/(treatments[0].levels* treatments[1].levels) * (esMean/ esSD_AOV) <sup>2</sup>
5	1,3	$n (a-1)b(c-1)(f/\sigma)^2$	$n*df1(5)*k/(ac)*(f/\sigma)^2$	samplesize * df1(5)*k/(treatments[0].levels* treatments[2].levels) * (esMean/esSD_AOV) <sup>2</sup>
6	2,3	$n a(b-1)(c-1)(f/\sigma)^2$	$n*df1(6)*k/(bc)*(f/\sigma)^2$	samplesize * df1(6)*k/(treatments[1].levels* treatments[2].levels) * (esMean/esSD_AOV) <sup>2</sup>
7	1,2,3	n (a-1)(b-1)(c-1) $(f/\sigma)^2$	$n*df1(7)*k/(abc)*(f/\sigma)^{2}$	samplesize * df1(7)*k/ $\prod_{i=0}^{2}$ (treatments[i].levels) * (esMean/esSD_AOV) <sup>2</sup>

#### Loop 1:

```
df1(0) = a - 1 = treatments[0].levels - 1 \\ df1(1) = b - 1 = treatments[1].levels - 1 \\ df1(2) = c - 1 = treatments[2].levels - 1 \\ df1(3) = (a - 1)(b - 1) = (treatments[0].levels - 1)(treatments[1].levels - 1) \\ df1(4) = (a - 1)(c - 1) = (treatments[0].levels - 1)(treatments[2].levels - 1) \\ df1(5) = (b - 1)(c - 1) = (treatments[1].levels - 1)(treatments[2].levels - 1) \\ df1(6) = (a - 1)(b - 1)(c - 1) = \prod_{i=0}^{2} (treatments[i].levels - 1)
```

#### Loop 2:

```
dft(0) = df1(0) / treatments[0].levels \\ dft(1) = df1(1) / treatments[1].levels \\ dft(2) = df1(2) / treatments[2].levels \\ dft(3) = df1(3) / treatments[0].levels / treatments[1].levels \\ dft(4) = df1(4) / treatments[0].levels / treatments[2].levels \\ dft(5) = df1(5) / treatments[1].levels / treatments[2].levels \\ dft(6) = df1(6) / treatments[0].levels / treatments[1].levels / treatments[2].levels \\ i = 0 to 6 \\ k = treatments[0].levels * treatments[1].levels * treatments[2].level \\ lambda(i) = samplesize * dft(i) * k * (esMean/esSD\_AOV)^2
```

# Parallel Single Outcome Power/Effect/Sample considerations

Each experimental subject gets exactly one level for each treatment and/or manipulation, and a single outcome measurement is taken at multiple fixed times for each experimental subject. The design is "one-way".

#### Model

For the outcome measure  $Y_{ijk}$  for i treatment, j time number and k replicated subject in the treatment group, the measurement model is given by

$$Y_{ijk} = \mu + \alpha_i + \tau_j + \gamma_{ij} + A_{ik} + E_{ijk},$$

#### where

- $\mu$ : overall mean of outcome measure
- $\alpha_i$ : effect of treatment
- $\tau_i$ : effect of time
- $\gamma_{ij}$ : interaction effect of time/treatment
- $A_{ik}$ : 0 mean, variance  $\sigma_{BS}^2$ , random effect of subject k in treatment i
- $E_{ijk}$ : 0 mean, variance  $\sigma_{ws}^2$ , random measurement error.

### The number of treatments, time points and subjects are

- g: total number of groups (treatment)
- t: total number of time points (repeated part)
- n: total number subjects in each treatment group

The total number of subjects is n\*g, and the total number data points is n\*g\*t.

#### The standard deviations are

- $\sigma_{ws}$ : the within subjects standard deviation
- ullet  $\sigma_{{\scriptscriptstyle BS}}$ : the between subjects standard deviation

# Webapp notes

# **Input parameters**

Symbol	Description	Variable Name
α	Significance level (probability of rejecting a true null, i.e. Type I error probability)	sig
n	Number of subjects in each treatment/ factor group (aka sample size per group)	ss
$\sigma_{ m ws}$	Within subjects standard deviation	wsSD_RM
$\sigma_{ ext{ iny BS}}$	Between subjects standard deviation	bsSD_RM
t	Number of time points	treatments[0].levels
$\mu_{ ext{time}}$	Time effect size	treatments[0].es
k	Number of treatments/factors, $k = 1$	treatmentsTotal
$\{g_i\}_{i=1}^k$	Number of <b>levels</b> per treatment/Factor	treatments[i].levels
$\{\mu_{\operatorname{trt}_i}\}_{i=1}^k$	Treatment effect size	treatments[i].es
$\mu_{ m int}$	Interactive effect size	treatments[k+1].es

### **One Treatment Formula**

	Formula	Coding
Tim	e Effect	
$df_1$	t-1	treatments[0].levels – 1
$df_2$	(n-1)(t-1)g	(ss-1)*(treatments[0].levels-1)*treatments[1].levels
λ	$\frac{(n-1)(t-1)g}{(t-1)g\frac{n\mu_{time}^2}{\sigma_{WS}^2}}$	(treatments[0].levels-1) * treatments[1].levels * ss * (treatments[0].es / wsSD_RM) <sup>2</sup>
Mai	n Treatment Effect	
$df_1$	g-1	treatments[1].levels – 1
$df_2$	(n-1)g	(ss-1) * treatments[1].levels
λ	$t \cdot (g-1) \frac{n\mu_{trt}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$	treatments[0].levels*(treatments[1].levels-1) * ss*treatments[0].es² / (wsSD_RM² + treatments[1].levels* bsSD_RM²)
Inte	raction Effect	
	(t-1)(g-1)	(treatments[0].levels – 1) * (treatments[1].levels – 1)
$df_2$	(n-1)(t-1)g	(ss-1) * (treatments[0].levels - 1) * treatments[1].levels
λ	$\frac{(n-1)(t-1)g}{(t-1)(g-1)\frac{n\mu_{\text{int}}^2}{\sigma_{WS}^2}}$	(treatments[0].levels - 1) * (treatments[1].levels - 1) * ss * (treatments[2].es/wsSD_RM) <sup>2</sup>

### Parallel Two Outcome Power/Effect/Sample considerations

### Webapp notes

The power  $(1-\beta)$  calculation typically looks like

$$F(F^{-1}(\alpha, df_1, df_2), df_1, df_2, \lambda) = \Pr[\text{non-central } F \leq \text{central } F \text{ specified critical value}].$$
 (2)

where

- $\alpha$  is significance, the probability of rejecting a true null, i.e. Type I error probability
- $df_1$  and  $df_2$  degree of freedom of *F*-Distribution, degree of freedom on numerator and denominator respectively;
- $\lambda$  is non-centrality parameter, sometime denoted by ncp.

### **Input parameters**

Symbol	Description	Variable Name
α	Significance level (probability of rejecting a true null, i.e. Type I error probability)	sig
n	Number of subjects in each treatment/ factor group (aka sample size per group)	ss
$\sigma_{ ext{ws}}$	Within subjects standard deviation	wsSD_RM
$\sigma_{ ext{ iny BS}}$	Between subjects standard deviation	bsSD_RM
t	Number of time points	treatments[0].levels
$\mu_{ ext{time}}$	Time effect size	treatments[0].es
k	Number of treatments/factors, <i>k</i> =1, 2, 3	treatmentsTotal
$\{g_i\}_{i=1}^k$	Number of <b>levels</b> per treatment	treatments[i].levels
$\{\mu_{\operatorname{trt} i}\}_{i=1}^k$	Treatment effect size	treatments[i].es
$\mu_{ m int}$	Interactive effect size	treatments[k+1].es

#### **Two Treatment Formula**

	Formula	Coding	
Time Effect			
$df_1$	t-1	treatments[0].levels – 1	
	$(n-1)(t-1) g_1 g_2$	(ss - 1)*(treatments[0].levels - 1) * treatments[1].levels * treatments[2].levels	
λ	$(t-1)g_1g_2\frac{n\mu_{time}^2}{\sigma_{WS}^2}$	(treatments[0].levels-1) * treatments[1].levels * treatments[2].levels * ss * (treatments[0].es / wsSD_RM) <sup>2</sup>	
Mai	Main Treatment Effect		

$df_1$	$g_1 - 1$	treatments[1].levels – 1	
$df_2$		(ss - 1) * treatments[1].levels * treatments[2].levels	
λ	$t \cdot (g_1 - 1)g_2 \frac{n\mu_{trt1}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$	treatments[0].levels * (treatments[1].levels - 1) * treatments[2].levels * ss * treatments[1].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )	
Sec	ondary Treatment Effect		
$df_1$	$g_2 - 1$	treatments[2].levels – 1	
$df_2$	$(n-1) g_1 g_2$	(ss-1) * treatments[1].levels * treatments[2].levels	
λ	$tg_1(g_2-1)\frac{n\mu_{trt2}^2}{\sigma_{WS}^2+t\cdot\sigma_{BS}^2}$	treatments[0].levels * treatments[1].levels  * (treatments[1].levels - 1) * ss * treatments[2].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )	
Tim	e and Main Interaction Effect		
	$(t-1)\left(g_1-1\right)$	(treatments[0].levels - 1) * (treatments[1].levels - 1)	
$df_2$	$(n-1)(t-1) g_1 g_2$	(ss-1) * treatments[0].levels * (treatments[1].levels - 1)	
λ	$(n-1)(t-1) g_1 g_2$ $(t-1)(g_1-1)g_2 \frac{n\mu_{t_{-1}}^2}{\sigma_{WS}^2}$	(treatments[0].levels – 1) * (treatments[1].levels – 1) * ss * (treatments[2].es/wsSD_RM) <sup>2</sup>	
Tim	Time and Secondary Interaction Effect		
$df_1$	$(t-1)(g_2-1)$	(treatments[0].levels - 1) * (treatments[1].levels - 1)	
$df_2$	$(n-1)(t-1) g_1 g_2$	(ss-1) * treatments[0].levels * (treatments[1].levels - 1)	
λ	$(t-1)g_1(g_2-1)\frac{n\mu_{t_2}^2}{\sigma_{WS}^2}$	(treatments[0].levels – 1) * (treatments[1].levels – 1) * ss * (treatments[2].es/wsSD_RM) <sup>2</sup>	
Mai	n and Secondary Interaction E	ffect	
$df_1$	$(g_1-1)(g_2-1)$	(treatments[0].levels – 1) * (treatments[1].levels – 1)	
	$(n-1) g_1 g_2$	(ss-1) * treatments[0].levels * (treatments[1].levels - 1)	
λ	$t(g_1-1)(g_2-1)\frac{n\mu_{1_2}^2}{\sigma_{WS}^2+t\cdot\sigma_{BS}^2}$	(treatments[0].levels - 1) * (treatments[1].levels - 1) * ss * (treatments[2].es/wsSD_RM) <sup>2</sup>	
Tim	Time, Main and Secondary Interaction Effect		
$df_1$	$(t-1)(g_1-1)(g_2-1)$	(treatments[0].levels – 1) * (treatments[1].levels – 1)	
$df_2$	$(n-1)(t-1)g_1g_2$	(ss-1) * treatments[0].levels * (treatments[1].levels - 1)	
λ	$(n-1) (t-1) g_1 g_2$ $t(t-1)(g_1-1)(g_2-1) \frac{n\mu_{t12}^2}{\sigma_{WS}^2}$	(treatments[0].levels - 1) * (treatments[1].levels - 1) * ss * (treatments[2].es/wsSD_RM) <sup>2</sup>	

### Parallel Three Outcome Power/Effect/Sample considerations

### Webapp notes

The power  $(1-\beta)$  calculation typically looks like

$$F(F^{-1}(\alpha, df_1, df_2), df_1, df_2, \lambda) = \Pr[\text{non-central } F \leq \text{central } F \text{ specified critical value}].$$
 (2)

where

- $\alpha$  is significance, the probability of rejecting a true null, i.e. Type I error probability
- $df_1$  and  $df_2$  degree of freedom of *F*-Distribution, degree of freedom on numerator and denominator respectively;
- $\lambda$  is non-centrality parameter, sometime denoted by ncp.

### **Input parameters**

Symbol	Description	Variable Name
α	Significance level (probability of rejecting a true null, i.e. Type I error probability)	sig
n	Number of subjects in each treatment/ factor group (aka sample size per group)	ss
$\sigma_{ ext{ws}}$	Within subjects standard deviation	wsSD_RM
$\sigma_{ ext{ iny BS}}$	Between subjects standard deviation	bsSD_RM
t	Number of time points	treatments[0].levels
$\mu_{ ext{time}}$	Time effect size	treatments[0].es
k	Number of treatments/factors, $k=1, 2, 3$	treatmentsTotal
$\{g_i\}_{i=1}^k$	Number of <b>levels</b> per treatment	treatments[i].levels
$\{\mu_{\operatorname{trt} i}\}_{i=1}^k$	Treatment effect size	treatments[i].es
$\mu_{ ext{int}}$	Interactive effect size	treatments[k+1].es

#### **Three Treatment Formula**

	Formula	Coding			
Tim	Time Effect				
$df_1$	t-1	treatments[0].levels – 1			
$df_2$	$(n-1)(t-1) g_1 g_2 g_3$	(ss - 1)*(treatments[0].levels - 1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$(t-1)g_1g_2g_3\frac{n\mu_{time}^2}{\sigma_{WS}^2}$	(treatments[0].levels-1)  * Prod(treatments[i].levels, i = 1,2,3)  * ss * (treatments[0].es / wsSD_RM) <sup>2</sup>			
Main Treatment Effect					
$df_1$	$g_1 - 1$	treatments[1].levels – 1			

$df_2$	$(n-1) g_1 g_2 g_3$	(ss - 1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$t \cdot (g_1 - 1)g_2g_3 \frac{n\mu_{trt1}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$	treatments[0].levels * (treatments[1].levels - 1)  * treatments[2].levels * treatments[3].levels  * ss * treatments[1].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )			
Sec	ondary Treatment Effect				
$df_1$	$g_2 - 1$	treatments[2].levels – 1			
$df_2$	$(n-1) g_1 g_2 g_3$	(ss - 1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$tg_1(g_2-1)g_3\frac{n\mu_{trt2}^2}{\sigma_{WS}^2+t\cdot\sigma_{BS}^2}$	treatments[0].levels * treatments[1].levels  * (treatments[2].levels - 1) * treatments[3].levels  * ss * treatments[2].es²  / (wsSD_RM² + treatments[0].levels* bsSD_RM²)			
Tert	iary Treatment Effect				
$df_1$	$g_3 - 1$	treatments[3].levels – 1			
$df_2$	$(n-1) g_1 g_2 g_3$	(ss-1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$tg_1g_2(g_3-1)\frac{n\mu_{trt3}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$	treatments[0].levels * treatments[1].levels * treatments[2].levels * (treatments[3].levels - 1) * ss * treatments[3].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )			
Tim	e and Main Interaction Effect				
$df_1$	$(t-1)(g_1-1)$	(treatments[0].levels – 1) * (treatments[1].levels – 1)			
$df_2$	$(n-1)(t-1) g_1 g_2 g_3$	(ss-1)*(t-1)* Prod(treatments[i].levels, i = 1,2,3)			
λ	$(n-1)(t-1) g_1 g_2 g_3$ $(t-1)(g_1-1)g_2 g_3 \frac{n\mu_{t-1}^2}{\sigma_{WS}^2}$	(treatments[0].levels - 1) * (treatments[1].levels - 1) * treatments[2].levels * treatments[3].levels * ss * (treatments[4].es/wsSD_RM) <sup>2</sup>			
Tim	e and Secondary Interaction Effection	et			
$df_1$	$(t-1)(g_2-1)$	(treatments[0].levels – 1) * (treatments[2].levels – 1)			
$df_2$	$(n-1)(t-1) g_1 g_2 g_3$	(ss-1)*(t-1)* Prod(treatments[i].levels, i = 1,2,3)			
	$(t-1)g_1(g_2-1)g_3\frac{n\mu_{t^2}^2}{\sigma_{WS}^2}$	(treatments[0].levels – 1) * treatments[1].levels * (treatments[2].levels – 1) * treatments[3].levels * ss * (treatments[5].es/wsSD_RM) <sup>2</sup>			
Tim	e and Tertiary Interaction Effect				
$df_1$	$(t-1)(g_3-1)$	(treatments[0].levels - 1) * (treatments[3].levels - 1)			
$df_2$	$(n-1)(t-1) g_1 g_2 g_3$	(ss-1)*(t-1)* Prod(treatments[i].levels, i = 1,2,3)			
λ	$(t-1)g_1g_2(g_3-1)\frac{n\mu_{t_3}^2}{\sigma_{WS}^2}$	(treatments[0].levels - 1) * treatments[1].levels * treatments[2].levels * (treatments[3].levels - 1) * ss * (treatments[6].es/wsSD_RM) <sup>2</sup>			
Mai	Main and Secondary Interaction Effect				
$df_1$	$(g_1-1)(g_2-1)$	(treatments[1].levels - 1) * (treatments[2].levels - 1)			
$df_2$	$(n-1) g_1 g_2 g_3$	(ss - 1) * Prod(treatments[i].levels, i = 1,2,3)			

λ	$t(g_1 - 1)(g_2 - 1)g_3 \frac{n\mu_{1_2}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$				
3.5	1 T	/ (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )			
Maı	Main and Tertiary Interaction Effect				
$df_1$	$(g_1-1)(g_3-1)$	(treatments[1].levels - 1) * (treatments[3].levels - 1)			
$df_2$	$(n-1) g_1 g_2 g_3$	(ss - 1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$t(g_1 - 1)g_2(g_3 - 1)\frac{n\mu_{1_2 3}^2}{\sigma_{WS}^2 + t \cdot \sigma_{BS}^2}$	treatments[0].levels * (treatments[1].levels - 1)  * treatments[2].levels * (treatments[3].levels - 1)  * ss * treatments[?].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )			
Sec	Secondary and Tertiary Interaction Effect				
$df_1$	$(g_2-1)(g_3-1)$	(treatments[2].levels - 1) * (treatments[3].levels - 1)			
$df_2$	$(n-1) g_1 g_2 g_3$	(ss-1) * Prod(treatments[i].levels, i = 1,2,3)			
λ	$tg_1(g_2-1)(g_3-1)\frac{n\mu_{2_3}^2}{\sigma_{WS}^2+t\cdot\sigma_{BS}^2}$	treatments[0].levels * treatments[1].levels  * (treatments[2].levels - 1) * (treatments[3].levels - 1)  * ss * treatments[?].es <sup>2</sup> / (wsSD_RM <sup>2</sup> + treatments[0].levels* bsSD_RM <sup>2</sup> )			
Moı	More than two Interaction Effect: the user should call for help				