Abstract

In analyzing data from a medical device, the researcher is often faced with data across the range of a biological analyte that may not satisfy the usual assumption for analysis of variance. Friedman's S Statistic is a useful nonparametric statistic when considering a randomized complete block design (2-way layout) which may be used when the usual assumptions required for analysis of variance (ANOVA) are not met. However, calculation of Friedman's S is tedious when applied to large data sets.

This paper presents an example of three manufacturing material sources (pilot lots) to prove manufacturing process capability when patient values are used to determine analyte response. The model under consideration is the usual 2-way ANOVA with lot as a main effect ($t_i$), and patient as a blocking variable. The hypotheses to be tested are $H_0: t_i = t_j$ vs. $H_a: t_i \neq t_j$, $i,j=1,...,k$.

This document also presents an automated method for converting a data set from continuous to ranked response using Proc RANK, 2-way ANOVA on the ranks using Proc ANOVA, and finally calculation of Friedman's S from results obtained within SAS.

Introduction

Friedman's S is useful when considering a randomized complete block design (2-way layout), where the blocks can be considered a "nuisance" variable. The model under consideration is:

$$Y_{ij} = \mu + t_i + \tau_j + e_{ij}$$

Where

$Y_{ij} =$ observed response  
$\mu =$ overall mean  
$t_i =$ blocking variable (nuisance effect)  
$\tau_j =$ treatment effect of interest  
$e_{ij} =$ random error

The Hypotheses to be tested are $H_0: t_i = t_j$ vs. $H_a: t_i \neq t_j$, $i,j=1,...,k$. The test is useful in that it requires no assumption of underlying distribution of the data. A problem is encountered when applied to large data sets, in that calculation of the statistic is tedious. This document presents a semi-automated method for the exact test, and consideration is given to an approximate method. An example taken from a product evaluation is presented to illustrate the methods.

Automation

SAS® software may be used to automate calculation of the S statistic. Hollander[1] notes that

$$S = \frac{12}{k(k+1)} \sum_{i=1}^{k} (R_i - \bar{R}_i)^2$$

and then calculate $S = \frac{12}{k(k+1)} \text{SS Treatment}$

where SS Treatment is the treatment sum of squares obtained by the usual ANOVA performed on the ranks of the data.

Procedure:

1. Obtain ranks from Proc RANK.
2. Obtain SST from ANOVA using GLM.
3. Calculate S as follows:

   No ties:

   $$S = \frac{12}{k(k+1)} \text{SS Treatment}$$

   Ties:

   $$M' = \frac{12}{nk(k+1)} \sum_{j=1}^{g} \left( \frac{1}{k} \sum_{i=1}^{k} \frac{t_i^2}{s_i^2} - k \right)$$

and then calculate $S=S'(M')\text{SS Treatment}$. The adjustment for ties was the most difficult piece to code, but once you have adjusted for ties, the code is general to all cases. The second summation in the denominator is summing the cube of the size of tied groups over the number of tied groups, and then subtracting the number of groups being compared. For instance, one row of three untied observations gives 11, 12 and 13 all equal to 1. Thus we have the sum of $1^2 + 1^2 + 1^2 = 3$. If we have a tie of say the first two groups, $g=2$ (that is we have one group of two ties, and one group with one "tie"). In this case, this will be the sum of $2^2 + 1^2 = 5$ for that row. In the case that all three observations are tied, $g=1$ group, and we obtain the sum of $3^2 = 9$. The algorithm which we implemented actually ignores the number of groups, but assigns the value of zero to the jth group in the event of a tie, which simplified the coding and still provides accurate results.

Hollander[1], page 141, is the source of the formula and test data set which we used to prove the method, before using it in our research example. In this example, three techniques of rounding first base in baseball are considered, with the desired outcome being to determine...
if one method leads to shorter times to reach second base. The response variable is measured across 22 ball players. Within each player (row), the response times are ranked for each method. This data set was analyzed using the SAS software code listed below.

/* Header Information **********************************************/
/* Filename: Friedtie Sas                              */
/* Author: Tim Beck and Sandy Weinert  */
/* Date: 12/07/93                          */
/* Purpose: To demonstrate SAS code useful to obtaining Friedman's S statistic */

/* Set Print Options *******************************************/
options ps=60 is=80 page=n=1;

/* Read in the data set *******************************************/
data first;  
  infile 'friedtstdat' firstobs=2;  
  input player$ method$ resp;  
run;

/* Sort the data set *******************************************/
proc sort data=first;  
  by player method;  
run;

/* Calculate the ranks placing them into the rankresp variable */
proc rank data=first out=rankdata;  
  var resp;  
  ranks rankresp;  
  by player;  
run;

/* Create a title *******************************************/
Title3 'ANOVA Using Ranks';

/* Perform ANOVA on the ranks *******************************************/
proc anova data=rankdata;  
  class player method;  
  model rankresp=player method;  
  means method Tukey t lines;  
run;

/* Sort ranked data for transpose into table *******************************************/
proc sort data=rankdata out=rankdata;  
  by player method;  
run;

/* Create the rank table *******************************************/
proc transpose data=rankdata out=tablrank;  
  drop=_NAME_ _LABEL_;  
  by player;  
run;

/* Set the variable for the number of groups *******************************************/
%let k=3;

/* Calculate number of groups and ties *******************************************/
data ties (drop=mergevar);  
  set tablrank;  
  array rank{1:3} A B C;  
  g=&k;  
  array tie{&k};  
  do i=1 to &k;  
    tie{i}=1;  
  end;
run;

/* Obtain Chi Square Quantile and Probability (large sample est) */
data chi;  
  set S;  
  prob_chl=1-probchi(S,&k-1);  
  chi_sq=cinv(0.05,&k-1);  
run;

/* Print pertinent information of the statistic *******************************************/
proc print;  
  var M N SS CHI_SQ PROB_CHI;  
run;

/* End of code *******************************************/

In the above code, Proc RANK assigned ranks to the responses within each row. These were placed into the.
variable called rankre5p (any eight character name may be used). Next, Proc GLM was used to obtain the sum of squares of the treatment (SST), in this case 10.64. Column ranks were summed in the Proc PRINT step. The data contained four ties between two methods. Using the above formulae, we obtain the following output.

Output of Friedman’s S using SAS Software

<table>
<thead>
<tr>
<th>OBS</th>
<th>M</th>
<th>N</th>
<th>SS</th>
<th>CHI_SQ</th>
<th>PROB_CHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0476</td>
<td>22</td>
<td>10.6364</td>
<td>11.1429</td>
<td>0.10259</td>
</tr>
</tbody>
</table>

M’=0.0476, S’=(0.0476)(22)(10.64)=11.1 which is the expected result listed in Hollander[1].

Approximate Method

The SAS software documentation[2] lists an approach suggested by Conover[3], which references a further article by Iman[4]. Basically, the approach is similar to the above in that the ranks are computed as in the normal S calculation, but the usual ANOVA is applied and the F-statistic for the treatment effect is used. Iman’s article maintained that the F approximation is to be preferred to the χ² approximation for small number of blocks and treatments. We performed ANOVA on the ranks obtained, and performed a multiple means analysis (Tukey’s Studentized Range Test), also listed in the above code. In this case, we conclude that the treatments are different with 95% confidence, with the lower ranked method being the desired method. This is consistent with Friedman’s S in Hollander[1]. Please refer to the articles listed at the end of this paper for discussions of the appropriate use of this technique.

Application to a Research Problem

Data were collected to compare three sources of a material to be used in production of a device for monitoring a certain biological analyte. The experimental design allowed blocking by donor (volunteers which provided blood for testing), where each material was tested on each donor’s specimen. For the sake of this presentation, all data were subjected to a linear transformation which preserved the relative error structures, but obscures the actual data and experimental purpose.

Bias from a reference method is the response of interest. The data are heteroscedastic over the range, and a variance stabilizing transformation (empirically derived) was used for the normal ANOVA. Example code is listed below.

```
* Header Information                                   *
* Filename : Friedman.Sas                               *
Author : Tim Beck and Sandy Weinert                    *
Date : 12/07/93                                         *

Purpose : To demonstrate SAS code necessary for
generation of Ranks and obtaining SST for exact
Friedman’s procedure */
* Set Printed Page Options ***************/
  options ps=60 ls=60 pageno=1;
/* Read in raw data from file *******************/
data raw;
infile ’test.dat’ firstobs=5;
input donor ref lot conc source;
bias=conc-ref;
run;
/* Perform transformation for usual ANOVA***********/
data xformed;
  set raw;
bias= [place your variance stabilization transformation on bias here];
run;
/* Set title for output *************************/
title1 h=2’Evaluation of Three Material Sources’;
/* Sort data set for means grouping *************/
proc sort data=raw;
  by source donor;
run;
/* Collapse data into means for two-way rank table******/
proc means data=rawnoprint;
  by source donor;
  var bias;
  output out=meanbias mean=mbias;
run;
/* Sort data for ranking ***************************/
proc sort data=meanbias;
  by donor source;
run;
/* Calculate ranks by donor for each method*********/
proc rank data=meanbias out=biasrank;
  var mbias;
  ranks rankbias;
  by donor;
run;
/* Print the ranked data ***************************/
proc print data=biasrank;
run;
/* Sort data for table generation *******************/
proc sort data=biasrank out=biasrank(keep=donor source rankbias);
  by donor source rankbias;
run;
/* Transpose ranked data for tabular presentation******/
proc transpose data=biasrank out=tabirank
  (drop= _NAME_ _LABEL_);
  by donor;
  id source;
  var rankbias;
run;
/* Print, summing for total rank information*********/
proc print;
  sum AAA BBB CCC;
run;
```
/* Transpose means output for rank table ***************/
proc transpose data=meanbias out=tablmean
(drop=_NAME__LABEL__);
   by donor;
   id source;
   var mbias;
run;
/* Print this table ***********************************/
proc print;
run;
/* Set title to tell one output from the other ***********/
Title3 'ANOVA Using Ranks';
/* Perform ANOVA on the ranks ************************/
proc anova data=biasrank;
   class donor source;
   model rankbias=donor source;
   means source tukey t;
run;
/* Again change the title for what follows *************/
Title3 'ANOVA Using Transformation for Variance Stabilization';
/* Perform the usual ANOVA on the raw data ************/
proc anova data=xformed;
   class donor source;
   model bias=source donor;
   means source tukey t llines;
run;
/* Calculate the number of ties from the ranks *********/
%let k=3;
data ties (drop=i j);
   set tablrank;
array rankr{1:3} AM BBB CCC;
g=&k;
array tie{&k};
do i=1 to &k;
   tie{i}=0;
   do j=i+1 to &k;
      if rankr{i}=rankr{j} then do;
         tie{i}=tie{i}+tie{j};
         tie{j}=0;
      end;
   end;
tie_sum=0;
   do i=1 to &k;
      if tie{i}=0 then g=g-1;
      tie_sum=tie_sum+tie{i}*&3;
   end;
tie_sum=tie_sum-&k;
run;
/* Print the table of rank information *****************/
proc print;
   sum AM BBB CCC Tie_Sum;
run;
/* Intermediate data manipulations and calculations*****/
data M (keep=M mergevar rows);
   retain summ(0) rows;
   set ties nobs=n end=lastone;
   summ=summ+tie_sum;
   if lastone;
   M=12/((k+3*(k-1))/2-1)/summ);
mergevar=1;
   rows=n;
run;
/* Obtain SST from GLM (ANOVA)***************************/
proc glm data=biasrank noprint outstat=SS_data;
   class donor source;
   model rankbias=donor source;
run;
/* Isolate SST from GLM Output **********************/
data SS_data (keep=SS mergevar);
   set SS_data;
   if _TYPE_="SS3" and _Source_='SOURCE';
   mergevar=1;
run;
/* Merge intermediates and calculate S ***************/
data S (drop=mergevar);
   merge M SS_data;
   by mergevar;
   S=M*rows*SS;
   rename rows=N;
run;
/* Obtain chi-square and probability for large sample*****/
data chi;
   set S;
   prob_chi=1-probchi(S,&k-1);
   chi_sq=cinv(0.05,&k-1);
run;
/* Print the output on a table ***********************/
proc print;
   var M N SS S CHI SQ PROB_CHI;
run;

The code listed above performs several tasks, which are highlighted in the comments immediately above each section. In this case, each donor was measured on three instruments for each source, where the instruments were determined to be equivalent. The final ANOVA made use of this repetition, but for the sake of the rank transformation, the data were reduced to the average of each set of readings for each material for each donor. This allowed for the simplified blocking structure required for the analysis on the ranks. After obtaining the means, the rank procedure was applied as in the previous example. Next, ANOVA was performed on the ranks. Finally, ANOVA was performed using the original data set with the variance stabilizing transformation. The following is output from the above code.

Output of the intermediate rank table, illustrating ties and number of groups.

<table>
<thead>
<tr>
<th>OBS</th>
<th>DONOR</th>
<th>AAA</th>
<th>BBB</th>
<th>CCC</th>
<th>G</th>
<th>TIE1</th>
<th>TIE2</th>
<th>TIE3</th>
<th>TIE_SUM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>101</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>102</td>
<td>2.0</td>
<td>1.0</td>
<td>3.0</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>103</td>
<td>3.0</td>
<td>1.0</td>
<td>2.0</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>189</td>
<td>2.5</td>
<td>1.0</td>
<td>2.5</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>190</td>
<td>220</td>
<td>2.0</td>
<td>1.0</td>
<td>3.0</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>191</td>
<td>221</td>
<td>2.0</td>
<td>1.0</td>
<td>3.0</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>192</td>
<td>222</td>
<td>1.5</td>
<td>1.5</td>
<td>3.0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

---

487.0 254.5 410.5 66
Output of Friedman's S using SAS Software

<table>
<thead>
<tr>
<th>OBS</th>
<th>M</th>
<th>N</th>
<th>S</th>
<th>CHI-SQ</th>
<th>PROB_CHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>.0052840</td>
<td>182</td>
<td>146.296</td>
<td>143.383</td>
<td>0.10259</td>
</tr>
</tbody>
</table>

From the ANOVA on the ranks output, we obtained the SST = 146.26. There were n = 192 donors, and k = 3 materials being tested. Eleven of these groups had ties of size 2. The exact S was calculated as

$$S^* = \left(\frac{1}{(192)(3)(4)}\right) \left(\begin{array}{c} 1 \\ 2 \end{array}\right)^{111.6}$$

Here again, the $\chi^2$ approximation is justified due to the large number of observations. This leads us to reject $H_0$: that the treatments are equal, and conclude $H_a$: that at least one of the treatments is not equal to the other two.

Turning again to the approach using ANOVA on the ranks, we obtain the following from the same code.

**ANOVA on the Ranks**

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Sum of Squares</th>
<th>Mean Square</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>193</td>
<td>58762.784461</td>
<td>304.574013</td>
<td>4.60</td>
<td>0.0001</td>
</tr>
<tr>
<td>Error</td>
<td>1534</td>
<td>101513.069618</td>
<td>66.175404</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected Total</td>
<td>1727</td>
<td>160296.854099</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R-Square: 0.366714, C.V. = 8.1348266, MSE = 0.607964

**Tukey's Means Comparison on the Original Transformed Response**

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Sum of Squares</th>
<th>Mean Square</th>
<th>F Value</th>
<th>Pr &gt; F</th>
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</thead>
<tbody>
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<td></td>
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<td>Corrected Total</td>
<td>1727</td>
<td>160296.854099</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R-Square: 0.366714, C.V. = 8.1348266, MSE = 0.607964

Means with the same letter are not significantly different.

Tukey Grouping

| DONOR | 191 | 433494.441966 | 227.717989 | 3.44    | 0.0001 |

Finally, we compare these results to our best parametric estimate of the truth, which is the original ANOVA on the data which was transformed to satisfy the usual assumptions for analysis of variance.

**ANOVA on the Original Transformed Response**

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Sum of Squares</th>
<th>Mean Square</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>193</td>
<td>58762.784461</td>
<td>304.574013</td>
<td>4.60</td>
<td>0.0001</td>
</tr>
<tr>
<td>Error</td>
<td>1534</td>
<td>101513.069618</td>
<td>66.175404</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected Total</td>
<td>1727</td>
<td>160296.854099</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R-Square: 0.366714, C.V. = 8.1348266, MSE = 0.607964

Tukey's Studentized Range (HSD) Test for variable: BIAS

| Alpha= 0.05 df= 1534 MSE= 66.1754 |
| Critical Value of Studentized Range= 3.318 |
| Minimum Significant Difference= 1.1245 |

Means with the same letter are not significantly different.

Tukey Grouping

| DONOR | 191 | 433494.441966 | 227.717989 | 3.44    | 0.0001 |

The usual ANOVA on the transformed data suggested that all three sources differ. Rank transformation (Friedman's S) and F approximation (ANOVA on the ranks) yielded similar results.

**Conclusions**

SAS software simplified the task of ranking the data, and performing ANOVA on the ranks, as well as providing results in the calculation of Friedman's S on large data sets.

**References**

Posters


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