

**Benjamini-Hochberg method (1995) for “false discovery rate”,**

<http://www.jstor.org/stable/2346101> ;

implemented in Statistical Analysis of Microarrays (SAM) and BRBTOOLS from the National Cancer Institute's Biometric Research Branch.

*Number of errors committed when testing  $m$  null hypotheses*

	<i>Declared non-significant</i>	<i>Declared significant</i>	<i>Total</i>
True null hypotheses	<b>U</b>	<b>V</b>	$m_0$
Non-true null hypotheses	<b>T</b>	<b>S</b>	$m - m_0$
	$m - \mathbf{R}$	<b>R</b>	$m$

B-H is a classical frequentist technique. False discovery rate could be defined as

$$\text{FDR} = Q_e = E(\mathbf{Q}) = E\{\mathbf{V}/(\mathbf{V} + \mathbf{S})\} = E(\mathbf{V}/\mathbf{R}).$$

Here  $\mathbf{R} = \#$  declared significant.

What if  $\mathbf{R}$  can equal 0? The  $Q_e$  will be infinite.

And when all null hypotheses are true, then all discoveries are false and  $\text{FDR}=1$ .

Instead B&H define

$$\text{FDR} = P(\bar{\mathbf{R}} > 0) E(\mathbf{V}/\mathbf{R} | \mathbf{R} > 0).$$

The BH procedure is:

let  $k$  be the largest  $i$  for which  $P_{(i)} \leq \frac{i}{m} q^*$ ;

then reject all  $H_{(i)}$   $i = 1, 2, \dots, k$ .

Then FDR is no bigger than  $q^*$ .

Example: An randomized clinical trial of treatments rt-PA versus APSAC when myocardial infarction occurs. There are 15 different clinical endpoints.

The 15 P values are ranked. Here are the first few with the critical cutoff values with  $q^*=0.05$ .

	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>					
<b>Pvalue</b>	<b>0.0001</b>	<b>0.0004</b>	<b>0.0019</b>	<b>0.0095</b>	0.0201	0.0278	0.0298	...	1
<b>cutoff</b>	<b>0.0033</b>	<b>0.0067</b>	<b>0.0100</b>	<b>0.0133</b>	0.0167	0.0200	0.0233	...	0.05

The first 4 hypotheses are “significant” with this rule. (In bold face)

Suppose we tweak the results. Decrease the 4th P value just a little:

	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>5</i>				
<b>Pvalue</b>	<b>0.0001</b>	<b>0.0004</b>	<b>0.0019</b>	<b>0.0095</b>	<b>0.0151</b>	0.0278	0.0298	...	1
<b>cutoff</b>	<b>0.0033</b>	<b>0.0067</b>	<b>0.0100</b>	<b>0.0133</b>	<b>0.0167</b>	0.0200	0.0233	...	0.05

Great, now the 5<sup>th</sup> is significant.

Now increase the 4<sup>th</sup> P value slightly:

	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>					
<b>Pvalue</b>	<b>0.0001</b>	<b>0.0004</b>	<b>0.0019</b>	<b>0.0135</b>	<b>0.0151</b>	0.0278	0.0298	...	1
<b>cutoff</b>	<b>0.0033</b>	<b>0.0067</b>	<b>0.0100</b>	0.0133	0.0167	0.0200	0.0233	...	0.05

Suddenly the 5<sup>th</sup> is ALSO not significant. Why not? Does this make sense? The data for the 5<sup>th</sup> test has not changed at all. That’s typical that weird things happen in frequentist approaches to multiple comparisons. It’s unsatisfying to many people.