A two-stage adaptive design can increase power for multiple comparisons

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Benjamini and Hochberg procedure

1. *independent* tests and $\alpha_* \in (0, 1)$ is control target.

2. $m$ statistics $\{t_i\}$, p-values, $\{p_i\}$.

3. Rank: $p(1) \leq p(2) \leq \cdots \leq p(m)$

4. Find largest $k$ such that $p(k) \leq k \cdot \alpha_*/m$.

5. Reject hypotheses with $k$: smallest p-values

$\Rightarrow$ False Discovery Rate $\leq \alpha_*$
## Decisions for an experiment

<table>
<thead>
<tr>
<th>True State</th>
<th>Decision</th>
<th>Reject</th>
<th>Accept</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_0$ True</td>
<td></td>
<td>$j$</td>
<td>$n - j$</td>
</tr>
<tr>
<td>$H_0$ False</td>
<td></td>
<td>$k - j$</td>
<td>$(m - n) - (k - j)$</td>
</tr>
</tbody>
</table>

- $k$: number of observations in the second group
- $m$: total number of observations in the second group
- $j$: number of observations in the first group
- $m - n$: number of observations in the second group that are not in the first group
- $n$: total number of observations in the first group
- $k - j$: number of observations in the second group that are not in the first group
Expected power

Expected power is the average number of null hypotheses we should reject that we do reject.

\[
\mathbb{E} \left[ \frac{(K - J)}{(m - n)} \right] = \sum_{k=0}^{m} \sum_{j} \left[ \frac{(k - j)}{(m - n)} \right] \Pr\{(K = k) \cap (J = j)\}
\]
Exact power

![Graph showing the relationship between Expected Power and Mean of Alternative.]

Number in Each Sample:
- 5
- 10
- 15

Glueck et al., CIS, 2008
Glueck et al., IJB, 2008
Adaptive design for multiple comparisons

- Benjamini and Yekutieli (2006) Biometrika
- Reiner-Benaim et al. (2007) Bioinformatics
- Blanchard and Roquain (2008) EJS
Problem

- Power decreases as the number of hypotheses increases
- Many hypotheses are null, not alternative, so we are wasting power on testing null hypotheses
- Reducing the number of hypotheses by discarding nulls, and thus enriching the proportion of alternatives should improve power
Adaptive FDR procedure

- Estimate the number of nulls
- Choose a truncation point so that for hypotheses with p-values less than truncation point, the estimated proportion of alternatives achieves a threshold
- Conduct a multiple comparisons procedure only on the hypotheses whose p-values are less than the truncation point
Results

• Fast
• Increases power by more than 10%
• Maintains false discovery rate