Adaptive Truncated Sequential Tests and the Bonferroni Procedure

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A Simple Method to Construct Sequential Tests

- $X_1, \ldots, X_n$ ... i.i.d. random variables
- $X_k = (X_1, \ldots, X_k)$ first $k$ observations
- $f : \mathbb{R}^n \to \{0\} \cup [1, \infty)$ with $E_{H_0}\{f(X_n)\} = \alpha$

A truncated sequential test

Reject $H_0$ after the $k$-th observation, if

$$E_{H_0}\{f(X_n) | X_k\} \geq 1$$

1. Type I error rate $\leq \alpha$
2. Under appropriate conditions:
   Type I error rate $\rightarrow \alpha$ as $n \rightarrow \infty$
Some comments

• \( E\{f(X_n)|X_n\} = f(X_n) \).
• In the final analysis the test rejects whenever
  \[ f(X_n) \geq 1. \]
• Let \( \varphi \in \{0, 1\} \) be the decision function of any test. With \( f(X_n) = \varphi \) the proposed procedure (typically) gives the fixed sample test.
Example

Testing Scenario

- Test of
  \[ H_0 : \mu = 0 \text{ against } H_1 : \mu > 0 \]
  for the mean of i.i.d. \( N(\mu, 1) \) distributed observations.
- \( n \) . . . maximal sample size
- \( p = 1 - \Phi\left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} X_n \right) \) . . . p-value of fixed sample z-test
A Family of Sequential Tests

\[ f(p) = \begin{cases} 
\gamma & \text{if } p \leq \alpha / \gamma \\
0 & \text{otherwise} 
\end{cases} \quad (\gamma \geq 1) \]
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\[ f(p) = \begin{cases} \gamma & \text{if } p \leq \frac{\alpha}{\gamma} \\ 0 & \text{otherwise} \end{cases} \quad (\gamma \geq 1) \]
Level and Conditional Expectation

\[ f(p) = \begin{cases} \gamma & \text{if } p \leq \alpha/\gamma \\ 0 & \text{otherwise} \end{cases} \]

- \( E_{H_0}\{f(p)\} = \gamma \frac{\alpha}{\gamma} = \alpha \)
- \( E_{H_0}\{f(p)|X_k\} = \gamma \left[ 1 - \Phi \left( \frac{z_{1-\alpha/\gamma} - \sqrt{\frac{1}{n} \sum_{i=1}^{t} X_k}}{\sqrt{1 - k/n}} \right) \right] \)

Corresponds to stochastic curtailment stopping rule (LAN, SIMON, HALPERIN, 1982).
An example path

\[ f(p) = \begin{cases} 
2 & \text{if } p \leq \alpha/2 \\
0 & \text{otherwise} 
\end{cases} \]
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$$f(p) = \begin{cases} 
\gamma & \text{if } p \leq \frac{\alpha}{\gamma} \\
0 & \text{otherwise} 
\end{cases}$$

- $E_{H_0}(f(p)|X_k) = 1 \iff$
  $$\sum_{i=1}^{k} X_i = z_{1-\alpha/\gamma} \sqrt{n} - z_{1-1/\gamma} \sqrt{n} - k = a(k)$$

- Special cases:
  - $\gamma = 1$: fixed sample case
  - $\gamma = 2$: $a(k) = z_{1-\alpha/2}$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$
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$\gamma = 1.8$

![Graph showing sequential boundaries for the partial sums with $\gamma = 1.8$.]
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1.3$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1.1$
Sequential Boundaries for the partial sums \( \sum_{i=1}^{k} X_i \)
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1.01$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 2.0$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 100.0$
Sequential Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1000.0$
The sequential procedure controls the Type I error rate

Let $\psi_k := E_{H_0}\{ f(X_n) | X_k \}$ and define the stopping time

$$T := \begin{cases} 
  n & \text{if all } \psi_k < 1 \\
  \min(k : \psi_k \geq 1) & \text{otherwise}
\end{cases}$$

The sequential test is given by

$$\varphi = \min(\psi_T, 1)$$

Proof:

$\psi_k$ is a martingale. Optional stopping theorem:

$$P(\varphi = 1) = E\{\min(\psi_T, 1)\} \leq E\{\psi_T\} = \psi_0 = E\{f(X_n)\} = \alpha$$
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Asymptotics

Proposition

Assume $f$ is a bounded, monotonic function of an asymptotically linear test statistics.

Then asymptotically (as $n \to \infty$)

1. the sequential test has level $\alpha$.
2. Assume $P_{H_0}\{f(X_n) = 1\} = 0$. Then

\[ P\{ T < n | H_0 \text{ is rejected} \} = 1. \]

Applications

Sign Test, Binomial Test, z-Tests, t-Tests, Likelihood Ratio Tests
Sequential Tests with Futility Stopping

- $f : \mathbb{R}^n \to (-\infty, 0) \cup [1, \infty)$ with $E_{H_0}\{f(X_n)\} = \alpha$
- Reject $H_0$ after the $k$-th observation, if
  $$E_{H_0}\{f(X_n)\mid X_k\} \geq 1$$
- Accept $H_0$ after the $k$-th observation, if
  $$E_{H_0}\{f(X_n)\mid X_k\} \leq 0$$
- For asymptotically linear test statistics:
  Type I error rate $\rightarrow \alpha$ for $n \rightarrow \infty$
A Family of Tests with Futility Stopping

\[ f(p) = \begin{cases} 
\gamma & \text{if } p \leq \alpha \\
-\alpha \frac{\gamma - 1}{1 - \alpha} & \text{otherwise}
\end{cases}, \quad E_{H_0}\{f(p)\} = \alpha \]
A Family of Tests with Futility Stopping

\[ f(p) = \begin{cases} 
\frac{\gamma}{1-\alpha} & \text{if } p \leq \alpha \\
-\alpha \frac{\gamma-1}{1-\alpha} & \text{otherwise}
\end{cases} \]

\[ E_{H_0}\{f(p)\} = \alpha \]

\[ \gamma = 2 \]
A Family of Tests with Futility Stopping

$$f(p) = \begin{cases} \frac{\gamma}{\alpha} & \text{if } p \leq \alpha \\ -\alpha \frac{\gamma^{-1}}{1-\alpha} & \text{otherwise} \end{cases}$$

$$E_{H_0}\{f(p)\} = \alpha$$

$$\gamma = 3$$
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1.05$
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 1.2$
Boundaries for the partial sums \( \sum_{i=1}^{k} X_i \)

\( \gamma = 1.5 \)
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$
Boundaries for the partial sums $\sum_{i=1}^{k} X_i$

$\gamma = 4.0$
Uniform Improvement of the Bonferroni Test

- $H_A, H_B \ldots$ considered null hypotheses
- $X^A_n, X^B_n \ldots$ data vectors for $H_A, H_B$.
- $p_A, p_B \ldots$ univariate p-values for $H_A, H_B$
- The Bonferroni test for $H = H_A \cap H_B$ is given by
  \[
  \varphi^B = \min\{1_{\{p_A \leq \alpha/2\}}, 1_{\{p_B \leq \alpha/2\}}\}.
  \]

- Let $f(p_A, p_B) = 1_{\{p_A \leq \alpha/2\}} + 1_{\{p_B \leq \alpha/2\}}$.
- $E_H\{f(p_A, p_B)\} = \alpha$, whatever the dependency structure.
- $\varphi^B \leq f(p_A, p_B)$
Sequential improvement of the Bonferroni Test

Reject $H = H_A \cap H_B$ after the $k$-th observation, if

$$E_H[1_{\{p_A \leq \alpha/2\}}|X_k^A] + E_H[1_{\{p_B \leq \alpha/2\}}|X_k^B] \geq 1$$

- Rejects whenever the classical Bonferroni test rejects
- Compared to the fixed sample Bonferroni test:
  - higher power
  - lower expected sample size
  - asymptotically exhausts the level for all dependence structures
Simulation Study

- Tests for the means of normal data
- Bivariate normal data with correlation $\rho$
Type I Error Rates

\[-\quad \alpha \quad \text{Level} \quad \frac{\alpha}{2} \quad \rho\]

- Bonferroni Test
- Sequential Test

\( n = 275 \)
\( \alpha = 0.05 \)
Power to reject $H_A \cap H_B$

- Bonferroni Test
- Sequential Test

$n = 275$
\(\alpha = 0.05\)
\(\mu_1 = 0.15\sigma\)
\(\mu_2 = 0.15\sigma\)
Expected Sample Size

- Bonferroni Test  -  Sequential Test

\[ n = 275 \]
\[ \alpha = 0.05 \]
\[ \mu_1 = 0.15 \sigma \]
\[ \mu_2 = 0.15 \sigma \]
Some Comments

- The sequential test rejects the intersection hypothesis after the $k$-th observation, if
  \[
  \sum_{i=1}^{k} (X_i^A + X_i^B) \geq 2\sqrt{n}z_{1-\alpha/2}
  \]

- The asymptotic $\alpha$ spending function is ($t = k/n$)
  \[
  \alpha(t) = 2 \left[ 1 - \Phi \left( \frac{\sqrt{2}z_{1-\alpha/2}}{\sqrt{t(1-\rho)}} \right) \right]
  \]
The Asymptotic $\alpha$-Spending Function

$\rho = -1.0$
The Asymptotic $\alpha$-Spending Function

$\rho = 0.0$

$t = k/n$

$\alpha(t)$
The Asymptotic $\alpha$-Spending Function

\[ \alpha(t) = \rho \frac{t}{n} \]

\[ \rho = 0.2 \]
The Asymptotic $\alpha$-Spending Function

\[ \alpha(t) = \rho = 0.4 \]
The Asymptotic $\alpha$-Spending Function

\[ \alpha(t) = \rho = 0.6 \]

\[ t = k/n \]
The Asymptotic $\alpha$-Spending Function

$$\rho = 0.8$$
The Asymptotic $\alpha$-Spending Function

\[ \rho = 1.0 \]
Generalizations

- Tests for elementary hypotheses with the closure principle
  - Test the intersection hypothesis with the sequential Bonferroni test
  - Test the elementary hypotheses with the sequential test defined by
    \[ 2 \cdot 1_{\{p \leq \alpha/2\}} \]
- Weighted Bonferroni test for \( m \)-hypotheses
- General cut-off tests (Röhmel & Streitberg, 1987)
Adaptive Sequential Tests

- Truncated sequential test defined by
  \[ f : \mathbb{R}^n \rightarrow \{0\} \cap [0, 1] \]
- interim analysis after \( k \) observations
- choose a sample size \( m \) and a secondary sequential trial defined by a function \( g \)
  \[ g : \mathbb{R}^m \rightarrow \{0\} \cap [0, 1], \quad E\{g(X'_m)\} = E\{f(X_n)|X_k\} \]
  where \( X'_m \) denotes the vector of future observations.

MÜLLER & SCHÄFER, 2004
Summary

- Simple construction principle for truncated sequential tests
- Incorporating futility stopping
- Uniform improvement of Bonferroni tests and other cut-off tests
- Easily extended to an adaptive test