A Bayesian Approach to Stepwise Simultaneous Testing

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Outline

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Frequentist stepwise multiple testing procedures

Comparing the ordered test statistics or associated p-values with a set of critical values in a stepwise fashion towards identifying the set of true and false null hypotheses.

- *Step-down methods* – starts with testing the most significant hypothesis and continues until an acceptance occurs or all hypotheses are rejected.
- *Step-up methods* – starts with testing the least significant hypothesis and continues until a rejection occurs or all the hypotheses are accepted.
- *Generalized step-up-down method of order r* (Tamhane, Liu, and Dunnett 1998) – starts with testing the rth least significant hypothesis.
  - ▷ acceptance $\Longrightarrow$ test continues in step-up manner
  - ▷ rejection $\Longrightarrow$ test continues in step-down manner

Bayesian multiplicity adjustment

- Why multiplicity adjustment for Bayesians
  - ▷ Berry (1988)
  - ▷ Breslow (1990)
  - ▷ Berry and Hochberg (1999)
- Bayesian multiple comparisons procedures
  - ▷ Duncan (1965): Bayesian decision-theoretic approach
  - ▷ Waller and Duncan (1969): hyper-prior distribution for the unknown ratio of between-to-within variances
  - ▷ Tamhane and Gopal (1993): comparisons of treatments with a control under additive overall loss function
  - ▷ Westfall, Johnson and Utts (1997): prior probability adjustment
  - ▷ Gopalan and Berry (1998): Dirichlet process prior for all configurations of hypotheses
  - ▷ Shaffer (1999): semi-Bayesian method

Current status of Bayesian testing of multiple hypotheses

- Bayesian hypothesis testing and model selection
  - ▷ Pairwise Bayes factors – Berger (1999); Berger and Pericchi (1996, 2001)
  - ▷ Multiple and partial Bayes factors – Bertolino, Piccinato, and Racugno (1995)
- Features of existing Bayesian testing procedures
  - ▷ Single step
  - ▷ Large number of families (configurations)
  - ▷ Intractable configurations of hypotheses with large family of hypotheses
  - ▷ computationally extensive

Bayesian Hypothesis Testing (I)

- Distributional setups
  - ▷ Let $\mathbf{X} = \{\mathbf{X}_1, \ldots, \mathbf{X}_k\}$ be independent samples from k populations, each with pdf
  $$f(\mathbf{x}_i|\theta_i) = \prod_{1 \le j \le n_i} f(x_i|\theta_i), \quad i = 1, \ldots, k$$
  - ▷ Let the $\theta_i, i = 1, \ldots, k$,be independent with the first stage prior $\pi_1(\theta_i|\lambda)$ and the second stage prior for $\lambda = (\lambda_1, \lambda_2)$ being $\pi_2(\lambda) = \pi_{21}(\lambda_1|\lambda_2)\pi_{22}(\lambda_2)$.
  - ▷ $H_i : \boldsymbol{\theta} \in \Theta_i$ against $\bar{H}_i : \boldsymbol{\theta} \in \bar{\Theta}_i$, for $i = 1, \ldots, k$, where $\boldsymbol{\theta} = \{\theta_1, \ldots, \theta_k\}$, $\Theta_i \cap \bar{\Theta}_i = \emptyset$ and $\Theta_i \cup \bar{\Theta}_i = \Omega$.
- Posterior probability of H_i given $\mathbf{X}$
$$P(H_i|\mathbf{X}) = \int_{\Theta_i} \pi(\boldsymbol{\theta}|\mathbf{X}) d\boldsymbol{\theta}$$

Bayesian Hypothesis Testing (II)

- Posterior probability of H_i given $\mathbf{X}$ (cont'd)

  where

$$\pi(\boldsymbol{\theta}|\mathbf{X}) = [m(\mathbf{X})]^{-1} f(\mathbf{X}|\boldsymbol{\theta})\pi(\boldsymbol{\theta}),$$

$$f(\mathbf{X}|\boldsymbol{\theta}) = \prod_{1 \le i \le k} f(\mathbf{X}_i|\theta_i),$$

$$\pi(\boldsymbol{\theta}) = \int \prod_{1 \le i \le k} \pi_1(\theta_i|\lambda)\pi_2(\lambda)d\lambda,$$

  and

$$m(\mathbf{X}) = \int_\Omega f(\mathbf{X}|\boldsymbol{\theta})\pi(\boldsymbol{\theta})d\boldsymbol{\theta}.$$

- $P(\bar{H}_i|\mathbf{X}) = 1 - P(H_i|\mathbf{X})$

- Marginal Bayes factor of H_i

$$B_i = \frac{P(H_i|\mathbf{X})}{1 - P(H_i|\mathbf{X})} \cdot \frac{1 - \pi_{i0}}{\pi_{i0}},$$

Bayesian Hypothesis Testing (III)

- Marginal Bayes factor of H_i (cont'd)
  with
  $$\pi_{i0} = \int_{\Theta_i} \pi(\boldsymbol{\theta}) d\boldsymbol{\theta}.$$

- For testing $H = \cap_{i=1}^k H_i$ against $\bar{H} = \cup_{i=1}^k \bar{H}_i$,
  $$B = \frac{\int_H \pi(\boldsymbol{\theta}|\mathbf{X}) d\boldsymbol{\theta}}{1 - \int_H \pi(\boldsymbol{\theta}|\mathbf{X}) d\boldsymbol{\theta}} \cdot \frac{1 - \int_H \pi(\boldsymbol{\theta}) d\boldsymbol{\theta}}{\int_H \pi(\boldsymbol{\theta}) d\boldsymbol{\theta}}.$$

- If $\lambda = (\lambda_1, \lambda_2)$ is known
  $$B = \frac{\prod_{1 \le i \le k} B_i}{\prod_{1 \le i \le k}(1 + B_i) - \prod_{1 \le i \le k} B_i} \cdot \frac{1 - \prod_{1 \le i \le k} \pi_{i0}}{\prod_{1 \le i \le k} \pi_{i0}}.$$

- If $\pi_{i0} = 1 - \pi_{i0}$ for all i's
  $$B = (2^k - 1) \frac{\prod_{1 \le i \le k} B_i}{\prod_{1 \le i \le k}(1 + B_i) - \prod_{1 \le i \le k} B_i}.$$

A Bayesian Stepwise Simultaneous Testing Procedure (I)

- Let $B_{(1)} \le \cdots \le B_{(k)}$ be the ordered values of the marginal Bayes factors $B_1, \ldots, B_k$, and $B_{(j)}$ correspond to $H_{(j)}$.
- If the strength of evidence for $H_{(j)}$ is weak, then the strength of evidence for $H_{(i)}$ should be weaker for all $i < j$;
- If the strength of evidence for $H_{(j)}$ is strong, then the strength of evidence for $H_{(l)}$ should be stronger for all $l > j$.
- $\binom{k}{r}$: $\bar{H}_{(1)} \cdots \bar{H}_{(r)} H_{(r+1)} \cdots H_{(k)}$
  $\Downarrow$
  $\left\{H_{(1)}, \ldots, H_{(k)}\right\}, \left\{\bar{H}_{(1)}, H_{(2)}, \ldots, H_{(k)}\right\}, \ldots,$
  $\left\{\bar{H}_{(1)}, \ldots, \bar{H}_{(k-1)}, H_{(k)}\right\}, \left\{\bar{H}_{(1)}, \ldots, \bar{H}_{(k)}\right\}.$
- Define

$$H^{(r)} = \left\{\cap_{i=1}^{r} \bar{H}_{(i)}\right\} \cap \left\{\cap_{i=r+1}^{k} H_{(i)}\right\}$$

for $r = 0, 1, \ldots, k$ with $\bar{H}_0 = \Omega$.

A Bayesian Stepwise Simultaneous Testing Procedure (II)

- Stepwise Bayes factor for $H^{(r)}$ to any of $H^{(r+1)}, \ldots, H^{(k)}$

$$B^{(r)} = \frac{P(H^{(r)}|\mathbf{X})}{\sum_{r+1 \leq i \leq k} P(H^{(i)}|\mathbf{X})} \cdot \frac{\sum_{r+1 \leq i \leq k} \pi(H^{(i)})}{\pi(H^{(r)})} \tag{1}$$

where $\pi(H^{(r)})$ is the prior probability of $H^{(r)}$, $r = 0, 1, \ldots, k-1$.

- The proposed procedure

  Step 0. Start with $r = 0$, i.e., the intersection of all the k null hypotheses, calculate $B^{(0)}$. If $B^{(0)} > c$, then accept $H^{(0)} = \cap_{i=1}^{k} H_{(i)}$ and stop; if $B^{(0)} \leq c$, then reject $H_{(1)}$ go to the next step.

  ...

  Step r. Calculate $B^{(r)}$. If $B^{(r)} > c$, then accept $H^{(r)}$ and stop; if $B^{(r)} \leq c$, then reject all $H_{(i)}$ for $i \leq r+1$ and go to the next step.

  ...

  Step k-1. Calculate $B^{(k-1)}$. If $B^{(k-1)} > c$, then accept $H^{(k-1)}$ and stop; if $B^{(k-1)} \leq c$, then reject all $H_{(i)}$ for $i \leq k$.

- The choice of c: Berger, Boukai, and Wang (1997).

Some features of the proposed procedure

- Step-down multiple testing procedure
- Two main steps
  - ▷ Specification of target families of true and false null hypotheses
  - ▷ stepwise search for the most plausible one of these families
- Considerable reduction in the size of set of families from 2^k to $k+1$
- Systematic improvement of the search for the “right” family by incorporating information gathered at every step
- Practically feasible in terms of keeping track of various configurations
- Computationally economic

Testing multiple point null hypotheses (I)

- $H_i : \theta_i = \theta_{i0}$, $i = 1, \ldots, k$, against $\bar{H}_i : \theta_i \neq \theta_{i0}$, $i = 1, \ldots, k$.
- Conditional prior given λ

$$\pi_1(\theta_i|\lambda) = \pi_{i0} I(\theta_i = \theta_{i0}) + (1 - \pi_{i0}) g_1(\theta_i|\lambda) I(\theta_i \neq \theta_{i0}).$$

- If θ_{i0} is known
  - ▷ Marginal Bayes factor of H_i

$$\begin{aligned} P(H_i|\mathbf{X}) &= [m(\mathbf{X})]^{-1} \int \Bigg[\pi_{i0} f(\mathbf{X}_i|\theta_{i0}) \prod_{1 \leq j \leq k}^{(-i)} \Big\{ \pi_{j0} f(\mathbf{X}_j|\theta_{j0}) \\ & \quad + (1 - \pi_{j0}) f^*(\mathbf{X}_j|\lambda) \Big\} \Bigg] \pi_2(\lambda) d\lambda, \end{aligned} \tag{2}$$

where $\quad f^*(\mathbf{X}_j|\lambda) = \int f(\mathbf{X}_j|\theta_j) g_1(\theta_j|\lambda) d\theta_j, \quad j = 1, \ldots, k,$

$$m(\mathbf{X}) = \int \Bigg[\prod_{1 \leq j \leq k} \Big\{ \pi_{j0} f(\mathbf{X}_j|\theta_{j0}) + (1 - \pi_{j0}) f^*(\mathbf{X}_j|\lambda) \Big\} \Bigg] \pi_2(\lambda) d\lambda,$$

Testing multiple point null hypotheses (II)

- If θ_{i0} is known (cont'd)
  - ▷ Posterior probability of $H^{(r)}$ given $\mathbf{X}$

$$P(H^{(r)}|\mathbf{X}) = [m(\mathbf{X})]^{-1} \int \Big[\prod_{1 \le i \le r} \big\{(1-\pi_{i0}) f^*(\mathbf{X}_i|\lambda)\big\} \prod_{r+1 \le i \le k} \big\{\pi_{i0} f(\mathbf{X}_i|\theta_{i0})\big\}\Big] \pi_2(\lambda) d\lambda, \quad (3)$$

  - ▷ Stepwise Bayes factor for testing $H^{(r)}$

$$B^{(r)} = \frac{P(H^{(r)}|\mathbf{X})}{\sum_{r+1 \le j \le k} P(H^{(j)}|\mathbf{X})} \cdot \sum_{r+1 \le j \le k} \left(\prod_{r+1 \le i \le j} \frac{1-\pi_{i0}}{\pi_{i0}} \right). \quad (4)$$

  - ▷ If $\lambda = (\lambda_1, \lambda_2)$ is known

$$B^{(r)} = \left[\sum_{r+1 \le j \le k} \left(\prod_{r+1 \le i \le j} \frac{1-\pi_{i0}}{\pi_{i0}} \frac{1}{B_i} \right) \right]^{-1} \left[\sum_{r+1 \le j \le k} \left(\prod_{r+1 \le i \le j} \frac{1-\pi_{i0}}{\pi_{i0}} \right) \right]. \quad (5)$$

Testing multiple point null hypotheses (III)

- If $\theta_{10} = \cdots = \theta_{k0} \equiv \theta_0$ and θ_0 is an unknown parameter of control group
  - ▷ Posterior probability of H_i given $\mathbf{X}$

$$P(H_i|\mathbf{X}) = \frac{1}{m_0(\mathbf{X})} \int \Big[\int f(\mathbf{X}_0|\theta_0)\pi_{i0} f(\mathbf{X}_i|\theta_0) \prod_{1\le j\le k}^{(-i)} \{\pi_{j0} f(\mathbf{X}_j|\theta_0) + (1-\pi_{j0}) f^*(\mathbf{X}_j|\lambda)\} \pi_1(\theta_0|\lambda) d\theta_0 \Big] \pi_2(\lambda) d\lambda, \quad (6)$$

where

$$m_0(\mathbf{X}) = \int \Big[\int f(\mathbf{X}_0|\theta_0) \prod_{1\le j\le k} \{\pi_{j0} f(\mathbf{X}_j|\theta_0) + (1-\pi_{j0}) f^*(\mathbf{X}_j|\lambda)\} \pi_1(\theta_0|\lambda) d\theta_0 \Big] \pi_2(\lambda) d\lambda.$$

  - ▷ Posterior probability of $H^{(r)}$ given $\mathbf{X}$

$$P(H^{(r)}|\mathbf{X}) = [m_0(\mathbf{X})]^{-1} \iint \Big[f(\mathbf{X}_0|\theta_0) \Big\{ \prod_{1\le j\le r} (1-\pi_{j0}) f^*(\mathbf{X}_j|\lambda) \prod_{r+1\le j\le k} \pi_{j0} f(\mathbf{X}_j|\theta_0) \Big\} \pi_1(\theta_0|\lambda) d\theta_0 \Big] \pi_2(\lambda) d\lambda. \quad (7)$$

Testing Multiple One-Sided Null Hypotheses (I)

- $H_i : \theta_i \le \theta_{i0}, i = 1, \dots, k$ against $\bar{H}_i : \theta_i > \theta_{i0}, i = 1, \dots, k$.
- If θ_{i0} is known
  - ▷ Posterior probability of H_i and $H^{(r)}$ given $\mathbf{X}$ are, respectively

$$P(H_i|\mathbf{X}) = [m^*(\mathbf{X})]^{-1} \int \left[f_0^*(\mathbf{X}_i|\lambda) \prod_{1 \le j \le k}^{(-i)} \left\{ f^*(\mathbf{X}_j|\lambda) \right\} \right] \pi_2(\lambda) d\lambda. \qquad (8)$$

$$P(H^{(r)}|\mathbf{X}) = [m^*(\mathbf{X})]^{-1} \int \left[\prod_{1 \le j \le r} \left\{ f_1^*(\mathbf{X}_j|\lambda) \right\} \prod_{r+1 \le j \le k} \left\{ f_0^*(\mathbf{X}_j|\lambda) \right\} \right] \pi_2(\lambda) d\lambda, \quad (9)$$

where

$$m^*(\mathbf{X}) = \int \left[\prod_{1 \le j \le k} \left\{ f^*(\mathbf{X}_j|\lambda) \right\} \right] \pi_2(\lambda) d\lambda, \; f^*(\mathbf{X}_j|\lambda) = \int f(\mathbf{X}_j|\theta_j) \pi_1(\theta_j|\lambda) d\theta_j,$$

$$f_0^*(\mathbf{X}_j|\lambda) = \int_{\theta_j \le \theta_{j0}} f(\mathbf{X}_j|\theta_j) \pi_1(\theta_j|\lambda) d\theta_j, \text{ and } f_1^*(\mathbf{X}_j|\lambda) = \int_{\theta_j > \theta_{j0}} f(\mathbf{X}_j|\theta_j) \pi_1(\theta_j|\lambda) d\theta_j.$$

Testing Multiple One-Sided Null Hypotheses (II)

- If θ_{i0} is known (cont'd)
  - ▷ Stepwise Bayes factor for $H^{(r)}$ given $\mathbf{X}$

$$B^{(r)} = \frac{P(H^{(r)}|\mathbf{X})}{\sum_{r+1\le i\le k} P(H^{(i)}|\mathbf{X})} \cdot \frac{\sum_{r+1\le i\le k} \pi_0(H^{(i)})}{\pi_0(H^{(r)})}, \qquad (10)$$

where

$$\pi_0(H^{(r)}) = \int \Big[\prod_{1\le i\le r} \Big\{ \int_{\theta_i > \theta_{i0}} \pi_1(\theta_i|\lambda)d\theta_i \Big\} \prod_{r+1\le i\le k} \Big\{ \int_{\theta_i \le \theta_{i0}} \pi_1(\theta_i|\lambda)d\theta_i \Big\} \Big] \pi_2(\lambda)d\lambda.$$

- If $\theta_{10} = \cdots = \theta_{k0} \equiv \theta_0$ and θ_0 is an unknown parameter of control group
  - ▷ posterior probability of H_i

$$\begin{aligned} P(H_i|\mathbf{X}) &= [m_0^*(\mathbf{X})]^{-1} \int \Big[\int f(\mathbf{X}_0|\theta_0) f_0^*(\mathbf{X}_i|\lambda) \pi_1(\theta_0|\lambda) d\theta_0 \\ &\quad \prod_{1\le j\le k}^{(-i)} \{f^*(\mathbf{X}_j|\lambda)\} \Big] \pi_2(\lambda) d\lambda \qquad (11) \end{aligned}$$

Testing Multiple One-Sided Null Hypotheses (III)

- If θ_{i0} is unknown and $\theta_{10} = \cdots = \theta_{k0} \equiv \theta_0$
  - ▷ posterior probability of H_i (cont'd)
    where
$$m_0^*(\mathbf{X}) = \int \Big[\prod_{0 \le j \le k} \{f^*(\mathbf{X}_j|\lambda)\} \Big] \pi_2(\lambda) d\lambda.$$
  - ▷ Posterior probability of $H^{(r)}$ given $\mathbf{X}$

$$P(H^{(r)}|\mathbf{X}) = [m_0^*(\mathbf{X})]^{-1} \int \Big[\int f(\mathbf{X}_0|\theta_0) \prod_{1 \le j \le r} \{f_1^*(\mathbf{X}_j|\lambda)\} \prod_{r+1 \le j \le k} \{f_0^*(\mathbf{X}_j|\lambda)\} \pi_1(\theta_0|\lambda) d\theta_0 \Big] \pi_2(\lambda) d\lambda. \quad (12)$$

Multiple Testing with A Standard Using Point Null Hypotheses (I)

- $X_{ij} \sim N(\theta_i, \sigma^2)$
- Prior density $g_1(\theta_i|\xi, \sigma^2) = N(\mu, \xi\sigma^2)$, for some known μ and ξ, with $\pi_2(\sigma^2) \propto (\sigma^2)^{-1}$.
- Null hypotheses $H_i : \theta_i = \theta_0$ versus $\bar{H}_i : \theta_i \neq \theta_0$, $i = 1, \ldots, k$, for some known θ_0.

Example 1. Mee, Shah, and Lefante (1987) (MSL) present a method for comparing k independent means with a known standard [data from Romano (1977)].

- Ten ball bearings are randomly selected from each of four production lines.
- MSL employ their procedure and conclude that process 2 is out of control. By applying the proposed Bayesian stepwise simultaneous testing procedure to the data with $\mu = 1$ mm, we come to the same conclusion (Table 1)

Multiple Testing with A Standard Using Point Null Hypotheses (II)

Table 1: Summary Statistics and Marginal and Stepwise Bayes Factors for Ball Bearing Data

Process	Mean	Sample Variance	n	B_i	r	$B^{(r)}$
2	1.406	0.18345	10	0.091	0	0.044
1	1.194	0.08392	10	0.734	1	1.978
4	1.176	0.05920	10	0.945	2	2.629
3	1.129	0.17021	10	1.878	3	22.512

Multiple Testing with An Unknown Control Using Point Null Hypotheses (I)

- Prior density $\pi_1(\theta_i|\xi, \sigma^2) = N(\mu, \xi\sigma^2), i = 0, \ldots, k.$ and $\pi_2(\sigma^2) \propto (\sigma^2)^{-1}$.
- Null hypotheses $H_i : \theta_i = \theta_0$ versus $\bar{H}_i : \theta_i \neq \theta_0$, $i = 1, \ldots, k$, for unknown parameter θ_0 of commonly referenced group.

Example 2. [Steele, R. et al (1980)] Toxicological effects of six different chemical solutions on young mice

- Comparisons of the six solutions with the control (group 0) and not on the comparisons among the six solutions.
- Dunnett's two-sided single-step confidence interval method: solutions 3 and 6 are significantly more toxic than the control in inhibiting mouse growth [Westfall, Tobias, Rom, Wolfinger, and Hochberg (1999), pp54-56].
- Our method with prior mean $\mu = 90$ and $\xi = 2$ concludes that groups 3, 6, and 2 are significantly different from the control in terms of toxicological effects (Table 2).

Multiple Testing with An Unknown Control Using Point Null Hypotheses (IV)

Table 2: Summary Statistics and Marginal and Stepwise Bayes Factors for Mouse Growth Data

Group	Mean	Std. Dev.	n	B_i	r	$B^{(r)}$
3	72.14	8.41	4	0.02	0	0.23
6	74.24	7.81	4	0.03	1	0.34
2	80.48	12.68	4	0.12	2	0.81
5	84.68	18.35	4	0.28	3	1.25
4	91.88	9.44	4	0.94	4	2.53
1	95.90	23.89	4	1.57	5	5.21
0	105.38	13.44	4			

Multiple Testing with An Unknown Control Using One-Sided Null Hypotheses (I)

- $H_i : \theta_i \leq \theta_0$ versus $\overline{H}_i : \theta_i > \theta_0$, $i = 1, \cdots, k$, with θ_0 being the unknown mean of the control group.
- Prior densities $IG(a/2, b/2)$ for σ^2 and ξ.

Example 3. [White and Froeb (1980)] The effect of smoking on pulmonary health:

- Subjects were assigned, based on their smoking habits, to one of six groups — non-smokers (NS), passive smokers (PS), non-inhaling smokers (NI), light smokers (LS), moderate smokers (MS), and heavy smokers (HS).
- A sample of 1050 female subjects, 50 from non-inhaling group and 200 from each of the remaining groups, were selected and data on their pulmonary function (forced vital capacity, FVC) were recorded.
- Smoking effects on individual's pulmonary health relative to non-smokers.
- Dunnett's one-sided method: there is a significantly difference in mean FVC between non-smokers and light, moderate and heavy smokers [Hsu (1996)].
- The proposed Bayesian procedure with $\mu = 3.30$: same conclusion (Table 3).

Multiple Testing with An Unknown Control Using One-Sided Null Hypotheses (III)

Table 3: Summary Statistics and Marginal and Stepwise Bayes Factors for Smoking and Pulmonary Health Data

Group (#)	Mean	Std. Dev.	n	B_i	r	$B^{(r)}$
HS (5)	2.55	0.38	200	0.01	0	0.33
MS (4)	2.80	0.38	200	0.04	1	0.85
LS (3)	3.15	0.39	200	0.22	2	0.97
NI (2)	3.19	0.52	50	0.49	3	1.24
PS (1)	3.23	0.46	200	1.07	4	1.43
NS (0)	3.35	0.63	200			

Remarks and Conclusions

- Equivalent results to those obtained from frequentist methods.
- Multiple testing involving normal means with unequal variances
- Simultaneous testing of means and variances from multiple normal populations
- Wide scope of applications: Applicable to many multiple testing problems with a non-hierarchical family of hypotheses
- Bayesian false discovery rate (FDR)
- Bayesian step-up procedure
- Bayesian generalized step-up-down procedure
- Bayesian credible interval approach
- Robustness: intrinsic Bayes factor and fractional Bayes factor