On Multiple Decision-Making

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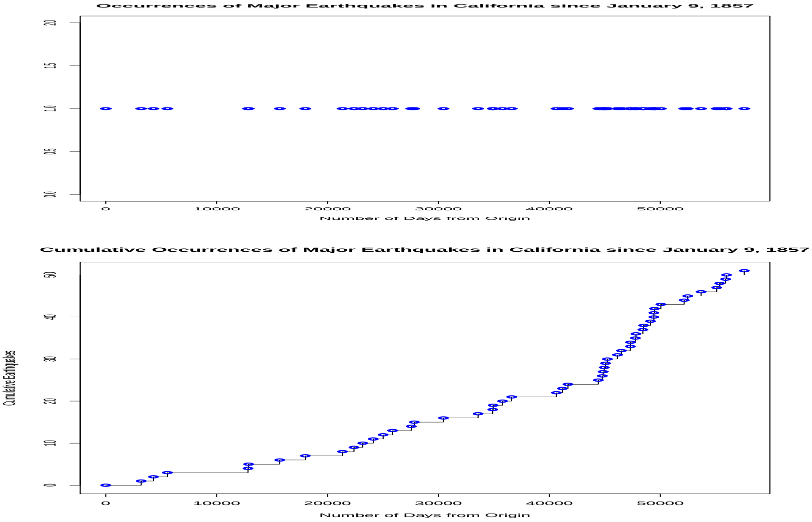
Major Earthquakes in California, 1857-2015

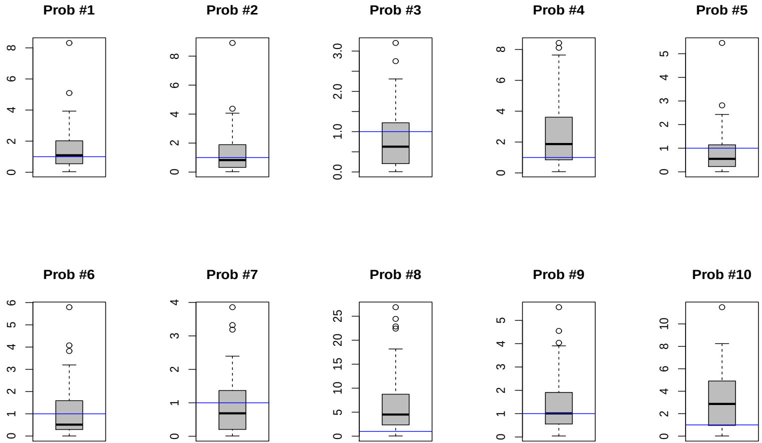


Questions: From an HPP(λ)? If so, is $MTBE = \lambda^{-1} > 1000$ days?

Multiple Testing Problem

$M = 10$ HPPs

Which of the 10 HPPs have $\lambda < 1$ Based on the $n = 50$ Observations?



Individual Decision Functions

- Decision Problems: $m \in \{1, 2, \ldots, M\}$
- Model (since HPP):

$$X_{m1}, X_{m2}, \ldots, X_{mn} \quad IID \quad Exp(\lambda_m)$$

- Hypotheses:

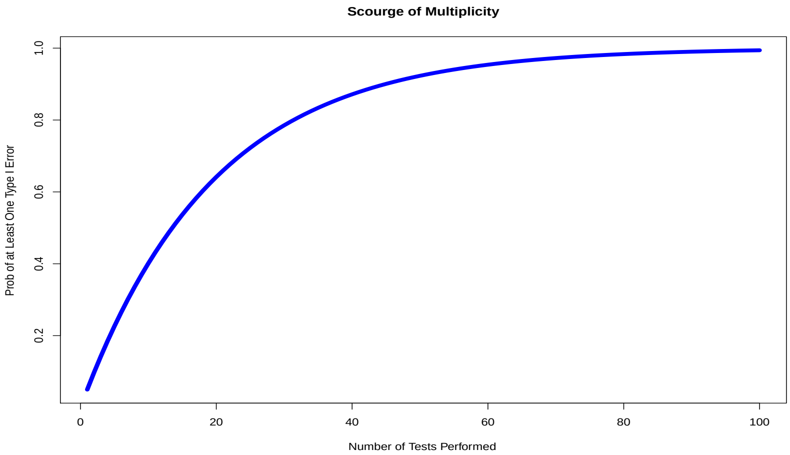
$$H_{m0} : \lambda_m \geq 1 \quad versus \quad H_{m1} : \lambda_m < 1$$

- Level of Significance: α, e.g., 0.05.
- Decision Function:

$$\delta_m(\mathbf{x}_m) = I\left\{2\sum_{i=1}^{n} X_{mi} > \chi^2_{2n;\alpha}\right\}$$

That is, decide for H_{m1} if $2S_m = 2\sum_{i=1}^{n} X_{mi} > \chi^2_{2n;\alpha}$.

Perils of Multiple Decision-Making: Fixed α



Relevance of Multiple Decisions

- Post-hoc analysis after a significant ANOVA test.
- Variable selection in regression problems.
- Genetic and/or proteomics studies.
- Engineering and reliability settings.
- Business and/or financial (investment) situations.
- University admission of students.
- Sporting decisions.
- Examples in yesterday's talks.

The General Multiple Decision Problem

- To discover the value (truth) of a parameter vector

$$\theta = (\theta_1, \theta_2, \ldots, \theta_M) \in \Theta = \{0, 1\}^M$$

- $\theta_m = 1$ means the mth alternative hypothesis H_{m1} is true.
- $\theta_m = 0$ means the mth null hypothesis H_{m0} hypothesis is true.
- Decision Maker's Goal: To choose an action vector

$$a = (a_1, a_2, \ldots, a_M) \in \mathfrak{A} = \{0, 1\}^M$$

- $a_m = 1$ means decide $\theta_m = 1$, called a discovery; $a_m = 0$ means decide $\theta_m = 0$, a non-discovery.

False and Missed Discoveries

- False Discovery [Type I Error]: action $a_m = 1$ when $\theta_m = 0$.

$$a_m(1 - \theta_m) = 1$$

- Missed Discovery [Type II Error]: action $a_m = 0$ when $\theta_m = 1$.

$$(1 - a_m)\theta_m = 1$$

- Practical Consequences of Errors of Decision:
  - False Discovery: Ends up *Chasing Noise as Signal!*
  - Missed Discovery: *Overlooking Key to Solving Problem.*
  - Reported results **NOT** Reproducible.
  - Non-Reproducible Results: Crisis in Science. [John Ionnadis]

Globally Assessing Multiple Actions: Losses

- Family-wise error indicator (FWEI):

$$L_0(a,\theta) = I\left\{\sum_{m=1}^{M} a_m(1-\theta_m) > 0\right\} = \text{At least one Type I Error?}$$

- False Discovery Proportion (FDP):

$$L_1(a,\theta) = \frac{\sum_{m=1}^{M} a_m(1-\theta_m)}{\max\{\sum_{m=1}^{M} a_m, 1\}} = \frac{\#\ of\ \ False\ \ Discoveries}{\#\ of\ \ Discoveries}$$

- Missed Discovery Proportion (MDP):

$$L_2(a,\theta) = \frac{\sum_{m=1}^{M}(1-a_m)\theta_m}{\max\{\sum_{m=1}^{M} \theta_m, 1\}} = \frac{\#\ of\ \ Missed\ \ Discoveries}{\#\ \ Discoverables}$$

Making Multiple Decisions from Data, Possibly BIG

- Obtain data (e.g., microarrays, brain data, Netflix, etc.):

$$X \in \mathfrak{X} = \text{Data Space}$$

- X maybe an $M \times n$ matrix; could be more complex.
- Probabilistic Structure:

$$X \sim P, \quad P \text{ is a Joint Probability Distribution}$$

- Marginal Components (Data and Distribution):

$$X_m = z_m(X) \in \mathfrak{X}_m \quad \text{and} \quad X_m \sim P_m = P z_m^{-1}$$

- Marginal Parameters: $\theta_m = \theta_m(P_m)$
- An Example:

$$\theta_m = 1 \Longleftrightarrow P_m \in \{N(\mu_m, \sigma_m^2) : \mu_m \geq 0, \sigma_m^2 > 0\}$$

Multiple Decision Functions

- Multiple Decision Function:

$$\delta : \mathfrak{X} \text{ (Data Space) } \to \mathfrak{A} = \{0,1\}^M \text{ (Action Space)}$$

- $\delta = (\delta_1, \delta_2, \ldots, \delta_M)$ with $\delta_m : \mathfrak{X} \to \{0,1\}$
- Remark: δ_m may use the whole data, not just X_m.
- $\mathfrak{D}$: space of multiple decision functions.
- $\mathcal{M}_0 = \{m : \theta_m = 0\}$ and $\mathcal{M}_1 = \{m : \theta_m = 1\}$
- Structure: $\{\delta_m(X) : m \in \mathcal{M}_0\}$ is an independent collection, and is independent of $\{\delta_m(X) : m \in \mathcal{M}_1\}$.
- $\{\delta_m(X) : m \in \mathcal{M}_1\}$ need NOT be an independent collection.

Risk Functions: Averaged Losses

- Given a $\delta \in \mathfrak{D}$: Family-Wise Error Rate (FWER):

$$R_0(\delta, P) = E[L_0(\delta(X), \theta(P))]$$

- False Discovery Rate (FDR):

$$R_1(\delta, P) = E[L_1(\delta(X), \theta(P))]$$

- Missed Discovery Rate (MDR):

$$R_2(\delta, P) = E[L_2(\delta(X), \theta(P))]$$

- Goal: Choose $\delta \in \mathfrak{D}$ with small risks, whatever P is.

Weak and Strong FWER or FDR Control by an MDF δ

- Weak FWER or FDR Control at Level q: For any P_0 with $\theta_m(P_0) = 0$ for all m,

$$R_0(\delta, P_0) \leq q \quad \text{or} \quad R_1(\delta, P_0) \leq q.$$

- Strong FWER or FDR Control at Level q: For *any* P,

$$R_0(\delta, P) \leq q \quad \text{or} \quad R_1(\delta, P) \leq q.$$

- Question: Could we obtain classes of MDFs strongly controlling the FWER or FDR?
- Game-theoretic aspects: 'Nature' vs cooperating multiple 'players'.

Revisiting Single Decision Problem

- Two Population Distributions:

$$F = N(\mu_1, \sigma^2), \text{ Treated}; \quad G = N(\mu_0, \sigma^2), \text{ Control}$$

- Decision Problem is to choose between

$$H_0 : \mu_1 = \mu_0 \Leftrightarrow \theta = 0$$
$$H_1 : \mu_1 > \mu_0 \Leftrightarrow \theta = 1$$

- H_0 usually STATUS QUO; H_1 usually RESEARCH hypothesis.
- Decision based on random samples:

$$\mathbf{X} = (X_1, X_2, \ldots, X_m) \sim F; \quad \mathbf{Y} = (Y_1, Y_2, \ldots, Y_n) \sim G$$

- Decision Function: $(\mathbf{x}, \mathbf{y}) \mapsto \delta(\mathbf{x}, \mathbf{y}) \in [0, 1]$
- $\delta(\mathbf{x}, \mathbf{y})$ is probability of deciding for H_1.

T-Test Procedure

- T-Test Statistic:

$$T(\mathbf{X}, \mathbf{Y}) = \frac{\bar{X} - \bar{Y}}{S_p\sqrt{\frac{1}{m} + \frac{1}{n}}}; \quad S_P^2 = \frac{(m-1)S_X^2 + (n-1)S_Y^2}{m+n-2}$$

- Decision Function of Size α:

$$\delta(\mathbf{x}, \mathbf{y}; \alpha) = I\left\{T(\mathbf{x}, \mathbf{y}) > \mathcal{T}^{-1}(1-\alpha, m+n-2)\right\}$$

- Alternative Approach: P-Value Statistic is

$$P(\mathbf{x}, \mathbf{y}) = \Pr\{T(\mathbf{X}, \mathbf{Y}) > T(\mathbf{x}, \mathbf{y}) | H_0\}$$

- Equivalent Decision Function:

$$\delta(\mathbf{x}, \mathbf{y}; \alpha) = I\{P(\mathbf{x}, \mathbf{y}) < \alpha\}$$

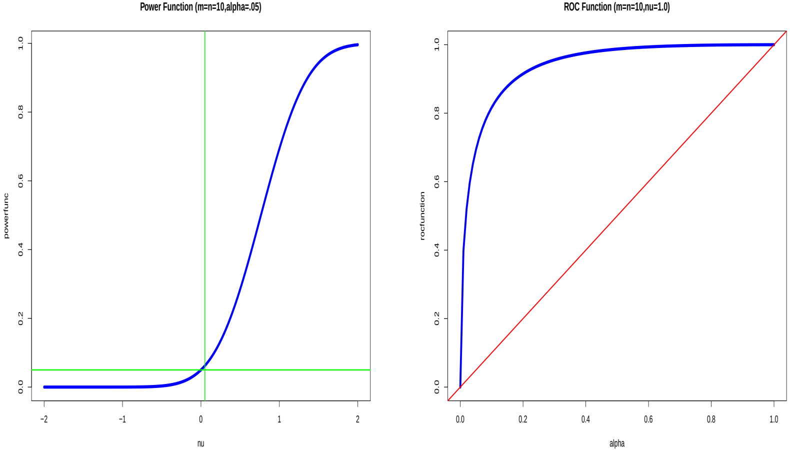
Power Function and ROC Function

- (Standardized) Effect Size: $\nu = (\mu_1 - \mu_0)/\sigma$
- An Important Function:

$$\pi(\nu;\alpha) = \Pr\{\delta(\mathbf{X},\mathbf{Y}) = 1 | \text{Effect Size is } \nu; \text{ Level } \alpha\}$$
$$= 1 - \mathcal{T}\left[\mathcal{T}^{-1}(1-\alpha, m+n-2), m+n-2, \sqrt{\frac{mn}{m+n}}\nu\right]$$

- Power Function: $\pi(\nu;\alpha)$ when viewed as function of effect size ν with level α fixed.
- ROC Function: $\pi(\nu;\alpha)$ when viewed as function of level α with effect size ν fixed.
- Sample Size Determination: for fixed ν, α, and value of power, solve for (m, n).

Plots of Power and ROC Functions



Decision Process and Multiple Decision Process

- In the two-sample T-test example, decision function depends on $\alpha \in [0,1]$. Leads to the notion of a decision process:

$$\Delta = (\delta(\mathbf{x}; \alpha) \equiv \delta(\alpha) : \alpha \in [0,1])$$

- For multiple decision problem: Multiple Decision Process:

$$\boldsymbol{\Delta} = (\Delta_m : m \in \mathcal{M} = \{1, 2, \ldots, M\})$$

- Decision Process for mth Component:

$$\Delta_m = (\delta_m(\alpha) : \alpha \in [0,1])$$

- Usual Approach: Pick a decision function δ_m from Δ_m using the same α.
- Common Choices for α: (weak) FWER Threshold of q use:

Bonferroni: $\alpha = q/M$; Sidak: $\alpha = 1 - (1-q)^{1/M}$

Notion of Size Function (Size-Picker)

- A size function is an

$$A : [0,1] \to [0,1],$$

continuous, strictly increasing, $A(0) = 0$, and $A(1) \leq 1$.

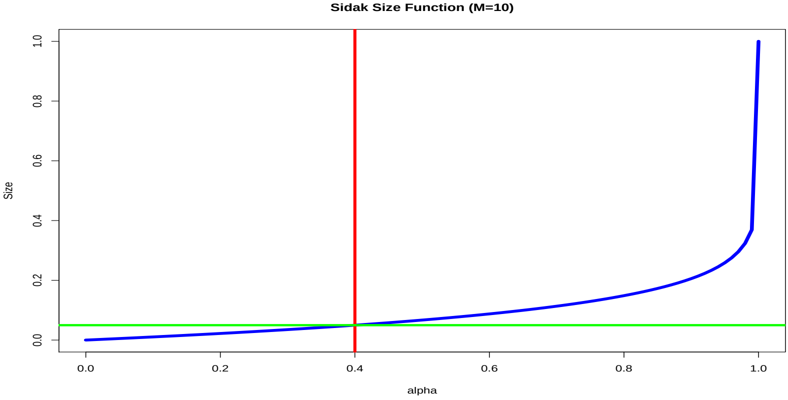
- Bonferroni size function: $A(\alpha) = \alpha/M$
- Sidak size function: $A(\alpha) = 1 - (1-\alpha)^{1/M}$

- $\mathfrak{S}$: collection of possible size functions.
- For a decision process Δ and a size function A, we choose the decision function from Δ via

$$\delta[A(\alpha)].$$

Illustration of Size Function

$$\text{Sidak: } A(\alpha) = 1 - (1-\alpha)^{1/10}$$



Multiple Decision Size Function

- For a multiple decision problem with M components, a multiple decision size function is

$$\mathbf{A} = (A_m : m \in \mathcal{M}) \quad \text{with} \quad A_m \in \mathfrak{S}.$$

- **Global Size Condition:**

$$1 - \prod_{m \in \mathcal{M}} [1 - A_m(\alpha)] = \alpha$$

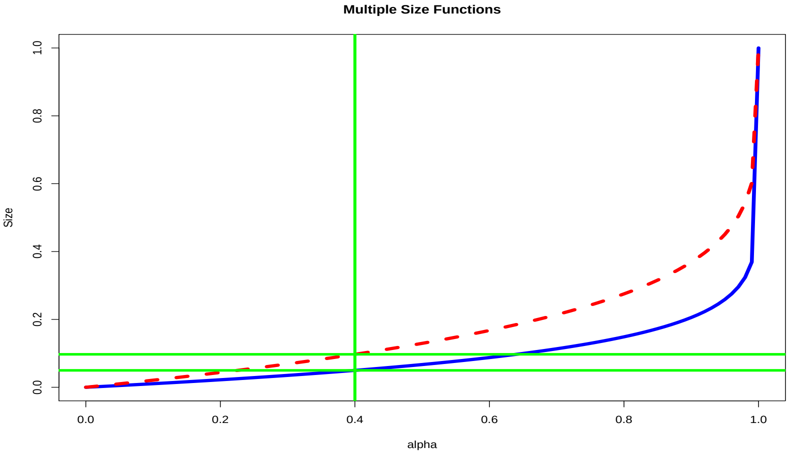
- Given a $\Delta = (\Delta_m : m \in \mathcal{M})$ and an $\mathbf{A} = (A_m : m \in \mathcal{M})$, multiple decision function is chosen according to

$$\delta(\alpha) = (\delta_m[A_m(\alpha)] : m \in \mathcal{M})$$

- Weak FWER of $\delta(\alpha)$:

$$R_0(\delta(\alpha), P) \quad = \quad 1 - \prod_{m \in \mathcal{M}} [1 - A_m(\alpha)] = \alpha$$

Illustration of Multiple Size Functions



Towards Strong FWER Control

Given a MDP $\Delta = (\Delta_m)$ and MDS $\mathbf{A} = (A_m)$, the MDF at α given by $\delta = (\delta_m[A_m(\alpha)], m \in \mathcal{M})$ has FWER:

$$\begin{aligned} R_0(\delta, P) &= E_P\left\{ I\left(\sum_{m=1}^{M} \delta_m[A_m(\alpha)][1-\theta_m(P)] > 0 \right) \right\} \\ &= P\left\{ \sum_{\mathcal{M}_0} \delta_m[A_m(\alpha)] > 0 \right\} \\ &= 1 - \prod_{\mathcal{M}_0} [1 - A_m(\alpha)] \\ &= 1 - \prod_{m=1}^{M} [1 - A_m(\alpha)]^{1-\theta_m(P)} \end{aligned}$$

Question: Given a FWER level q, what is the best α?

Nostalgia (for our Spanish Friends): **Paul, the Oracle!**

'Best' Choice of α

- An Oracle's Choice:

$$\alpha^{\dagger}(q;P) = \inf \left\{ \alpha \in [0,1] : \prod_{m=1}^{M} [1 - A_m(\alpha)]^{1-\theta_m(P)} < 1 - q \right\}$$

- But, P is unknown to us, hence $\theta_m(P)$ and $\alpha^{\dagger}(q;P)$ are unknown to us.
- However, we could estimate $\theta_m(P)$ by

$$\delta_m[A_m(\alpha)-].$$

- The Oracle's choice is then estimated by

$$\alpha^{\dagger}(q) = \inf \left\{ \alpha \in [0,1] : \prod_{m=1}^{M} [1 - A_m(\alpha)]^{1-\delta_m[A_m(\alpha)-]} < 1 - q \right\}$$

Strong FWER-Controlling MDF

- Chosen Multiple Decision Function:

$$\delta^\dagger(q) \equiv \left(\delta_m[A_m(\alpha^\dagger(q))] : m \in \mathcal{M}\right)$$

- Theorem (Peña, Habiger, Wu, 2011, Ann Stat; 2015, Metrika)
  Given a $\Delta = (\Delta_m)$ and an $\mathbf{A} = (A_m)$, the $\delta^\dagger(q)$ defined above has

$$R_0(\delta^\dagger(q), P) \leq q,$$

  whatever P is. Thus, it is an MDF achieving strong FWER control at level q.

Towards FDR Control

- Given MDP $\Delta = (\Delta_m)$ and MDS $\mathbf{A} = (A_m)$, the MDF

$$\delta(\alpha) = (\delta_m[A_m(\alpha)] : m \in \mathcal{M})$$

has FDR

$$R_1(\delta(\alpha), P) = E\left\{\frac{\sum \delta_m[A_m(\alpha)](1 - \theta_m(P))}{\sum \delta_m[A_m(\alpha)]}\right\}$$

- Observe:

$$E\left\{\sum \delta_m[A_m(\alpha)](1 - \theta_m(P))\right\} \leq \sum A_m(\alpha)$$

FDR-Controlling MDFs

- Let

$$\alpha^*(q) = \sup\left\{\alpha \in [0,1] : \sum_{m=1}^{M} A_m(\alpha) \le q \sum_{m=1}^{M} \delta_m[A_m(\alpha)]\right\}$$

- Chosen Multiple Decision Function:

$$\delta^*(q) \equiv (\delta_m[A_m(\alpha^*(q))] : m \in \mathcal{M})$$

- Theorem (Peña, et al, 2011, Ann Stat; 2015, Metrika)

Given a pair $(\Delta, \mathbf{A})$*, the MDF* $\delta^*(q)$ *achieves FDR control at level* q *in that*

$$R_1(\delta^*(q), P) \le q,$$

whatever P *is. [Remark: Needed is a Noether-type condition on* $\mathbf{A}$*.]*

Classes of MDFs Controlling FWER and FDR

- A class of strong FWER-controlling MDFs at threshold q is:

$$\mathfrak{D}^\dagger = \left\{\delta^\dagger(q;\Delta,\mathbf{A}) : \Delta \in \mathfrak{D}, \mathbf{A} \in \mathfrak{S}\right\}$$

- A class of FDR-controlling MDFs at threshold q is:

$$\mathfrak{D}^* = \{\delta^*(q;\Delta,\mathbf{A}) : \Delta \in \mathfrak{D}, \mathbf{A} \in \mathfrak{S}\}$$

- Remark: Sidak's sequential step-down strong FWER controlling MDF belongs to $\mathfrak{D}^\dagger$.
- Remark: Benjamini-Hochberg's (BH) step-up FDR controlling MDF belongs to $\mathfrak{D}^*$.
- Potential Utility: May choose best MDF in $\mathfrak{D}^\dagger$ or $\mathfrak{D}^*$ wrt the missed discovery rate.

Improving on the BH FDR-Controlling MDF

- **IDEA:** Given an MDP $\Delta = (\Delta_m : m \in \mathcal{M})$, find the optimal MDS $\mathbf{A}^* \equiv \mathbf{A}^*(\Delta) \in \mathfrak{S}$ achieving smallest MDR

$$R_2[(\Delta \circ \mathbf{A})(\alpha), P_1] = \frac{1}{M} \sum_{m=1}^{M} \{1 - \pi_m [A_m(\alpha)]\} .$$

- FWER-controlling MDF:

$$\delta^\dagger(q) = \delta^\dagger(q; \Delta, \mathbf{A}^*(\Delta))$$

- FDR-controlling MDF:

$$\delta^*(q) = \delta^*(q; \Delta, \mathbf{A}^*(\Delta))$$

- Use the best MDP Δ, e.g., MPs; UMPs; UMPUs; UMPIs.

Case with Simple Nulls and Simple Alternatives

- For each $m = 1, 2, \ldots, M$, $X_m \sim f_m$ and to decide between

$$H_{m0} : f_m = f_{m0} \Leftrightarrow \theta_m = 0$$

$$H_{m1} : f_m = f_{m1} \Leftrightarrow \theta_m = 1$$

- Neyman-Pearson MP Decision Process for each m has, with $L_m(x_m) = f_{m1}(x_m)/f_{m0}(x_m)$:

$$\delta_m(x_m; \alpha) = \begin{cases} 1 & \text{if} \quad L_m(x_m) > c_m(\alpha) \\ \gamma_m(\alpha) & \text{if} \quad L_m(x_m) = c_m(\alpha) \\ 0 & \text{if} \quad L_m(x_m) < c_m(\alpha) \end{cases}.$$

- ROC Functions:

$$\alpha \mapsto \pi_m(\alpha) \equiv \pi_m(\alpha; (f_{m0}, f_{m1}))$$

- Concave, continuous, increasing, and twice-differentiable.

Optimal Size Functions

Theorem (Peña, et al, 2011, Ann Stat & Metrika)

Multiple decision size function $(\alpha \mapsto A_m(\alpha) : \; m \in \mathcal{M})$ *is optimal if it satisfies the* $M+1$ *equilibrium conditions*

$$\text{For all } m \in \mathcal{M}: \quad \pi'_m[A_m(\alpha)][1 - A_m(\alpha)] = \lambda \quad \text{for some } \lambda \in \Re;$$

$$\sum_{\mathcal{M}} \log[1 - A_m(\alpha)] = \log(1 - \alpha).$$

Equivalent to

$$\left[\mathbf{I} - \frac{1}{M}\mathbf{J}\right] \kappa(\mathbf{z}) + \mathbf{l}(\mathbf{z}) = \mathbf{1}\left[\frac{1}{M}\log(1-\alpha)\right];$$

$\mathbf{z} = (A_m(\alpha), m = 1:M)^{\mathrm{t}}$, $\kappa(\mathbf{z}) = (\log[\pi'_m(z_m)], m = 1:M)^{\mathrm{t}}$, *and* $\mathbf{l}(\mathbf{z}) = (\log(1 - z_m), m = 1:M)^{\mathrm{t}}$.

With f_{m0} and f_{m1} Normal Distributions

- $X_m \sim N(\mu_m, \sigma = 1), m = 1, 2, \ldots, M$
- $H_{m0} : \mu_m = 0$ versus $H_{m1} : \mu_m = \gamma_m$
- For each m, Neyman-Pearson MP decision process.

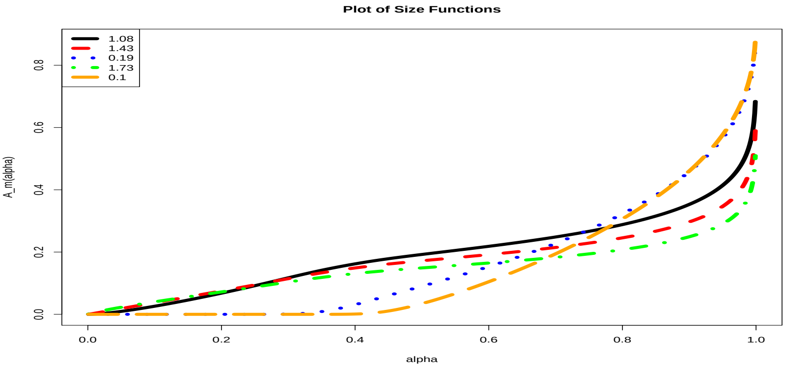
$$\Delta_m = (\delta_m(\alpha) : \alpha \in [0, 1])$$

$$\delta_m(x_m; \alpha) = I\{x_m \geq \Phi^{-1}(1 - \alpha)\}$$

- ROC Function for the *m*th NP MP Decision Process:

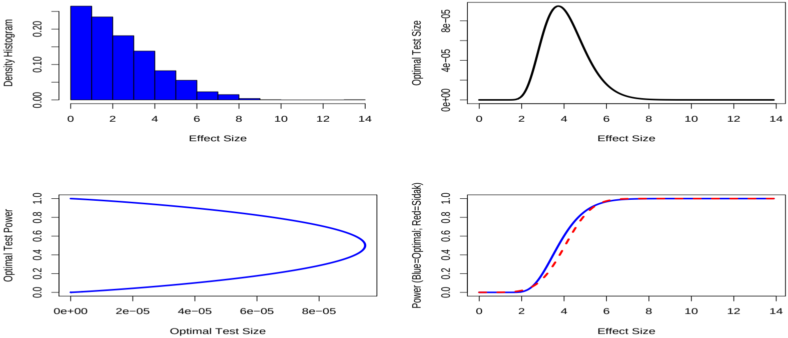
$$\pi_m(\alpha) = 1 - \Phi\left[\Phi^{-1}(1 - \alpha) - \gamma_m\right]$$

Shapes of Optimal Multiple Size Function: $M = 5$



Optimal Test Sizes vs Effect Sizes: $M = 2000$

Effect Sizes Generated Via: $\gamma_m \stackrel{IID}{\sim} |N(0,3)|$



Economic Aspect: A Size-Investing Strategy

- Do not invest your size on those where you will not make discoveries (small power) or those that you will certainly make discoveries (high power)!
- Concentrate on those where it is a bit uncertain, since your **differential gain** in overall discovery rate would be greater!
- On Some Interesting Consequences.
  - *On Graduate Student Advising.*
  - *US Presidential Election Strategy.*
  - Generally: Allocating Resources.

Simulations: Comparing BH with $\delta^*(q)$

Normally-distributed data; $q^* = 10\%$; $M = 100$; 1000 Replications

ν	p	δ_F^*-FDR	δ_F^*-MDR	δ^{BH}-FDR	δ^{BH}-MDR
1	0.1	9.14	87.10	9.02	90.02
1	0.2	8.21	84.05	8.78	87.38
1	0.4	5.92	80.12	5.88	83.73
2	0.1	9.79	66.10	9.24	67.93
2	0.2	7.68	58.25	7.94	59.93
2	0.4	5.74	49.29	6.10	50.90
4	0.1	8.37	10.44	8.62	12.36
4	0.2	7.72	5.93	7.81	8.22
4	0.4	5.69	3.80	6.14	5.72

With Exponentially-Distributed Data; 1000 reps; $p = \#$ of correct alternatives; $q = 20\%$; Effect Sizes $\xi_m \sim U[.25, .75]$

M	$n_m = n$	p	BH		$\delta^*(q)$	
			FDR	MDR	FDR	MDR
100	5	.2	15.93574	55.56008	16.03789	55.24426
100	10	.2	15.78390	38.48281	14.97451	38.12848
100	30	.2	16.09659	10.88535	14.93114	8.026157
100	5	.3	13.42253	46.06943	13.24371	45.90983
100	10	.3	13.76047	31.97512	13.65171	30.47509
100	30	.3	13.80077	5.639566	13.89979	2.626881
100	5	.5	10.37083	41.65425	10.06751	41.40670
100	10	.5	10.11820	26.34404	10.11692	23.57873
100	30	.5	10.03628	7.615538	9.590189	4.151696

Same Setting but Only Four Values of Effect Sizes

Effect Sizes Used

$$m = 1 : 25 : \ \xi_m = .1; \ m = 26 : 50 : \ \xi_m = .3$$

$$m = 51 : 75 : \ \xi_m = .5; \ m = 76 : 100 : \ \xi_m = .7$$

M	$n_m = n$	p	BH		$\delta^*(q)$	
			FDR	MDR	FDR	MDR
100	5	.2	16.3581	39.05525	15.79368	36.95671
100	10	.2	15.86433	26.73459	16.05328	22.97558
100	30	.2	16.0207	9.896752	15.76027	5.316628

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