Multiple Decision Making in the Face of Uncertainty

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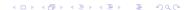
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Outline

- Some Motivating Problems.
- Multiple Decision Problems.
- Mathematical Framework (Decision Functions, Losses, Risks).
- Special Case: Optimal Choice Between Two Actions.
- Multiple Decision Processes.
- Multiple Decision Size Function.
- Class of FWER-Controlling MDFs.
- Class of FDR-Controlling MDFs.
- An Application to a Microarray Data Set.
- Towards Optimal MDFs.
- Applicability and Some Comparisons.



Some Motivating Questions and Areas of Relevance

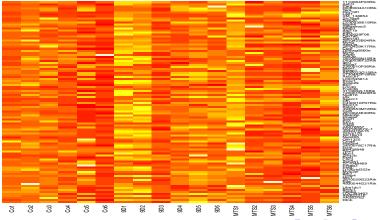
- Microarray data analysis: Which genes are relevant?
- Variable selection: Which of many predictors are relevant?
- Survival analysis: Which predictors affects a lifetime variable?
- ▶ Reliability: Which components in a system are relevant?
- ► Epidemiology: Spread of a disease in a geographical area.
- ▶ Oil (mineral) exploration: Where to dig?
- Business: Locations of business ventures.
- ▶ US Presidential Election: Where to focus resources to optimize electoral votes?
- Sporting Events: Predicting outcomes of World Cup soccer games.



A Microarray Data: HeatMap of Gene Expression Levels

First 100 genes out of 41267 genes in a colon cancer study at USC (M Peña's Lab). Three groups (Control; 9 Days; 2 Weeks) with 6 replicates each.





A Typical Variable Selection Problem

Model.

$$Y = \beta_0 + \sum_{j=1}^{M} \beta_j X_j + \epsilon$$

- ▶ M is large, but many β_j s are equal to zero.
- ▶ Observed Data: For j = 1, 2, ..., n,

$$(Z_j, \delta_j, X_{1j}, X_{2j}, \ldots, X_{Mj})$$

with

$$Z_j = \min(Y_j, C_j)$$
 and $\delta_j = I\{Y_j \le C_j\}$

Goal: To select the relevant predictor variables.



A Reliability (or Biological Pathways) Problem

- System is composed of components.
- ▶ Structure function, ϕ , relates components to system: series, parallel, series-parallel, etc.
- M potential components that could constitute a system. We do not know which components are relevant nor do we know the structure function.
- ▶ Question: Given data regarding states or lifetimes of system and components, to determine relevant components.
- ► Component lifetimes may be censored by system lifetime.
- Highly nonlinear types of relationships.



General Multiple Decision Problem

Discover the value of a parameter

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

- $\theta_m = 1$ means *m*th component is relevant; $\theta_m = 0$ means *m*th component is not relevant.
- Choose an action

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

▶ $a_m = 1$ means declare that $\theta_m = 1$, a discovery; $a_m = 0$ means declare $\theta_m = 0$, a non-discovery.



Assessing Actions via Losses

Family-wise error indicator (FWEI):

$$L_0(a,\theta) = I\left\{\sum_{m=1}^M a_m(1-\theta_m) > 0\right\}$$

► False Discovery Proportion (FDP):

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

Missed Discovery Proportion (MDP):

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



Illustration

ightharpoonup M = 10 Decisions to Make.

Truth or State of Reality:	$\theta = (1, 1, 0, 1, 0, 0, 0, 0, 0, 1)$
Action Taken:	a = (0, 1, 0, 1, 1, 0, 0, 0, 0, 0)

Agreements and Disagreements (in Tabular Form):

	Action (a)		
Truth (θ)	0	1	Total
0	5	1	6
1	2	2	4
Total	7	3	10

- ► Family wise error indicator (FWEI) = 1 (Type I)
- ▶ False discovery proportion (FDP) = 1/3 = .33 (Type I)
- ► Missed discovery proportion (MDP) = 2/4 = .50 (Type II)



Nostalgia: Paul, the Oracle!



Life is Tough: No Oracles, Just Statisticians!

Obtain a BIG data (e.g., microarrays, Netflix):

$$X \in \mathfrak{X}$$

Observable is Random:

$$X \sim P = \text{Unknown Probability Function}$$

Marginal Components:

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

Parameters of Interest:

$$\theta_m = \theta_m(P_m)$$

► Example:

$$\theta_m = 1 \iff P_m \in \{N(\mu, \sigma^2) : \mu > 0, \sigma^2 > 0\}$$



Multiple Decision Functions

Multiple Decision Function:

$$\delta: \mathfrak{X} \to \mathfrak{A} = \{0,1\}^M$$
 Note: $|\mathfrak{A}| = 2^M$

Components:

$$\delta = (\delta_1, \delta_2, \dots, \delta_M)$$
$$\delta_m : \mathfrak{X} \to \{0, 1\}$$

- ▶ 𝔄: space or collection of multiple decision functions.
- $\mathcal{M}_0 = \{ m : \theta_m = 0 \} \text{ and } \mathcal{M}_1 = \{ m : \theta_m = 1 \}$
- ▶ 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 over Possible Data

- ▶ 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):

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

- Expectations are with respect to $X \sim P$.
- ▶ Our Goal: Choose $\delta \in \mathfrak{D}$ with small risks, whatever P is.



Special Case: A Pair of Choices (M = 1)

- $\bullet \ \theta \in \Theta = \{0,1\}$
- ▶ $a \in \mathfrak{A} = \{0, 1\}$
- $L_0(a,\theta) = L_1(a,\theta) = aI(\theta=0)$
- $L_2(a, \theta) = (1 a)I(\theta = 1)$
- ▶ $X \sim P$ with $P \in \{P_0, P_1\}$.
- Assume P_0 and P_1 have respective densities:

$$f_0(x)$$
 and $f_1(x)$

- $R_0(\delta,\theta) = R_1(\delta,\theta) = P_0(\delta(X) = 1)I(\theta = 0)$
- $R_2(\delta, \theta) = [1 P_1(\delta(X) = 1)]I(\theta = 1)$



Types I and II Errors, Power, and Optimality

- $R_0(\delta, \theta)$: Type I error probability.
- $R_2(\delta, \theta)$: Type II error probability.
- Note

$$R_2(\delta, \theta = 1) = 1 - \pi(\delta)$$

where

$$\pi(\delta) = P_1(\delta(X) = 1) = POWER \text{ of } \delta.$$

▶ Desired Goal: Given Type I level $\alpha \in [0,1]$, find $\delta^*(\cdot; \alpha)$ with

$$R_0(\delta^*, \theta) \le \alpha$$
, for all θ ,

and

$$R_1(\delta^*, \theta) \leq R_1(\delta, \theta)$$
, for all θ ,

for any other δ with $R_1(\delta, \theta) \leq \alpha, \forall \theta$.



Neyman-Pearson MP Test δ_{α}^*

Neyman and Pearson (1933): optimal [most powerful]
 decision function of form

$$\delta_{\alpha}^{*}(x) = \begin{cases} 1 & \text{if} \quad f_{1}(x) > c(\alpha)f_{0}(x) \\ \gamma(x) & \text{if} \quad f_{1}(x) = c(\alpha)f_{0}(x) \\ 0 & \text{if} \quad f_{1}(x) < c(\alpha)f_{0}(x) \end{cases}$$

where $c(\alpha)$ and $\gamma(\alpha)$ satisfy

$$R_0(\delta_{\alpha}^*, \theta = 0) = \alpha.$$

- **Remark**: Depends on α , hence power depends on α .
- ▶ Leads to the notion of a decision process.



Concrete Example of a Decision Process

- ▶ Model: $X = (X_1, X_2, \dots, X_n) \stackrel{IID}{\sim} N(\mu, \sigma^2)$.
- ▶ Problem: Test $H_0: \mu \leq \mu_0$ [$\theta = 0$] vs $H_1: \mu > \mu_0$ [$\theta = 1$]
- **Decision Function**: *t*-test of size α given by

$$\delta(X;\alpha) = I\left\{\frac{\sqrt{n}(\bar{X} - \mu_0)}{S} \ge t_{n-1;\alpha}\right\}$$

- ▶ Decision function depends on the size index α .
- Decision Process:

$$\Delta = (\delta(\alpha) \equiv \delta(\cdot; \alpha) : \alpha \in [0, 1])$$

▶ Size Condition:

$$\sup\{E_P[\delta(X;\alpha)]:\theta(P)=0\}\leq\alpha$$



Multiple Decision Process

- ▶ Multiple decision problem with *M* components.
- Multiple Decision Process:

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

Decision Process for mth Component:

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

- **Example**: *t*-test decision process for each component.
- ▶ Usual Approach: Pick a 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 Functions

Size Function:

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

continuous, strictly increasing, A(0) = 0 and $A(1) \le 1$, and possibly differentiable.

- ▶ Bonferroni size function: $A(\alpha) = \alpha/M$
- ▶ Sidak size function: $A(\alpha) = 1 (1 \alpha)^{1/M}$
- ▶ S: collection of possible size functions.
- For decision process Δ and size function A, choose decision function from Δ via

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



Multiple Decision Size Function

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

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

▶ Condition:

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

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

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

▶ Weak FWER of $\delta(\alpha)$:

$$R_0(\delta(\alpha), P) = 1 - \prod [1 - A_m(\alpha)] \le \alpha$$



Neyman-Pearson Paradigm

- ► Control Type I error rate; minimize Type II error rate.
- ▶ Desired Type I error threshold: $q \in (0,1)$
- ▶ Weak Control: For P with $\theta_m(P) = 0$ for all m, want a δ with

$$R_0(\delta, P) \le q$$
 or $R_1(\delta, P) \le q$.

▶ Strong Control: Whatever P is, want a δ such that

$$R_0(\delta, P) \le q$$
 or $R_1(\delta, P) \le q$.

▶ And, if above Type I error control is achieved, we want to have $R_2(\delta, P)$ small, if not optimal.



Towards Strong FWER Control

Given a MDP $\Delta = (\Delta_m)$ and MDS $\mathbf{A} = (A_m)$, for the chosen δ at α , its FWER is

$$R_{0}(\delta, P) = E_{P} \left\{ I \left(\sum \delta_{m} [A_{m}(\alpha)] [1 - \theta_{m}(P)] > 0 \right) \right\}$$

$$= P \left\{ \sum_{\mathcal{M}_{0}} \delta_{m} [A_{m}(\alpha)] > 0 \right\}$$

$$= 1 - \prod_{\mathcal{M}_{0}} [1 - A_{m}(\alpha)]$$

$$= 1 - \prod_{\mathcal{M}_{0}} [1 - A_{m}(\alpha)]^{1 - \theta_{m}(P)}$$

Question: Given a threshold of q, what is the best α ?



'Best' Choice of α

Oracle Paul's Choice:

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

▶ But, P is unknown, hence $\theta_m(P)$ is also unknown. But we could estimate $\theta_m(P)$ by

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

▶ The Oracle's choice is then estimated by

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



Strong FWER-Controlling MDF

Chosen Multiple Decision Function:

$$\delta^{\dagger}(q) = \left(\delta_{m}[A_{m}(\alpha^{\dagger}(q))] : m \in \mathcal{M}\right)$$

▶ Theorem

Given a $\Delta=(\Delta_m)$ and an ${\bf A}=(A_m)$, the $\delta^\dagger(q)$ defined above has

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

whatever P is. That is, $\delta^{\dagger}(q)$ is an MDF achieving strong FWER control at level q.



Generalized P-Values

Definition

The *m*th component of the vector of generalized *P*-value statistic associated with Δ and $\bf A$ is

$$\alpha_m \equiv \alpha_m(\Delta, \mathbf{A}) = \inf\{\alpha \in [0, 1] : \delta_m[A_m(\alpha)] = 1\}$$

- ▶ Smallest size to decide in favor of $\theta_m = 1$ under (Δ, \mathbf{A}) .
- Ordered Generalized P-Value Statistics:

$$0 \equiv \alpha_{(0)} < \alpha_{(1)} < \alpha(2) < \ldots < \alpha_{(M)} < \alpha_{(M+1)} \equiv 1$$

Observe that for

$$\alpha \in [\alpha_{(k)}, \alpha_{(k+1)}) \iff \sum \delta_m[A_m(\alpha)] = k$$



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

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

Observe:

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



Optimal Choice of α

▶ Preceding considerations heuristically suggest the α :

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

Chosen Multiple Decision Function:

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

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

$$R_1(\delta^*(q), P) \leq q.$$



Classes of MDFs Controlling FWER and FDR

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

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

► 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 D[†].
- ▶ Remark: Benjamini-Hochberg's step-up FDR controlling MDF belongs to 𝒯*.
- ▶ Potential Utility: May choose best MDF in D[†] or D* wrt the missed discovery rate.



Famous FDR-Controlling MDF

- ▶ Benjamini-Hochberg (JRSS B, '95) paper. Most well-known FDR-controlling procedure.
- ▶ Let $P_1, P_2, ..., P_M$ be the ordinary P-values from the M tests.
- ▶ Let $P_{(1)} < P_{(2)} < ... < P_{(M)}$ be the ordered P-values.
- ► For FDR-threshold equal to q, define

$$K = \max \left\{ k \in \{0, 1, 2, \dots, M\} : P_{(k)} \le \frac{qk}{M} \right\}.$$

▶ BH MDF $\delta^{BH}(q) = (\delta^{BH}_m : m \in \mathcal{M})$ has

$$\delta_m^{BH}(X) = I\left\{P_m \le P_{(K)}\right\}, \ m \in \mathcal{M}.$$

Simple and easy-to-implement, but is it the BEST?

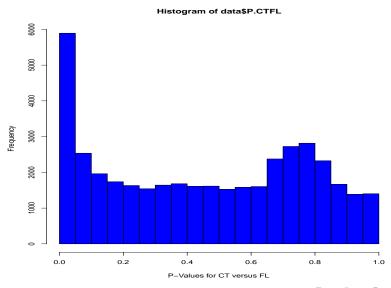


Applying BH Procedure to a Two-Group Microarray Data

- ► Agilent Technology microarray data set from M. Peña's lab. Jim Ryan of NOAA did the microarray analysis.
- ▶ M = 41267 genes.
- 2 groups, each group with 5 replicates.
- ► Applied *t*-test for each gene, using logged expression values. *P*-values obtained.
- ▶ Applied Benjamini-Hochberg Procedure with q = .15 to pick out the significant genes from the M = 41267 genes.
- Procedure picked out 2599 significant genes.
- ► Further analyzed the top (wrt to their *p*-values) 200 genes from these selected genes.
- Performed a cluster analysis on these 200 genes.

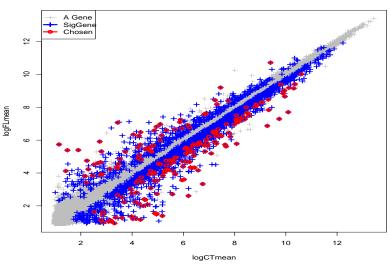


Histogram of the *P*-Values from the *t*-Tests

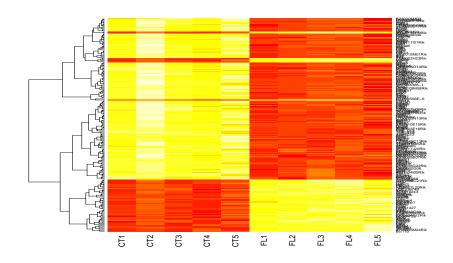


Scatterplot of the Pairwise Gene Means

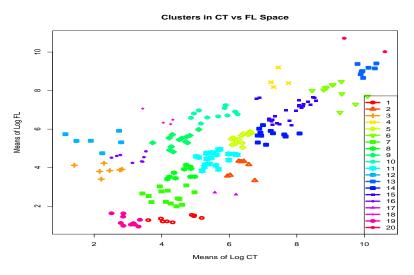
Significant and Chosen Genes



Heatmap of the 200 Top Genes



Pictorial Depiction of Gene Clusters of Top 200 Genes



BUT, Can We Obtain a Better MDF than BH?

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

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

- $\pi_m(\alpha) = POWER \text{ of } \delta_m(\alpha)$
- 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.



Role of Power or ROC Functions

- ▶ *P*-value based procedures ignore differences in powers.
- Neyman and Pearson: power germane in search for optimality.
- ▶ Power of *m*th Test: $\pi_m(\alpha) = E_{P_{m1}}\{\delta_m(X;\alpha)\}$
- ▶ ROC Function for *m*th Decision Process Δ_m :

$$\alpha \mapsto \pi_m(\alpha)$$

- ▶ ROC functions in the missed discovery rate.
- ► Enables exploiting differences in the ROC functions.
- ▶ Why Power or ROC Differences? Different effect sizes, decision processes, or dispersion parameters.
- ► EXCHANGEABILITY: EXCEPTION rather than RULE!



Case with Simple Nulls and Simple Alternatives

- ▶ Neyman-Pearson Most Powerful Decision Process for each *m*.
- ▶ ROC Functions:

$$\alpha \mapsto \pi_m(\alpha)$$

- ▶ ROC functions are concave, continuous, and increasing.
- Assume that they are also twice-differentiable.

Theorem

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

$$\forall m \in \mathcal{M}: \quad \pi'_m(A_m)(1-A_m) = \lambda \quad \textit{for some } \lambda \in \Re;$$

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



Example: Optimal Multiple Decision Size Function

- M = 2000
- ▶ For each m: $X_m \sim N(\mu_m, \sigma = 1)$
- ► Multiple Decision Problem: To test

$$H_{m0}$$
: $\mu_m = 0$ versus H_{m1} : $\mu_m = \gamma_m$.

- ▶ Effect Sizes: $\gamma_m \stackrel{IID}{\sim} |N(0,3)|$
- ▶ For each *m*, Neyman-Pearson MP decision process.

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

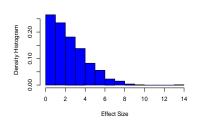
$$\delta_m(x_m;\alpha) = I\{x_m \ge \Phi^{-1}(1-\alpha)\}\$$

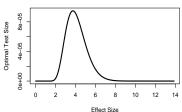
▶ Power or ROC Function for the *m*th NP MP Decision Process:

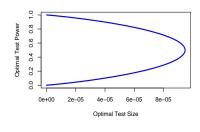
$$\alpha \mapsto \pi_m(\alpha) = 1 - \Phi \left[\Phi^{-1}(1 - \alpha) - \gamma_m \right]$$

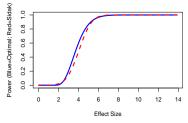


Optimal Test Sizes vs Effect Sizes











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)!
- Rather, concentrate on those where it is a bit uncertain, since your differential gain in overall discovery rate would be greater!
- Some Wicked Consequences
 - Departmental Merit Systems.
 - Graduate Student Advising.



BH MDF versus $\delta^*(q)$: $q^* = .1$; M = 20; 1000 Reps

ν	р	δ_{F}^{*} -FDR	$\delta_{\it F}^*$ -MDR*	δ^{BH} -FDR	δ^{BH} -MDR *
1	0.1	8.03	70.80	8.43	72.64
1	0.2	7.55	79.64	8.77	81.99
1	0.4	6.05	77.47	6.65	80.30
2	0.1	7.70	54.42	8.43	55.80
2	0.2	7.39	56.32	7.59	57.31
2	0.4	6.47	47.82	6.21	49.38
4	0.1	9.14	8.62	9.48	10.30
4	0.2	7.80	7.34	6.97	9.20
4	0.4	6.15	3.58	5.65	5.53

BH MDF versus $\delta^*(q)$: $q^* = .1$; M = 100; 1000 Reps

ν	р	δ_F^* -FDR	$\delta_{\it F}^*$ -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

Potential Applications and Concluding Remarks

- Microarray data analysis: which genes are important?
- Systems analysis (Biological Pathways?): which components (subsystems of genes) are relevant?
- Variable selection: which predictor variables are important?
- For each gene, component, or predictor variable, apply a decision function to decide whether, say, independence or dependence holds with respect to the response variable.
- ► Test for Independence: Kendall's procedure, for example.
- Use MDFs $\delta^{\dagger}(q)$ or $\delta^{*}(q)$.
- Issues of determining effect sizes to determine power or ROC functions still need further studies.
- Comparison with other methods, such as those using regularization?



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