3.27pt

Selected topics in the Analysis of Large Dimensional Data

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• Testing for Global Null and Multiple Testing

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- Model selection in multiple regression Information Criteria

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Major problem - multiple comparisons, multiple testing (in PCA selection of nonzero singular values)



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 Y_{ij} for $i=1,\ldots,n_2$ are iid with $E(Y_{ij})=\mu_{2j}$ and

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Gene j is associated with cancer if $\mu_{1j} \neq \mu_{2j}$

We test $H_{0j}: \mu_{1j}=\mu_{2j}$ with a t-test $t_j=rac{ar{X}_{.j}-ar{Y}_{.j}}{S(ar{X}_{.j}-ar{Y}_{.j})}$, where

 $S(ar{X}_{.j}-ar{Y}_{.j})$ is the estimate of the standard deviation of $ar{X}_{.j}-ar{Y}_{.j}$

 $X_{n_1 \times p}$ - expressions of p genes for n_1 healthy individuals $Y_{n_2 \times p}$ - expressions of p genes for n_2 cancer patients Assumption: X_{ii} for $i=1,\ldots,n_1$ are iid with $E(X_{ii})=\mu_{1i}$ and $Var(X_{ii}) = \sigma_{1i}^2 < \infty$ Y_{ii} for $i=1,\ldots,n_2$ are iid with $E(Y_{ii})=\mu_{2i}$ and $Var(Y_{ii}) = \sigma_{2i}^2 < \infty$ Gene j is associated with cancer if $\mu_{1i} \neq \mu_{2i}$ We test $H_{0j}: \mu_{1j}=\mu_{2j}$ with a t-test $t_j=rac{ar{X}_{.j}-ar{Y}_{.j}}{S(ar{X}:-ar{Y}_{.})},$ where $S(\bar{X}_{.i} - \bar{Y}_{.i})$ is the estimate of the standard deviation of $\bar{X}_{.i} - \bar{Y}_{.i}$ If n_1 and n_2 are large enough then $t_i \sim \mathcal{N}(\mu_i, 1)$ with $\mu_j = \frac{\mu_{1j} - \mu_{2j}}{\sigma_{1i} / \sqrt{n_1} + \sigma_{2i} / \sqrt{n_2}}$ and $H_{0j}: \mu_j = 0$

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 $H_{0i}: \mu_i = 0 \quad \text{vs} \quad \mu_i \neq 0$ Reject H_{0i} when $|X_i| > c$

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 vs $\mu_i \neq 0$

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 when $|X_i| > c$

Multiple comparison problem: if all μ_i s are equal to zero than $\max(|X_1|,\ldots,|X_p|) = \sqrt{2\log p}(1+o_p)$

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Thus to separate signal from noise we need $c=c(p)\to\infty$ as $p\to\infty$.

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Bonferroni procedure: Reject H_0 when

$$\max(|X_1|,\ldots,|X_p|) \geq \Phi^{-1}\left(1-rac{lpha}{2p}
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Probability of type I error:

$$P_{H_0}\left(\bigcup_{j=1}^{p}\{|X_j|>c_{Bon}\}\right)\leq \sum_{j=1}^{p}P(\{|X_j|>c_{Bon}\}=\alpha)$$

Exact type I error of Bonferroni

Due to independence

$$P(\textit{Type I Error}) = 1 - P_{H_0} \left(\bigcap_{j=1}^{p} \{|X_j| < c_{Bon} \} \right)$$
$$= 1 - \left(1 - \frac{\alpha}{p} \right)^p \to 1 - e^{-\alpha} = \alpha + o(\alpha)$$

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$$\alpha = 0.05$$
 , $n = 30000$, $P(Type\ I\ Error) \approx 0.0488$

Needle in haystack

Needle in haystack: for some $i\in\{1,p\}$, $\mu_i=\mu^p$ and for all $j\neq i, \ \mu_j=0$



How long needle can be found?

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Is there a test procedure which can find a shorter needle?

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Neyman-Pearson optimal test (maximal power for a given type I error) has the form

Reject H_0 for large values of $L(x) = \frac{L_A(x)}{L_0(x)}$

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Bayesian model for "needle in haystack" problem

$$H_0: \mu = (\mu_1, \dots, \mu_p) = 0$$

$$H_A: \mu \sim \frac{1}{\rho} \sum_{i=1}^{\rho} \delta_{\mu_i}$$

$$\delta_{\mu_i} : P(\{\mu_i = \mu^p, \mu_j = 0 \text{ for } j \neq i\}) = 1$$

Interpretation: under H_A there is just one signal of known magnitude μ^p but we do not know where and assume a uniform distribution over $i \in \{1, ..., p\}$.

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Interpretation - Bonferroni correction has asymptotically optimal detection region under the needle in haystack problem

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If $||\mu||^2/p \to 0$ then $\frac{||X||^2 - (p + ||\mu^2||)}{\sqrt{2p + 4||\mu||^2}} \to N(0,1)$

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Bayesian model for equally distributed signals:

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Power of Neyman-Pearson test converges to α when $\frac{||\rho||^2}{\sqrt{p}} \to 0$

Relationship between signal strength and the sparsity

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$$k=\sqrt{p}$$
 means equal to 5 - Bonferroni weak, chi-square test strong

What happens in the middle?

Sparse mixture model

Model:

$$H_0: \mu = 0, \quad H_A: \mu_1, \dots, \mu_p \quad \textit{iid} \quad (1 - \epsilon)\delta_0 + \epsilon \delta_\mu$$

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Neyman-Pearson test:

$$L = \prod_{i=1}^{p} [(1 - \epsilon) + \epsilon e^{\mu X_i - \mu^2/2}]$$

Ingster (1999) detection boundary

$$\epsilon^{p} = p^{-\beta}, \quad \frac{1}{2} < \beta < 1$$

when $\beta=1/2$ we have about $k=p^{-1/2}p=\sqrt{p}$ signals, when $\beta=1$ then the number of signals $k=p^{-1}p=1$ is equal to 1 (needle in the haystack)

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$$\rho(\beta) = \begin{cases} \beta - 1/2 & \text{for } 1/2 < \beta \le 3/4 \\ (1 - \sqrt{1 - \beta})^2 & \text{for } 3/4 \le \beta \le 1 \end{cases}$$

Neyman-Pearson test has the full asymptotic power if $r > \rho(\beta)$ and no asymptotic power if $r < \rho(\beta)$.



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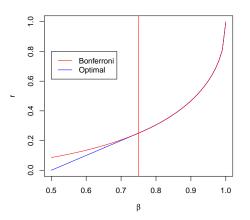
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Donoho and Jin (2004): Bonferroni detection boundary coincides with the optimal detection boundary if $\beta \geq 3/4$

Ingster detection boundary



Interpretation: When the number of needles increases than they can be substantially shorter than $\sqrt{2\log p}$ to be detected by Bonferroni.

Lesson learned from theory of testing the global hypothesis

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There is no a single optimal method for testing the global null hypothesis - the selection of the method should depend on the expectation on the signal sparsity.

Multiple testing

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H_0 false	Т	S	p_1
	W	R	р

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 $\alpha = 0.05, p_0 = 5000 \rightarrow E(V) = 250$

Multiple testing procedures

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Benjamini-Hochberg (1995) procedure:

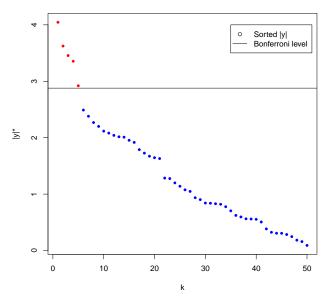
- (1) $|X|_{(1)} \ge |X|_{(2)} \ge \ldots \ge |X|_{(p)}$
- (2) Find the largest index i such that

$$|X|_{(i)} \ge \Phi^{-1}(1-\alpha_i), \quad \alpha_i = \alpha \frac{i}{2p},$$
 (1)

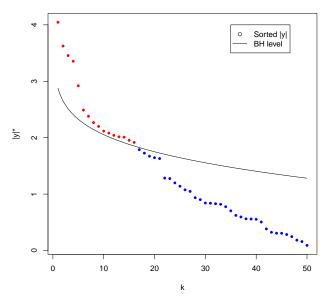
Call this index i_{SU} .

(3) Reject all $H_{(i)}$'s for which $i \leq i_{SU}$

Bonferroni correction



Benjamini and Hochberg correction



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where p_0 is the number of true null hypotheses, $p_0=|\{i:\mu_i=0\}|$ (Benjamini, Yekutieli, 2001) When test statistics are "positively correlated"then BH controls FDR at or below the level $\alpha\frac{p_0}{p}$. Independently of the correlation structure FDR is controlled at or below the level $\alpha\frac{p_0}{p}$ if $|X|_{(j)}$ is compared to $\Phi^{-1}\left(1-\frac{j\alpha}{2p\sum_{i=1}^p\frac{1}{i}}\right)$.

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Can we do better?

Bias-Variance Tradeoff

$$MSE(\hat{\mu}_i)=E(\hat{\mu}_i-\mu_i)^2=B_i^2+Var_i,$$
 where $B_i=E\hat{\mu}_i-\mu_i$ is the bias of $\hat{\mu}_i$

and $Var_i = E(\hat{\mu}_i - E(\hat{\mu}_i))^2$ is the variance of $\hat{\mu}_i$.

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Can we improve MSE by introducing some bias and reducing the variance ?

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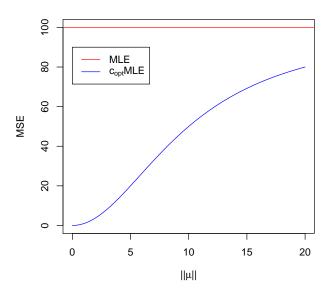
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Using elementary calculus we can show that the optimal value of \boldsymbol{c} is equal to

$$c_{opt} = argmin_{c \in R} MSE(c) = \frac{||\mu||^2}{||\mu||^2 + p\sigma^2} \in [0,1)$$
.

Improvement in MSE, $p = 100, \sigma = 1$



Shrinking towards the common mean

Consider an estimator

$$\hat{\mu}_d = (1-d)\hat{\mu}_{MLE} + dar{X}$$

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$$d_{opt} = \frac{\sigma^2}{\sigma^2 + Var(\mu)} \in (0, 1], \text{ with } Var(\mu) = \frac{1}{p-1} \sum (\mu_i - \bar{\mu})^2.$$

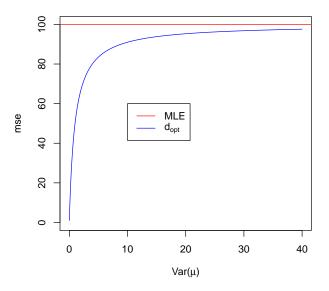
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 $d=1 \;\; ext{if and only if} \;\; \mu_1=\ldots=\mu_p$

Improvement in MSE, $p = 100, \sigma = 1$



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If p > 3 then for both J-S estimators it holds $E||\hat{\mu}_{IS} - \mu||^2 < E||\hat{\mu}_{MIF} - \mu||^2$

Hard thresholding

When signal is sparse even better results can be obtained by hard thresholding

$$\hat{\mu}_{i} = \begin{cases} X_{i} & \text{when} & H_{0i} \text{ is rejected} \\ 0 & \text{when} & H_{0i} \text{ is not rejected} \end{cases} , \tag{3}$$

where the decisions are made by Bonferroni or BH multiple testing procedures. Bonferroni is optimal for very sparse signals while BH "adapts" to the unknown sparsity (see Abramovich, Benjamini, Donoho and Johnstone, Ann.Statist. 2006)

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Hard thresholded estimator of μ using BH multiple testing rule adapts to the unknown sparsity and is asymptotically optimal in the sense discussed in (Abramovich, Benjamini, Donoho and Johnstone, Ann.Statist. 2006)