Competitors when Non-null, Varying Sample Size, log2-fold standard deviation, and π_0.

David Gerard

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Abstract

I compare MOUTHWASH to various competitors. I look at AUC and estimates of π_0. I also look at the Kendall's Tau between the p-values or lfdr's for the different methods.

1 Competitors

For each competitor, I performed two methods. The first method consisted of a two-step procedure:

1. Estimate $\hat{\beta}_{[2,i]}$ and it's corresponding standard error $\hat{s}_i$.
2. Run ASH on $\hat{\beta}_{[2,i]}$ and $\hat{s}_i$.

The second method was to just calculate a normal (or t, where appropriate) p-values from $\hat{\beta}_{[2,i]}/\hat{s}_i$.

The ASH methods provide an estimate of π_0. I obtained an estimate of π_0 from the p-values by the `qvalue` package in `R` [Storey, 2002]. In some cases for the quasi-binomial methods, the largest p-values were less than 0.9 and `qvalue` would return an error (because it uses the largest p-values to estimate the proportion of nulls). For these, I used the upper quartile of p-values to estimate the proportion of nulls. Maybe a bad idea.

The methods that Mengyin and I have coded to get $\hat{\beta}_{[2,i]}$ and $\hat{s}_i$ were

- VOOM [Law et al., 2014].
- RUVseq [Risso et al., 2014] followed by VOOM [Law et al., 2014] with the estimated confounding factors. Half of the factors were used as control genes. RUVseq is RUV2 on the log(counts + 1) matrix.
- SVAseq [Leek, 2014] followed by VOOM [Law et al., 2014] with the estimated confounding factors. SVAseq is SVA on the log(counts + 1) matrix.
- Quasi-binomial glm.
- RUVseq + quasi-binomial glm.
- SVAseq + quasi-binomial glm.
- MYRNA, which is just a quasi-binomial glm using the 75th percentile of the samples' counts as covariates [Langmead et al., 2010].
- MYRNA offset, which is just a quasi-binomial glm using the 75th percentile of the samples' counts as offsets [Langmead et al., 2010].
- DESeq2glm [Love et al., 2014].
- The robust regression version of CATE [Wang et al., 2015] on the log(counts + 1).
- The negative controls version of CATE [Wang et al., 2015] on the log(counts + 1).

- SVA [Leek and Storey, 2007] with the number of confounders estimated using the method of Buja and Eyuboglu [1992] on the log(counts + 1), followed by OLS.
- RUV2 [Gagnon-Bartsch et al., 2013] with 50% of the observations being control genes with the number of confounders estimated using the method of Buja and Eyuboglu [1992] on the log(counts + 1), followed by OLS.
- OLS on the log(counts + 1).
- The ridge-regression version of LEAPP [Sun et al., 2012] on the log(counts + 1).
- The soft-thresholding version of LEAPP [Sun et al., 2012] on the log(counts + 1).

Notes:

- "VOOM" means using VOOM [Law et al., 2014] to find weights for each observations, then fitting a linear model using LIMMA [Smyth, 2005].
- LEAPP does not easily provide standard errors, so I excluded it from the ASH analysis. But I still use it for the `qvalue` analysis.
- EdgeR was giving me trouble, so I excluded it.

The factor analysis part of MOUTHWASH was done with the quasi-mle approach of Bai et al. [2012] with the number of hidden confounders using the methods of Buja and Eyuboglu [1992] implemented in the `num.sv()` function in the `sva` package in `R`.

In summary, there are 31 methods that I compared in estimating π_0 and in their AUC:

1. MOUTHWASH
2. voom + ASH
3. Quasi-binomial GLM + ASH
4. MyrnaQB + ASH
5. Myrnaoffqb + ASH
6. RUVseq + voom + ASH
7. SVAseq + voom + ASH
8. RUVseq + Quasi-binomial GLM + ASH
9. SVAseq + Quasi-binomial GLM + ASH
10. DESeq2glm + ASH
11. OLS on log(counts + 1) + ASH
12. RUV2 on log(counts + 1) + ASH
13. SVA on log(counts + 1) + ASH
14. Robust Regression Cate + ASH
15. Negative Control CATE + ASH
16. voom + `qvalue`
17. Quasi-binomial GLM + `qvalue`
18. Myrnaqb + `qvalue`
19. Myrnaoffqb + `qvalue`
20. RUVseq + voom + `qvalue`
21. SVAseq + voom + `qvalue`
22. RUVseq + Quasi-binomial GLM + `qvalue`
23. SVAseq + Quasi-binomial GLM + `qvalue`
24. DESeq2glm + `qvalue`
25. OLS on log(counts + 1) + `qvalue`
26. RUV2 on log(counts + 1) + `qvalue`
27. SVA on log(counts + 1) + `qvalue`

28. Robust Regression CATE + `qvalue`
29. Negative Control CATE + `qvalue`
30. Soft-thresholding version of LEAPP+ `qvalue`
31. Ridge version of LEAPP+ `qvalue`

2 Simulation Study

I ran through 100 repetitions of generating data from GTEX lung data under the following parameter conditions:

- $n \in \{20, 40\}$,
- $p = 1000$,
- $\pi_0 \in \{0.5, 0.9\}$,
- $\sigma_{log2} \in \{1, 10\}$.

I extracted the most expressed p genes (excluding the top 5 expressed genes) from the GTEX lung data and n samples are chosen at random. Half of these samples are randomly given the "treatment" label 1, the other half given the "treatment" label 0. Of the p genes, $\pi_0 p$ were chosen to be non-null. Signal was added by the poisson-thinning approach in Mengyin's code with a mean log2-fold change of 0 and a standard deviation log2-fold change of σ_{log2}. That is

$$A_1, \ldots, A_{p/2} \sim N(0, \sigma^2_{log2}) \tag{1}$$

$$B_i = 2^{A_i} \text{ for } i = 1, \ldots, p/2. \tag{2}$$

If $A_i > 0$ then we replace $Y_{[1:(n/2),i]}$ with $Binom(Y_{[j,i]}, 1/B_i)$ for $j = 1, \ldots, n/2$. If $A_i < 0$ then we replace $Y_{[(n/2+1):n,i]}$ with $Binom(Y_{[j,i]}, B_i)$ for $j = n/2 + 1, \ldots, n$.

For each iteration, I calculated three things:

1. The pairwise Kendall's tau between the methods' lfdr's or p-values.
2. The AUC using either the lfdrs or p-values.
3. The estimates of π_0.

3 Results

For the frequentist procedures, I used the vector of p-values as the predictions and I used the vector of lfdr's from the ASH-like procedures for prediction. These were used to create ROC curves and calculate AUCs. In general, the AUC's were all very similar with the ash-like methods having slightly higher AUC. The two consistent winners are MOUTHWASH and CATE (negative control version) + ASH.

I present below the median Kendall's tau between each method. The methods are clustered using their Kendall's tau using the `hclust` function in `R` and the hierarchical clusterings are in the plots below. Graphical representations of the median Kendall's taus (with columns and rows sorted by the same ordering as the tree leaves) are also below. In general, there are usually four distinct clusters:

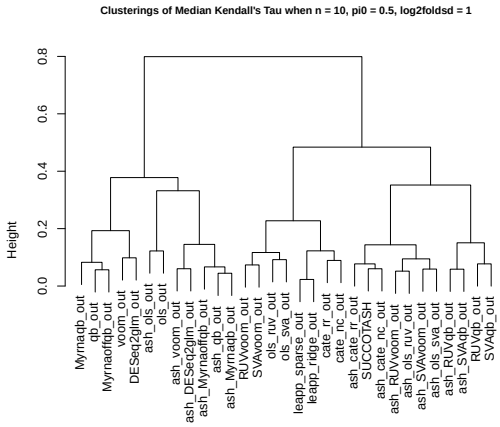
1. ASH + Confounder adjustment
2. ASH + no confounder adjustment
3. Frequentist + confounder adjustment, and

4. Frequentist + no confounder adjustment.

The Quasi-binomial GLM methods also usually cluster together. These observations don't always hold, but seem to be the biggest sources of clustering. MOUTHWASH (SUCCOTASH) is usually clustered with the ASH + confounder adjustment methods.

The median Kendall's tau can get quite low between the separate groups — as small as 0.2. This indicates that for many datasets, the rankings can be quite different. But now I'm thinking I should look at the rankings of only the most-significant genes.

From the p-values, I used the `qvalue` package [Storey, 2002] to estimate π_0. Estimates of π_0 are given from `ashr` for the ASH-like methods. MOUTHWASH (SUCCOTASH) performs the worst in estimating π_0, usually underestimating it. The ASH-like methods usually estimate π_0 to be smaller than their non-ASH counterparts.


Clusterings of Median Kendall's Tau when n = 10, pi0 = 0.5, log2foldsd = 1
Height
0.0
0.2
0.4
0.6
0.8
Mymaqb_out
qb_out
Mymaoffqb_out
voom_out
DESeq2glm_out
ash_ols_out
ols_out
ash_voom_out
ash_DESeq2glm_out
ash_Mymaoffqb_out
ash_qb_out
ash_Mymaqb_out
RUVvoom_out
SVAvoom_out
ols_ruv_out
ols_sva_out
leapp_sparse_out
leapp_ridge_out
cate_rr_out
cate_nc_out
ash_cate_rr_out
SUCCOTASH
ash_cate_nc_out
ash_RUVvoom_out
ash_ols_ruv_out
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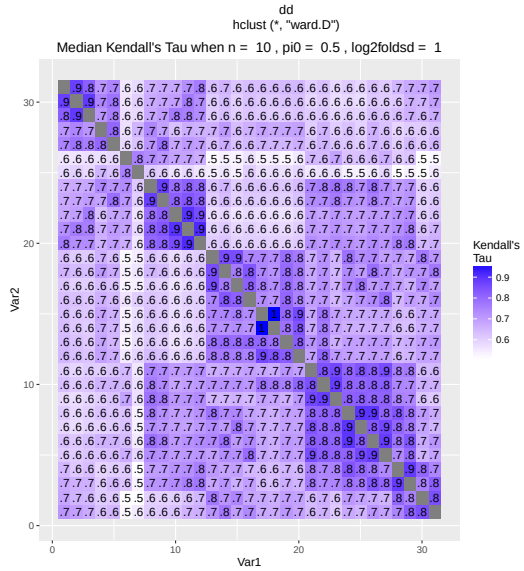
RUVqb_out
SVAqb_out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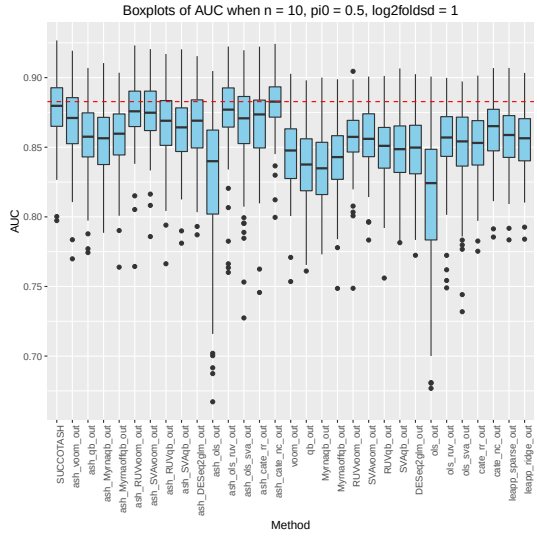
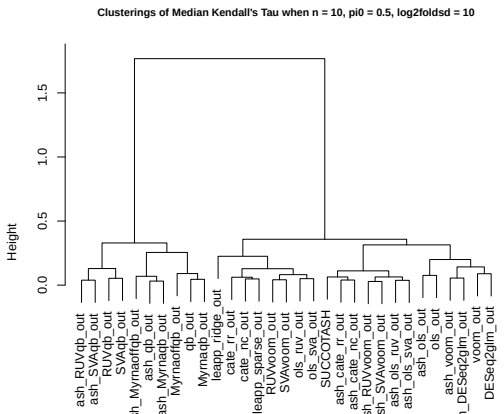
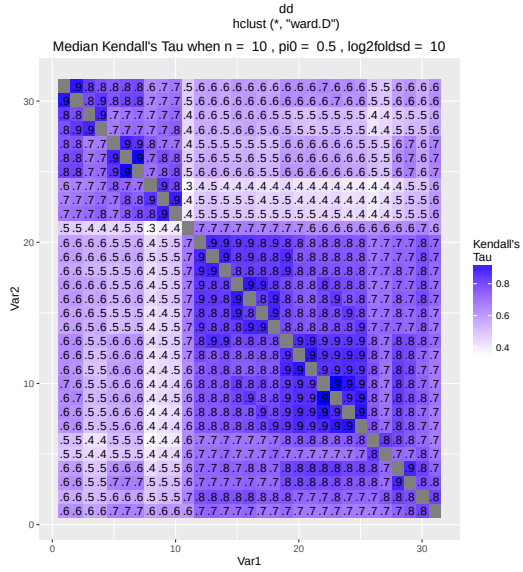
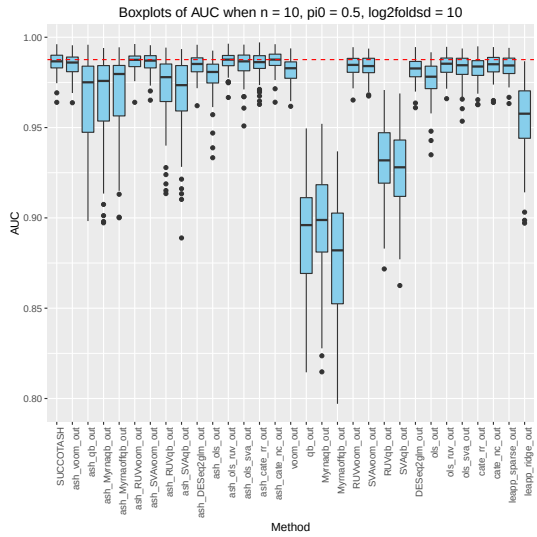
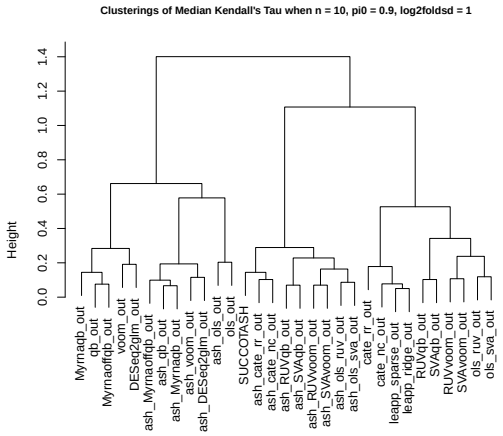
hclust (*, "ward.D")
Median Kendall's Tau when n = 10 , pi0 = 0.5 , log2foldsd = 1
Var2
Var1
0
10
20
30
Kendall's Tau
0.6
0.7
0.8
0.9
1


Boxplots of AUC when n = 10, pi0 = 0.5, log2foldsd = 1
AUC
0.70
0.75
0.80
0.85
0.90
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Mymaqb_out
ash_Mymaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Mymaqb_out
Mymaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Clusterings of Median Kendall's Tau when n = 10, pi0 = 0.5, log2foldsd = 10
Height
0.0
0.5
1.0
1.5
ash_RUVqb_out
ash_SVAqb_out
RUVqb_out
SVAqb_out
ash_Mymaoffqb_out
ash_qb_out
ash_Mymaqb_out
Mymaoffqb_out
qb_out
Mymaqb_out
leapp_ridge_out
cate_rr_out
cate_nc_out
leapp_sparse_out
RUVvoom_out
SVAvoom_out
ols_ruv_out
ols_sva_out
SUCCOTASH
ash_cate_rr_out
ash_cate_nc_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_ols_ruv_out
ash_ols_sva_out
ash_ols_out
ols_out
ash_voom_out
ash_DESeq2gim_out
voom_out
DESeq2gim_out


dd
hclust (*, "ward.D")
Median Kendall's Tau when n = 10 , pi0 = 0.5 , log2foldsd = 10
Var2
Var1
Kendall's Tau
0.8
0.6
0.4


Boxplots of AUC when n = 10, pi0 = 0.5, log2foldsd = 10
AUC
1.00
0.95
0.90
0.85
0.80
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Mymaqb_out
ash_Mymaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2gim_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Mymaqb_out
Mymaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2gim_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method



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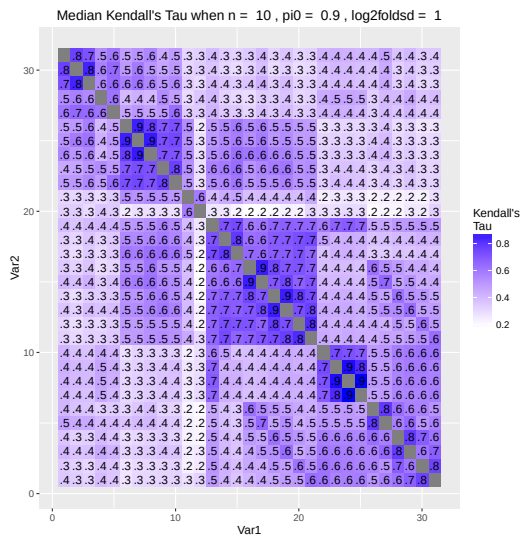
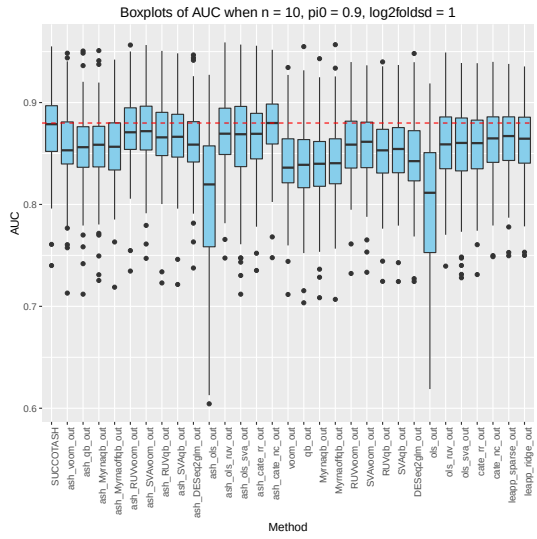
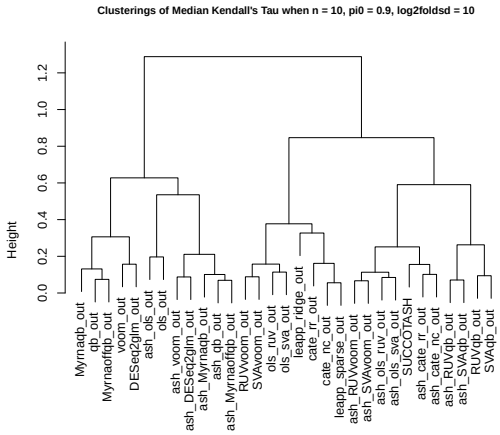
hclust (*, "ward.D")







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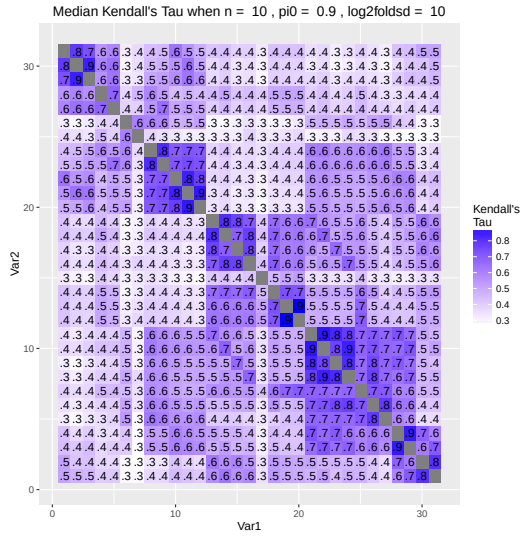
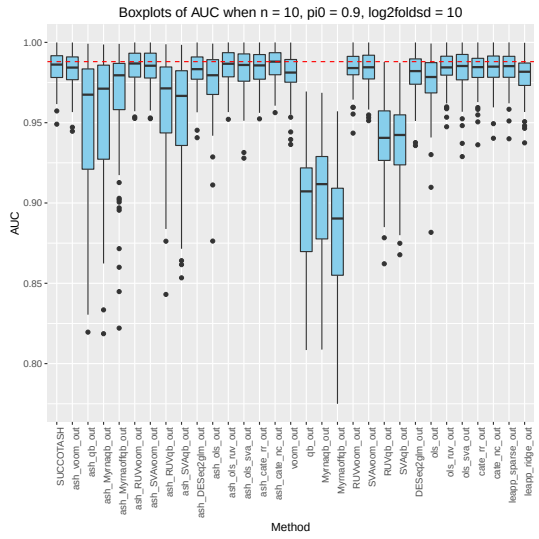
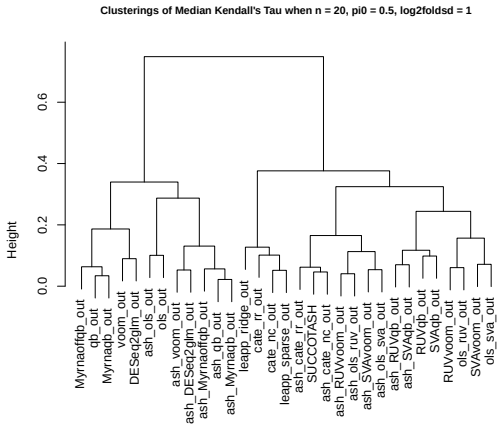
hclust (*, "ward.D")






Clusterings of Median Kendall's Tau when n = 20, pi0 = 0.5, log2foldsd = 1
Height
0.0
0.2
0.4
0.6
Mymaoffqb_out
qb_out
Mymaqb_out
voom_out
DESeq2glm_out
ash_ols_out
ols_out
ash_voom_out
ash_DESeq2glm_out
ash_Mymaoffqb_out
ash_qb_out
ash_Mymaqb_out
leapp_ridge_out
cate_rr_out
cate_nc_out
leapp_sparse_out
ash_cate_rr_out
SUCCOTASH
ash_cate_nc_out
ash_RUVvoom_out
ash_ols_ruv_out
ash_SVAvoom_out
ash_ols_sva_out
ash_RUVqb_out
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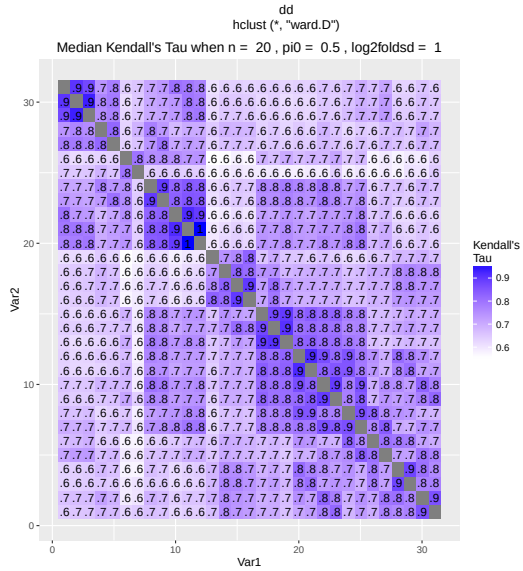
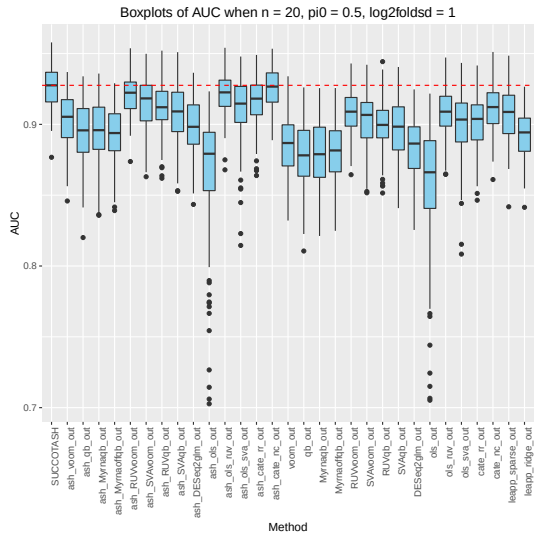
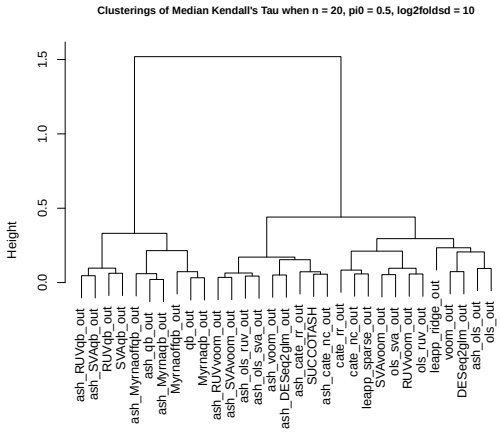
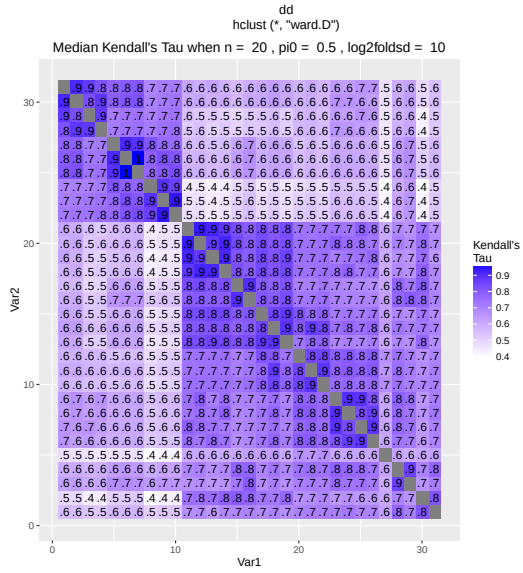
SVAvoom_out
ols_sva_out


dd
hclust (*, "ward.D")
Median Kendall's Tau when n = 20 , pi0 = 0.5 , log2foldsd = 1
Var2
Var1
Kendall's Tau
0.9
0.8
0.7
0.6
0
10
20
30


Boxplots of AUC when n = 20, pi0 = 0.5, log2foldsd = 1
AUC
0.7
0.8
0.9
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Mymaqb_out
ash_Mymaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Mymaqb_out
Mymaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Clusterings of Median Kendall's Tau when n = 20, pi0 = 0.5, log2foldsd = 10
Height
0.0
0.5
1.0
1.5
ash_RUVqb_out
ash_SVAqb_out
RUVqb_out
SVAqb_out
ash_Mynaoftqb_out
ash_qb_out
ash_Mynaqb_out
Mynaoftqb_out
qb_out
Mynaqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_ols_ruv_out
ash_ols_sva_out
ash_voom_out
ash_DESeq2glm_out
ash_cate_rr_out
SUCCOTASH
ash_cate_nc_out
cate_rr_out
cate_nc_out
leapp_sparse_out
SVAvoom_out
ols_sva_out
RUVvoom_out
ols_ruv_out
leapp_ridge_out
voom_out
DESeq2glm_out
ash_ols_out
ols_out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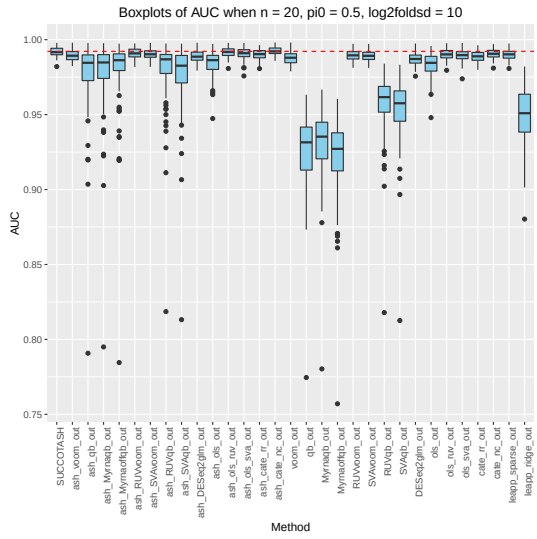
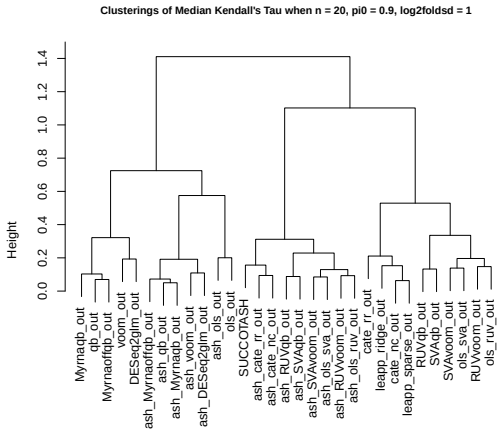
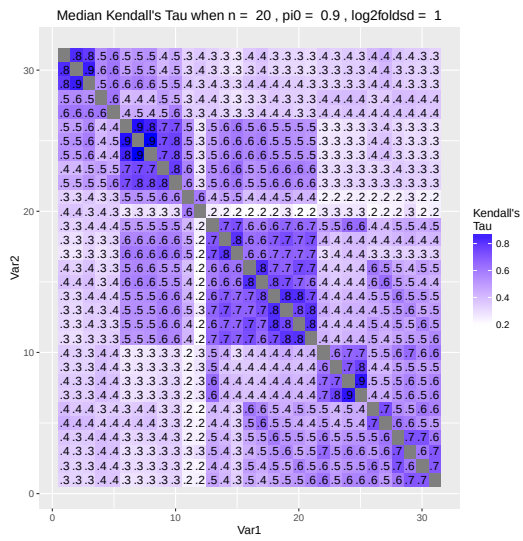
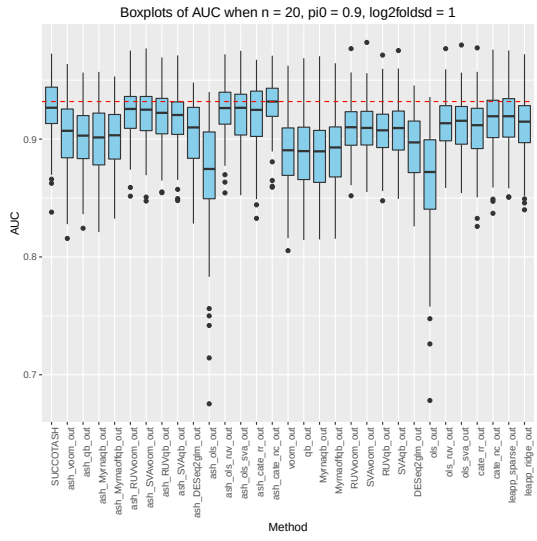
hclust (*, "ward.D")
Median Kendall's Tau when n = 20 , pi0 = 0.5 , log2foldsd = 10
Var2
Var1
Kendall's Tau
0.9
0.8
0.7
0.6
0.5
0.4

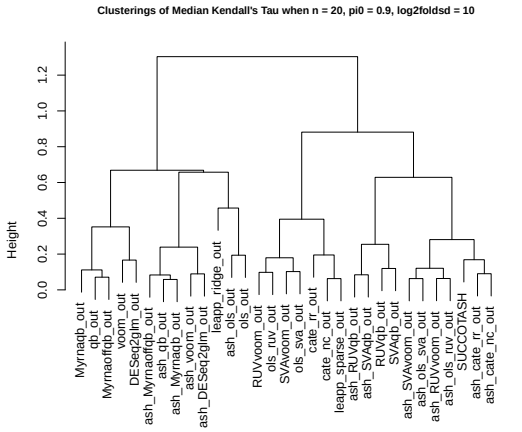

Boxplots of AUC when n = 20, pi0 = 0.5, log2foldsd = 10
AUC
1.00
0.95
0.90
0.85
0.80
0.75
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Mynaqb_out
ash_Mynaoftqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Mynaqb_out
Mynaoftqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method

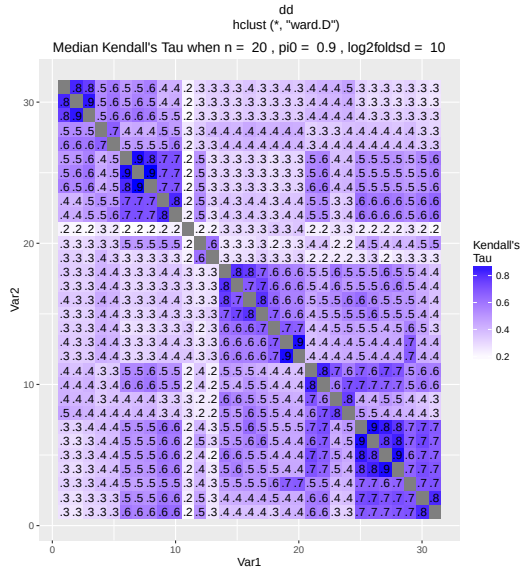


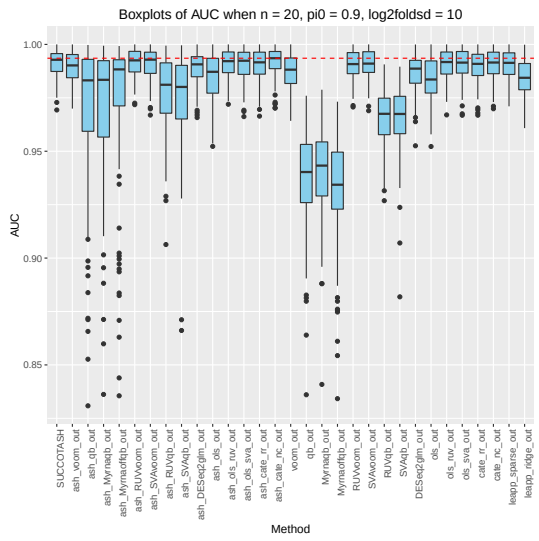
dd
hclust (*, "ward.D")

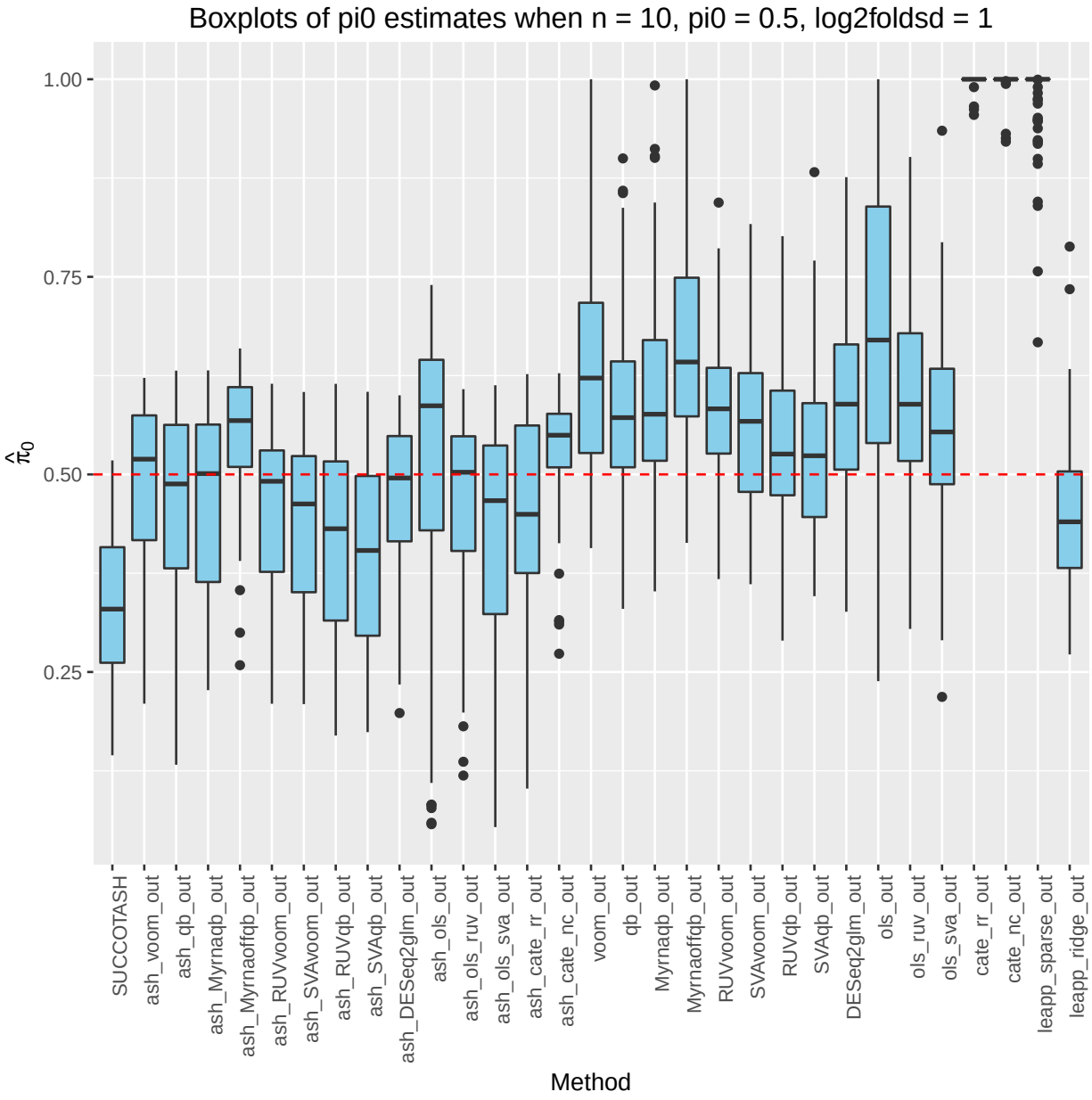


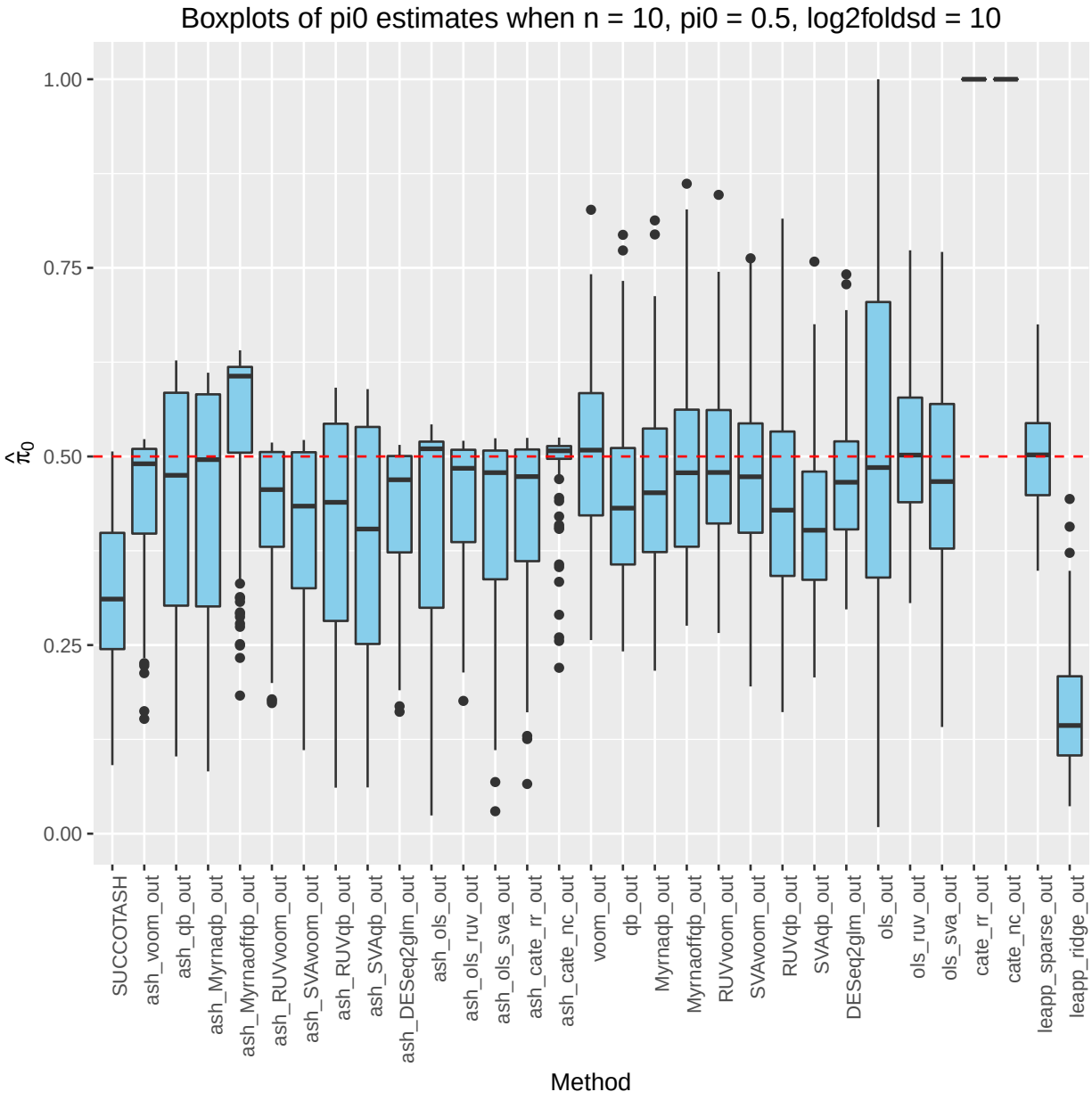


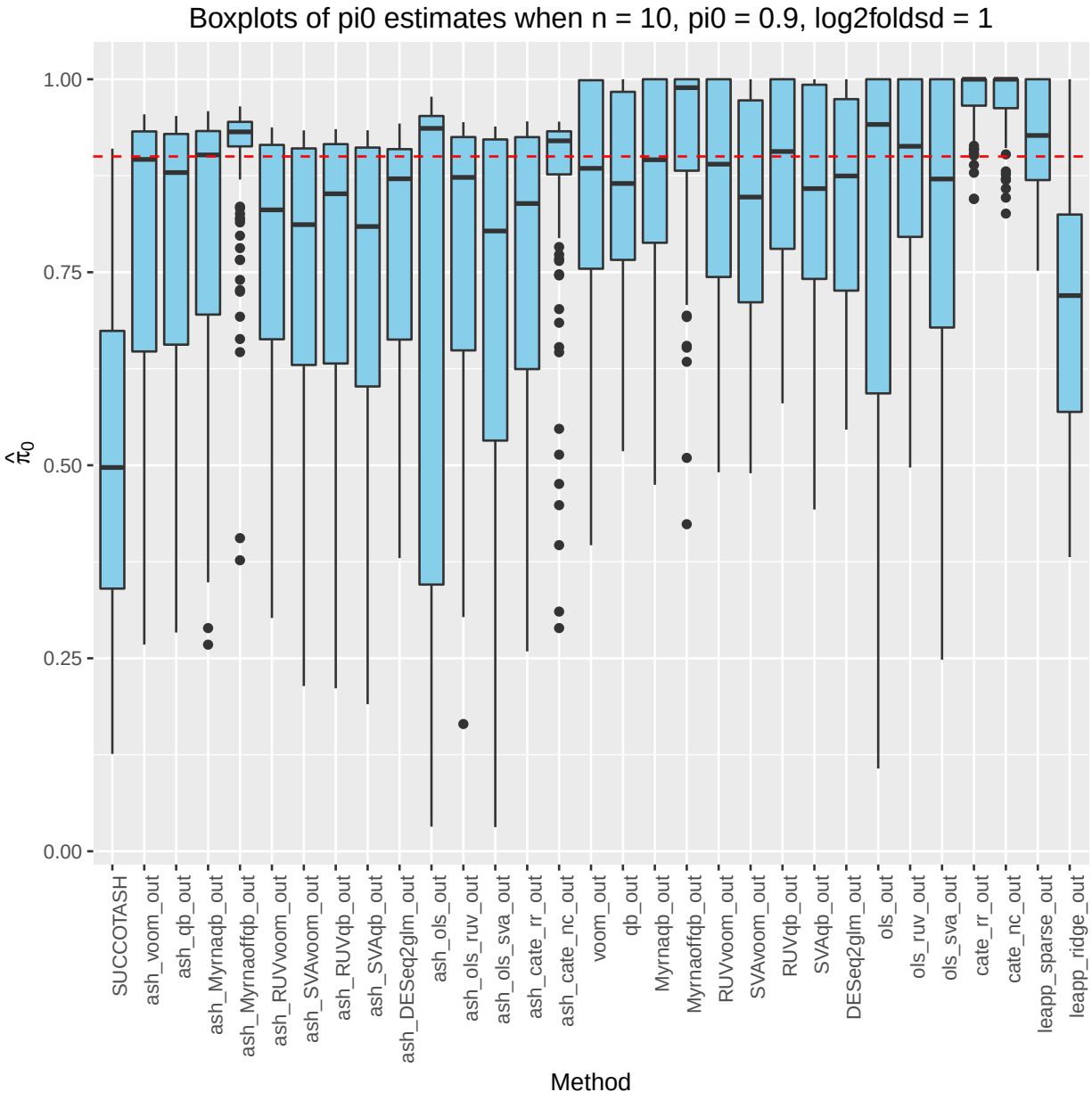

Clusterings of Median Kendall's Tau when n = 20, pi0 = 0.9, log2foldsd = 10
Height
0.0
0.2
0.4
0.6
0.8
1.0
1.2
Mynaqb_out
qb_out
Mynaoffqb_out
voom_out
DESeq2glm_out
ash_Mynaoffqb_out
ash_qb_out
ash_Mynaqb_out
ash_voom_out
ash_DESeq2glm_out
leapp_ridge_out
ash_ols_out
ols_out
RUVvoom_out
ols_ruv_out
SVAvoom_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
ash_RUVqb_out
ash_SVAqb_out
RUVqb_out
SVAqb_out
ash_SVAvoom_out
ash_ols_sva_out
ash_RUVvoom_out
ash_ols_ruv_out
SUCCOTASH
ash_cate_rr_out
ash_cate_nc_out

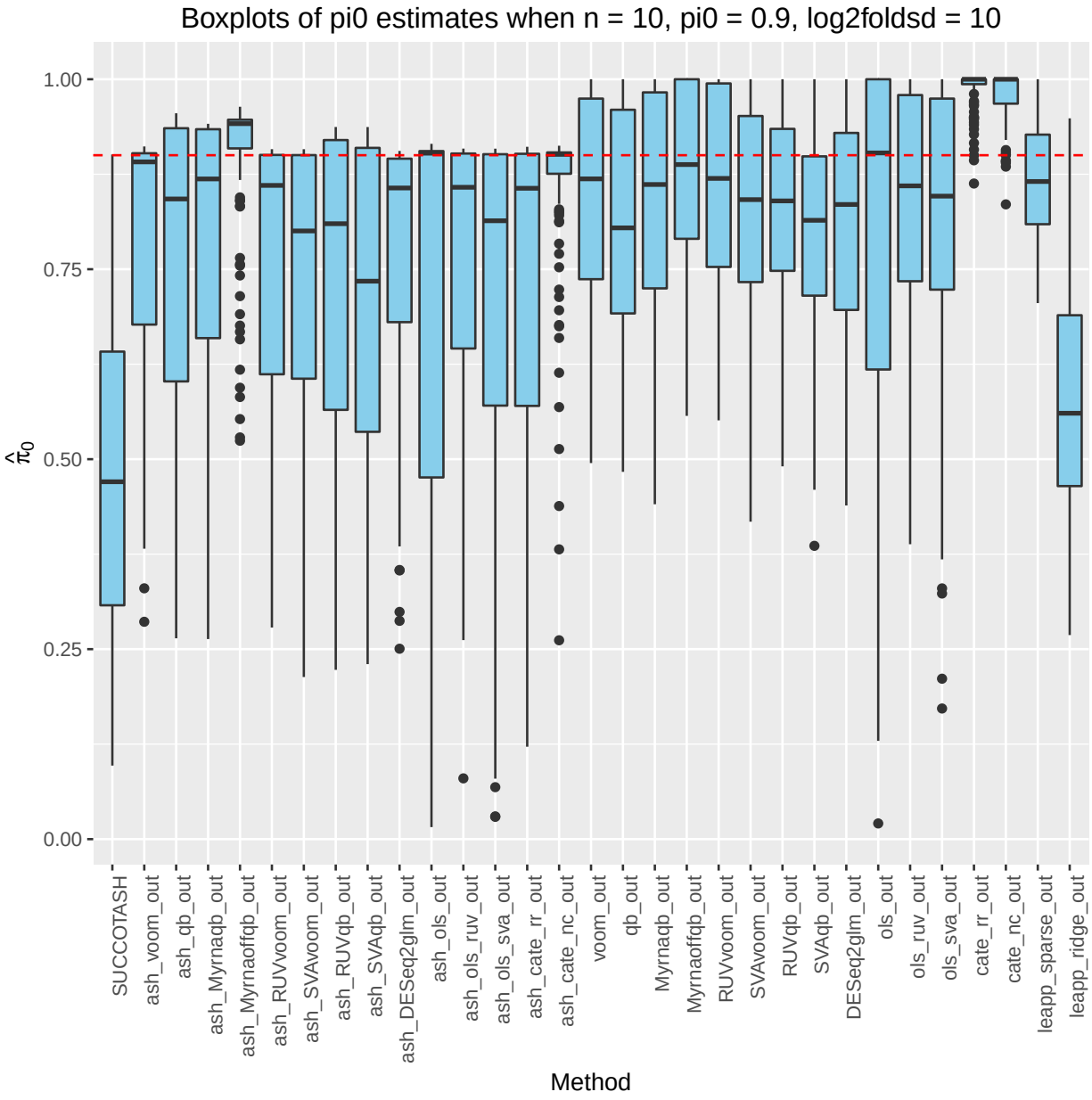

dd
hclust (*, "ward.D")
Median Kendall's Tau when n = 20 , pi0 = 0.9 , log2foldsd = 10
Var2
Var1
Kendall's Tau
0.8
0.6
0.4
0.2

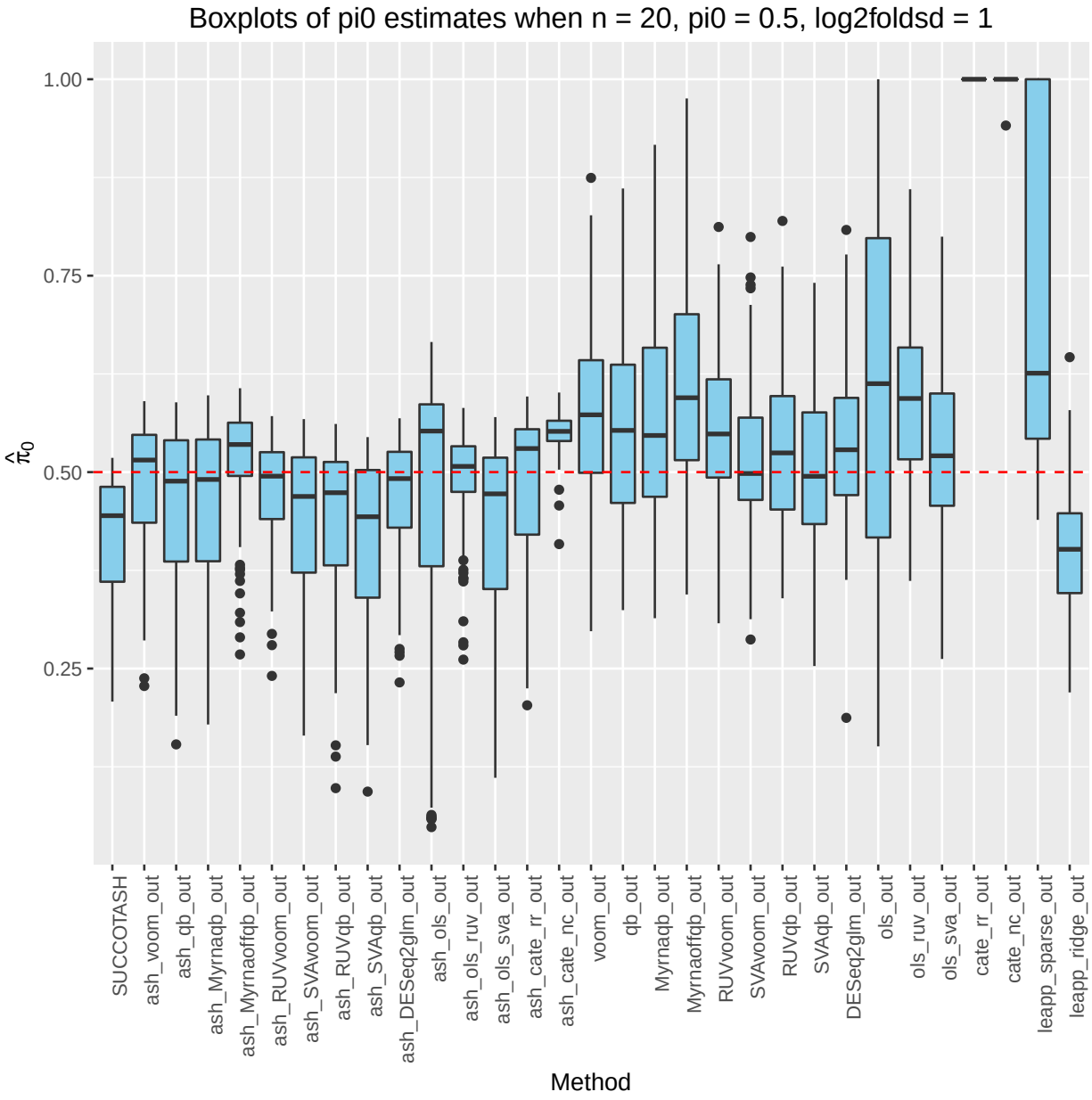

Boxplots of AUC when n = 20, pi0 = 0.9, log2foldsd = 10
AUC
1.00
0.95
0.90
0.85
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Mynaqb_out
ash_Mynaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Mynaqb_out
Mynaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method

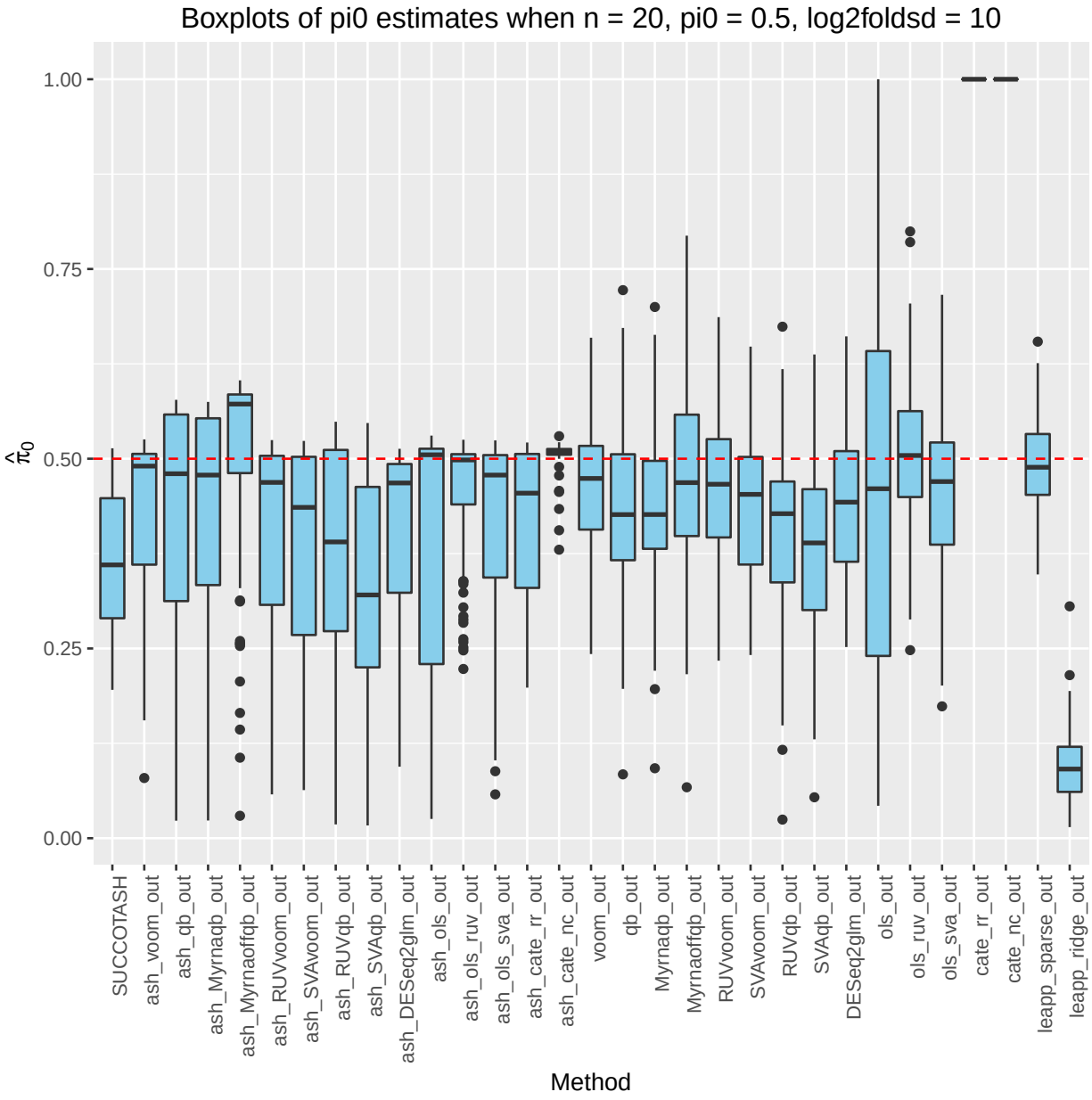

Boxplots of pi0 estimates when n = 10, pi0 = 0.5, log2foldsd = 1
1.00
0.75
0.50
0.25
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 10, pi0 = 0.5, log2foldsd = 10
1.00
0.75
0.50
0.25
0.00
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 10, pi0 = 0.9, log2foldsd = 1
1.00
0.75
0.50
0.25
0.00
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 10, pi0 = 0.9, log2foldsd = 10
1.00
0.75
0.50
0.25
0.00
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 20, pi0 = 0.5, log2foldsd = 1
1.00
0.75
0.50
0.25
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
ols_out
ols_ruv_out
ols_sva_out
cate_rr_out
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 20, pi0 = 0.5, log2foldsd = 10
1.00
0.75
0.50
0.25
0.00
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
RUVvoom_out
SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
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ols_sva_out
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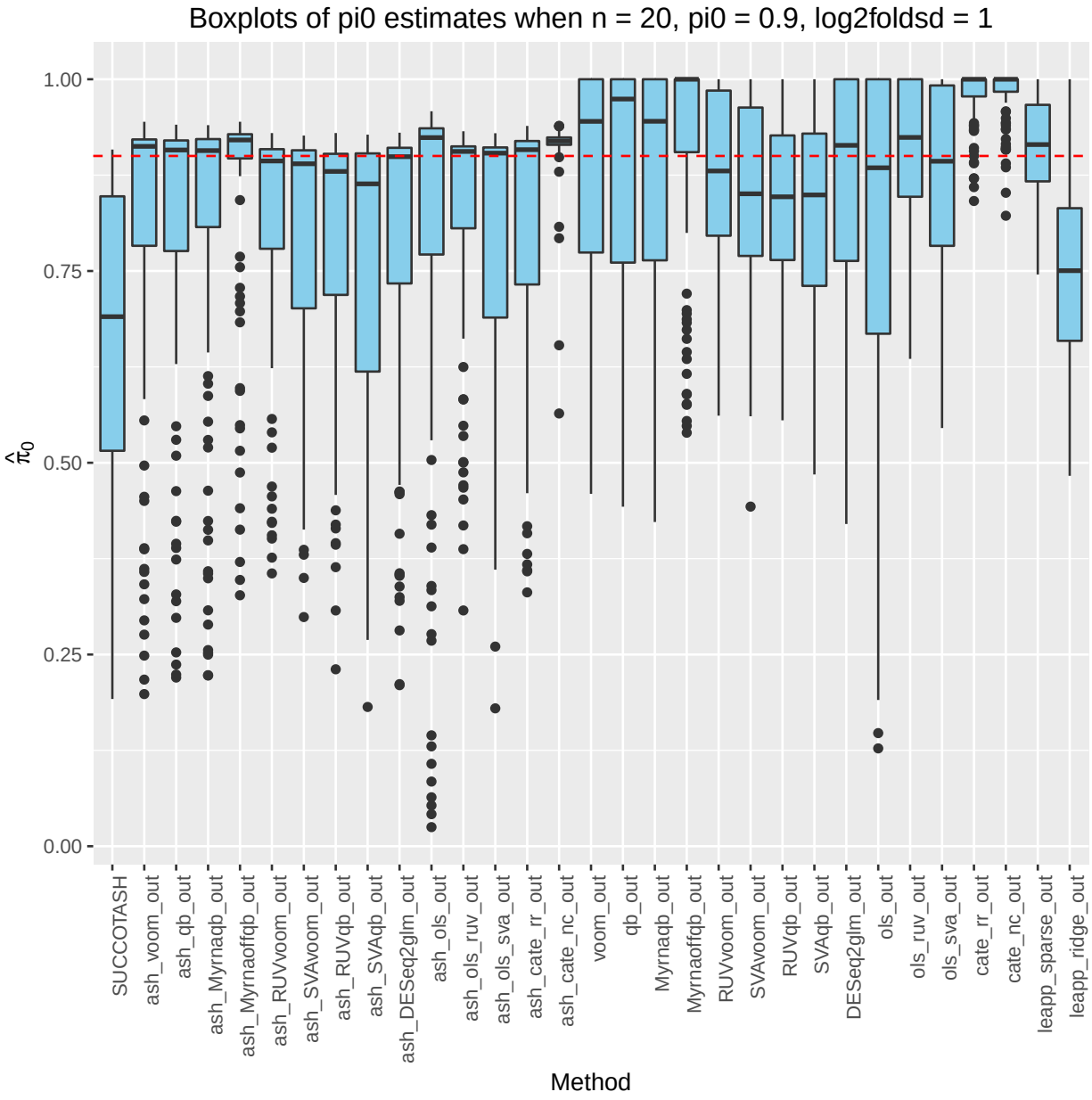
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method


Boxplots of pi0 estimates when n = 20, pi0 = 0.9, log2foldsd = 1
1.00
0.75
0.50
0.25
0.00
$\hat{\pi}_0$
SUCCOTASH
ash_voom_out
ash_qb_out
ash_Myrnaqb_out
ash_Myrnaoffqb_out
ash_RUVvoom_out
ash_SVAvoom_out
ash_RUVqb_out
ash_SVAqb_out
ash_DESeq2glm_out
ash_ols_out
ash_ols_ruv_out
ash_ols_sva_out
ash_cate_rr_out
ash_cate_nc_out
voom_out
qb_out
Myrnaqb_out
Myrnaoffqb_out
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SVAvoom_out
RUVqb_out
SVAqb_out
DESeq2glm_out
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ols_sva_out
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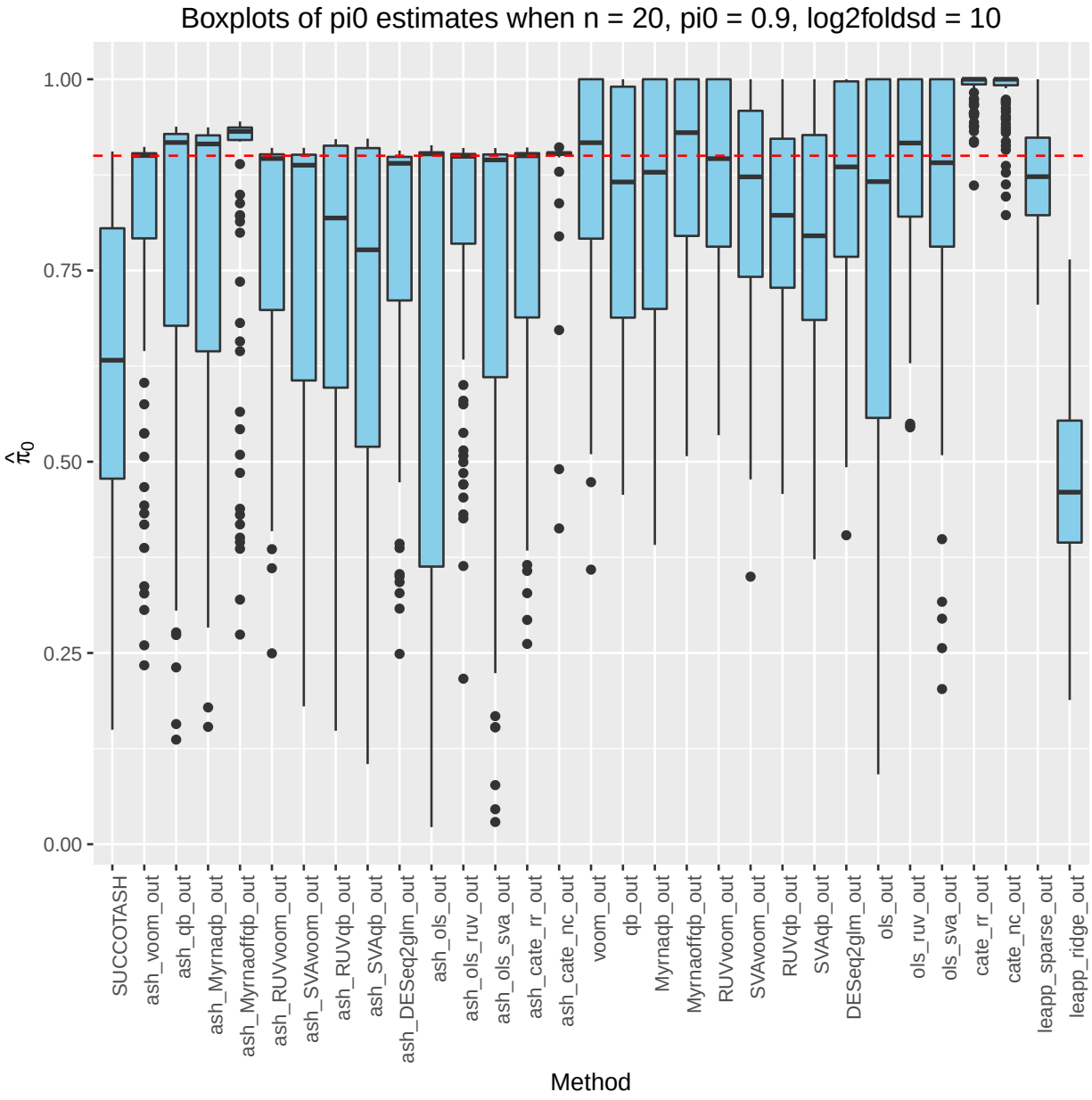
cate_nc_out
leapp_sparse_out
leapp_ridge_out
Method



References

Jushan Bai, Kunpeng Li, et al. Statistical analysis of factor models of high dimension. *The Annals of Statistics*, 40(1):436–465, 2012.

Andreas Buja and Nermin Eyuboglu. Remarks on parallel analysis. *Multivariate behavioral research*, 27(4):509–540, 1992.

J Gagnon-Bartsch, L Jacob, and TP Speed. Removing unwanted variation from high dimensional

data with negative controls. Technical report, Technical Report 820, Department of Statistics, University of California, Berkeley, 2013.

Ben Langmead, Kasper D Hansen, Jeffrey T Leek, et al. Cloud-scale rna-sequencing differential expression analysis with myrna. *Genome Biol*, 11(8):R83, 2010.

Charity W Law, Yunshun Chen, Wei Shi, and Gordon K Smyth. Voom: precision weights unlock linear model analysis tools for rna-seq read counts. *Genome Biol*, 15(2):R29, 2014.

Jeffrey T Leek. svaseq: removing batch effects and other unwanted noise from sequencing data. *Nucleic acids research*, page gku864, 2014.

Jeffrey T Leek and John D Storey. Capturing heterogeneity in gene expression studies by surrogate variable analysis. *PLoS Genet*, 3(9):1724–1735, 2007.

Michael I Love, Wolfgang Huber, and Simon Anders. Moderated estimation of fold change and dispersion for rna-seq data with deseq2. *Genome Biol*, 15(12):550, 2014.

Davide Risso, John Ngai, Terence P Speed, and Sandrine Dudoit. Normalization of rna-seq data using factor analysis of control genes or samples. *Nature biotechnology*, 32(9):896–902, 2014.

Gordon K Smyth. Limma: linear models for microarray data. In *Bioinformatics and computational biology solutions using R and Bioconductor*, pages 397–420. Springer, 2005.

John D Storey. A direct approach to false discovery rates. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 64(3):479–498, 2002.

Yunting Sun, Nancy R Zhang, Art B Owen, et al. Multiple hypothesis testing adjusted for latent variables, with an application to the agemap gene expression data. *The Annals of Applied Statistics*, 6(4):1664–1688, 2012.

Jingshu Wang, Qingyuan Zhao, Trevor Hastie, and Art B Owen. Confounder adjustment in multiple hypotheses testing. *arXiv preprint arXiv:1508.04178*, 2015.