RUVASH Using Maximum Number of Factors Allowed

Abstract

I run RUVASH always using the maximum number of factors allowed by the model, which is $n - k - 1$. As long as you limmashrink the variance estimates prior to inflation, RUVASH actually works pretty well. If you don't limmashrink the variances, then RUVASH performs horribly.

Simulation Setup

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

- $n \in \{10, 20, 40\}$,
- $p = 1000$.
- $\pi_0 \in \{0.5, 0.9, 1\}$,
- The alternative distribution being just a standard normal. New alternatives are generated every iteration.

I extracted the most expressed p genes from the GTEX muscle data and n samples are chosen at random. Half of these samples are randomly given the "treatment" label 1, the other half given the "control" label 0. Of the p genes, $\pi_0 p$ were chosen to be non-null. Signal was added by a Poisson-thinning approach, where the log-2 fold change was sampled from a standard normal. That is

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

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

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 $j = n/2 + 1, \ldots, n$.

I now describe the justification for this. Suppose that

$$Y_{ij} \sim Poisson(\lambda_j). \tag{3}$$

Let x_i be the indicator of treatment vs control for individual i. Let Ω be the set of non-null genes. Let Z be the new dataset derived via the steps above. That is

$$Z_{ij}|Y_{ij} = \begin{cases} Binom(Y_{ij}, 2^{A_j x_i}) & \text{if } A_j < 0 \text{ and } j \in \Omega \\ Binom(Y_{ij}, 2^{-A_j(1-x_i)}) & \text{if } A_j > 0 \text{ and } j \in \Omega \\ Y_{ij} & \text{if } j \notin \Omega. \end{cases} \tag{4}$$

Then

$$Z_{ij}|A_j, A_j < 0, j \in \Omega \sim Poisson(2^{A_j x_i} \lambda_j) \tag{5}$$

$$Z_{ij}|A_j, A_j > 0, j \in \Omega \sim Poisson(2^{-A_j(1-x_i)} \lambda_j), \tag{6}$$

and

$$E[\log_2(Z_{ij}) - \log_2(Z_{kj})|A_j, A_j < 0, j \in \Omega] \approx A_j x_i - A_j x_k, \text{ and} \tag{7}$$
$$E[\log_2(Z_{ij}) - \log_2(Z_{kj})|A_j, A_j > 0, j \in \Omega] \approx -A_j(1 - x_i) + A_j(1 - x_k). \tag{8}$$

if individual i is in the treatment group and individual k is in the control group, then this just equals A_j. I treat the A_j's as the true coefficient values when calculating the MSE.

Methods

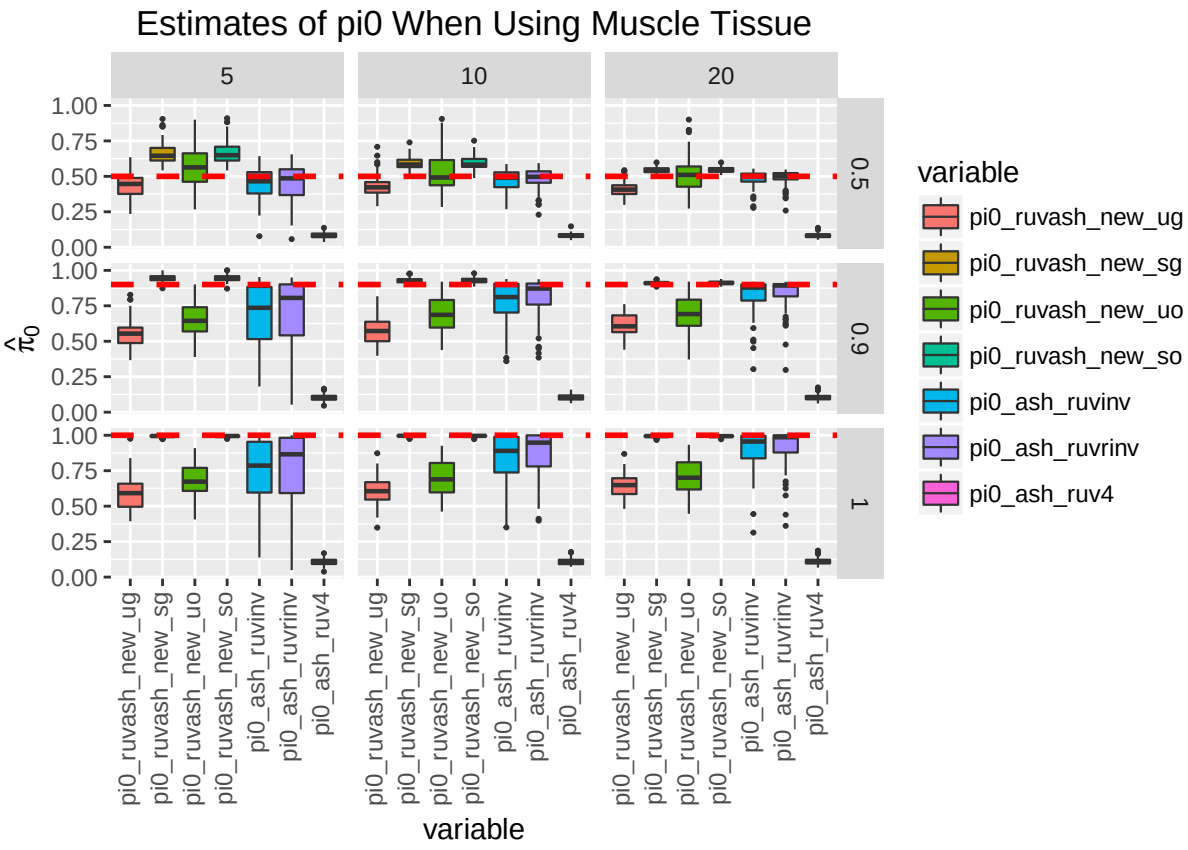
The notation in the plots below is:

- ruvash_new_ug: $\hat{\Sigma}$ is not limmashrunk and multply $\hat{\lambda}\hat{\Sigma}$ by the diagonal elements of $([X, Z]^T[X, Z])^{-1}$ and use GLS to estimate hidden confounders.
- ruvash_new_ug: $\hat{\Sigma}$ is limmashrunk and multply $\hat{\lambda}\hat{\Sigma}$ by the diagonal elements of $([X, Z]^T[X, Z])^{-1}$ and use GLS to estimate hidden confounders.
- ruvash_new_uo: $\hat{\Sigma}$ is not limmashrunk and multply $\hat{\lambda}\hat{\Sigma}$ by the diagonal elements of $([X, Z]^T[X, Z])^{-1}$ and use OLS to estimate hidden confounders.
- ruvash_new_uo: $\hat{\Sigma}$ is limmashrunk and multply $\hat{\lambda}\hat{\Sigma}$ by the diagonal elements of $([X, Z]^T[X, Z])^{-1}$ and use OLS to estimate hidden confounders.
- ash_ruvinv: Run ‘ruv::RUVinv‘ then ASH. RUVinv is RUV4 using the maximum allowed number of factors given the number of control genes, followed by a method-of-moments approach to estimating the variances that the RUV folks call the "inverse-method".
- ash_ruvrinv: A ridged version of RUV-inverse.
- ash_ruv4: Run ‘ruv::RUV4‘ followed by ASH (no variance inflation).

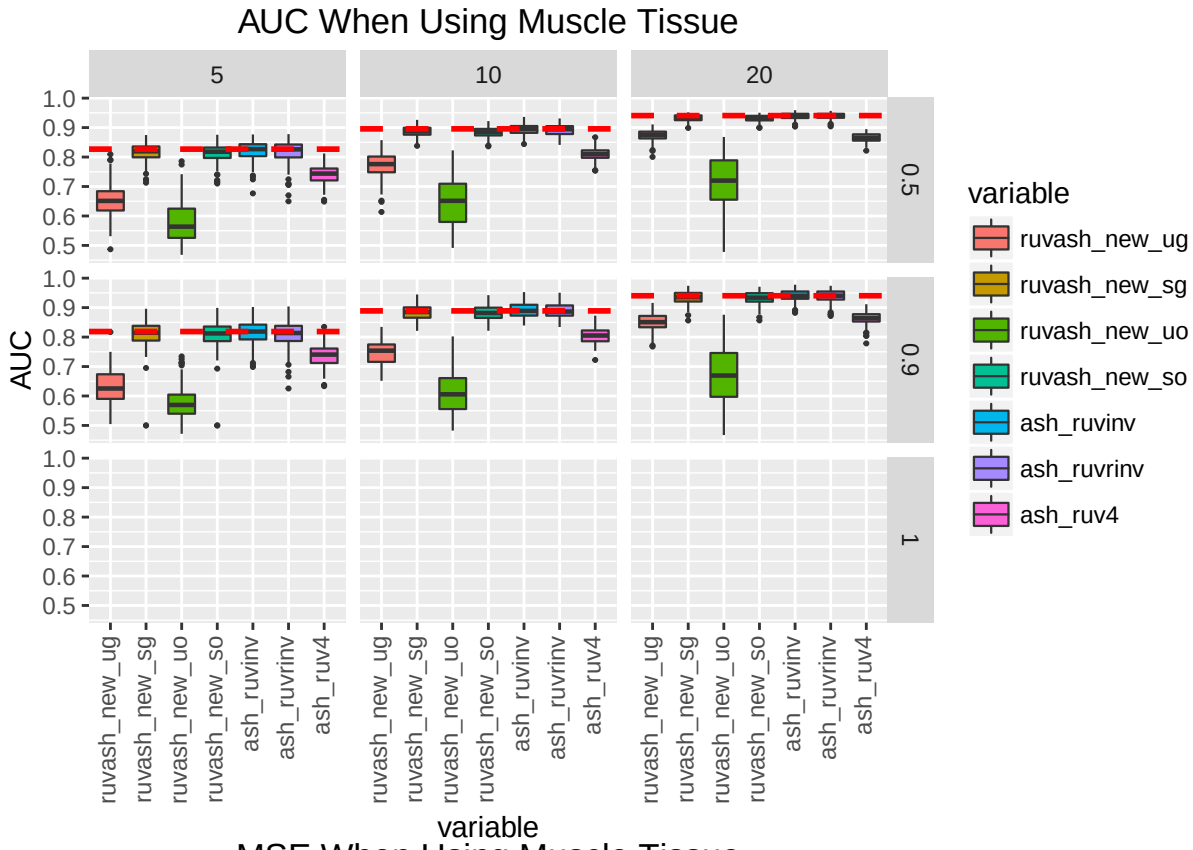
Results

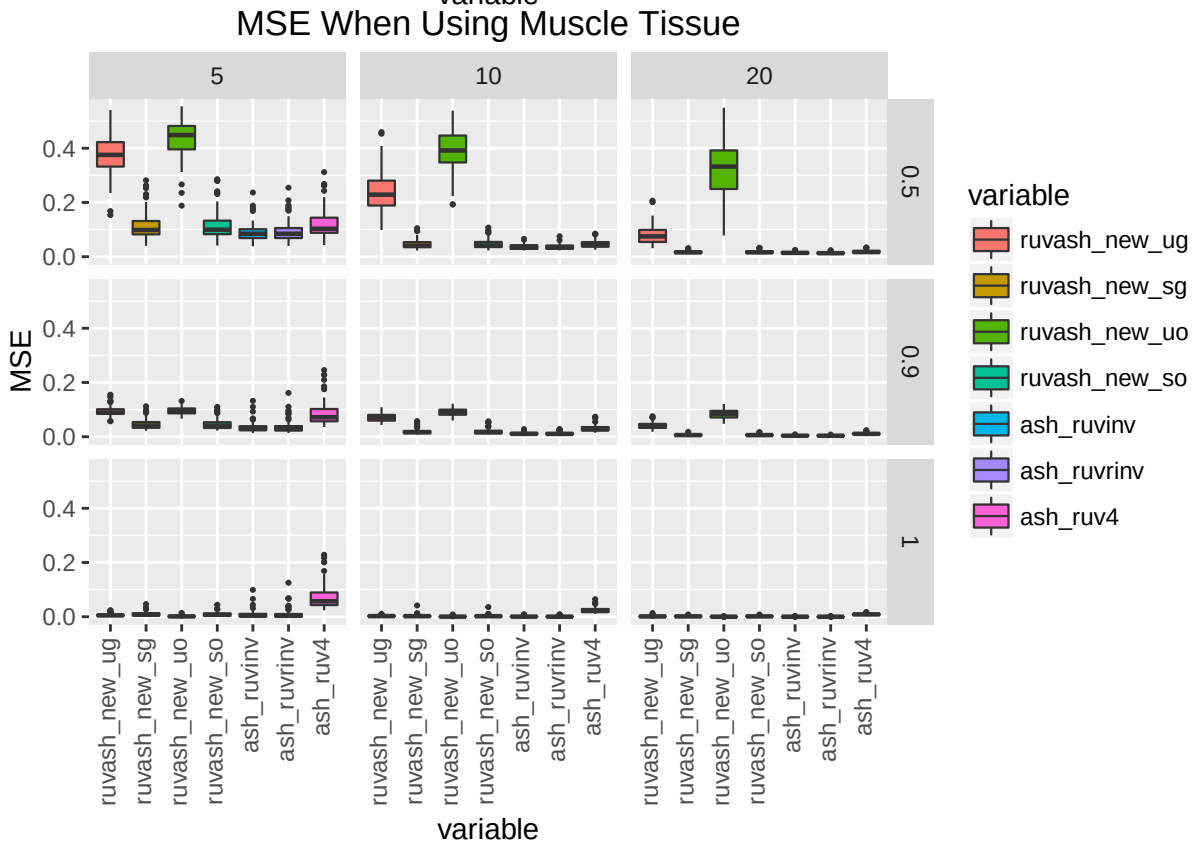
The scale estimates are ridiculous if you don’t limmashrink the variances prior to estimating the variance inflation parameter. RUVASH with limmashrink actually works really well.

Plots




```
## Warning: Removed 2100 rows containing non-finite values (stat_boxplot).
```



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## Warning: Removed 738 rows containing non-finite values (stat_boxplot).
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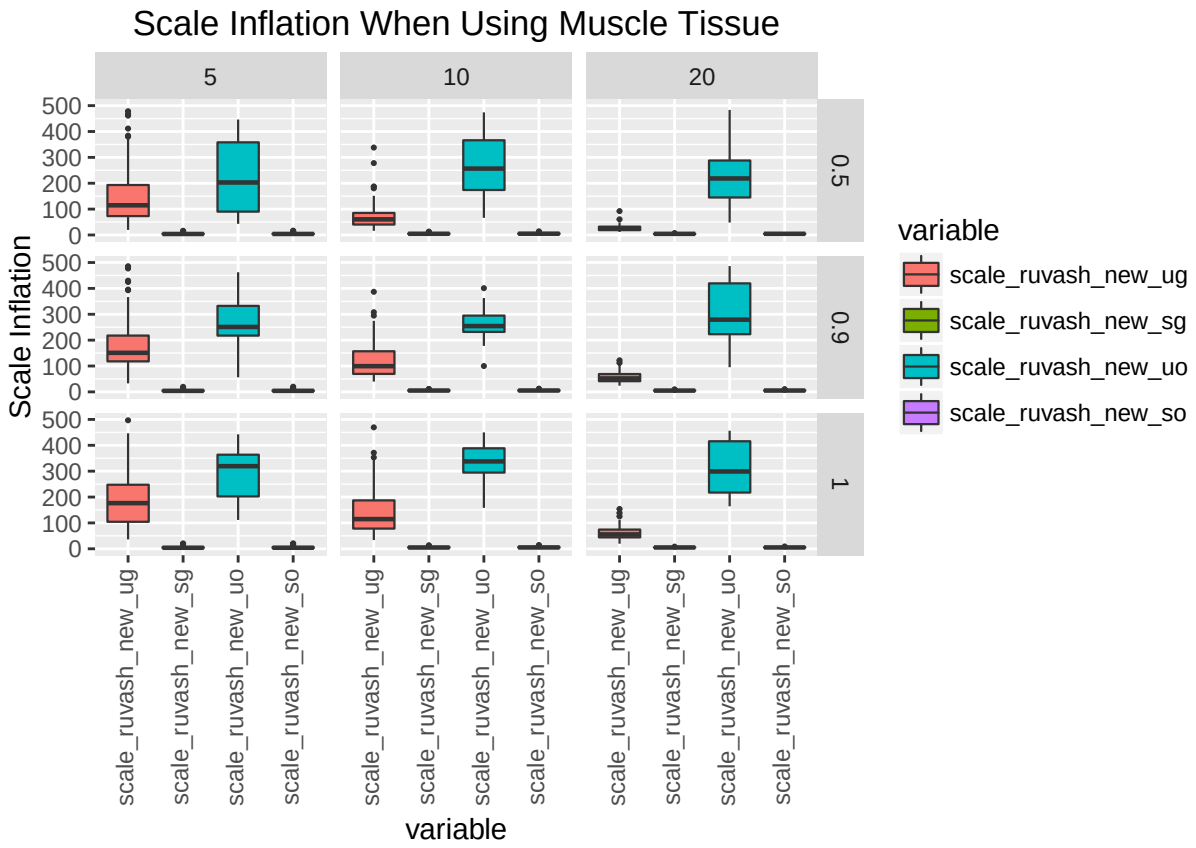


```
sessionInfo()
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## R version 3.3.1 (2016-06-21)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 14.04.4 LTS
##
## locale:
##  [1] LC_CTYPE=en_US.UTF-8       LC_NUMERIC=C
##  [3] LC_TIME=en_US.UTF-8        LC_COLLATE=en_US.UTF-8
##  [5] LC_MONETARY=en_US.UTF-8    LC_MESSAGES=en_US.UTF-8
##  [7] LC_PAPER=en_US.UTF-8       LC_NAME=C
##  [9] LC_ADDRESS=C               LC_TELEPHONE=C
## [11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
## [1] tidyr_0.4.1    reshape2_1.4.1 ggplot2_2.1.0
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_0.12.5      knitr_1.12.28    magrittr_1.5     munsell_0.4.3
##  [5] colorspace_1.2-6 R6_2.1.2         stringr_1.0.0    plyr_1.8.4
##  [9] dplyr_0.4.3      tools_3.3.1      parallel_3.3.1   grid_3.3.1
## [13] gtable_0.2.0     DBI_0.4          htmltools_0.3.5  yaml_2.1.13
## [17] digest_0.6.9     assertthat_0.1   formatR_1.3      evaluate_0.9
## [21] rmarkdown_0.9.6  labeling_0.3     stringi_1.0-1    compiler_3.3.1
```

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## [25] scales_0.4.0
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