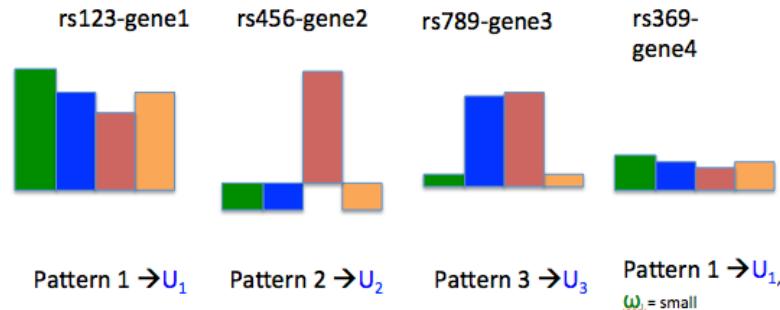
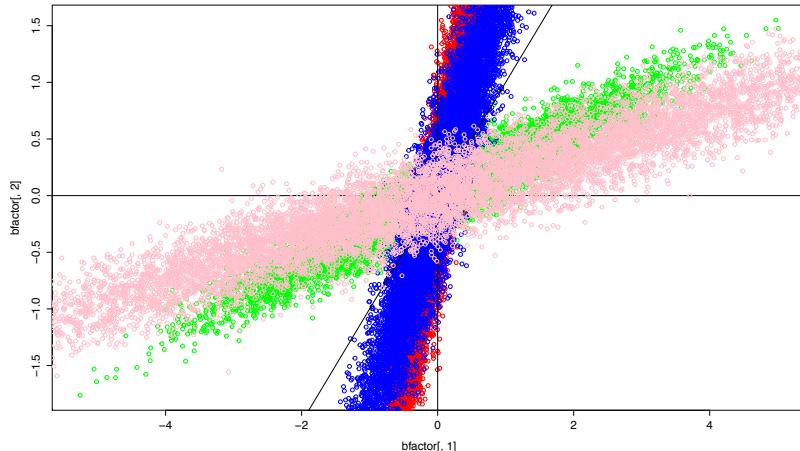


Paper Figures

Methods Outline

Patterns of Sharing



Capturing Continuous Effect

Whereas Configurations would assume all effect vectors fall on 45 degree or x y axis, quantitative configurations allow for consistent heterogeneity - e.g., consistently larger effects in tissue 1 vs 2, though active in both (show example from real data in results section)

Patterns of Sharing

Quantitative patterns express consistency relationships among tissues, with patterns learned from the data. SNPs may show strong evidence of arising from the same pattern in that their relative ratios among tissues are similar, but have effects that differ in absolute magnitude.

Schematic of Pipeline

- JxR matrix of summary statistics and their standard errors

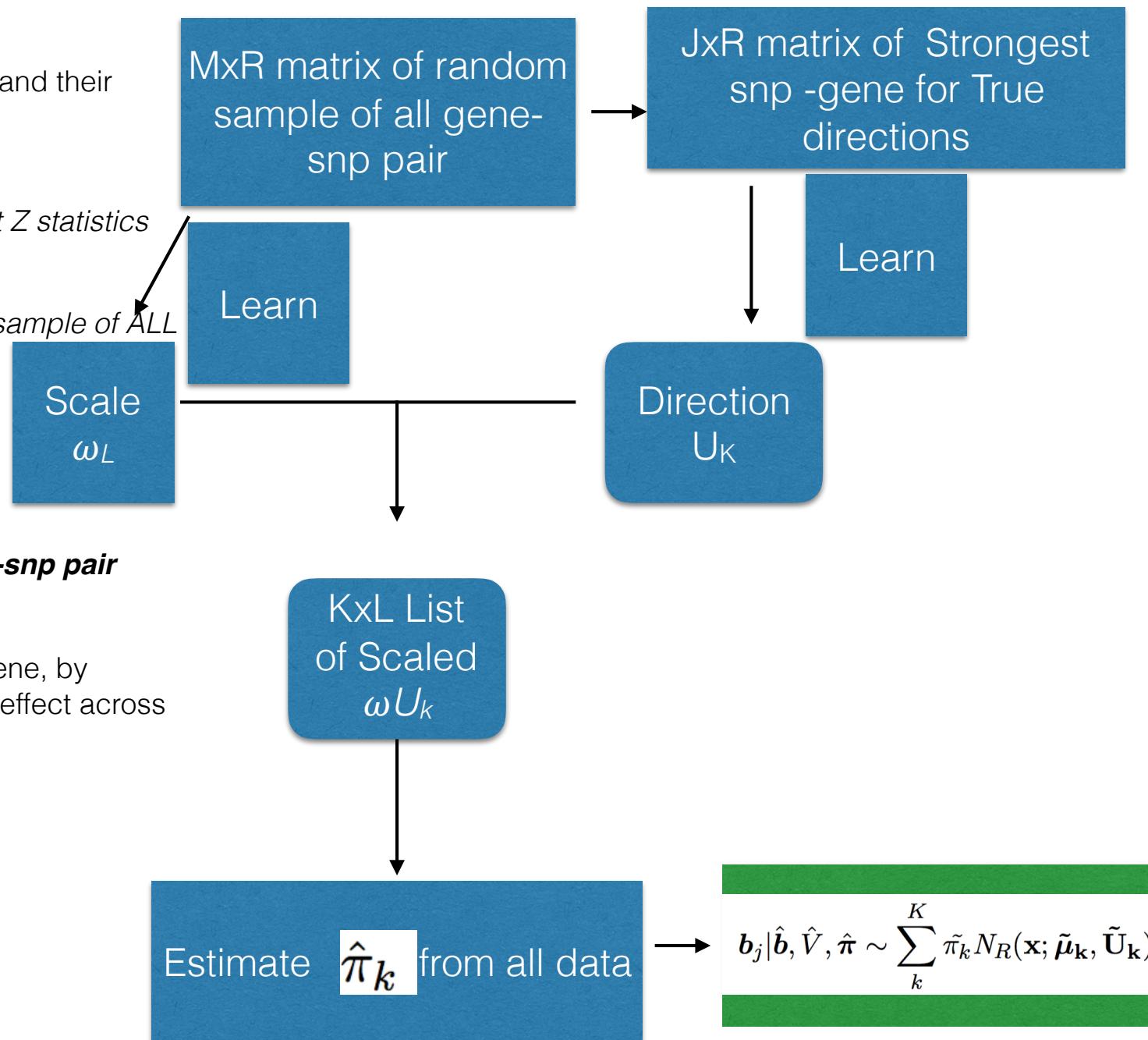
- **Prior:** Estimate U_k from strongest Z statistics

- Infer **prior** mixture weights from sample of ALL DATA

- Compute **posterior** on any gene-snp pair

- Report results on one QTL per-gene, by choosing SNP with max absolute effect across tissues

- Report effect size as **E(BIData)**



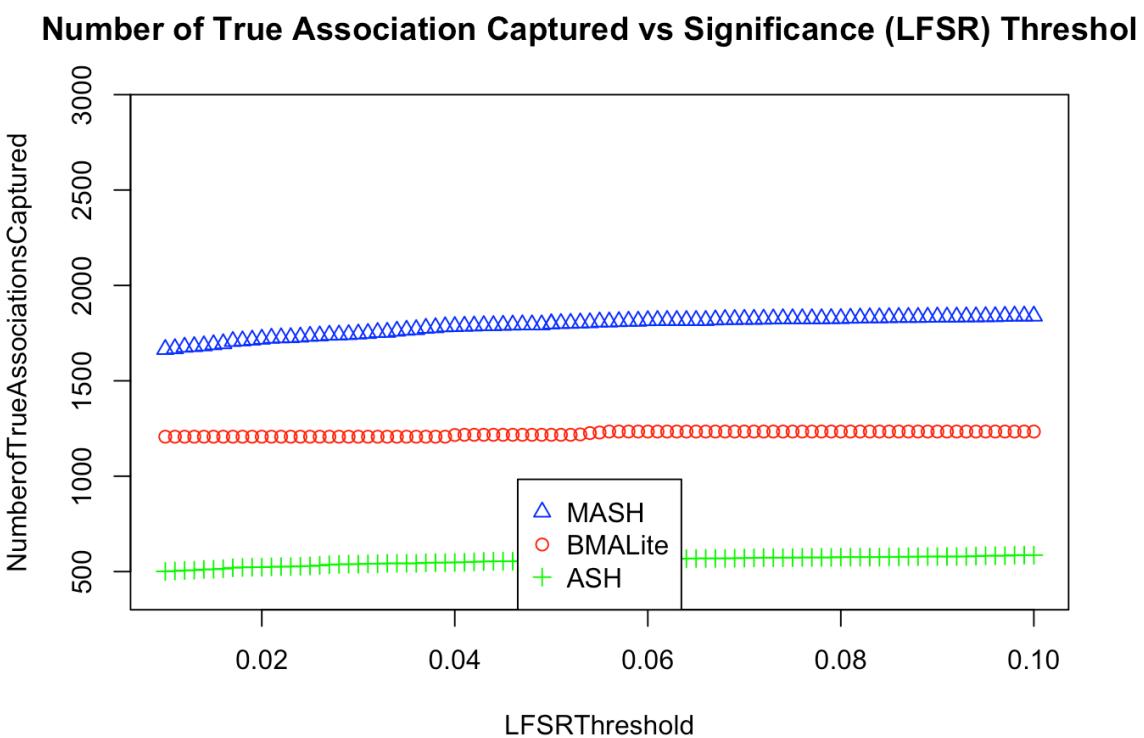
Pipeline

- JxR matrix of summary statistics and their standard errors
- **Prior:** Estimate U_k from strongest Z statistics
- Infer **prior** mixture weights from sample of ALL DATA
- Compute *posterior* **on any gene-snp pair**
- Report results on one QTL per-gene, by choosing snp with max absolute effect across tissues
- Report effect size as **E(BIData)**

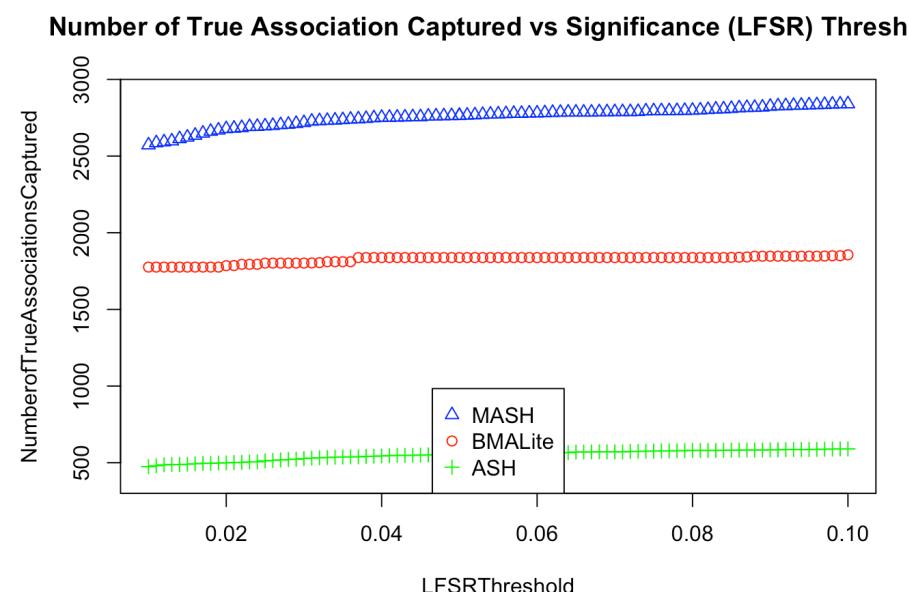
Results: Features of Method

- Power vs Accuracy in Simulations
- Adaptive Shrinkage in Real data: power increases over univariate methods

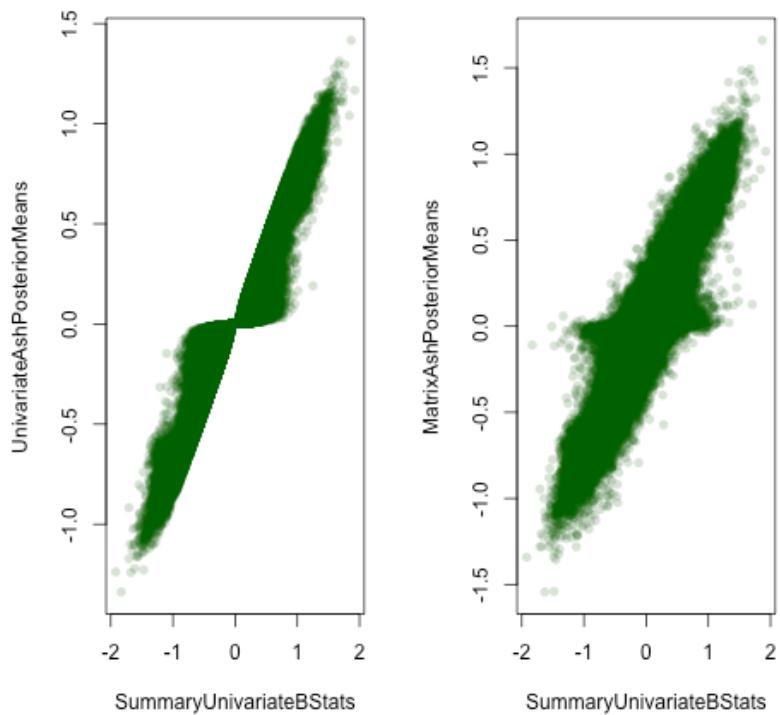
TSpecSim



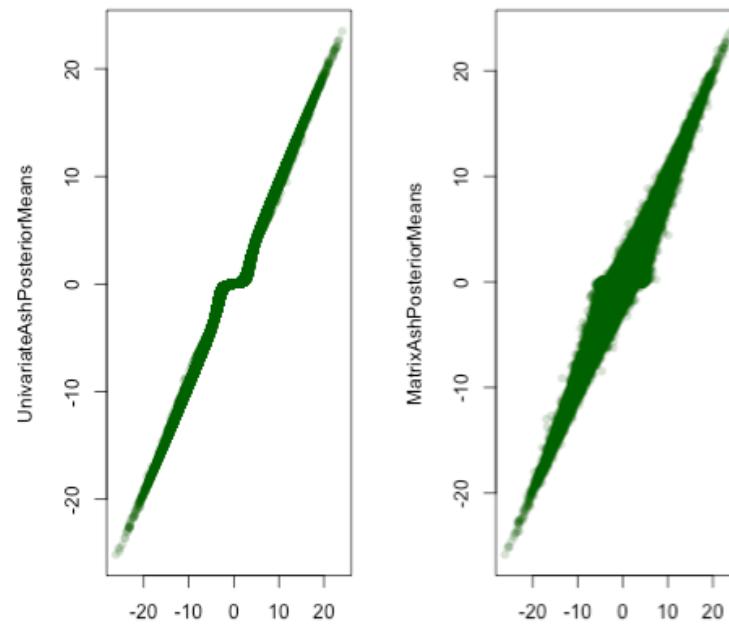
SharedSim



Univariate Ash MASH
 $E(B|Data)$ vs $B.mle$



Univariate Ash MASH
 $E(Z|Data)$ vs $Z.mle$



- Shrinkage according to abundance of small effects, standard error
- Now consider: for Z statistics of same size, nudging occurs meaning not all Z statistics are shrunk uniformly
- In this particular Data Set Sharing ***and small effects common***, ‘nudge’ effects small in some tissues but larger others towards bigger effects
- **Identify > 4x** as many significant associations
- One SNP per gene, $16K \times 44$ tissues = 707,036

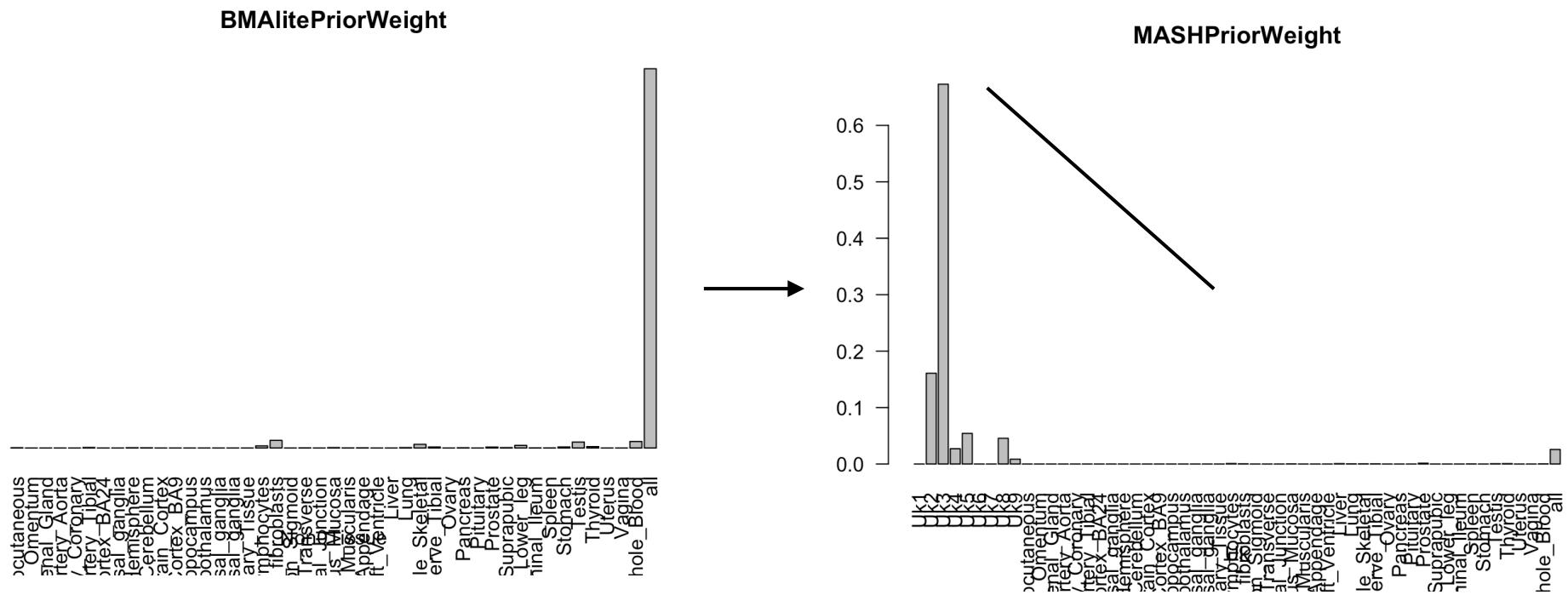
Matrix Ash Ash

Significant. b_{jr}	393414	91755
------------------------------------	---------------	-------

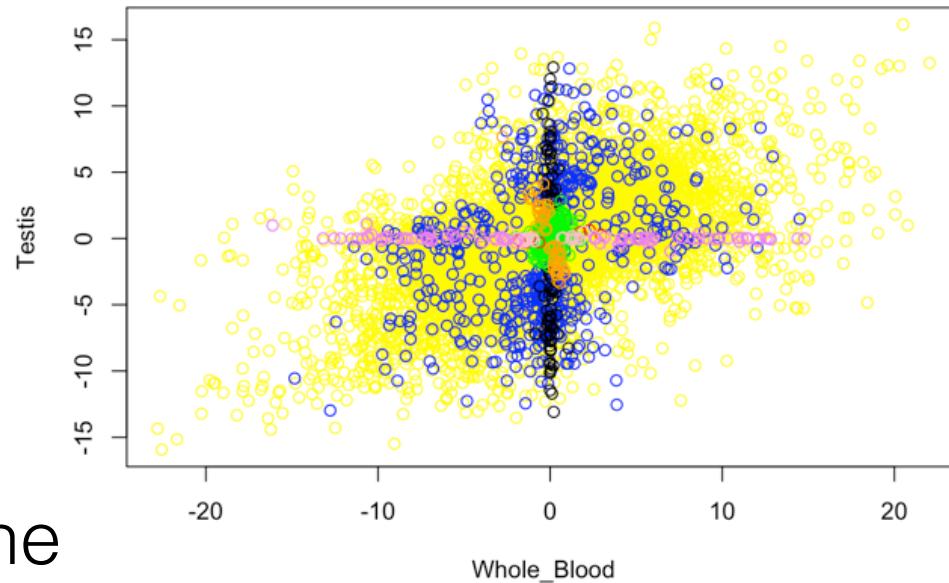
Results

New patterns of Sharing

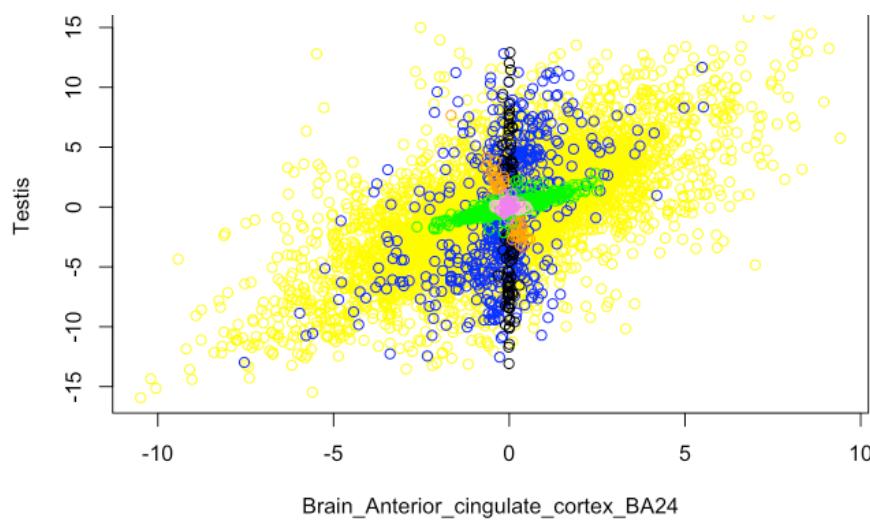
Parsing the Shared

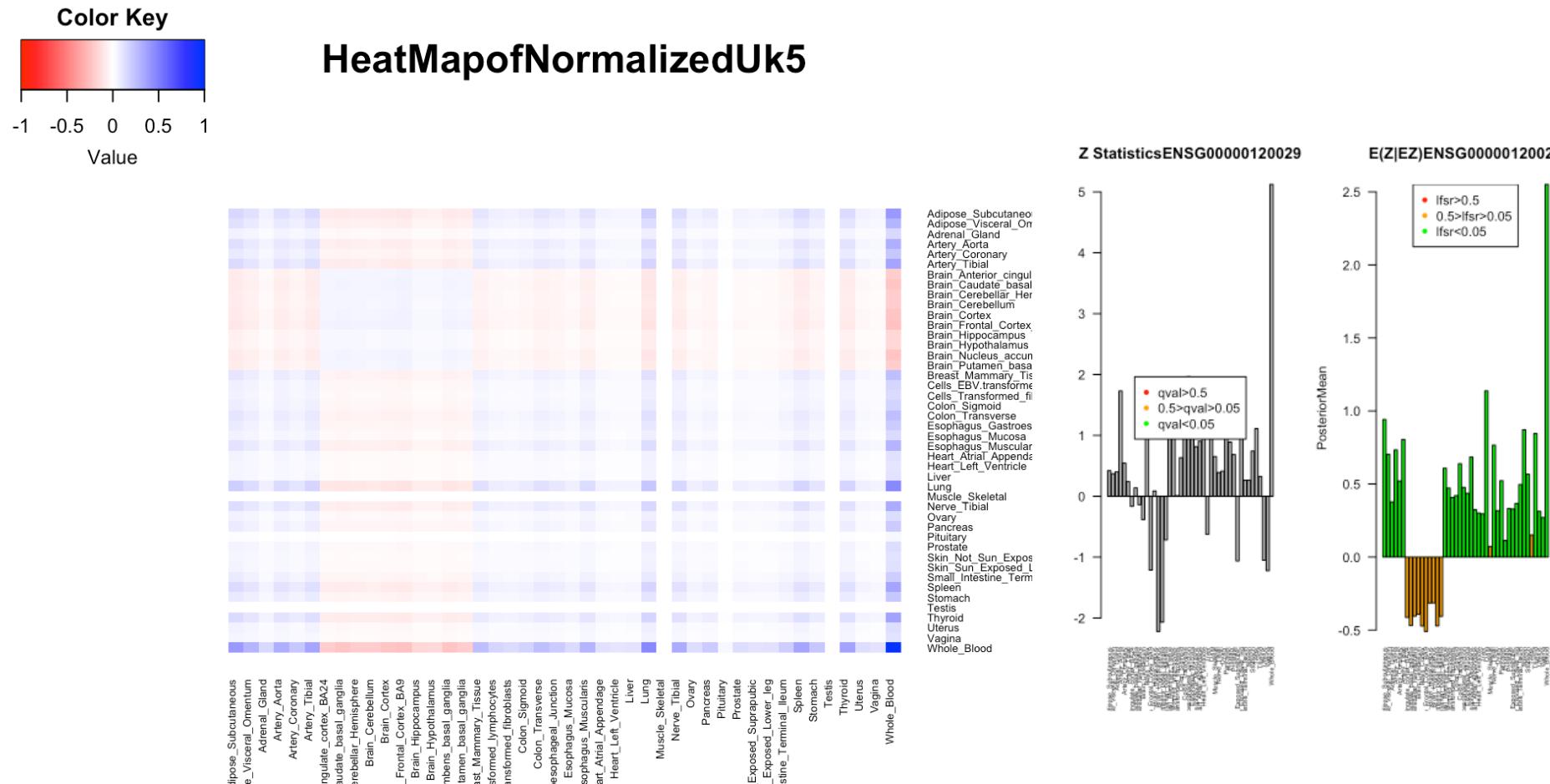


Patterns of Sharing



Critically: None
maximally
loaded on 1-1

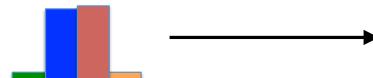
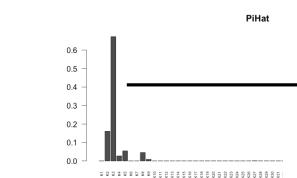




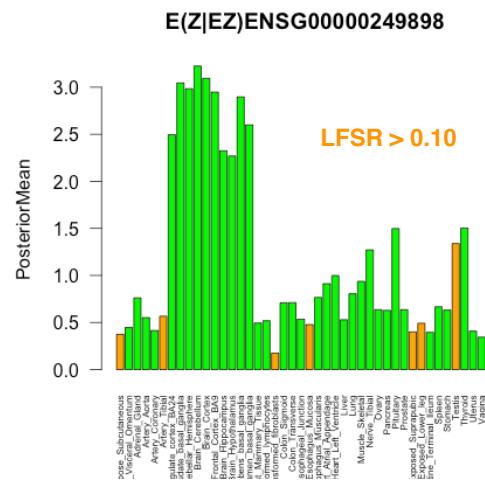
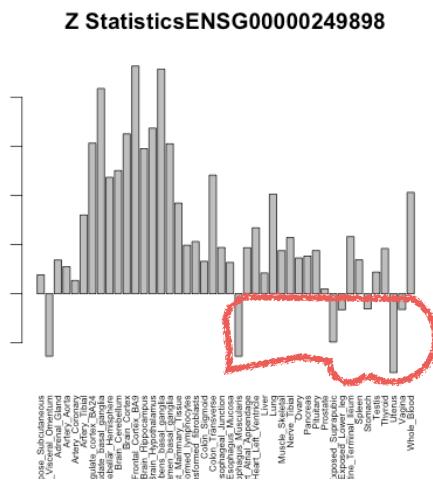
Emphasis on Sharing: What do the U_k capture?

$U_k = 3$

- Consistency in ‘sign’
- Heterogeneity in magnitude
- pattern with large effects in brain



Pattern 3 $\rightarrow U_3$



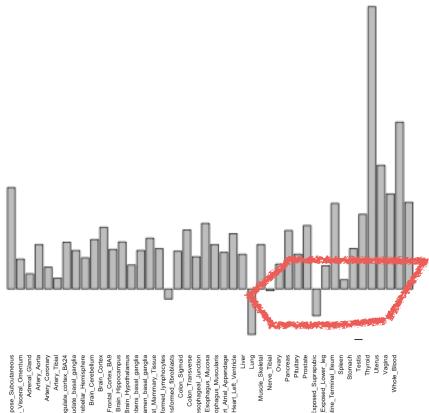
$U_k = 9$

Quantitative Tissue Specificity ...

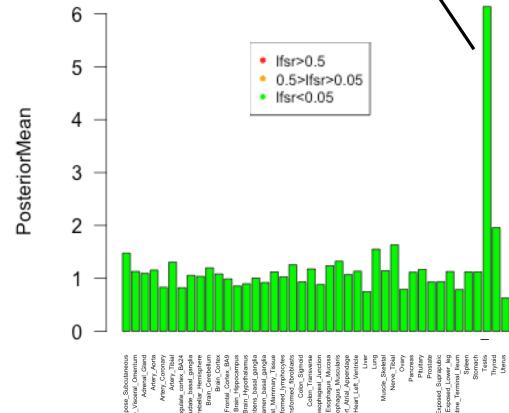
- Tissue-Specific in Testes and Whole Blood
- QUANTITATIVELY but not QUALITATIVELY
- Reverses off directions because of consistency



Z Statistics ENSG00000009830

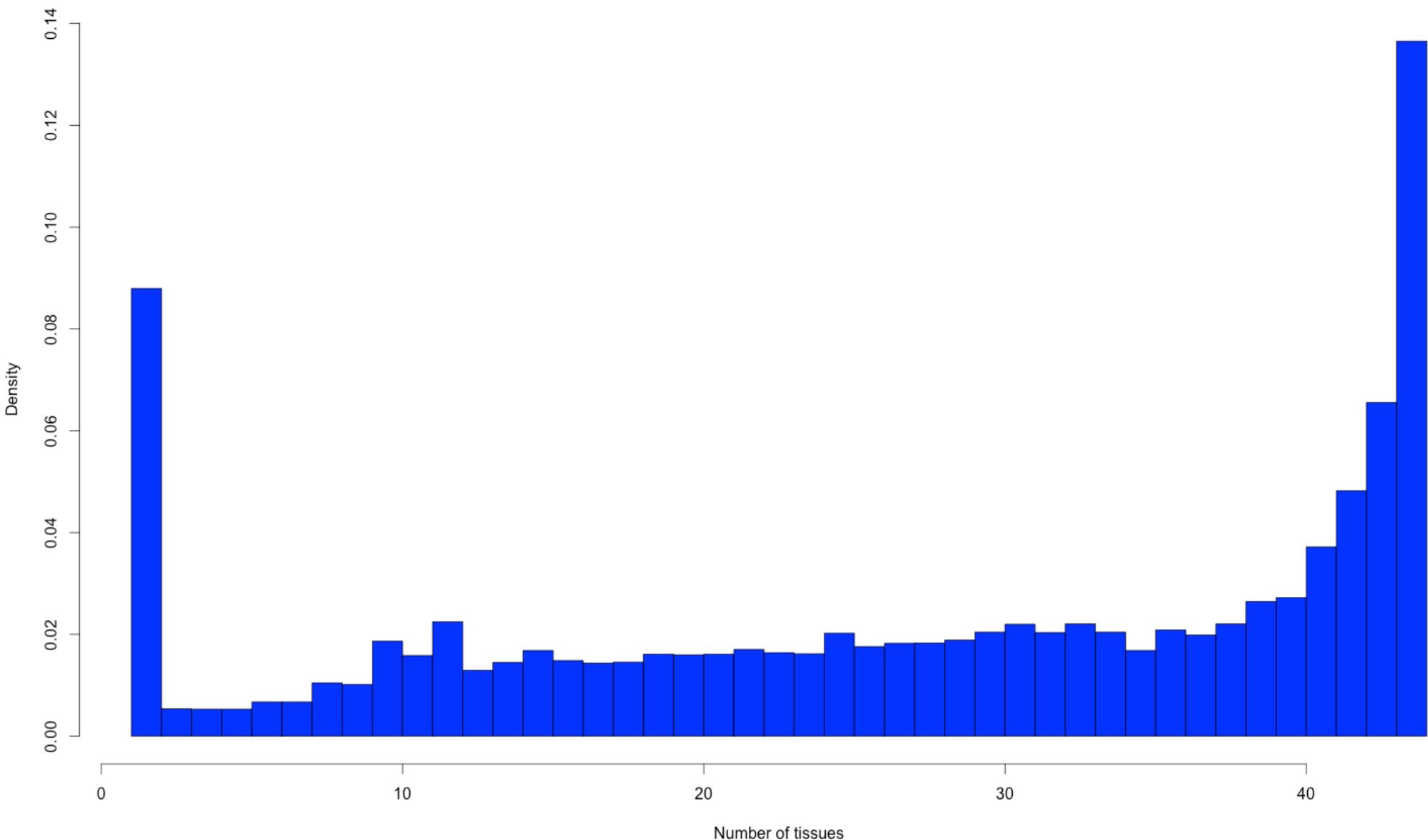


E(Z|EZ) ENSG00000009830

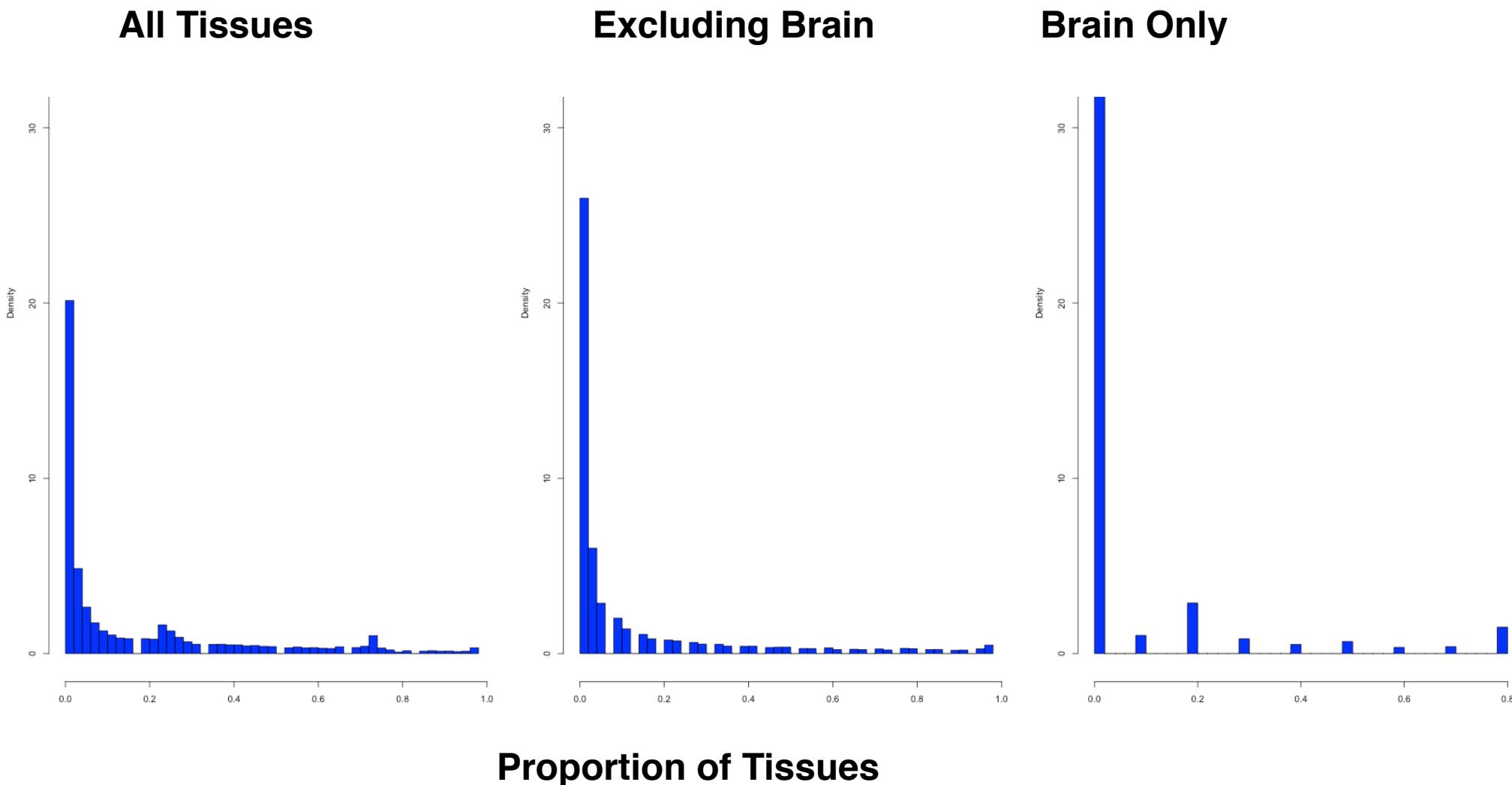


Quantitative Heterogeneity Plots

Number of Tissues in Which eQTL is Significant

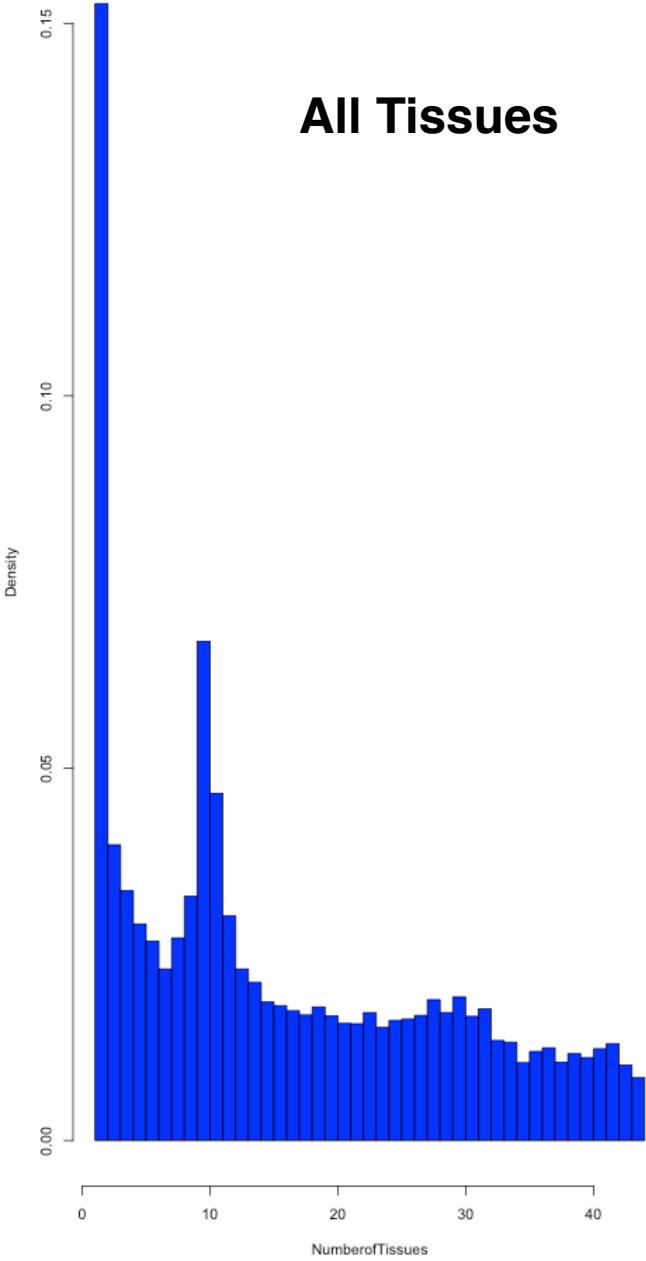


Proportion of Tissues in which Sign different than Max Effect

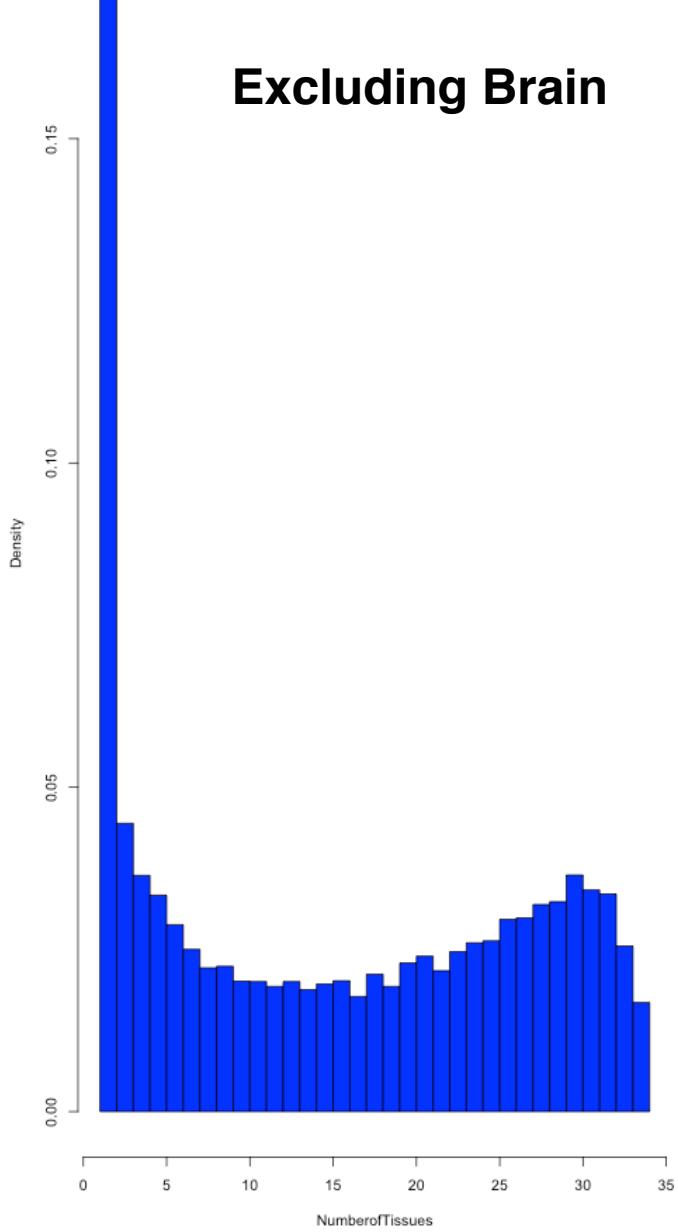


Number of Tissues in which Effect > 50% Max Effect

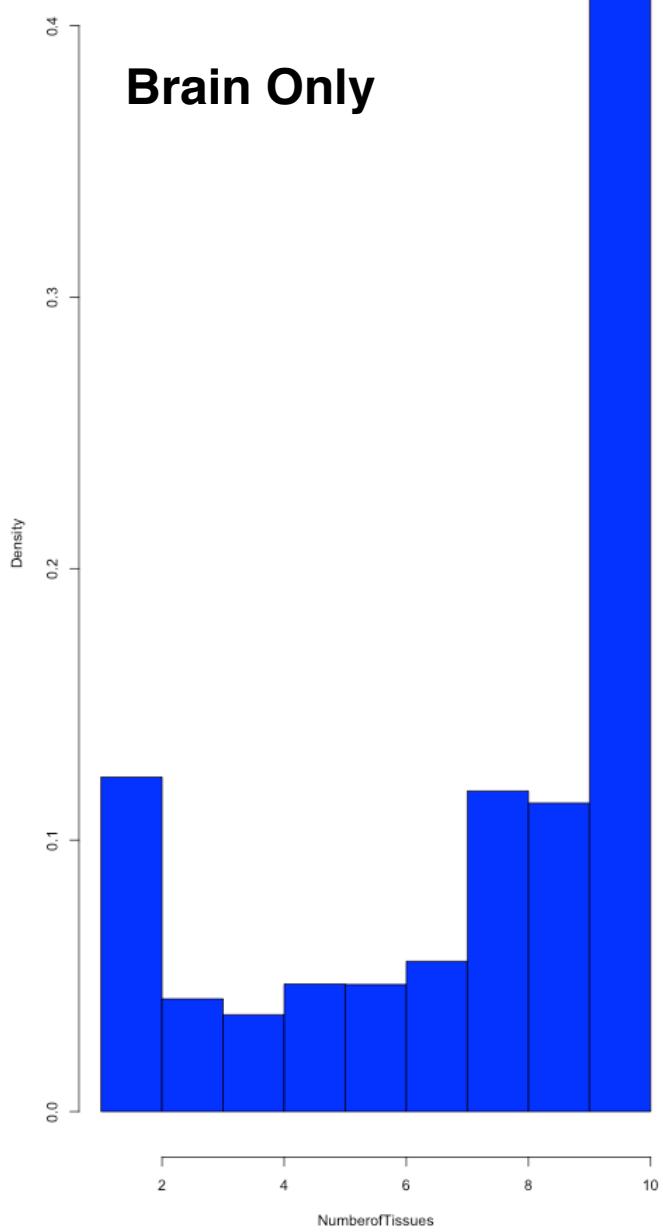
All Tissues



Excluding Brain

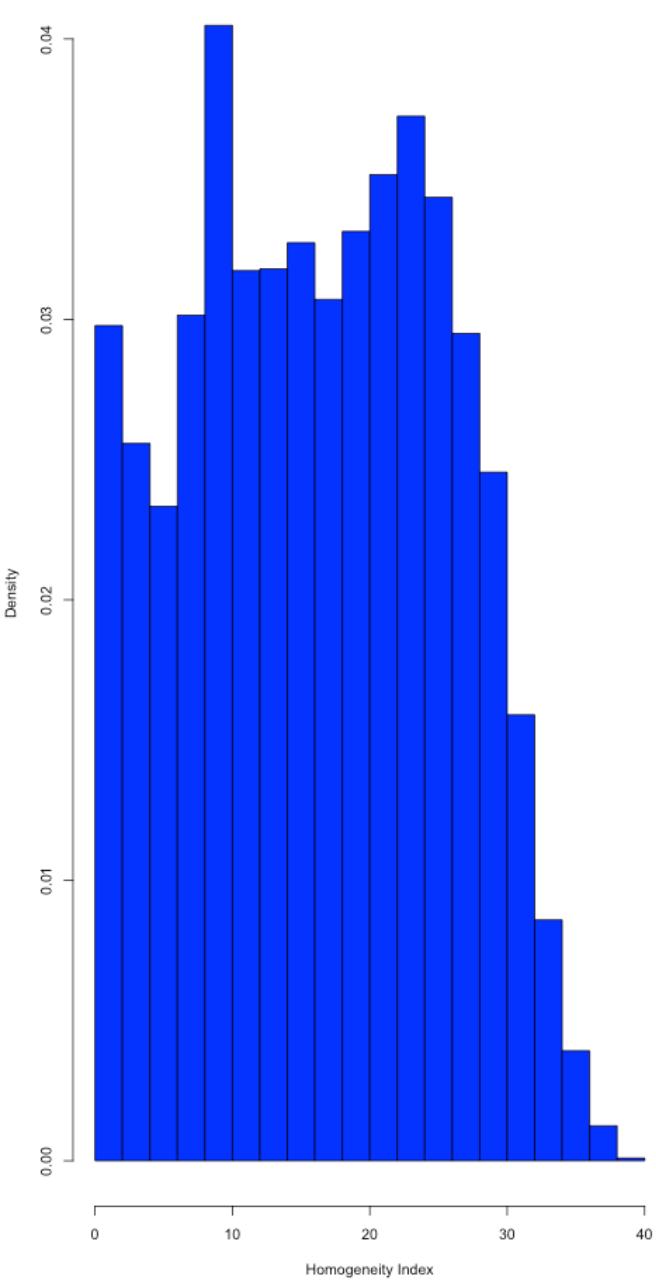


Brain Only

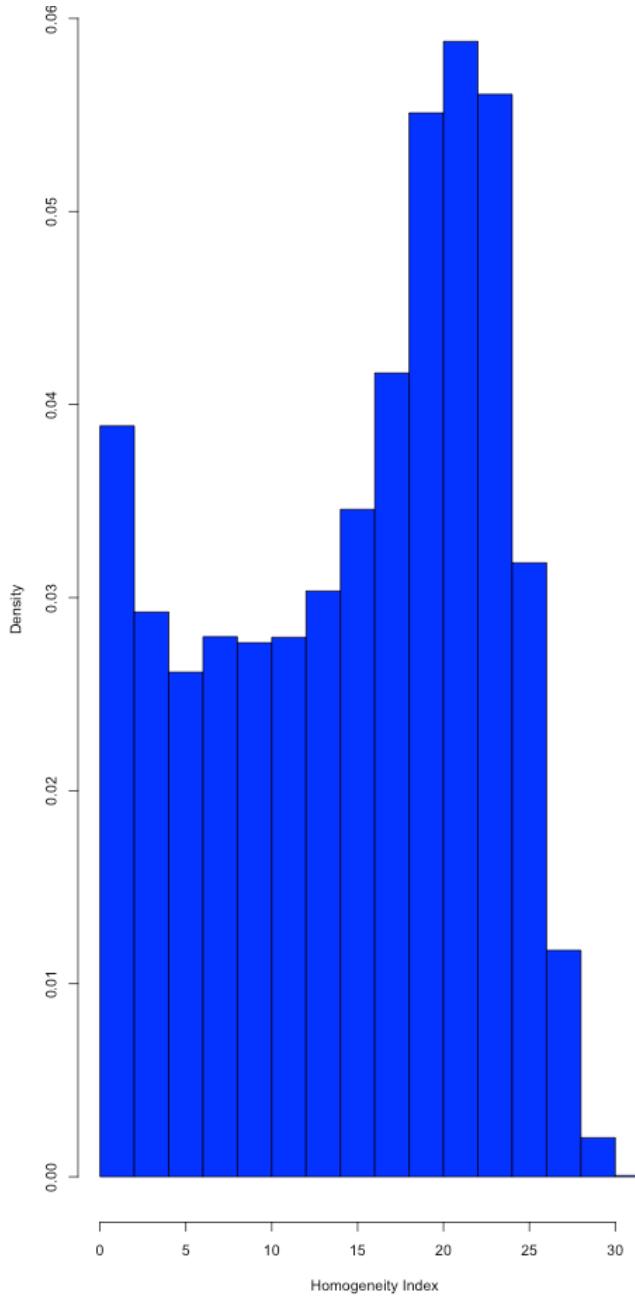


Sum of Normalize Bjr

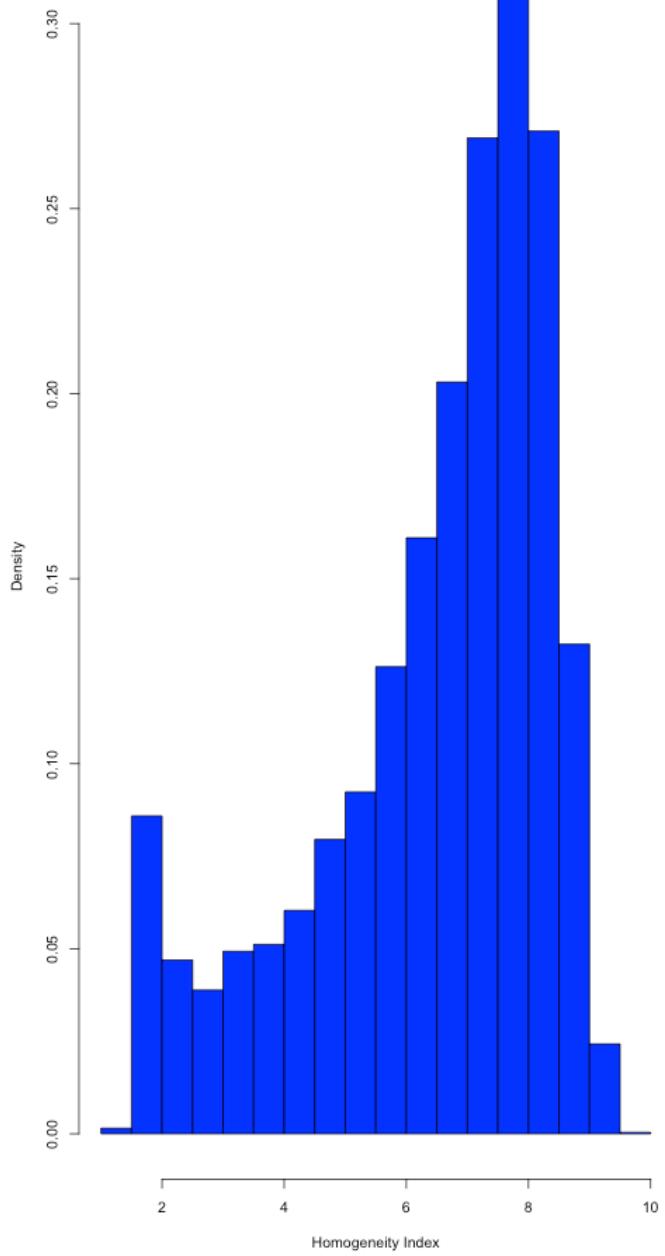
All Tissues



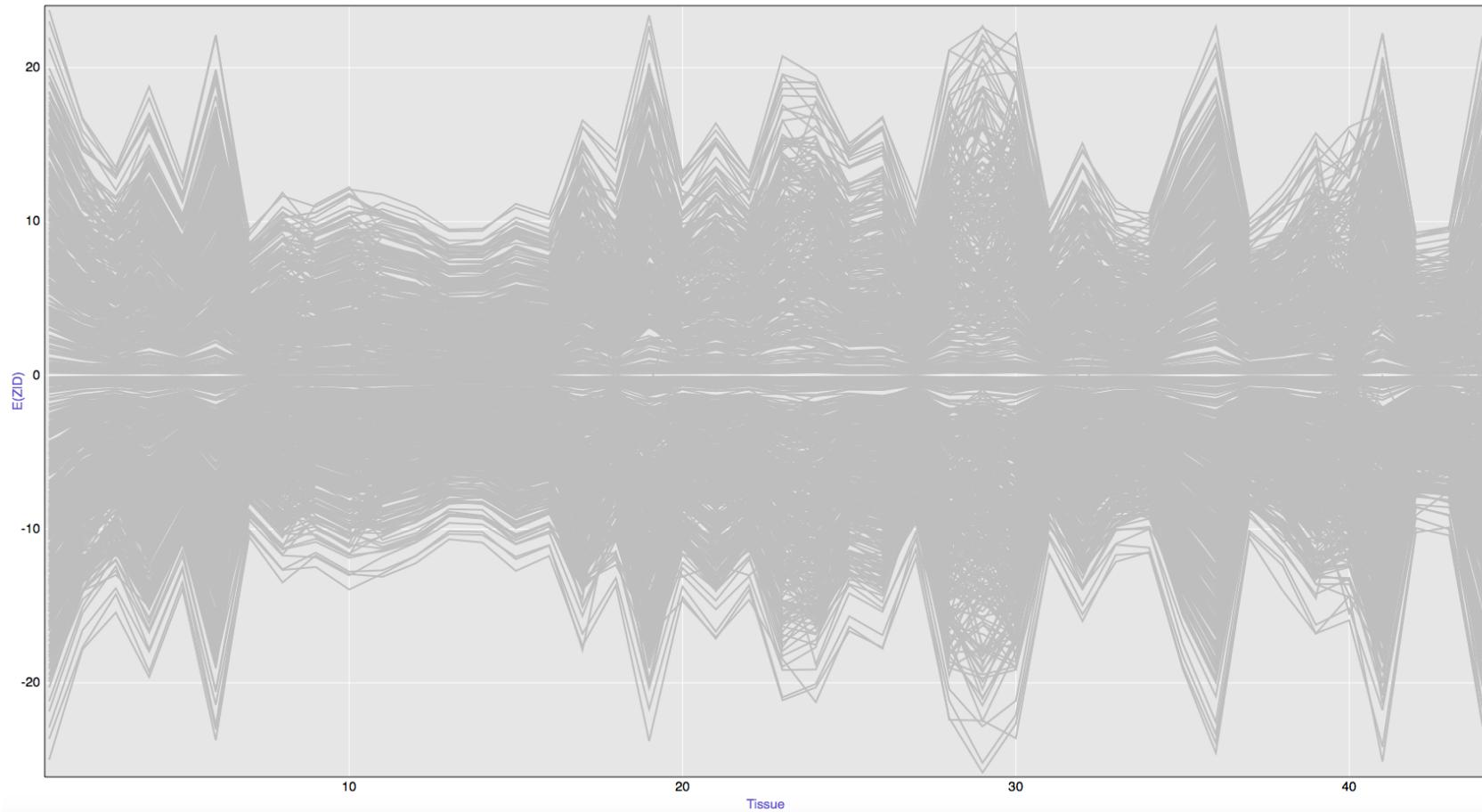
Excluding Brain



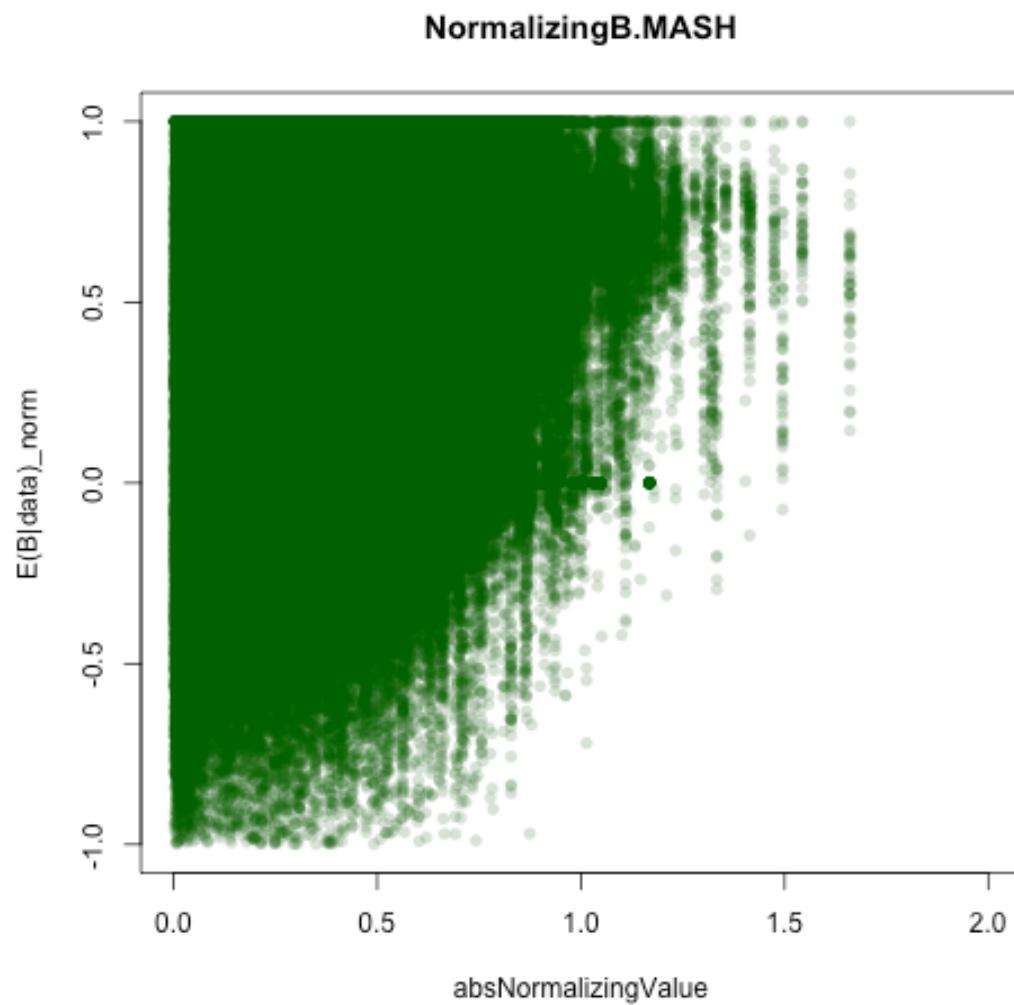
Brain Only



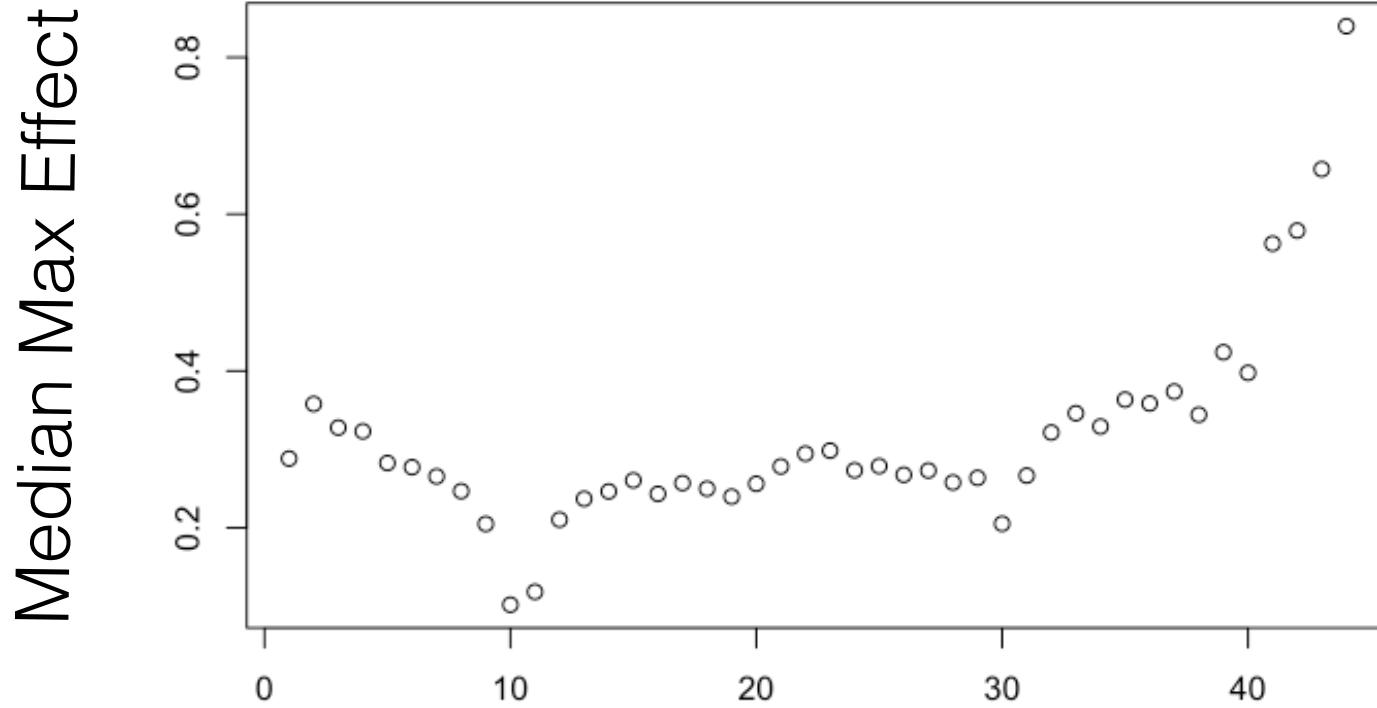
Homogeneous (i.e., hindex>40)



Homogeneity Index

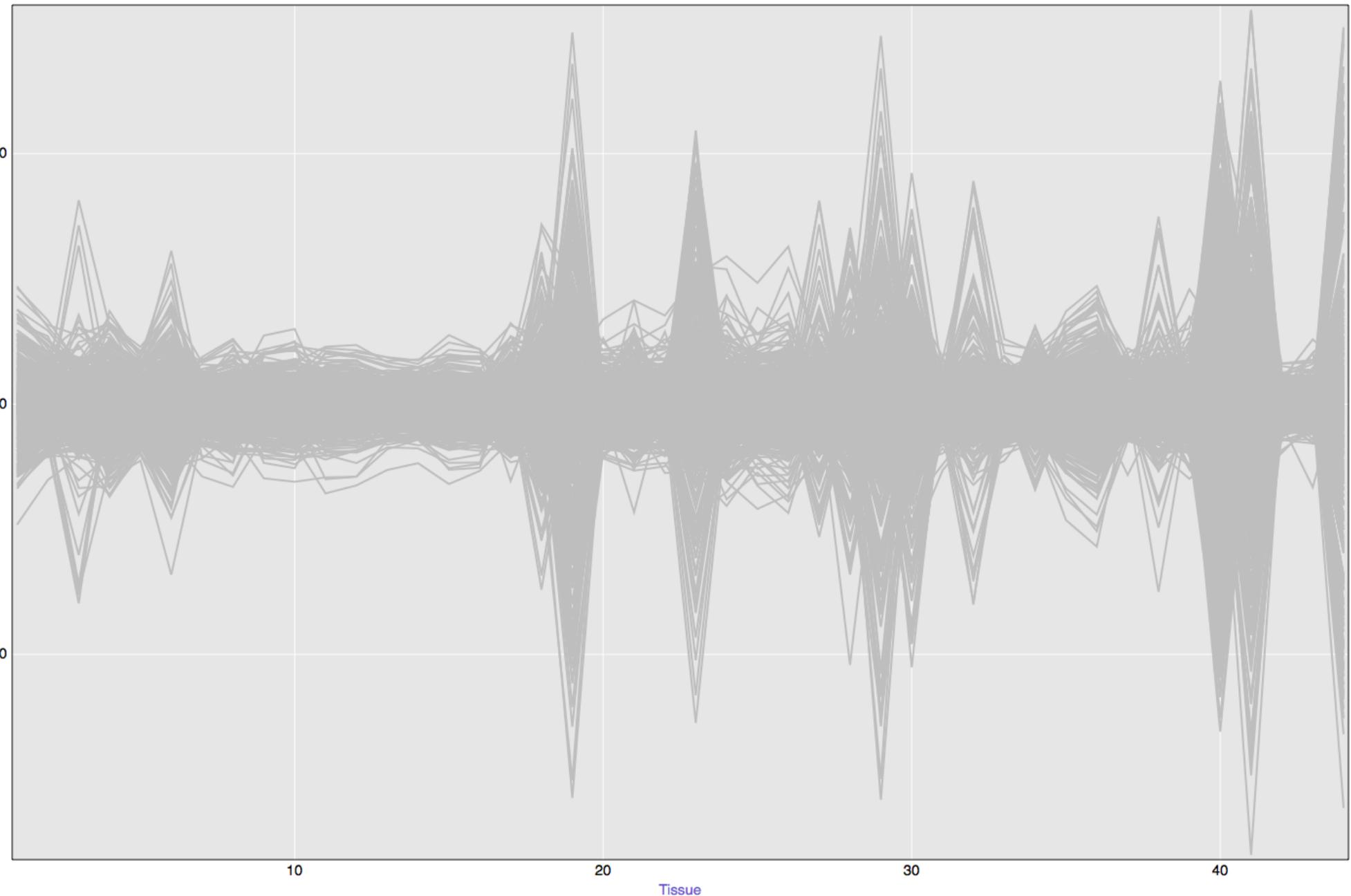


Median Max Abs Effect for eQTL with 's' homogenous tissues

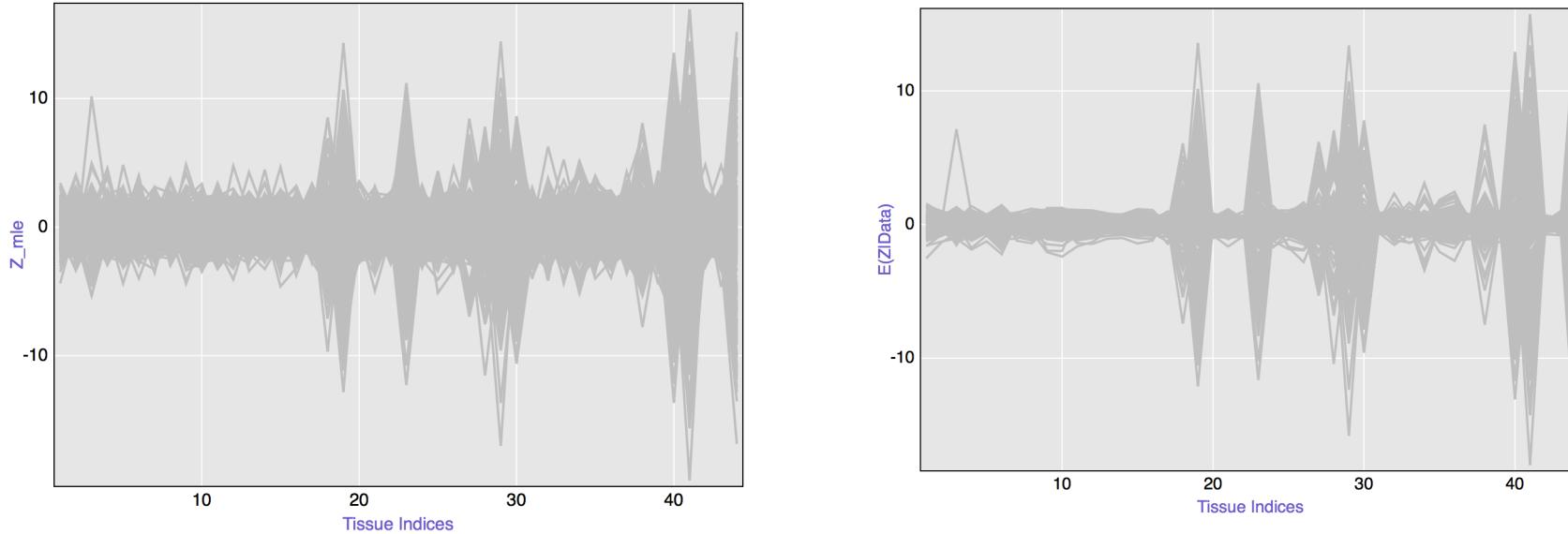


Number of Tissues That are 50% of max effect

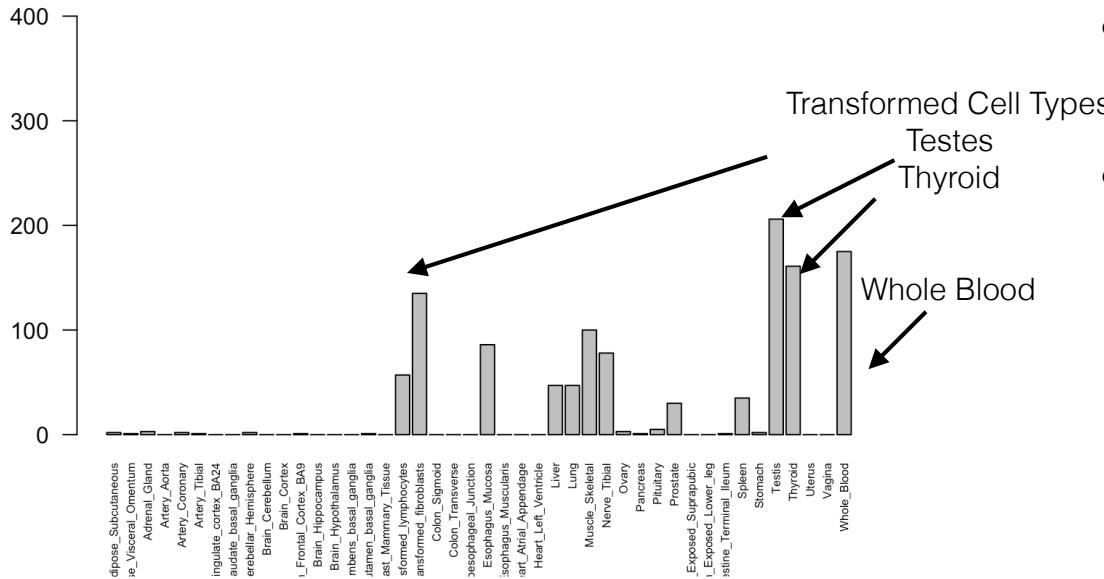
heterogenous (i.e., h.index<2)



Tissue Specificity



Number of eQTL

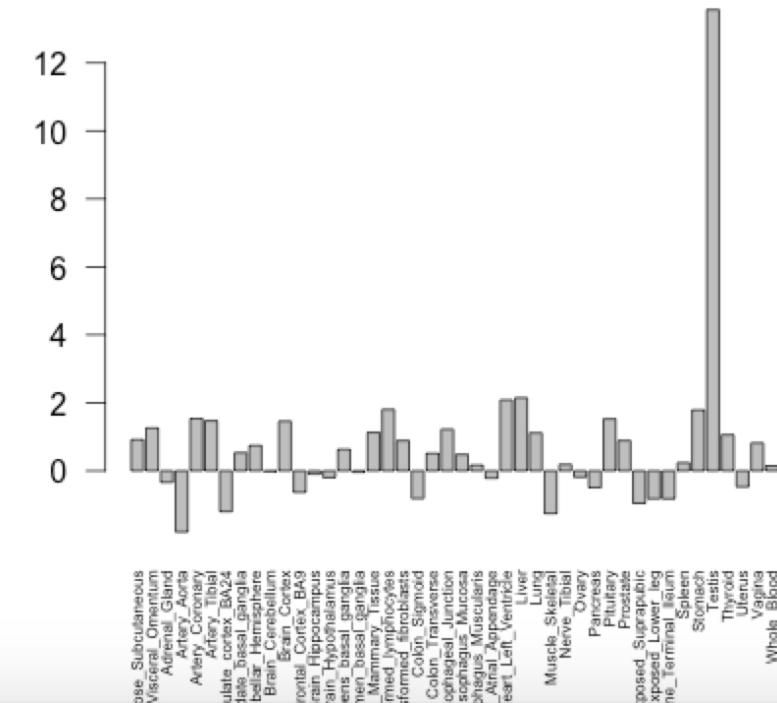


- ‘Smoothing’ of tissue specific effects
- Despite large amounts of sharing, still able to capture some patterns of ‘tissue specificity’

But also Tissue specificity *qualitatively* ...

- Enforced through '***eqtlbma-lite***' matrices 10:54 and 'learned' through some of our dimensional reduction matrices

Z Statistics ENSG00000131848



E(Z|EZ) ENSG00000131848

