

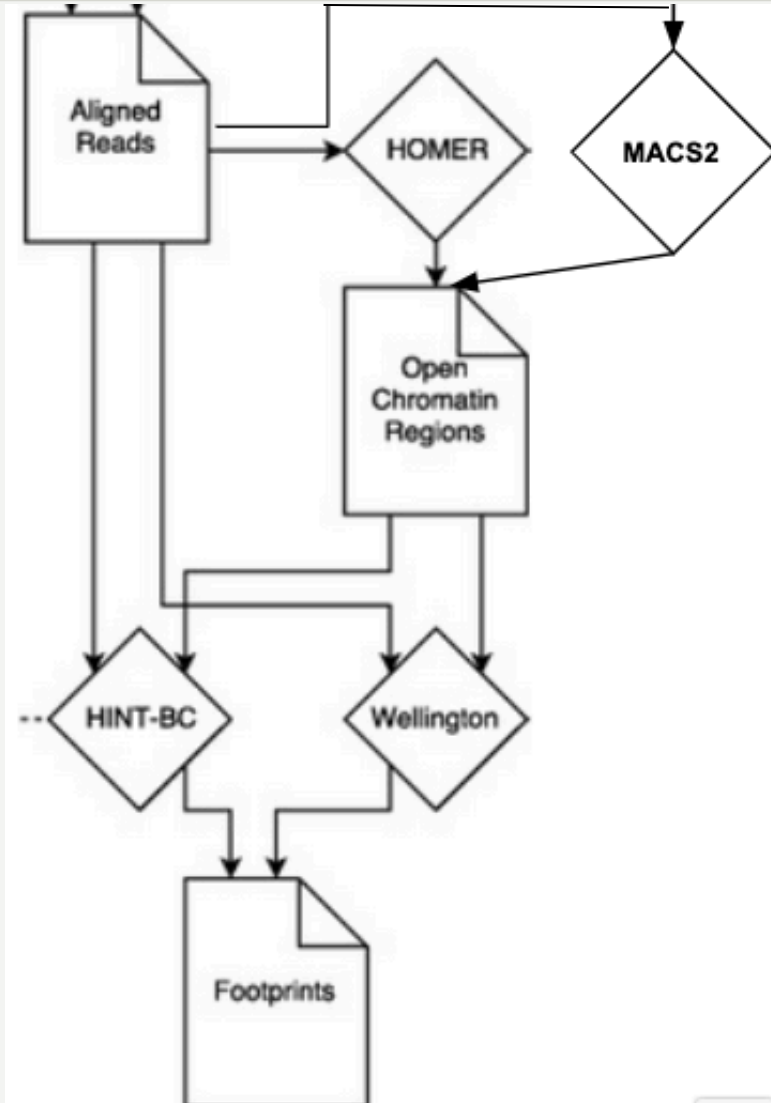
ATAC-seq evaluation

OS Projektvortrag, 6.12.



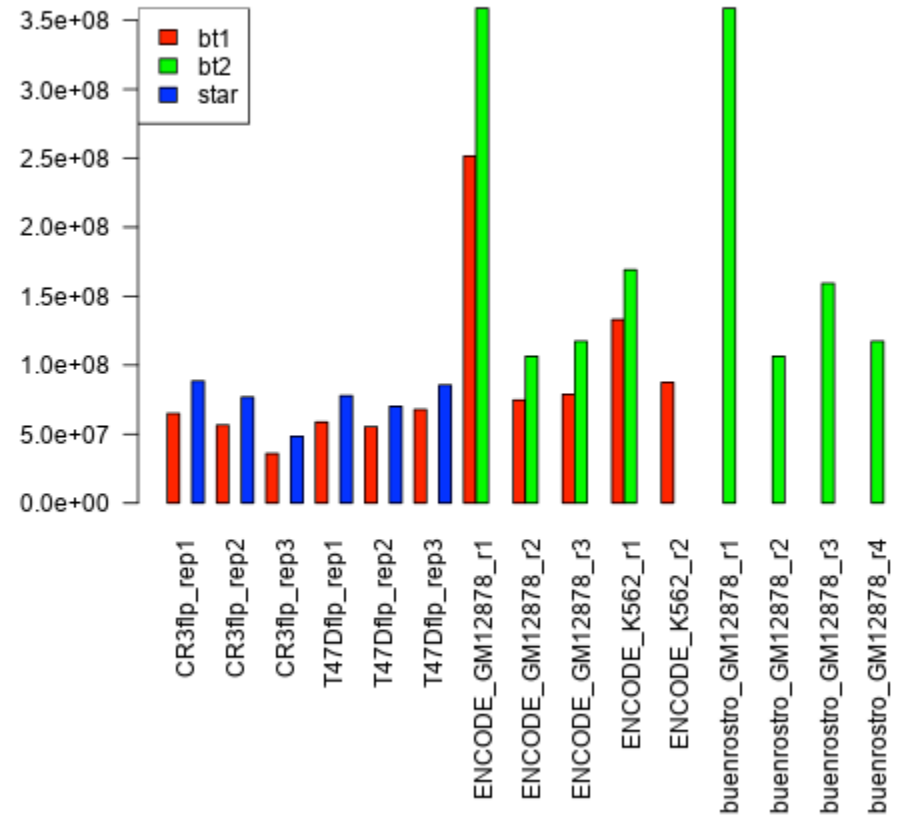


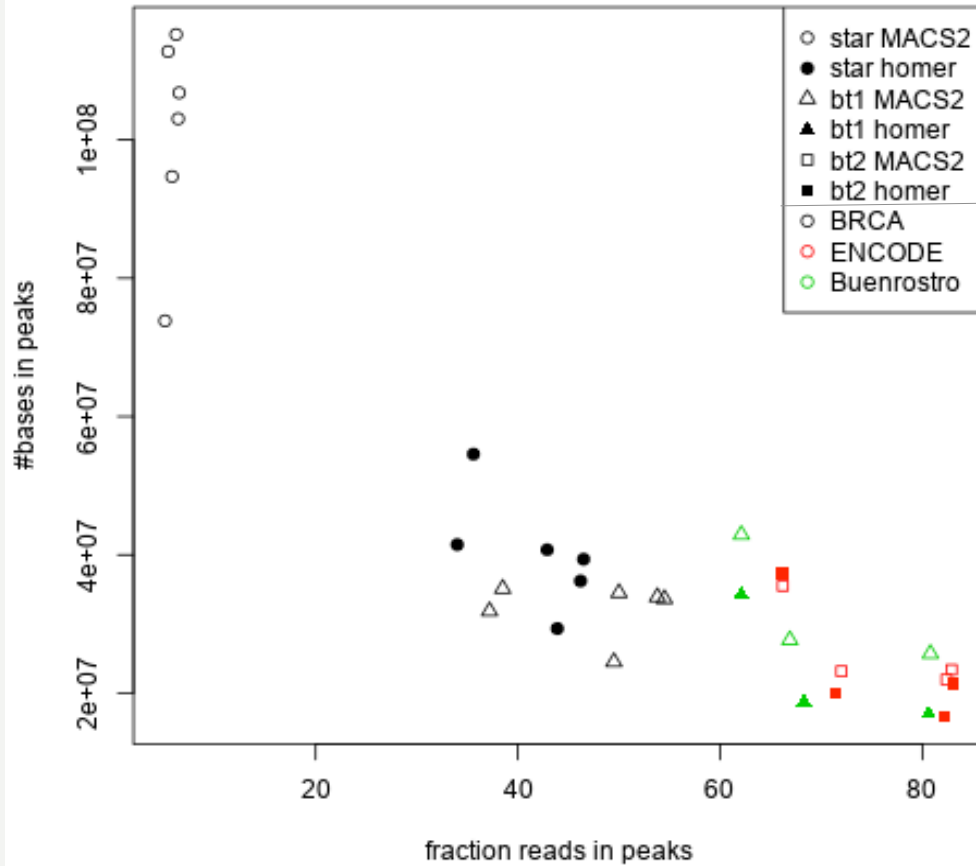
- ATAC-seq promises insights into regulation
- But how far is it possible?
- no good evaluation paper
- most biological papers stop at DHS
- use datasets with ChIP-seq for multiple TFs and ATAC-seq with replicates to evaluate footprint calling
- dataset should also be differential
- for different combinations of DHS and footprint callers
- also analyze reproducibility using replicates



- Breast Cancer:
 - ATAC-seq with 3 replicates
 - WT (T47D) and mutated GATA3 (CR3)
 - ChIP-seq for N/C-GATA3, FOXA1 and ERalpha
- ENCODE:
 - Schep et al. 2015
 - 3 replicates for GM12878, 2 for K562
 - ChIP-seq from ENCODE
- Buenrostro:
 - Buenrostro et al. 2013
 - 4 replicates for GM12878
 - ChIP-seq from ENCODE

Sequencing depth





Fraction of reads in DHS peaks
as quality measure

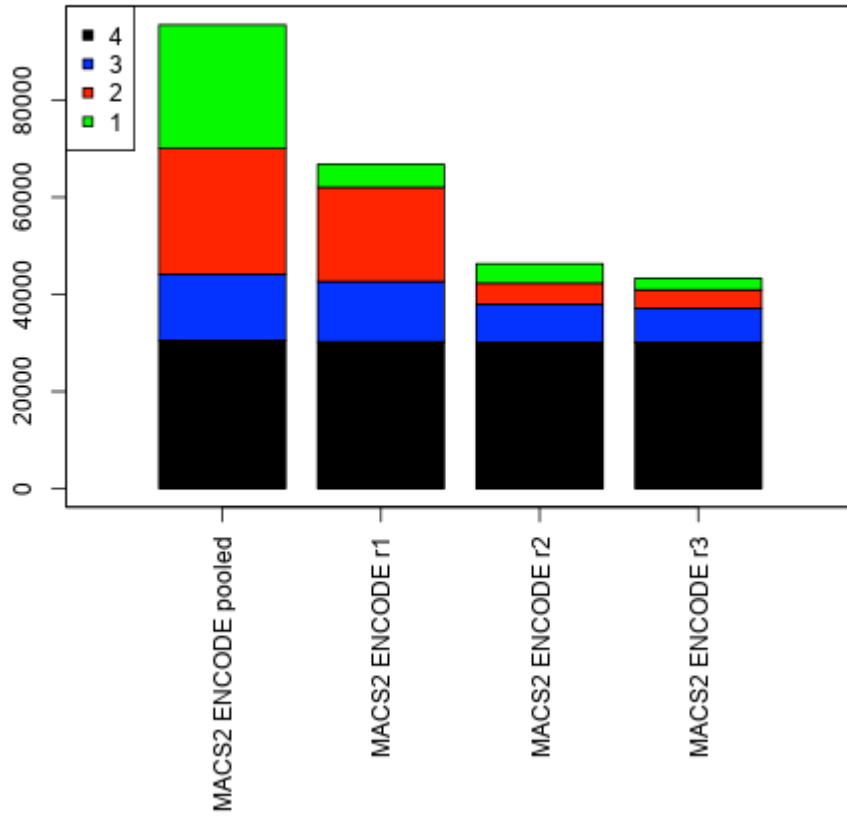
value around 40% considered
good



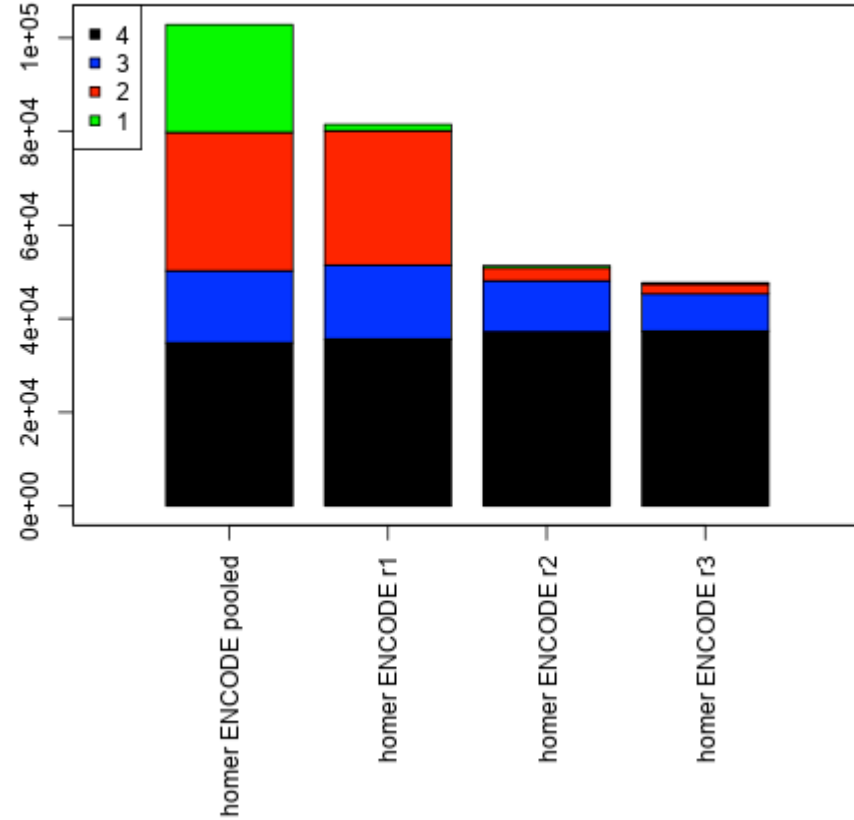
REPRODUCIBILITY



MACS2



homer

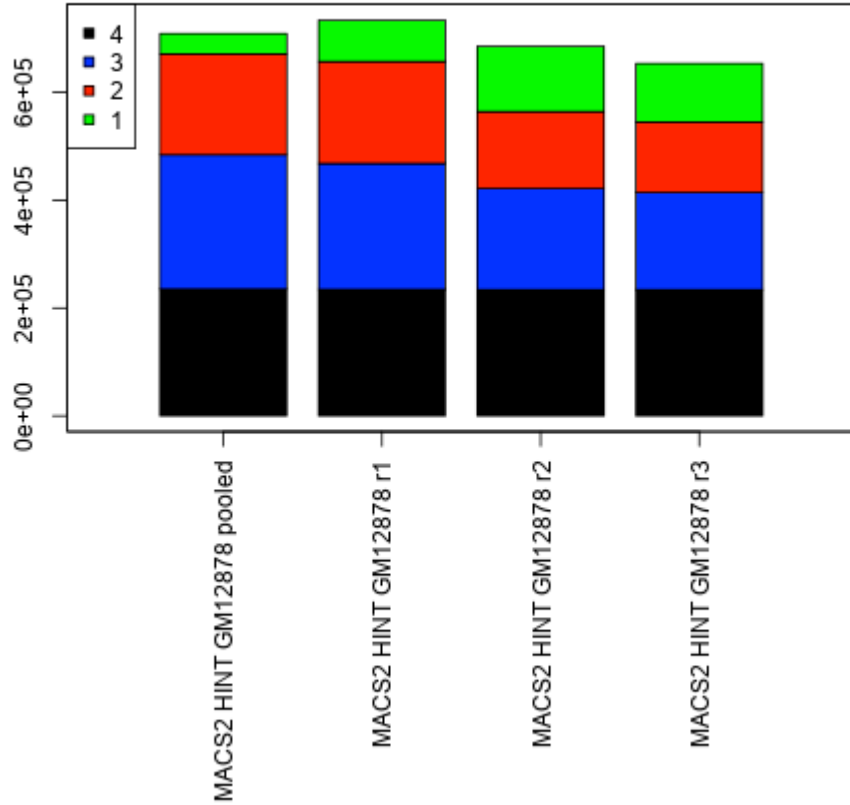


higher sequencing depth for r1 (250 mio vs 100 mio)

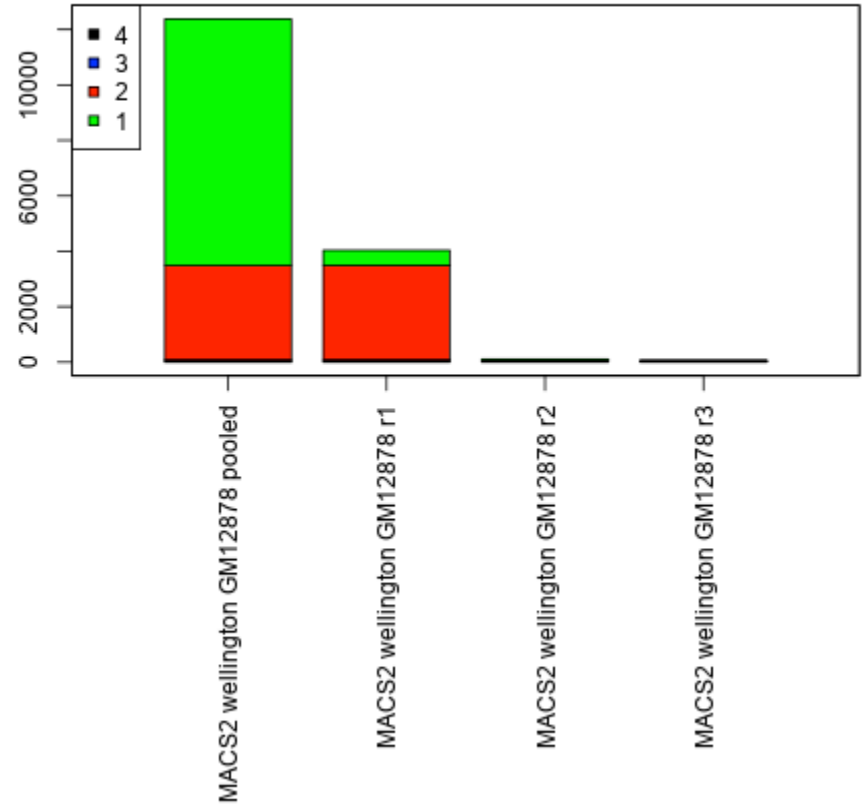
ENCODE dataset



MACS2 HINT



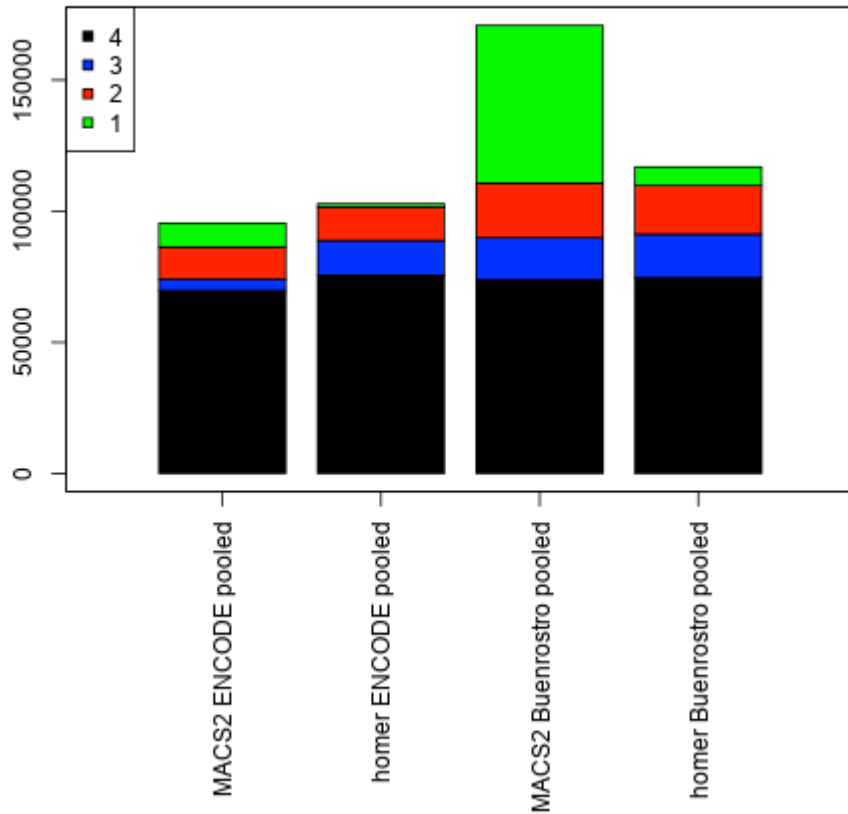
MACS2 wellington



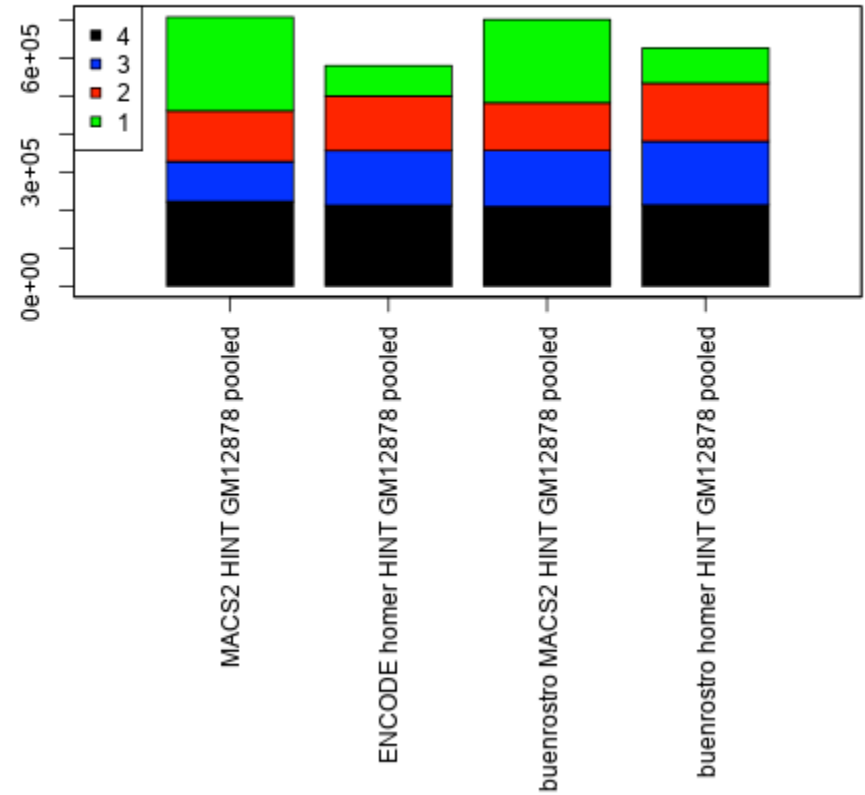


GM12878 cell line measured both in ENCODE and buenrostro datasets

DHS
(pooled replicates)

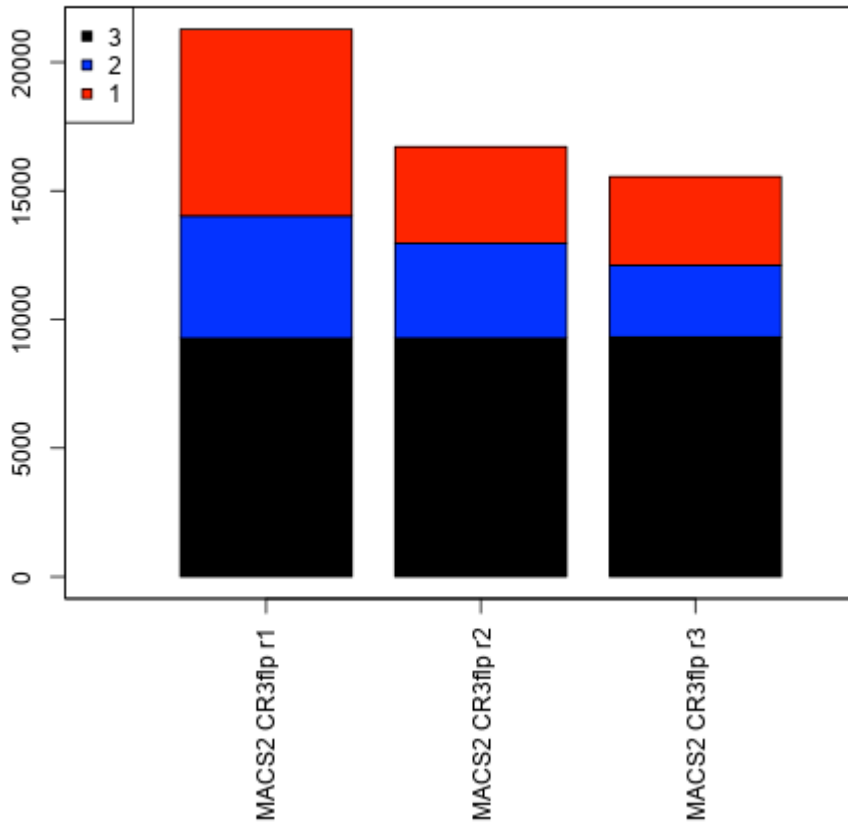


footprints
(pooled replicates)

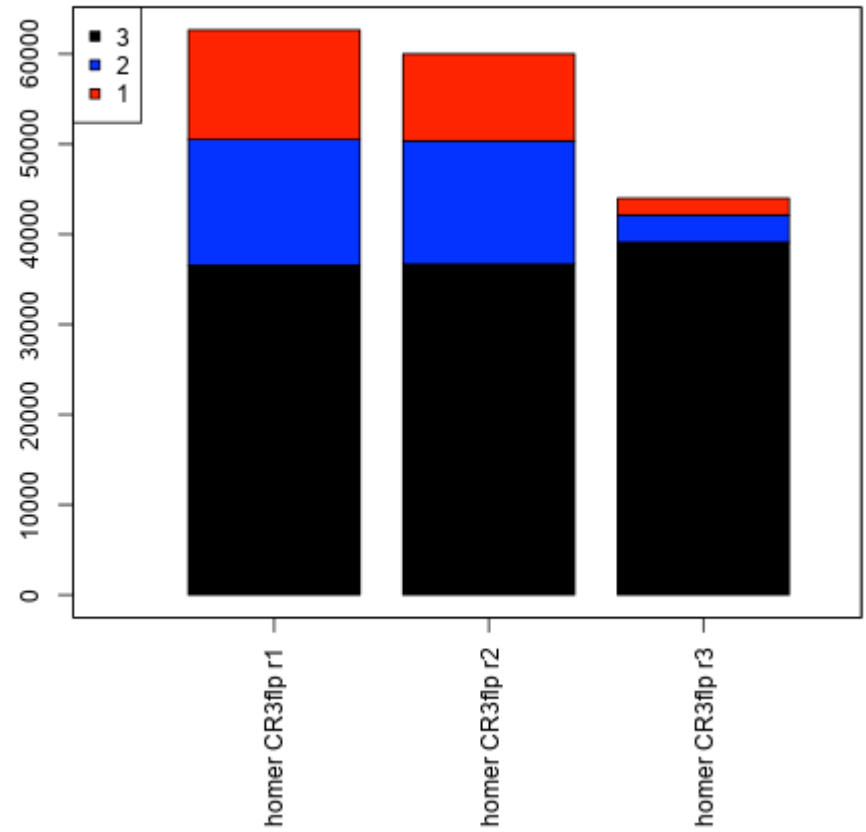




MACS2

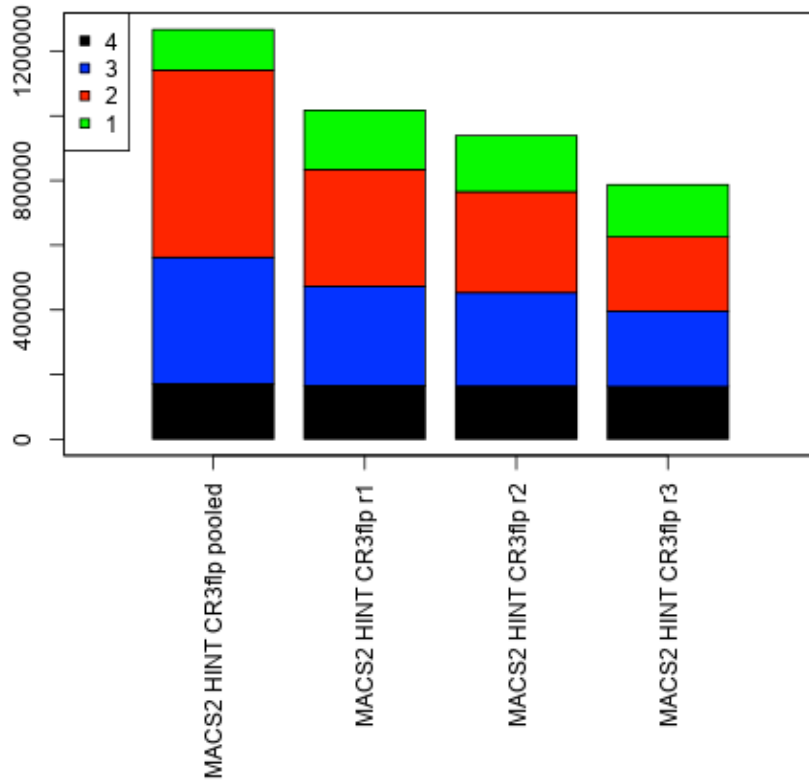


homer

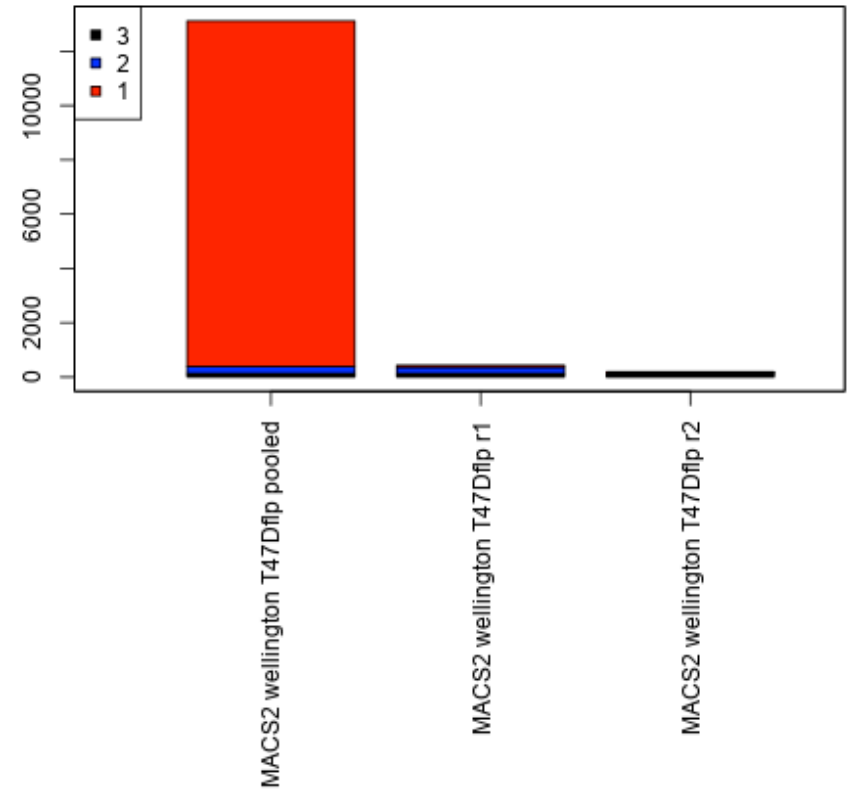




HINT

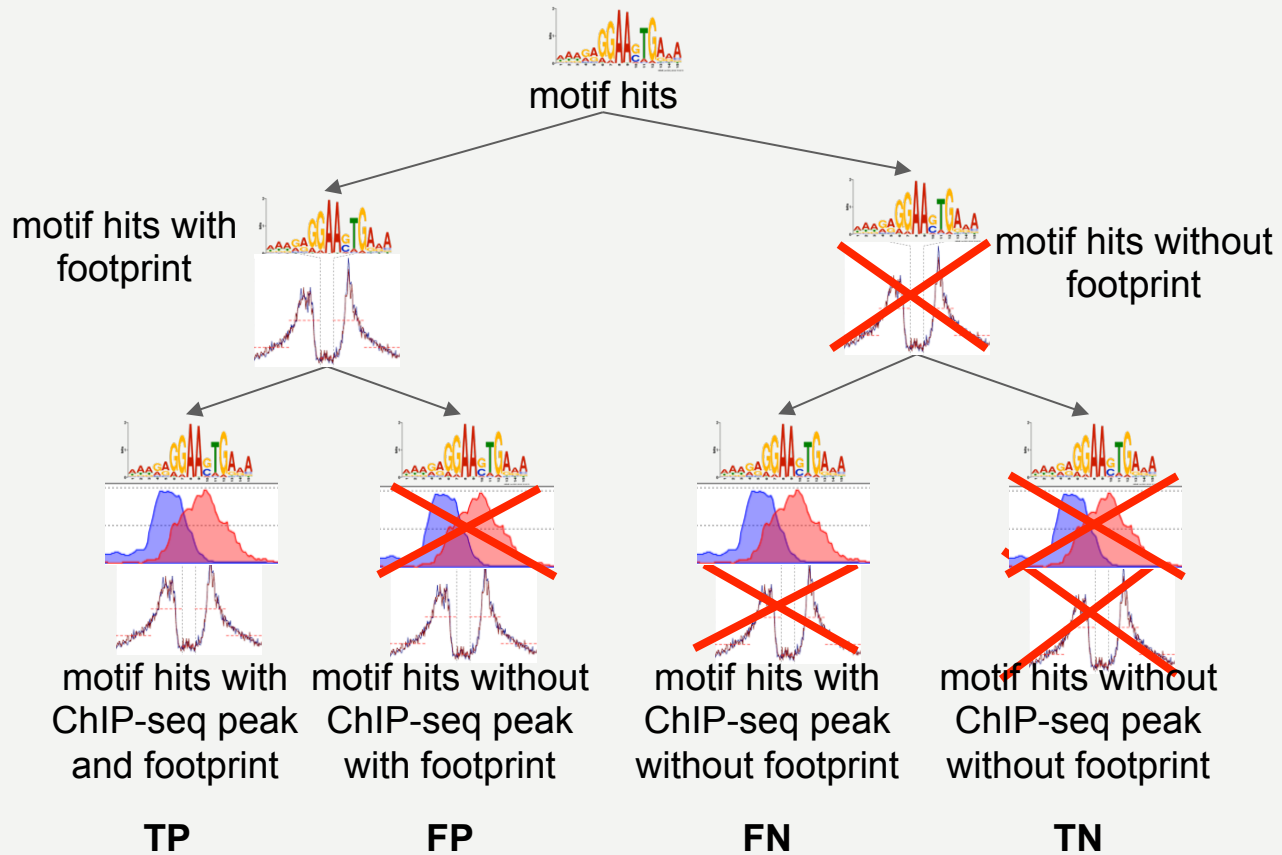


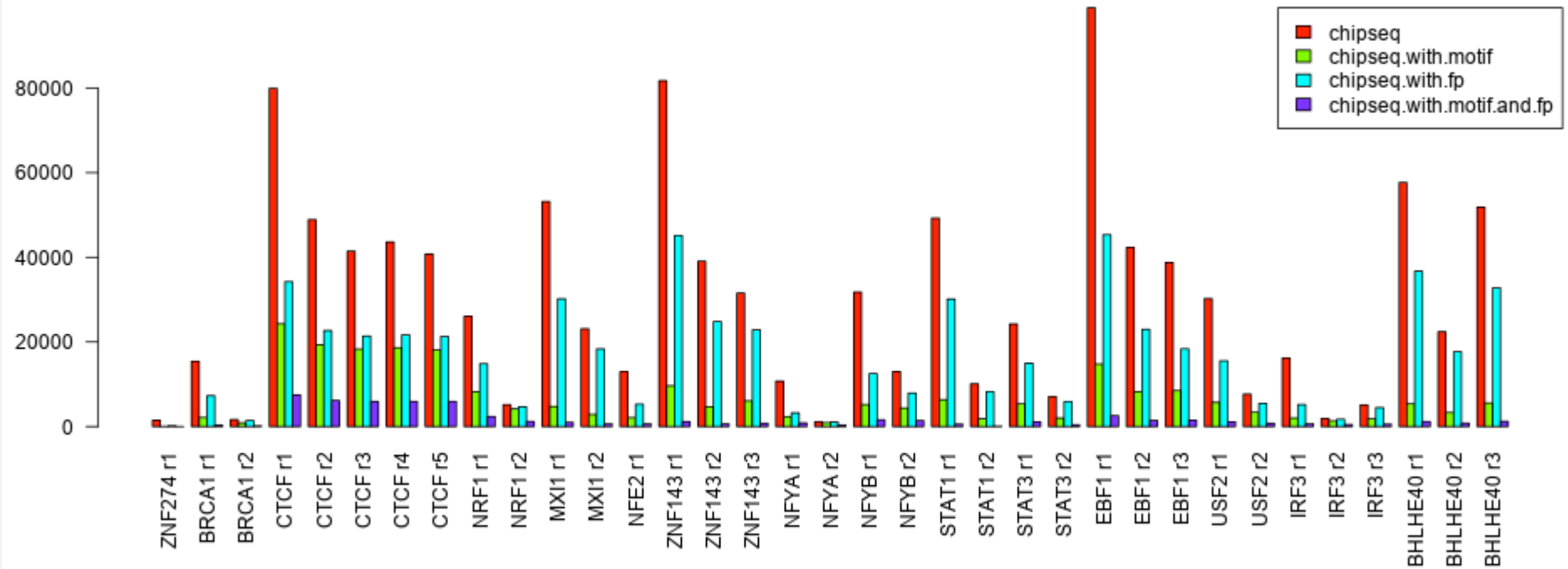
wellington





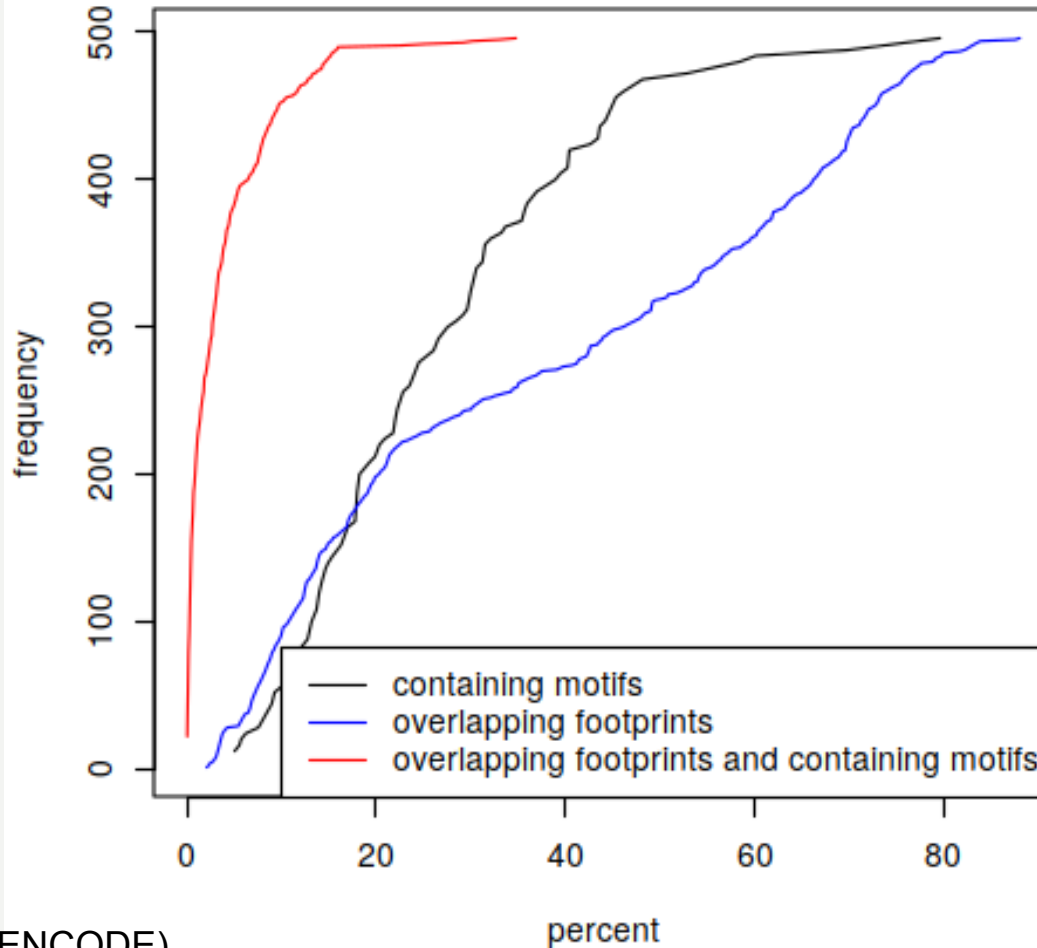
EVALUATION

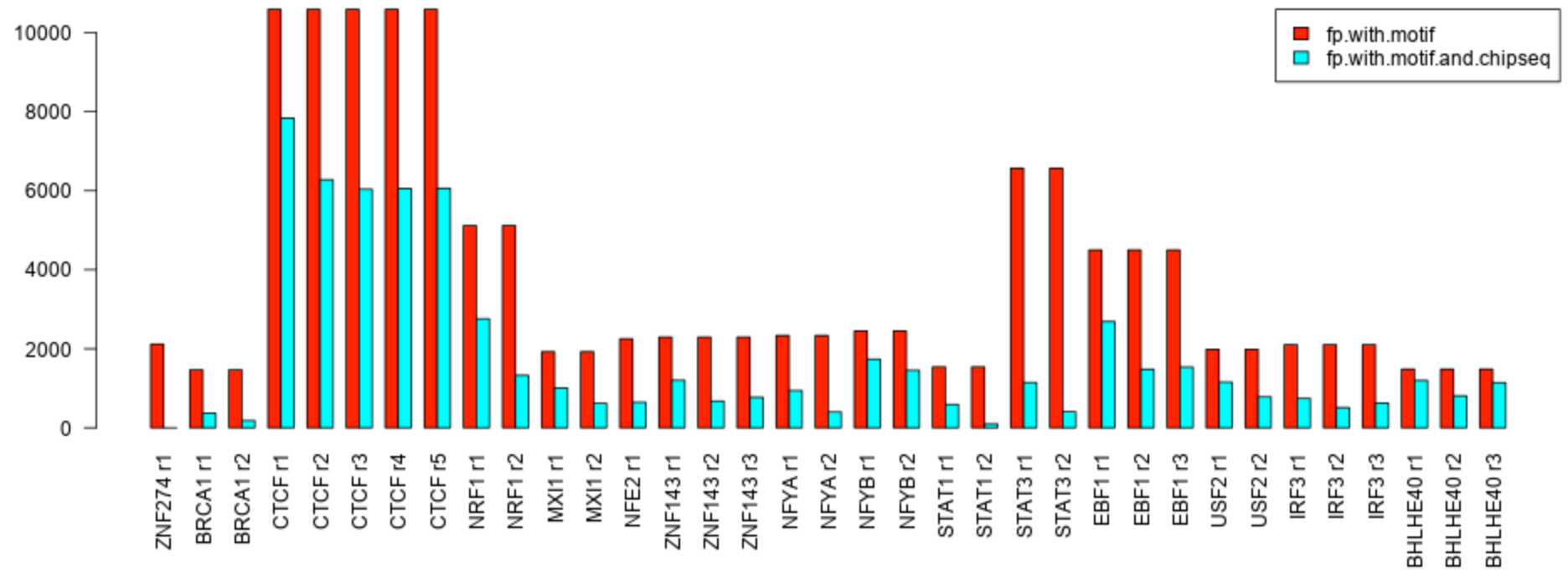






ChIP-seq peaks...





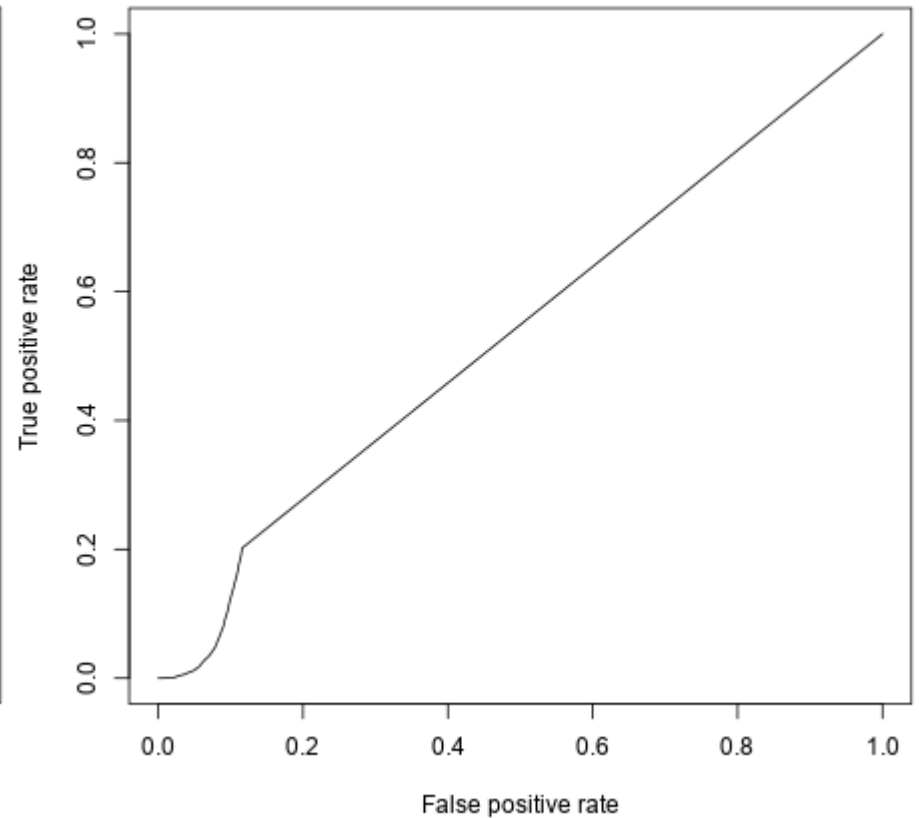
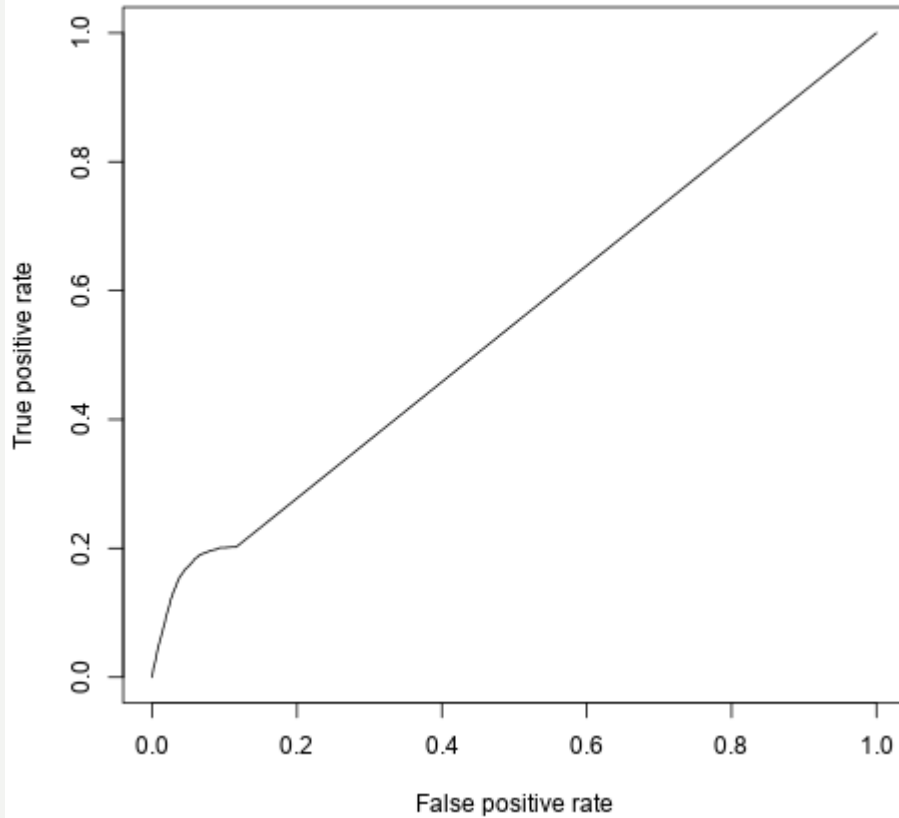


example ROC for NRF1

with reverse order footprint scores

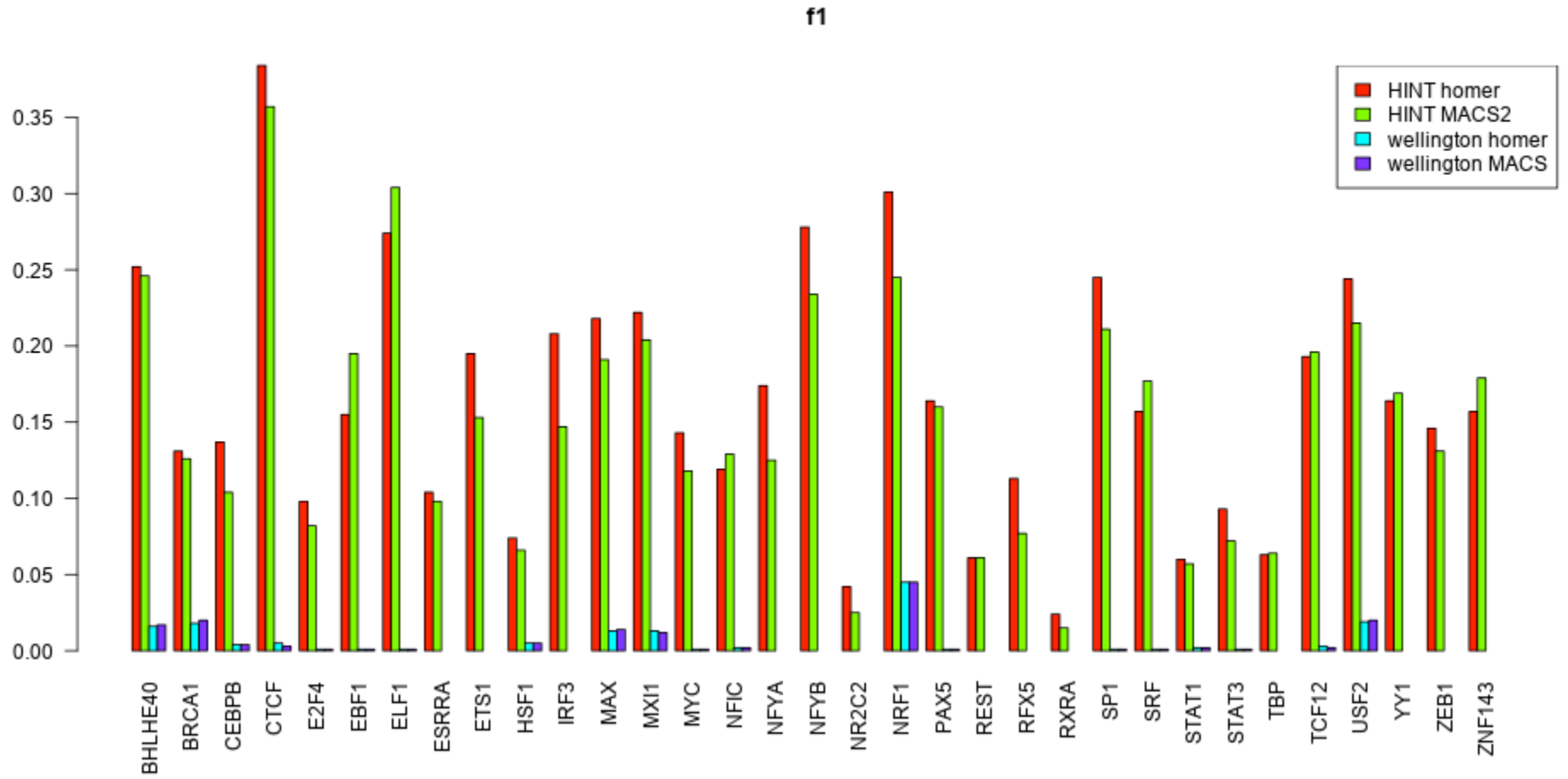
0.5494511

0.5366011



AUPRC: 0.48

0.41

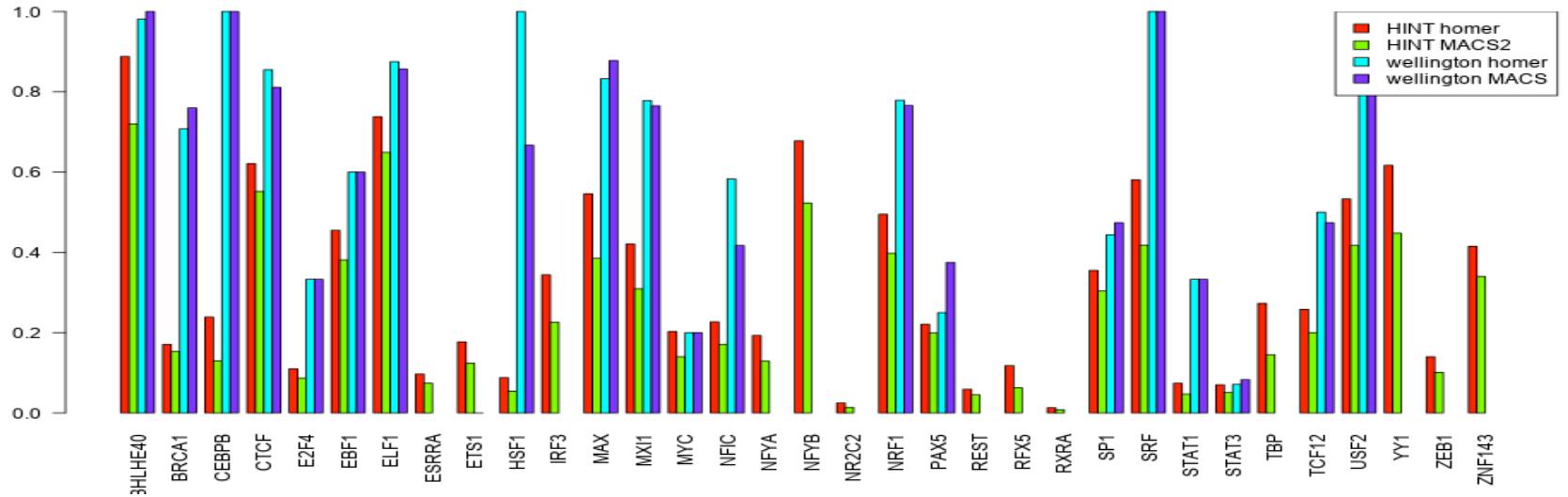


ENCODE dataset

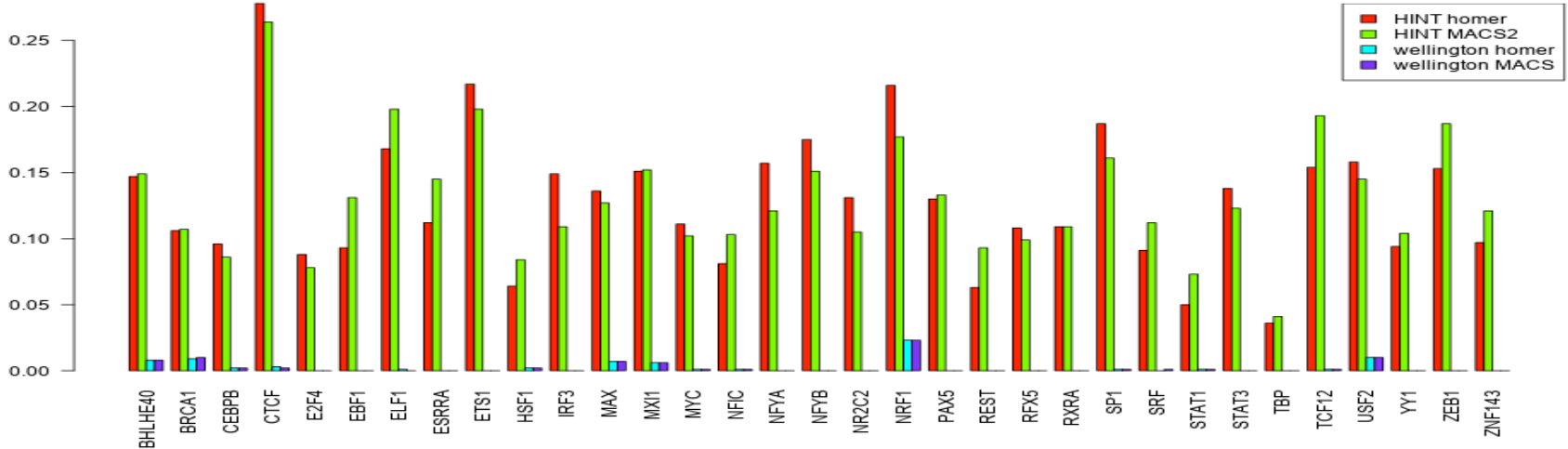
Precision and Recall

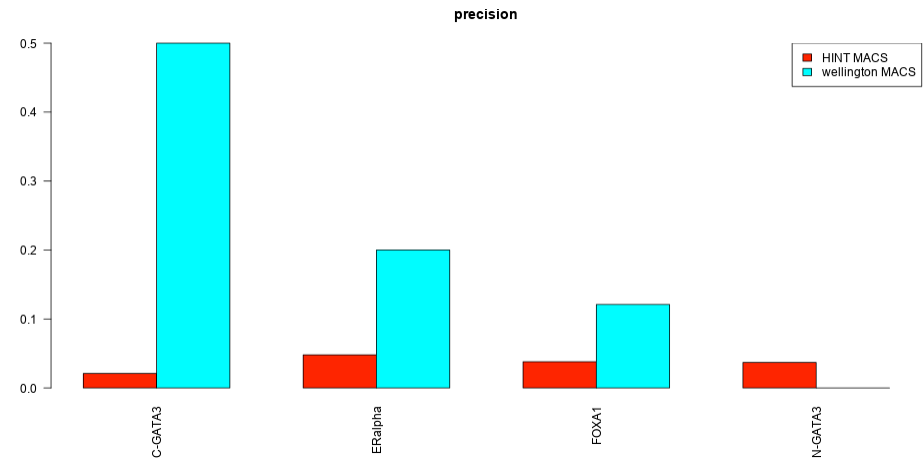
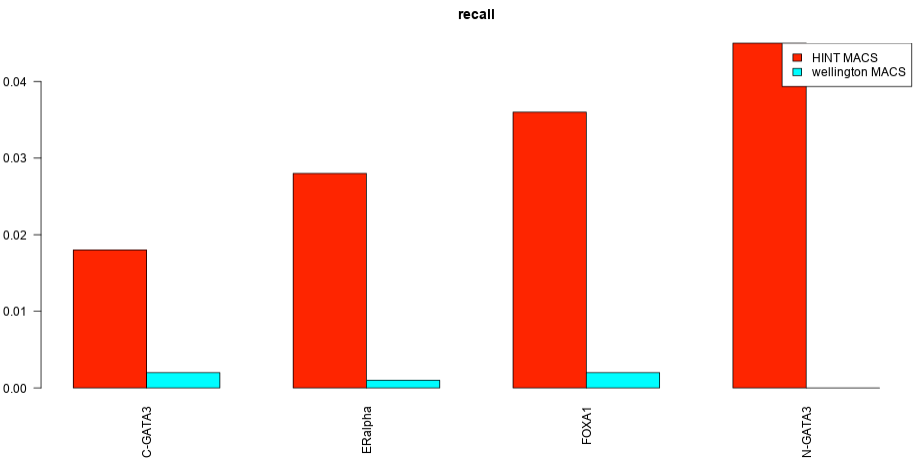
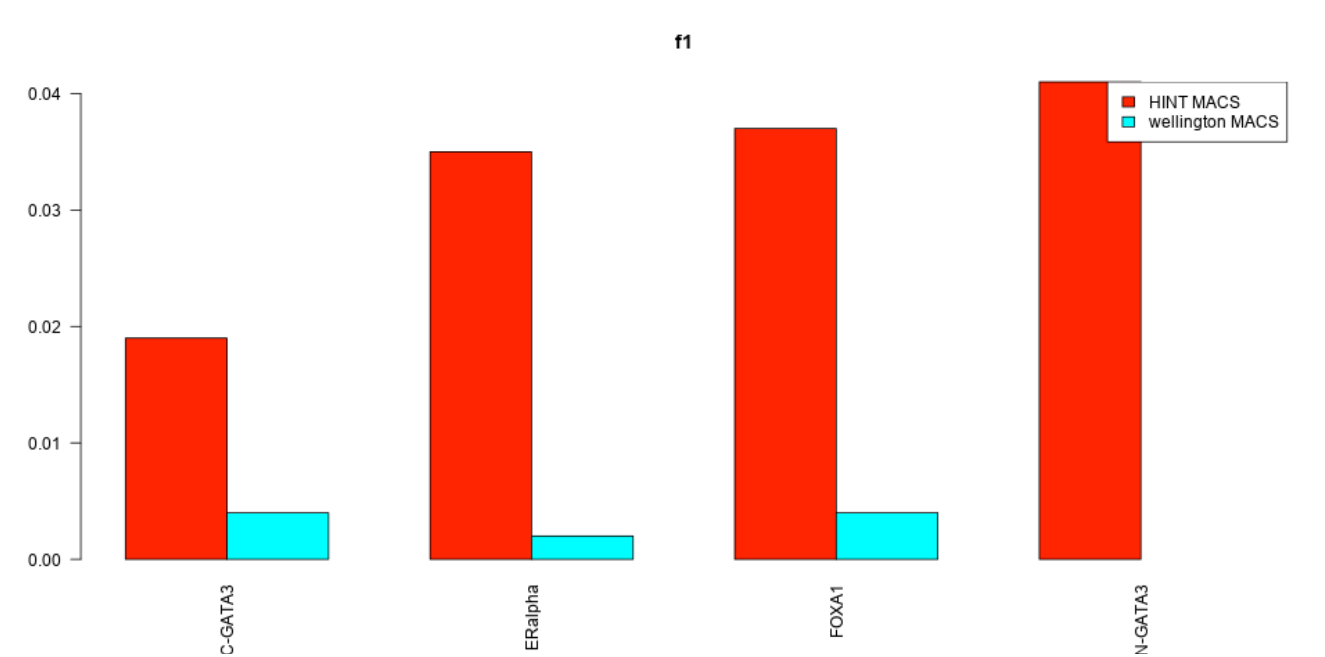


precision



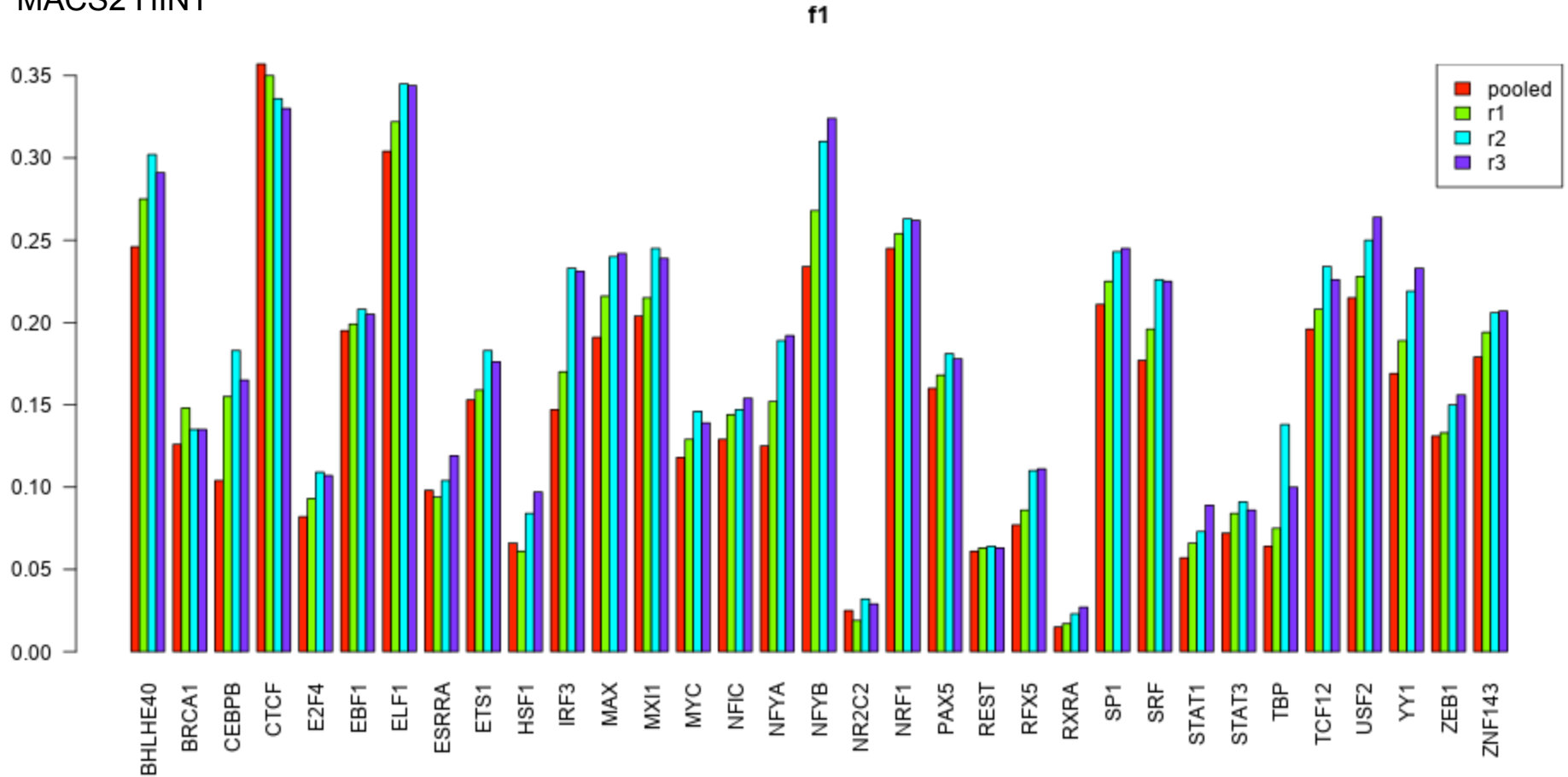
recall





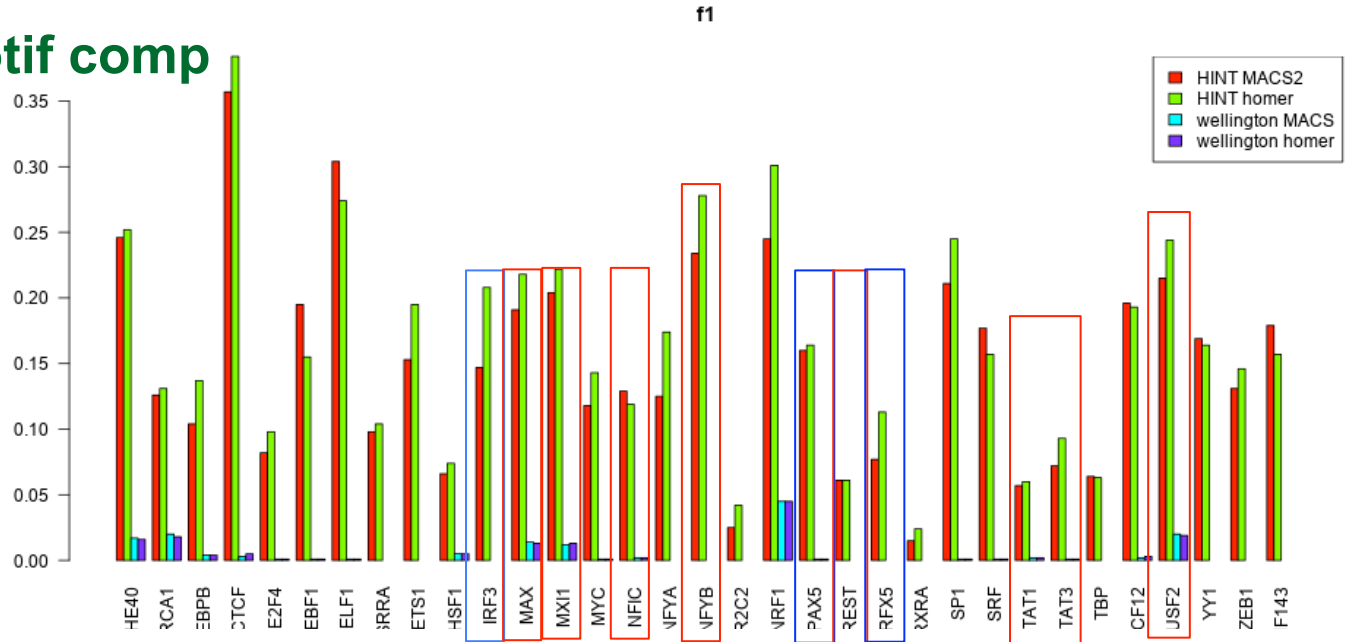


MACS2 HINT

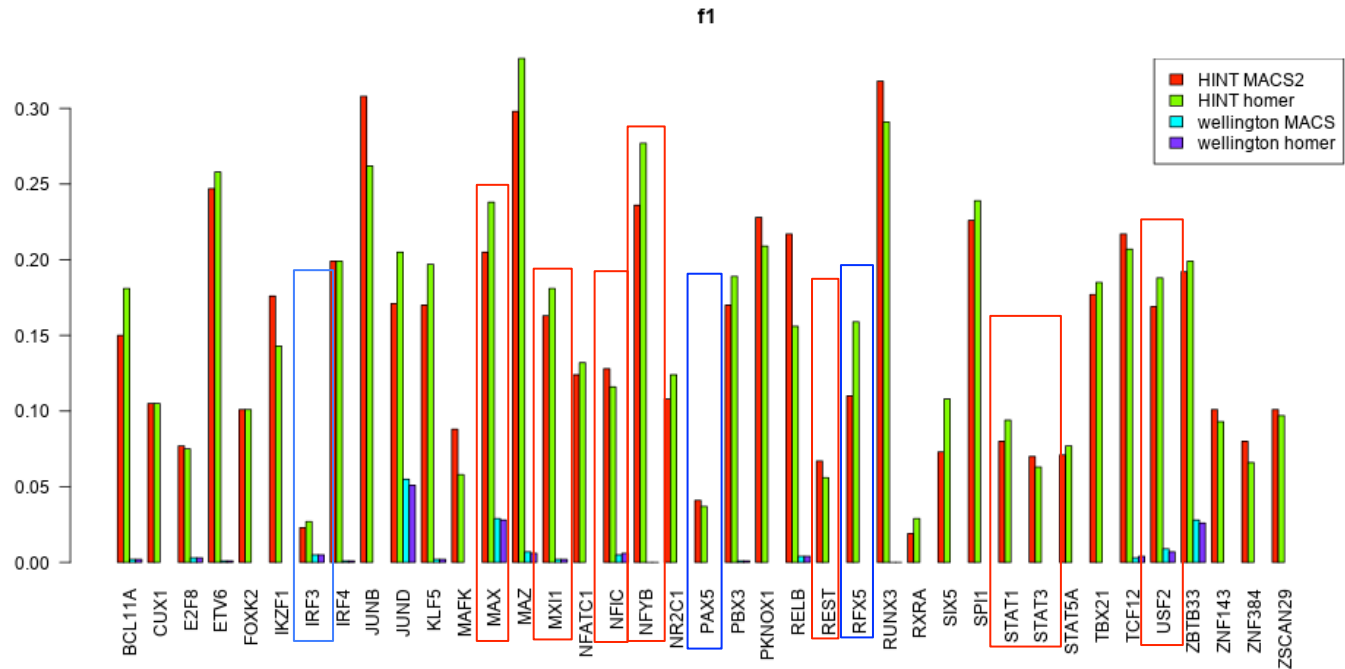


Motif comp

factorbook



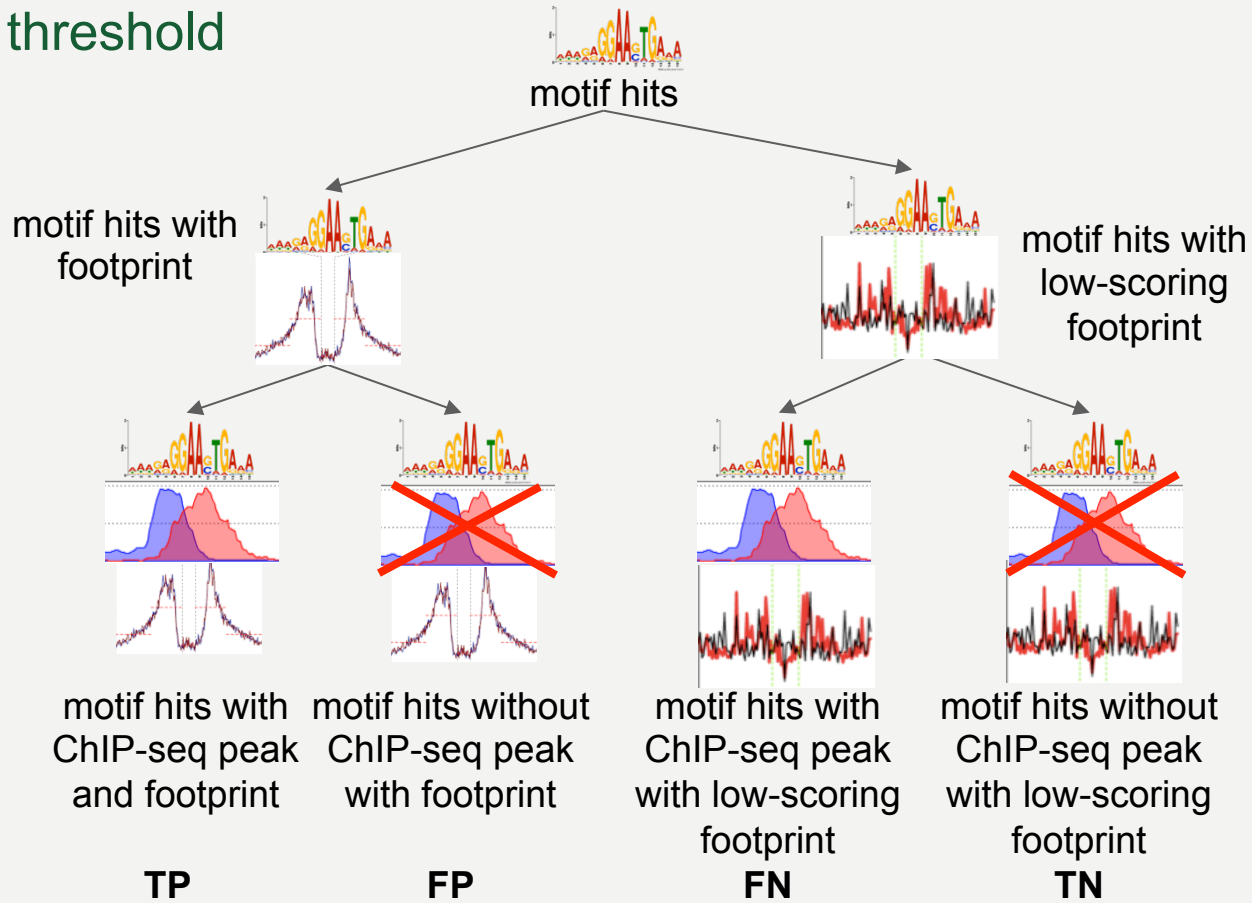
CisBP



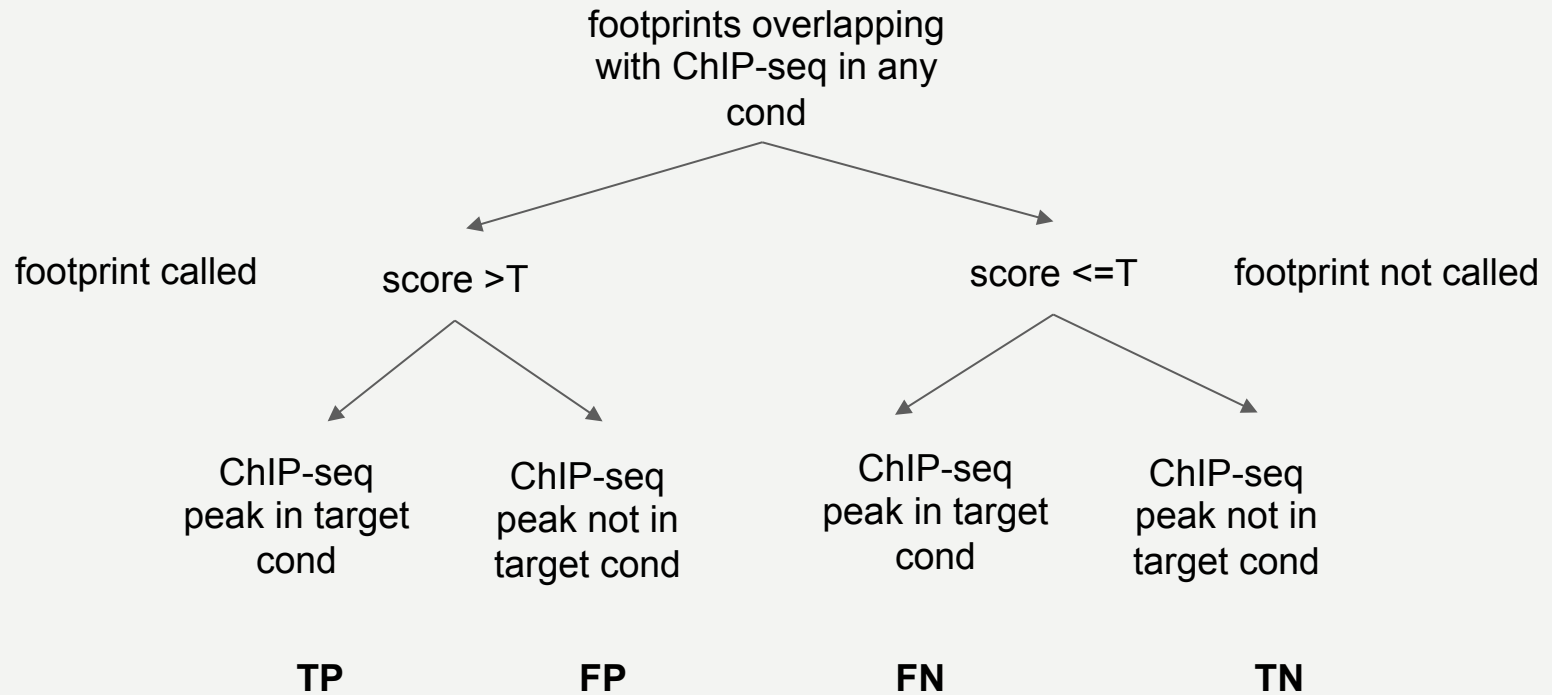
ALTERNATIVE EVALUATION MODES



restrict evaluation to called footprints -> negatives are footprints with scores below threshold

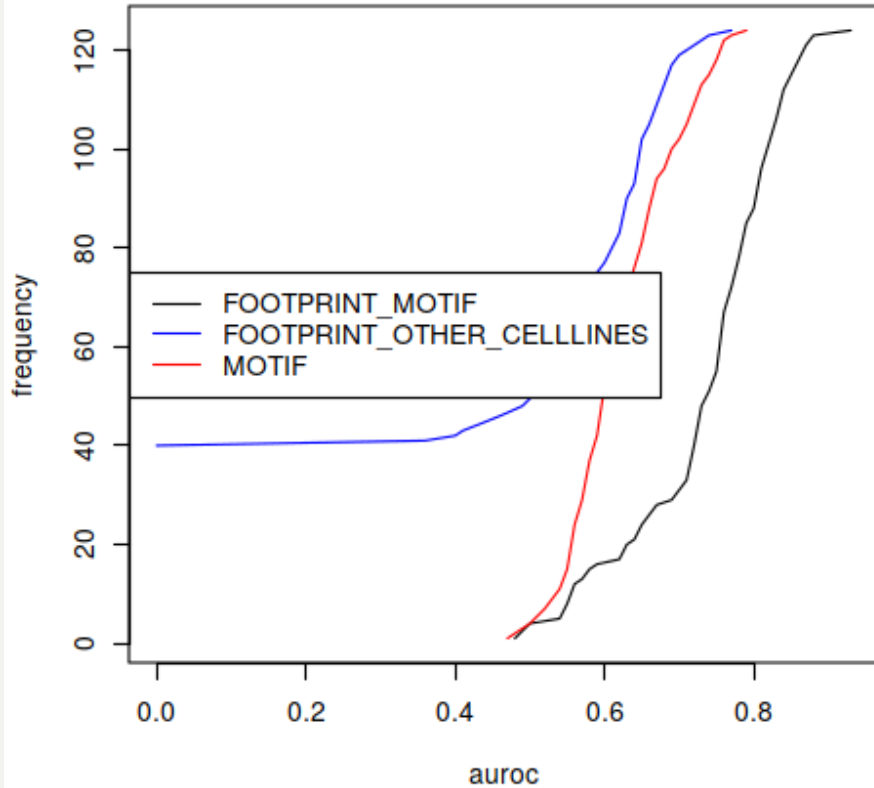


find TF-specific footprints not by motif but by compendium of ChIP-seq

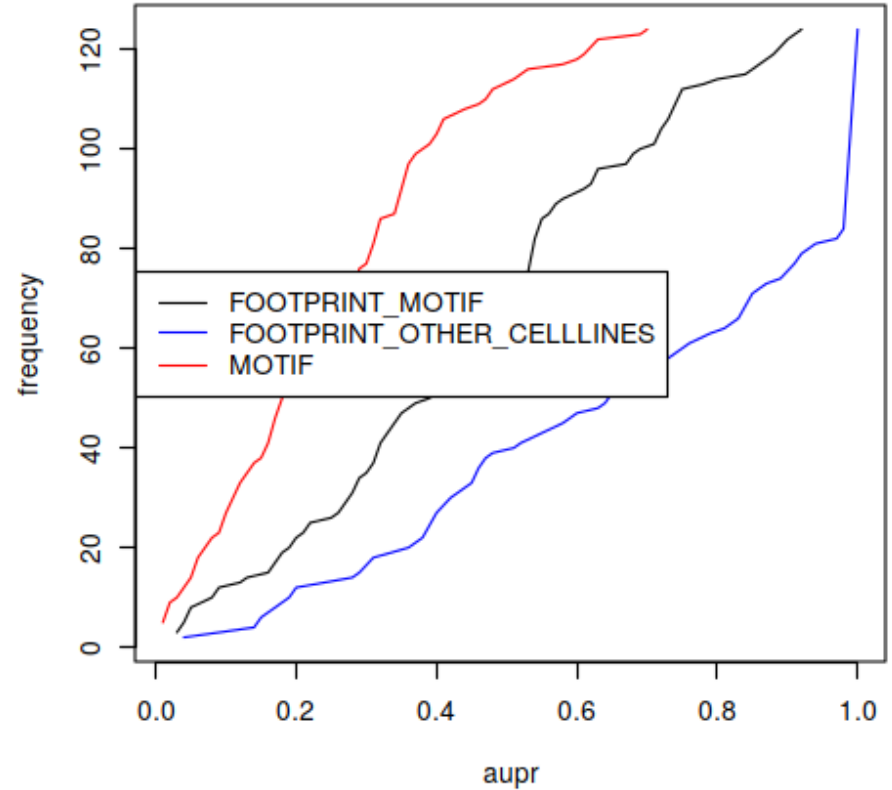




MACS2: HINT
on pooled



MACS2: HINT
on pooled





- motif-based AUROC can be misleading
- evaluation results generally disappointing
- reproducibility on DHS better than for footprints
- HINT performance comparable between replicates
 - → also not better for pooled replicates!
- Wellington recall dependent on sequencing depth
- different evaluation modes proposed to avoid motif/TN problems