ENGINE: an Enhancer-Gene Interaction dEtection method using robust feature extraction.

Part2: Tuning and feature selection

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Yale

Flowchart

Flowchart

408 positive set:K562 ChIA-PET intersect with MIT mix-membership prediction

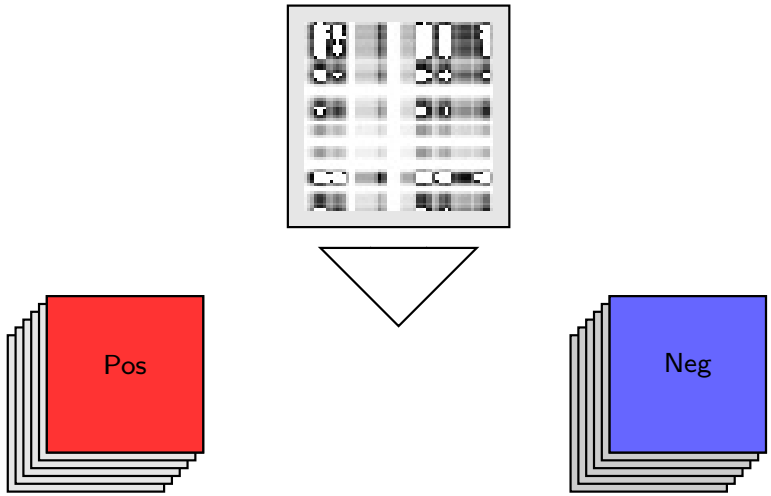
408 negative set:MCF7 specific ChIA-PET interactions

Data transformation

Flowchart

SURF: Speeded Up Robust Features, merits:

- Scale and image rotation invariant detectors and descriptors.
- blob detection
- ...

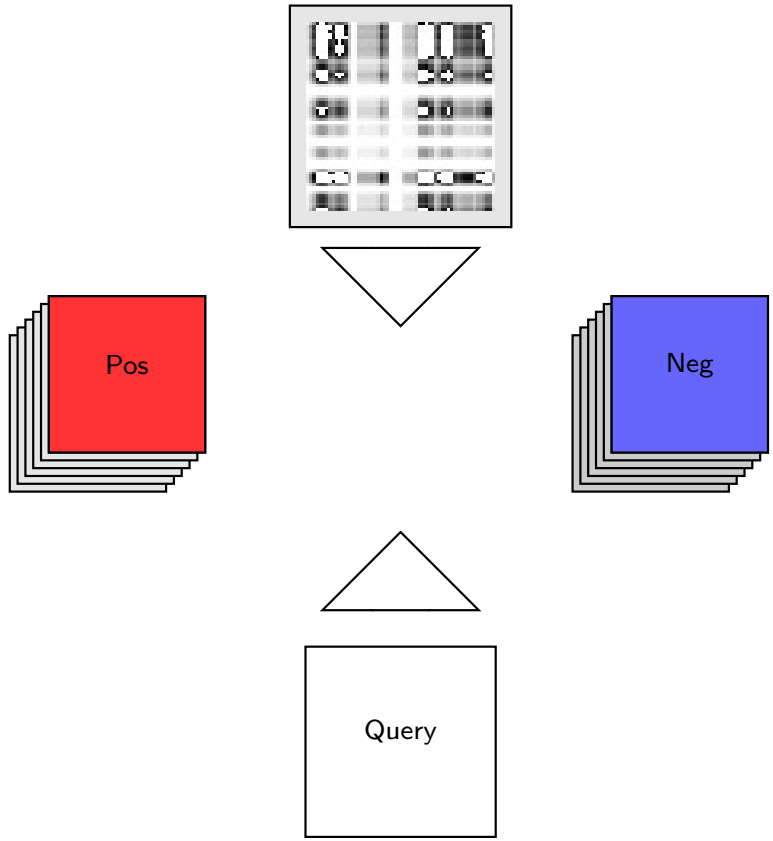


Flowchart

Feature S_i in $N_{j,k}$ matrix (feature sets), and recognition matrix

$$R_{i,j} = \begin{cases} 1, & \text{if } s_i = n_j \\ 0, & \text{otherwise} \end{cases} \quad (1)$$

The enrichment score:
$ES(i) = -\sum log(\frac{\sum_j R_{i,j}}{N}) - log(\frac{\sum_j \sum_k 1\{s_i = n_j\}}{\sum_j \sum_k 1})$.
The relative enrichment score
$RS = ES(positive) - ES(negative)$.
The lower of RS, the better!
use RandomForest to do classification.



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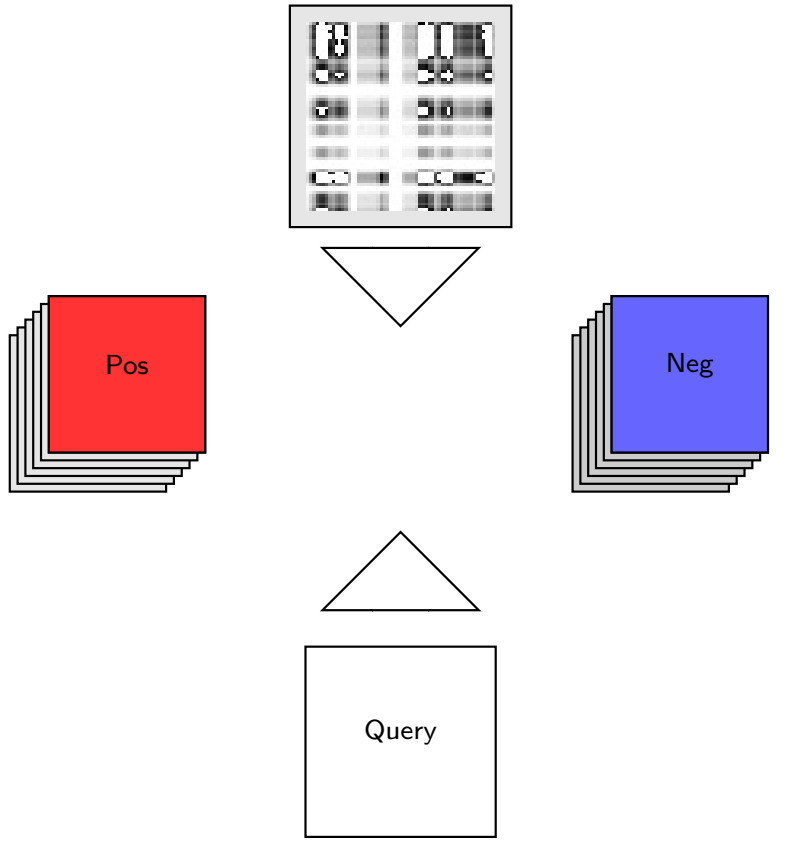
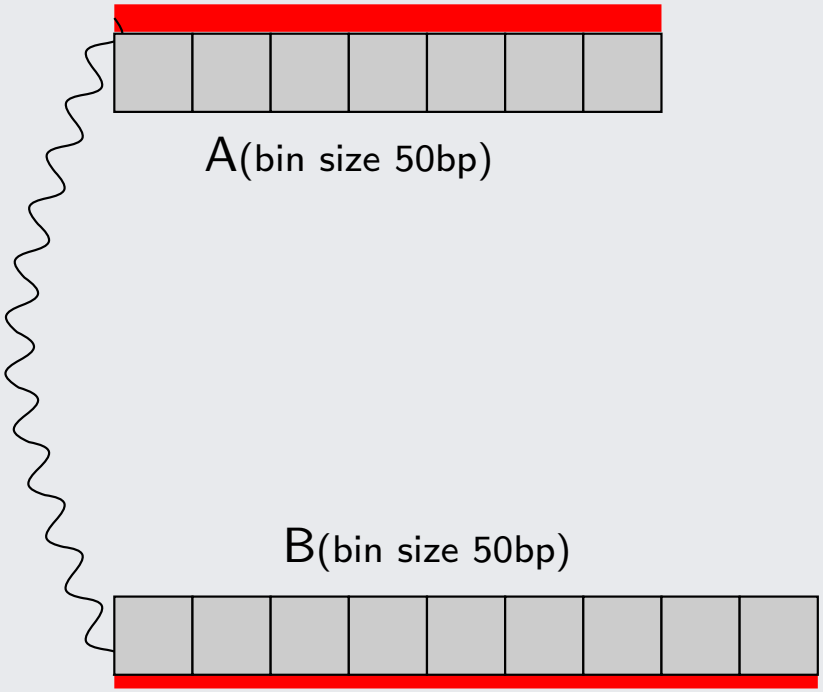
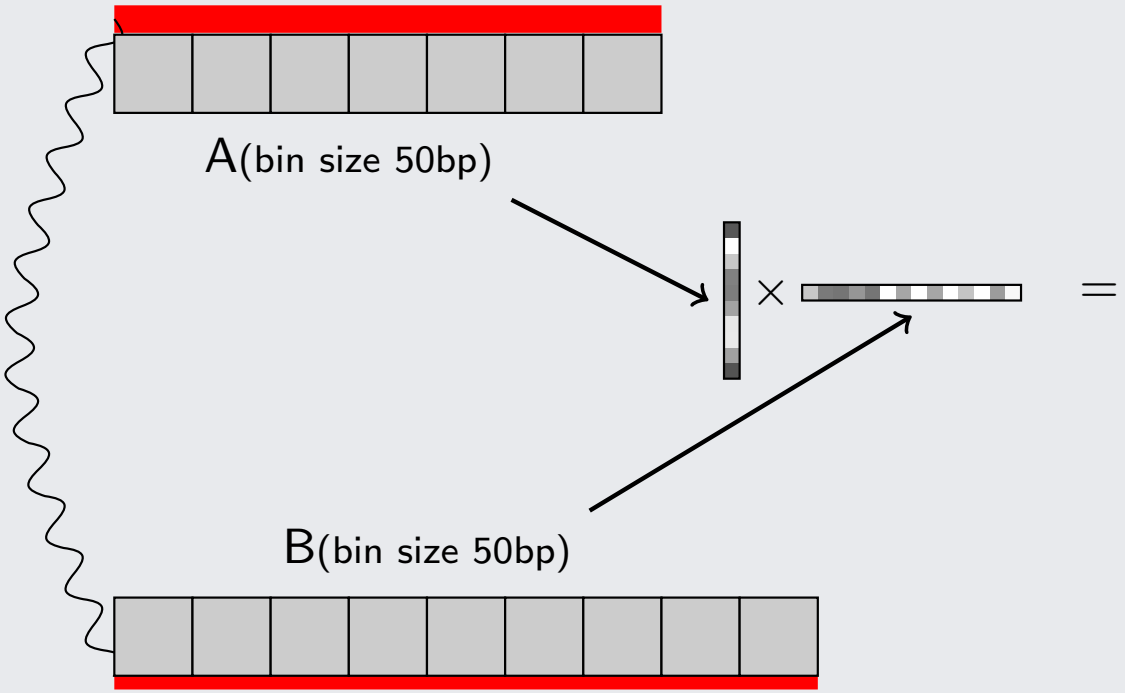


H3k27ac,H3k4me1,H3k4me2,H3k4me3,H3k9ac,
H3k9me1,H3k9me3,P300

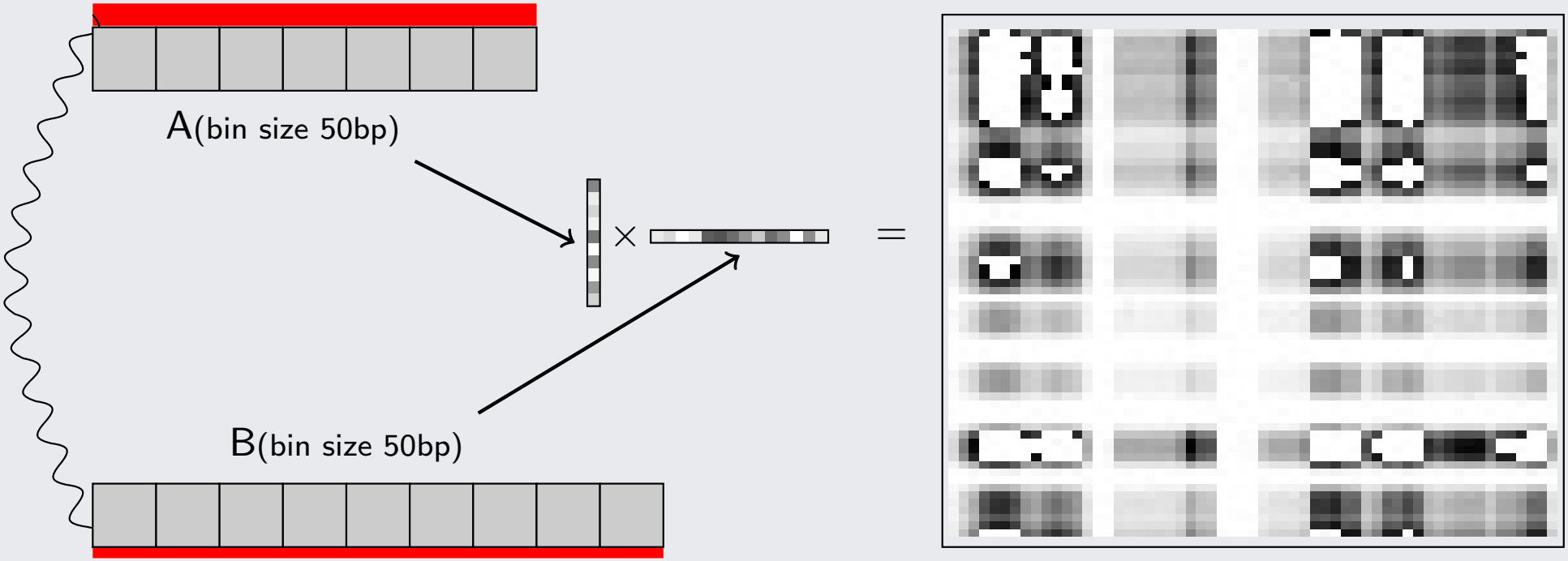
Psuedo Image transformation



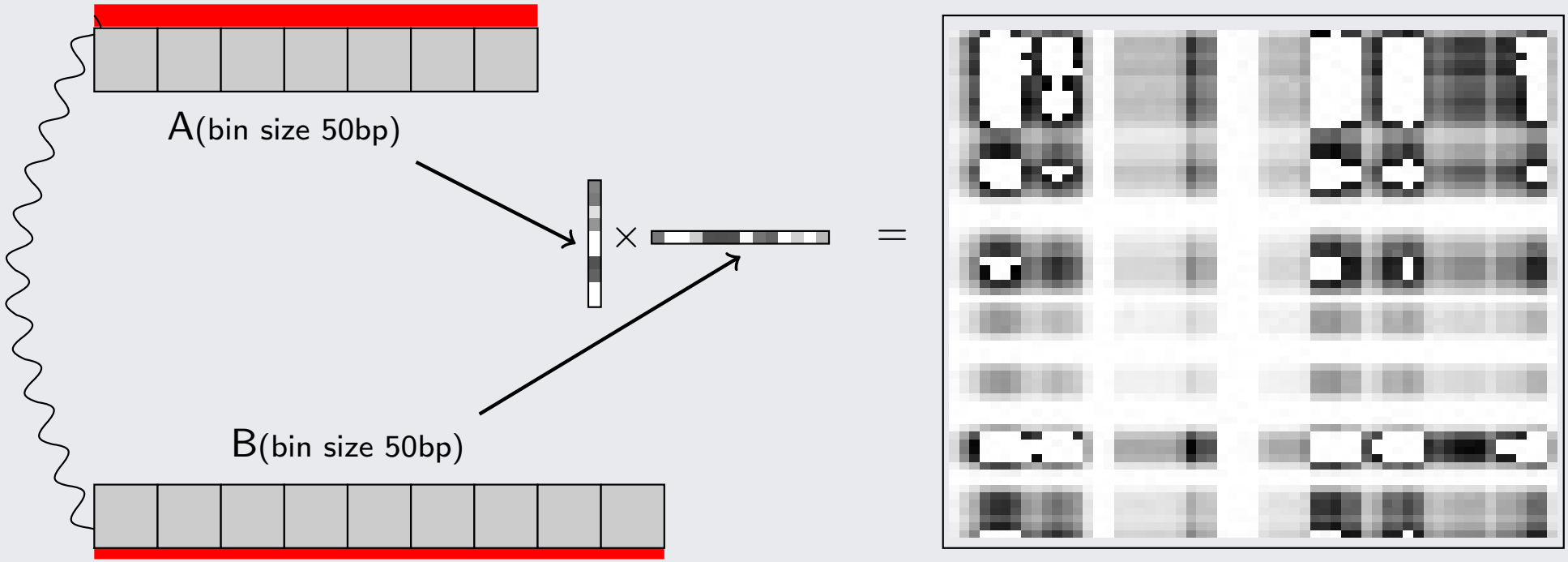
Psuedo Image transformation



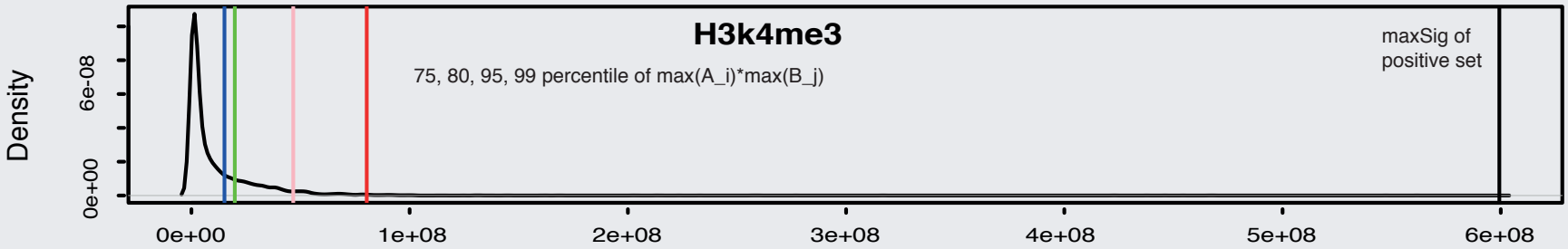
Psuedo Image transformation

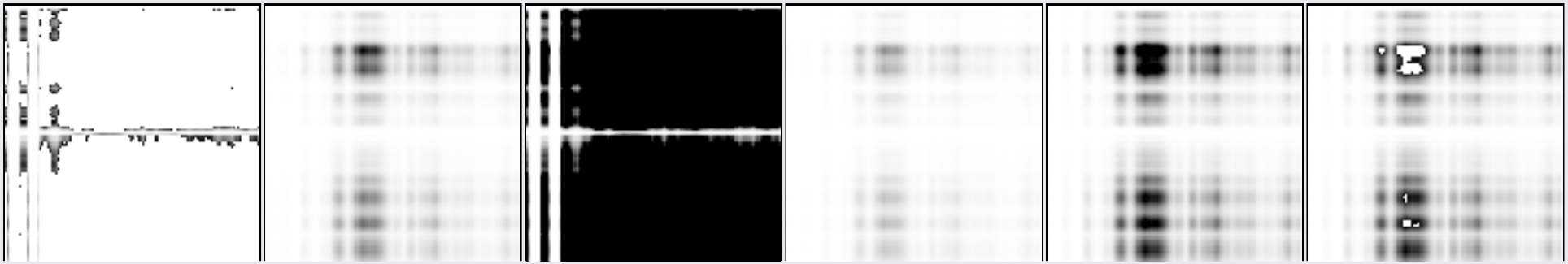


Psuedo Image transformation

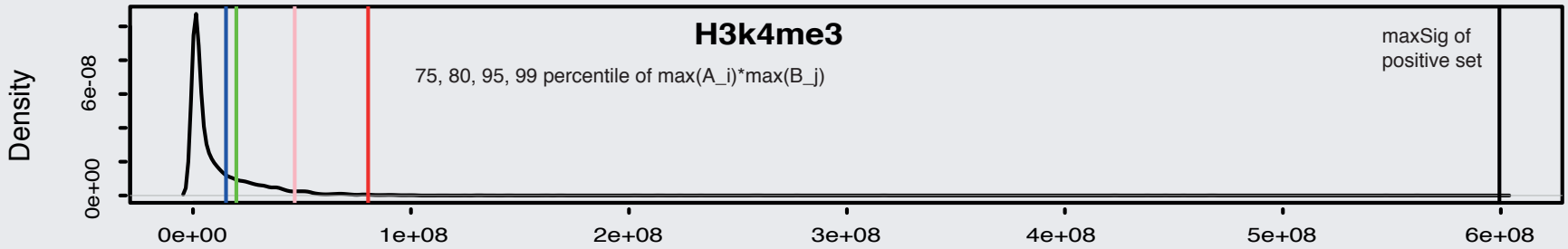


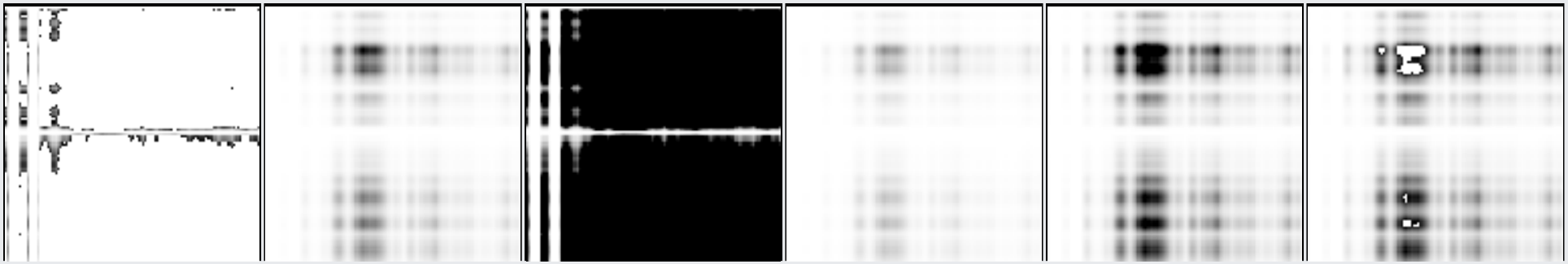
The range of signal is in [min(A)*min(B), max(A)*max(B)], then convert to grayscale psuedo image: integer in [0, 255].





1.5max(A,B) F | *maxA*, *maxB* | 1.5*max*(*A*, *B*)*C* | 99 perc | 75 perc C | 75 perc F





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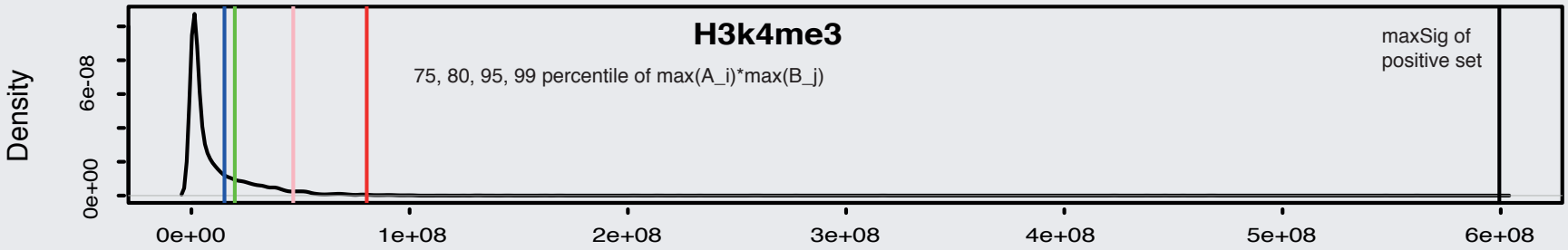
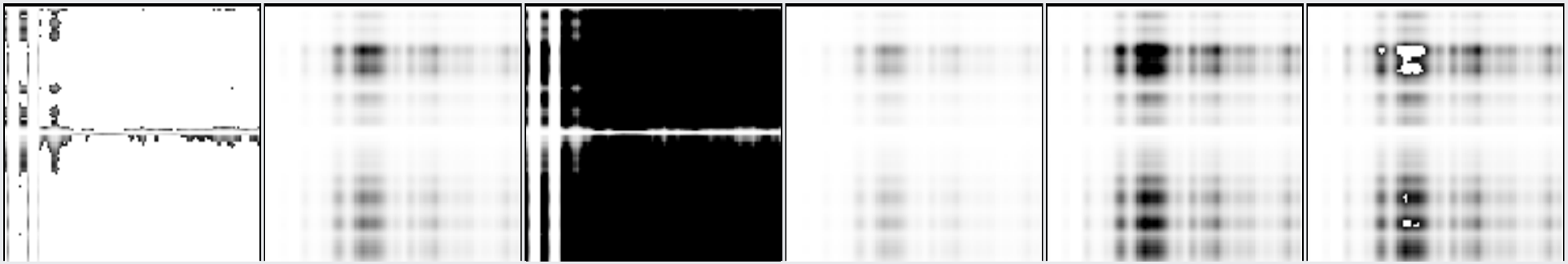
AUC: 0.94 | 0.92 | 0.94 | 0.9999 | 0.98 | 0.98





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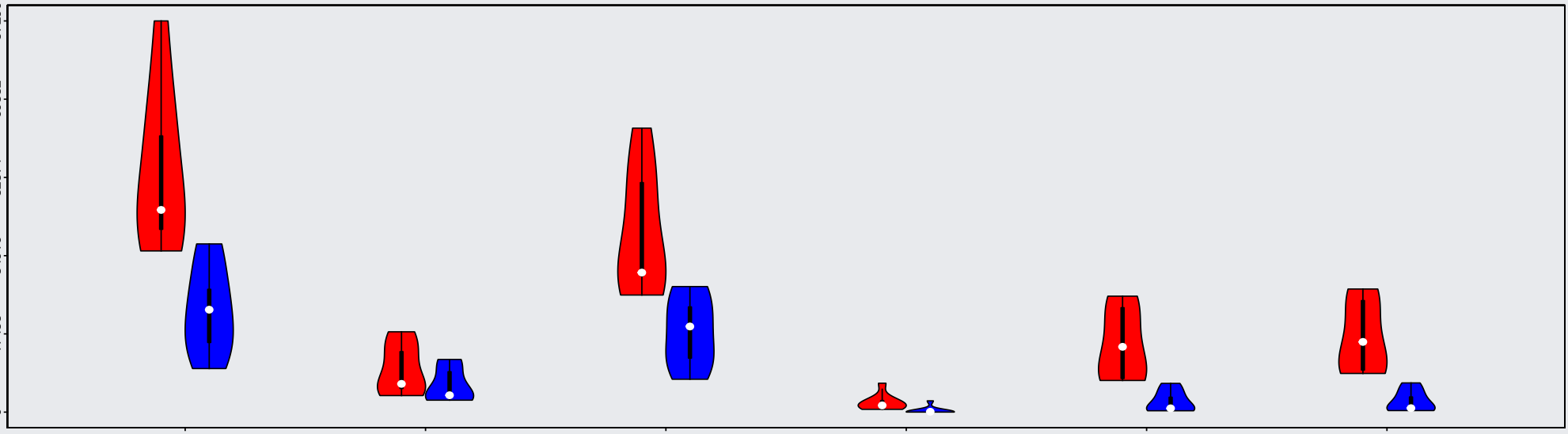

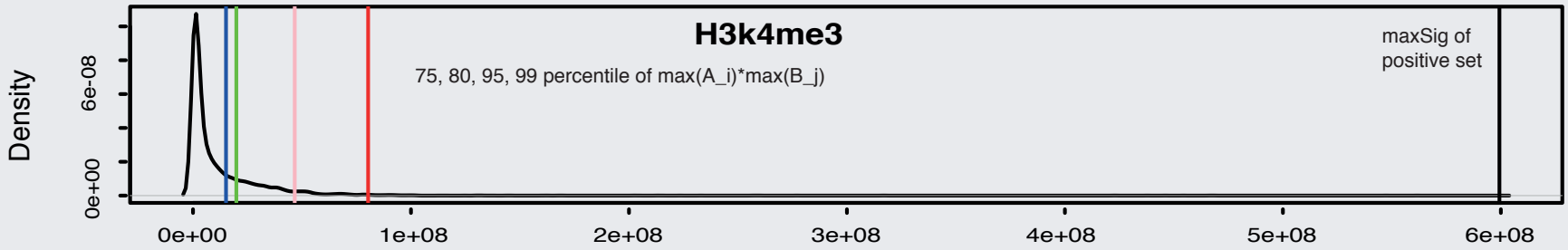

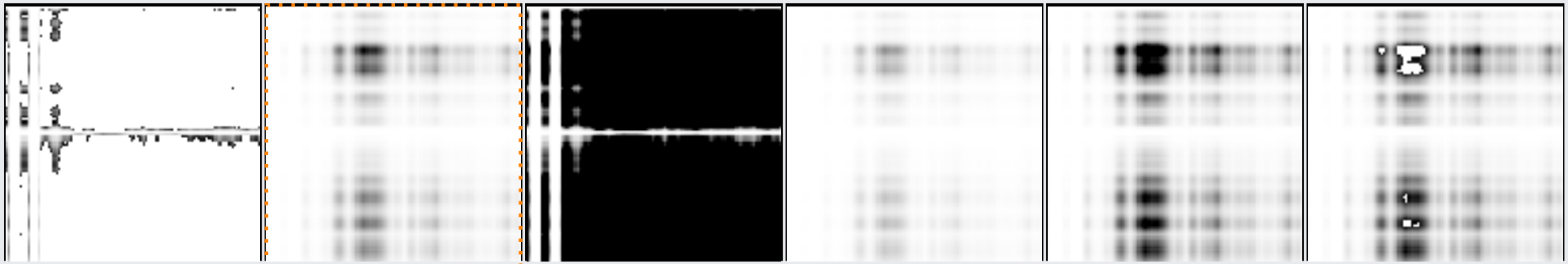

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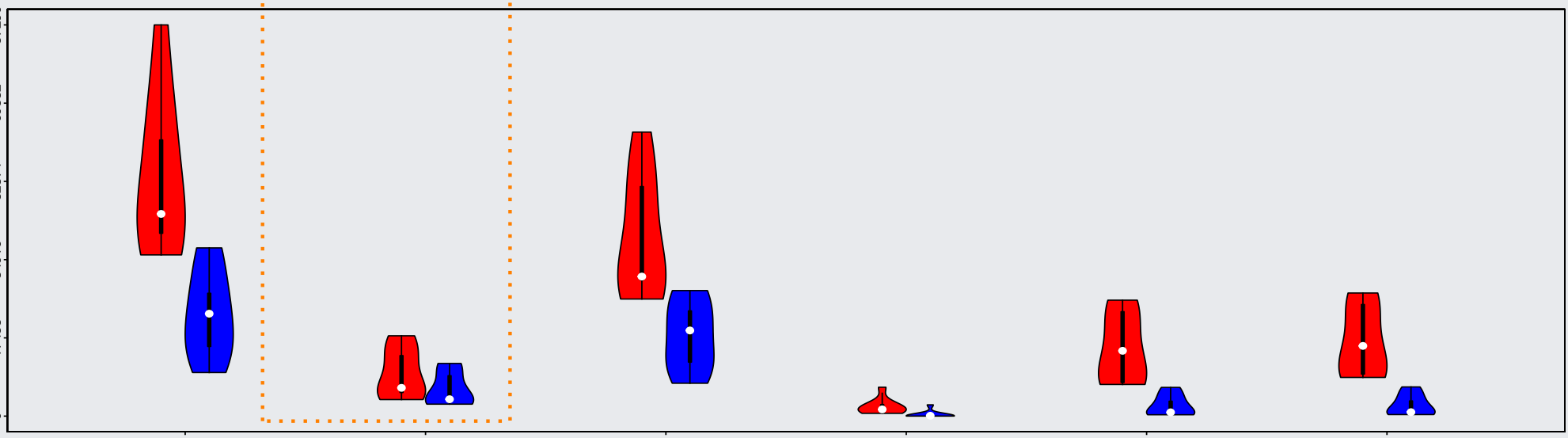
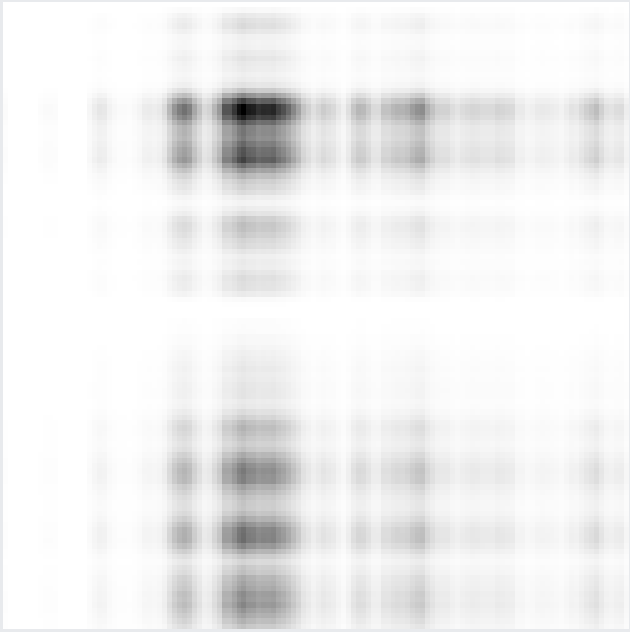


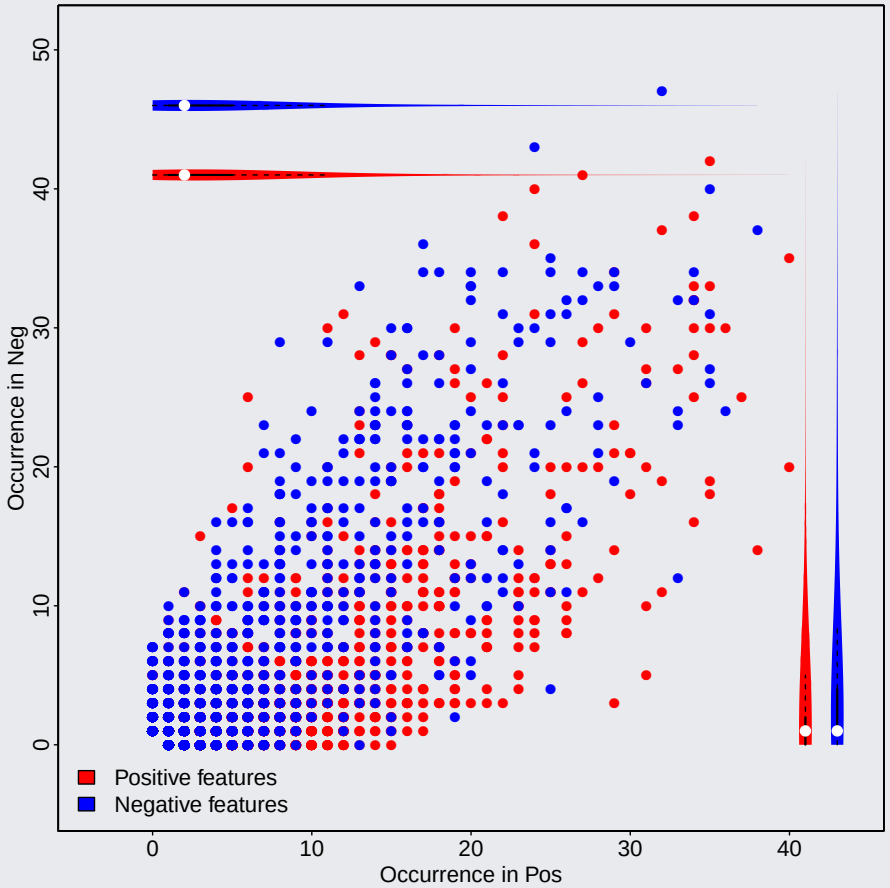
Heterogeneity; saturation affect feature detection; positive set have relative high signal

Additional negative dataset test

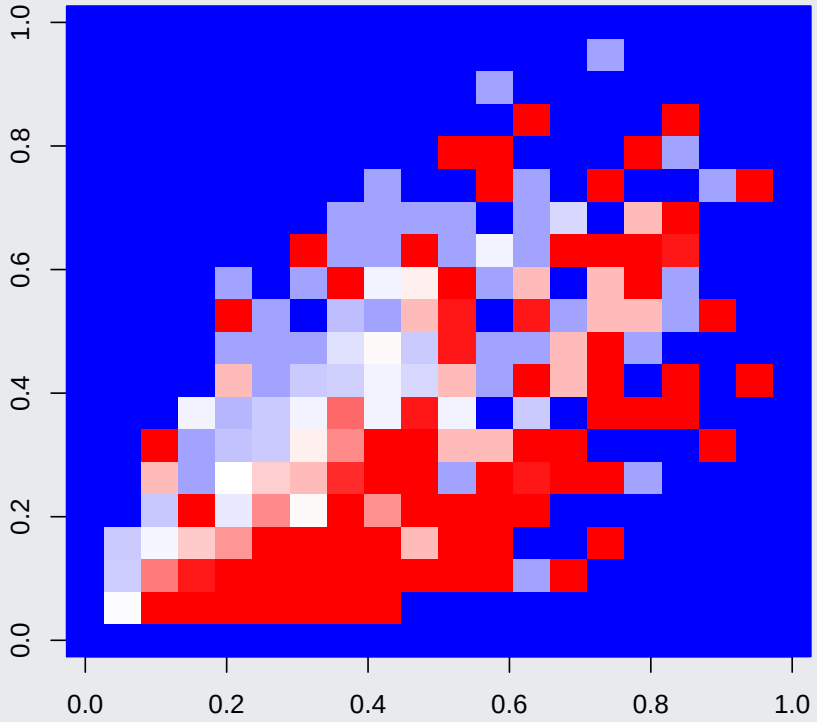


	Orignal negative dataset	Random shift region	Random signal
AUC	0.92	0.93	0.93

Feature selection

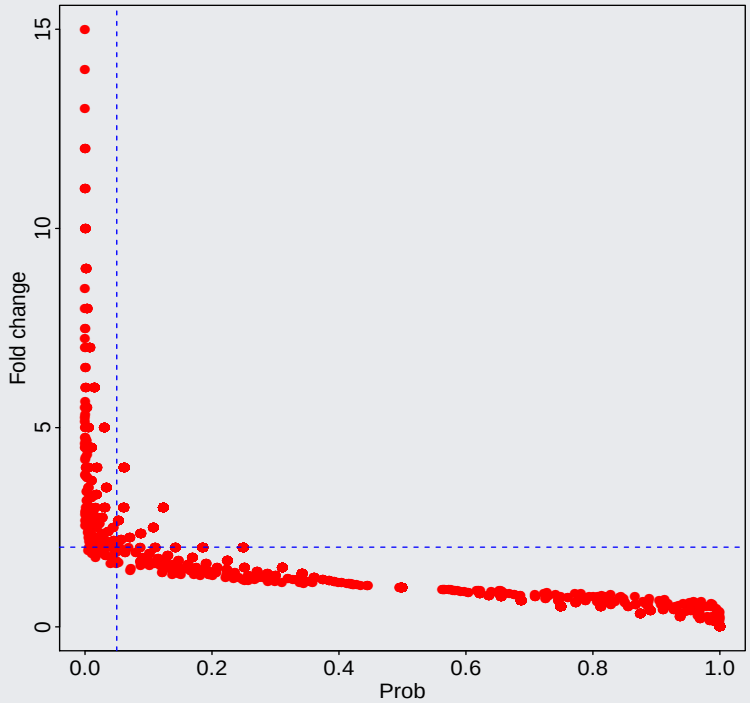


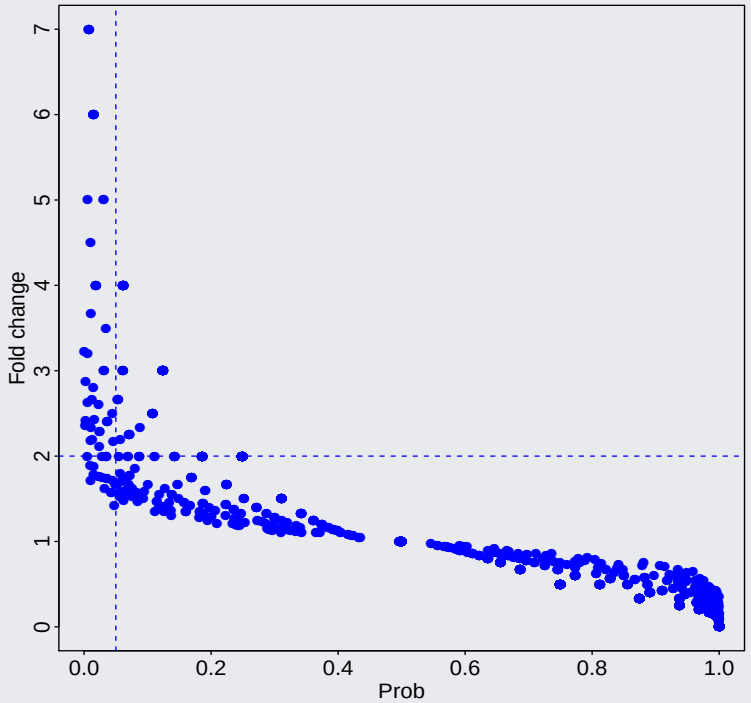
Feature distribution



$P(pos|neg)$ conditional density

Feature selection



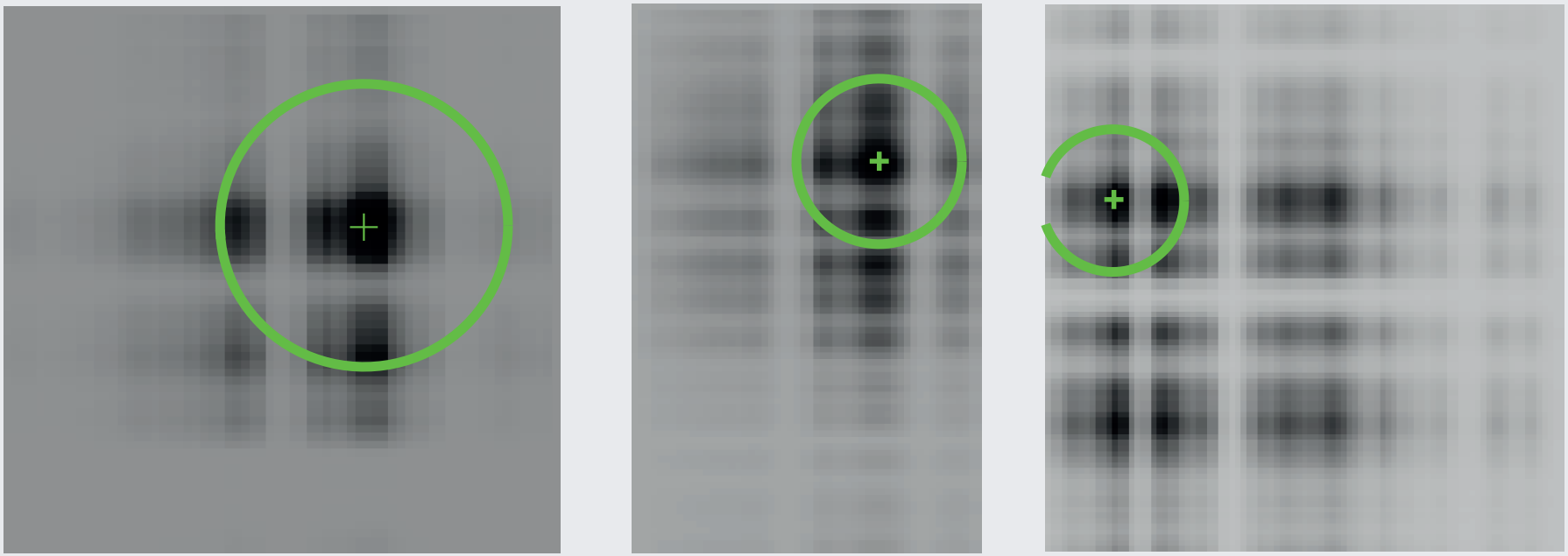


pvalue($= \sum(dhyper(pos\_hit : total\_hit, \#pos\_sample, \#neg\_sample, total\_hit))) < 0.05$ and FC>2, #pos_features in each marker:

H3k27ac	H3k4me1	H3k4me2	H3k4me3	H3k9ac	H3k9me1	H3k9me3	P300	nCpG
395	835	742	462	400	1427	2110	672	1228

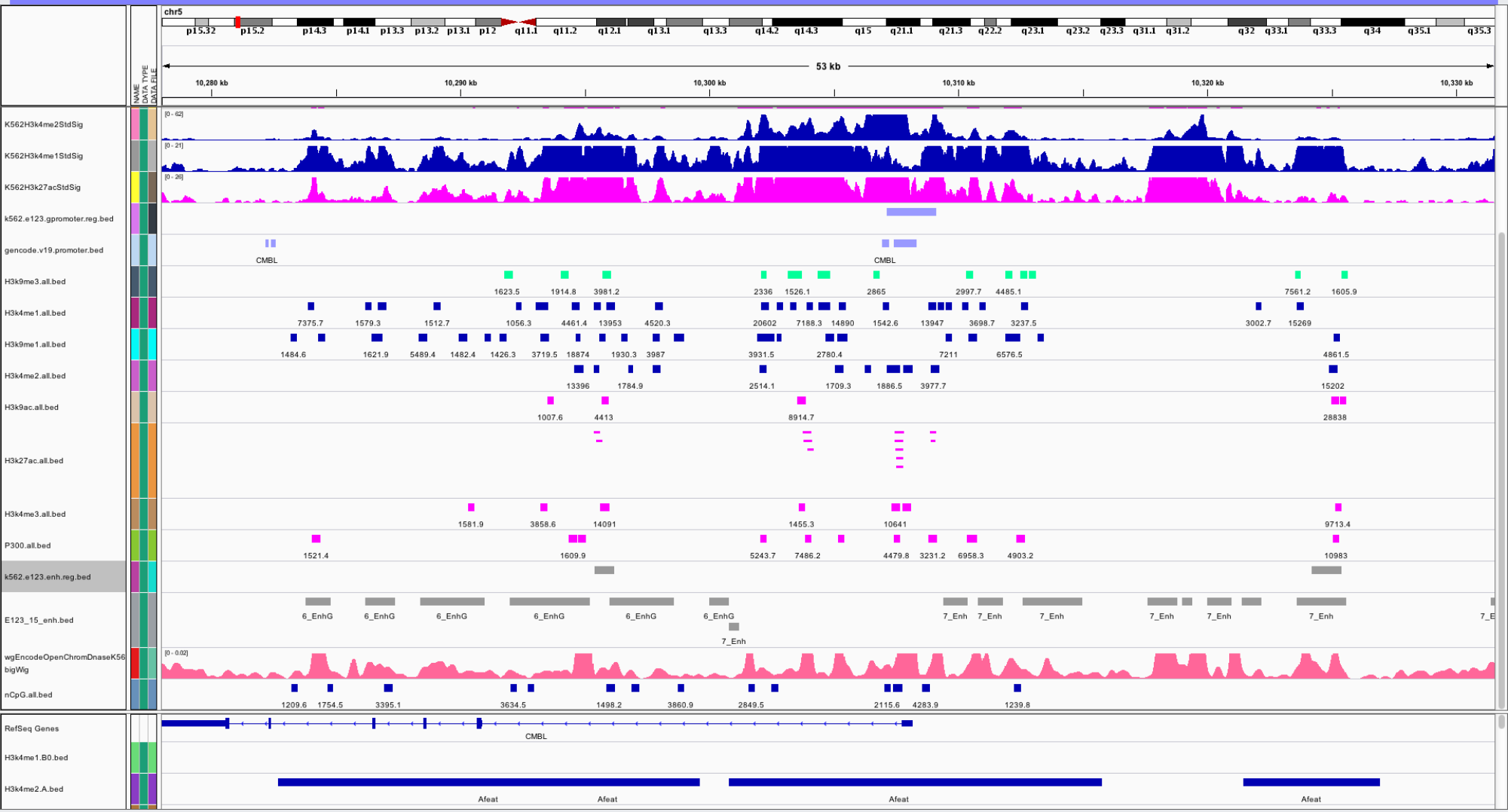
More #sig_features $\neq$ high importance;

Feature visualization



Example for top H3K27ac features

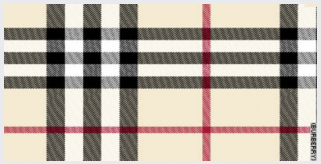
Feature visualization



Feature visualization

Feature visualization

Pattern



Future plan

Explore more biological function

evaluation using selected feature

Comparison with other software

whole genome predictioin