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

Part2: Tuning and feature selection

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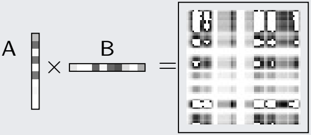
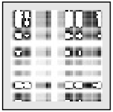
Flowchart

Flowchart



408 positive set:K562 ChIA-PET intersect with MIT mix-membership prediction
408 negative set:MCF7 specific ChIA-PET interactions

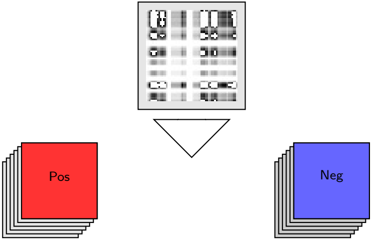
Data transformation



Flowchart

SURF: Speeded Up Robust Features, merits:

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

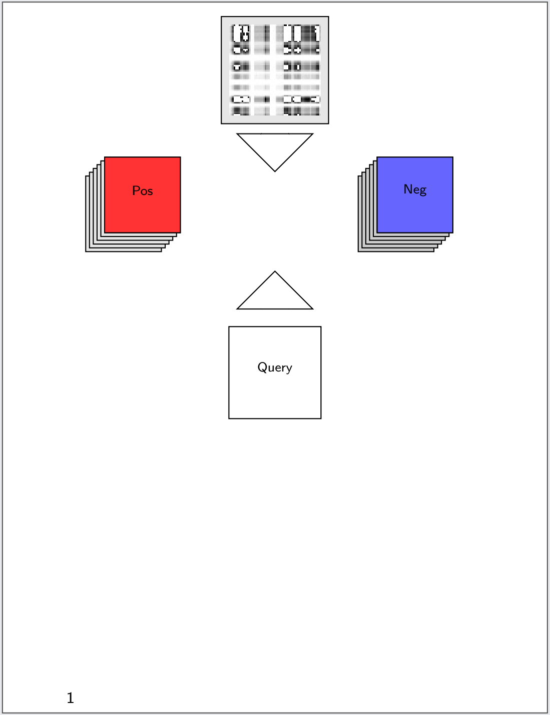


Flowchart

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

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

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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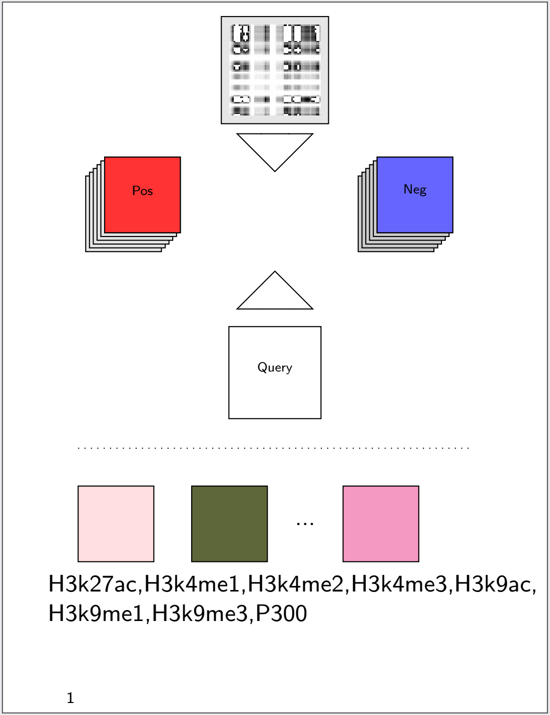
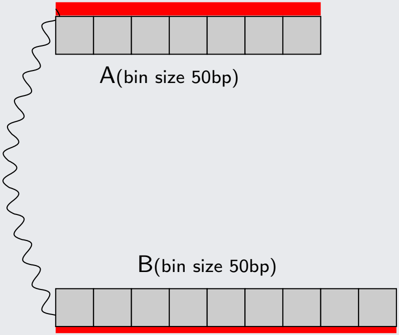
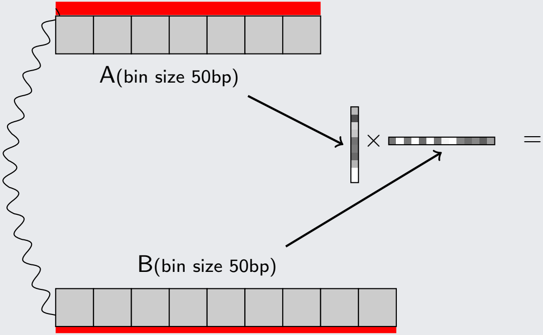


H3k27ac,H3k4me1,H3k4me2,H3k4me3,H3k9ac,
H3k9me1,H3k9me3,P300

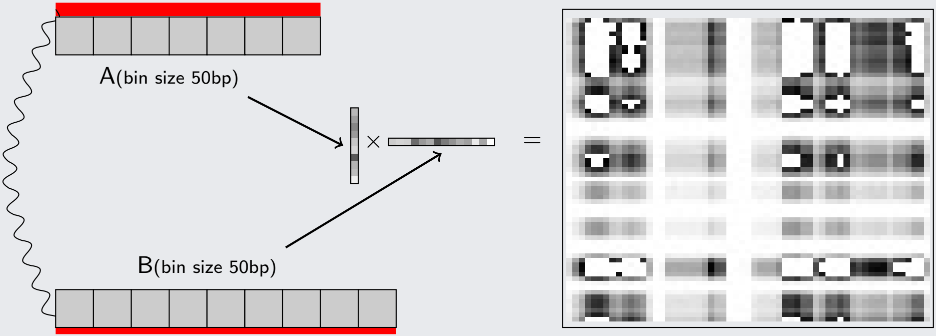
Psuedo Image transformation



Psuedo Image transformation



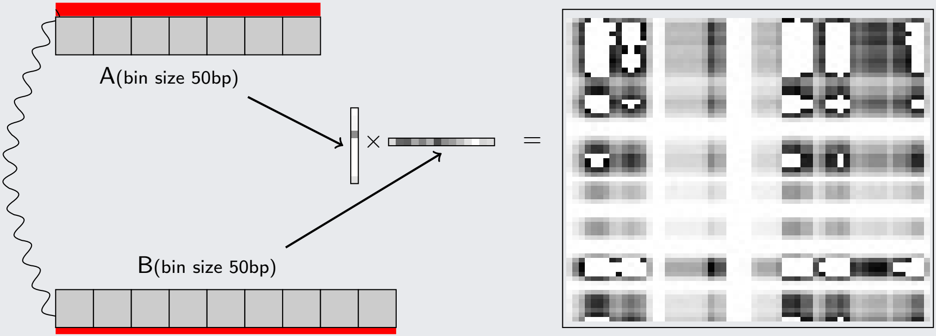
Psuedo Image transformation



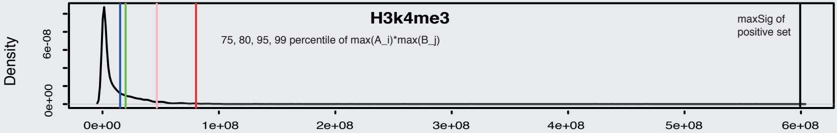
A(bin size 50bp)

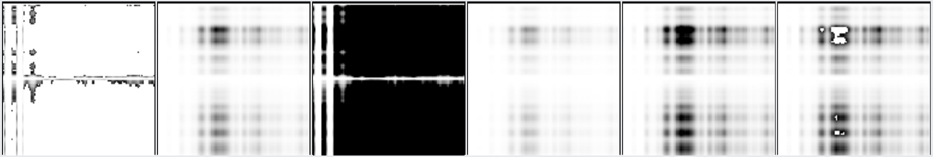
B(bin size 50bp)

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

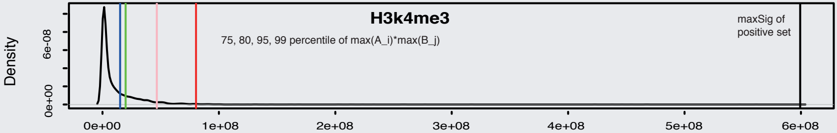
$maxA$, $maxB$

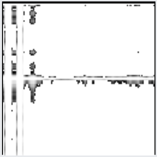
1.5$max(A, B)C$

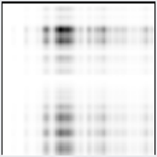
99 perc

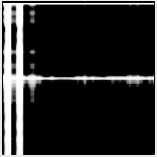
75 perc C

75 perc F




1.5max(A,B) F


$maxA$, $maxB$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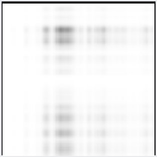
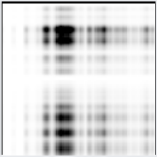
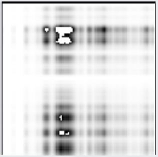
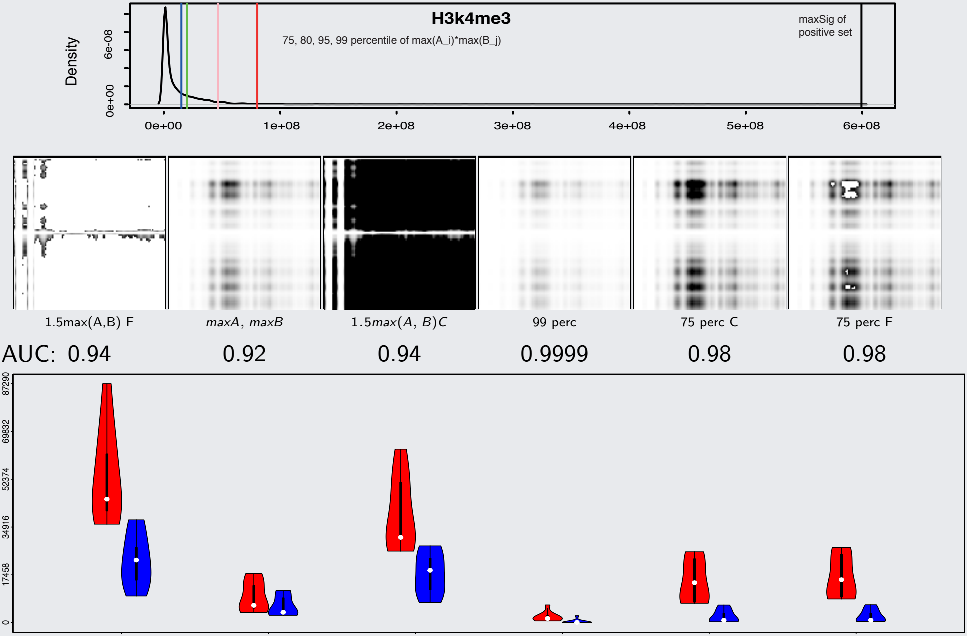
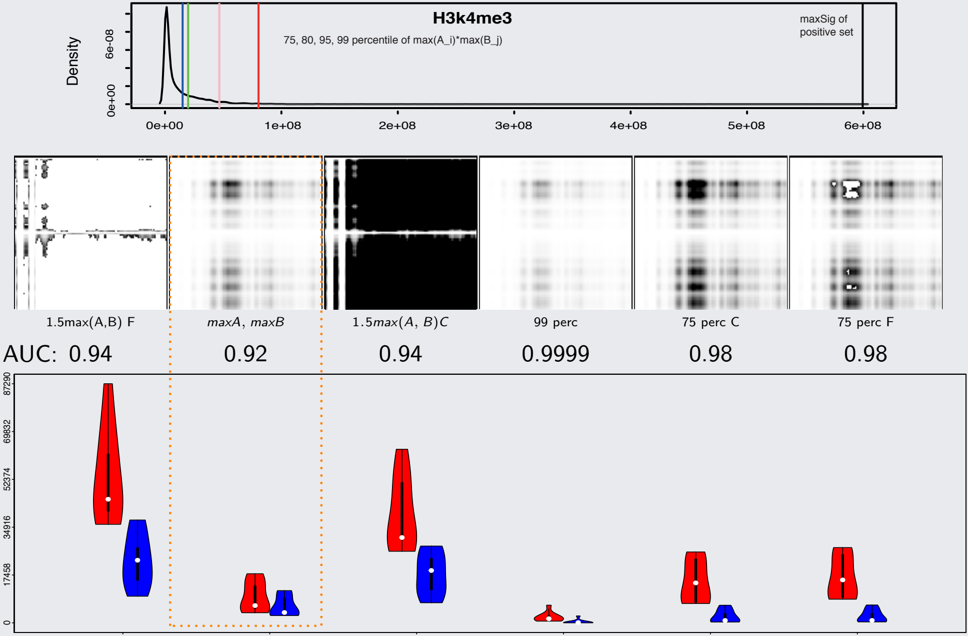

99 perc


75 perc C


75 perc F

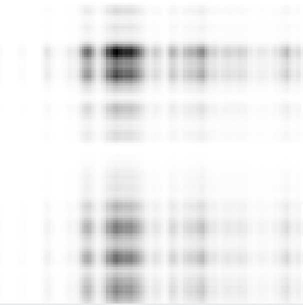
AUC: 0.94 0.92 0.94 0.9999 0.98 0.98


H3k4me3
75, 80, 95, 99 percentile of max(A_i)*max(B_j)
maxSig of
positive set
Density
0e+00
6e-08
0e+00
1e+08
2e+08
3e+08
4e+08
5e+08
6e+08
1.5max(A,B) F
maxA, maxB
1.5max(A, B)C
99 perc
75 perc C
75 perc F
AUC: 0.94
0.92
0.94
0.9999
0.98
0.98
0
17458
34916
52374
69832
87290



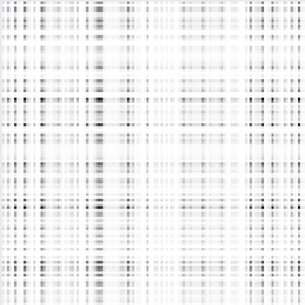
Heterogeneity; saturation affect feature detection; positive set have relative high signal

Additional negative dataset test



Orignal negative dataset

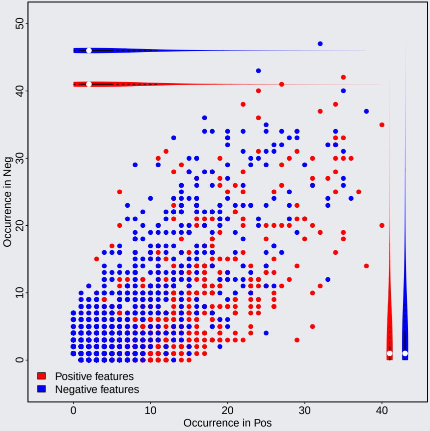
Random shift region



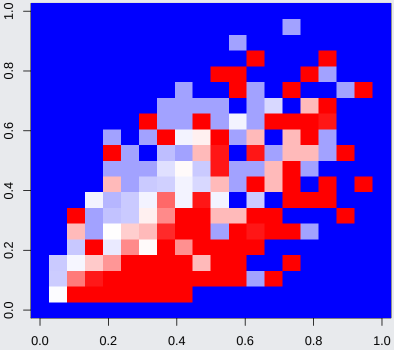
Random signal

AUC	0.92	0.93	0.93

Feature selection

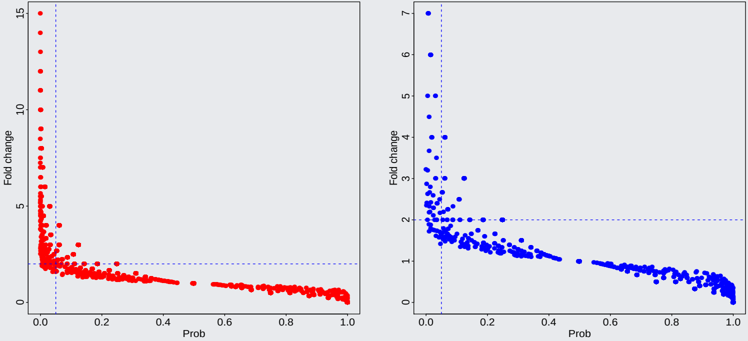


Feature distribution



$P(pos|neg)$ conditional density

Feature selection

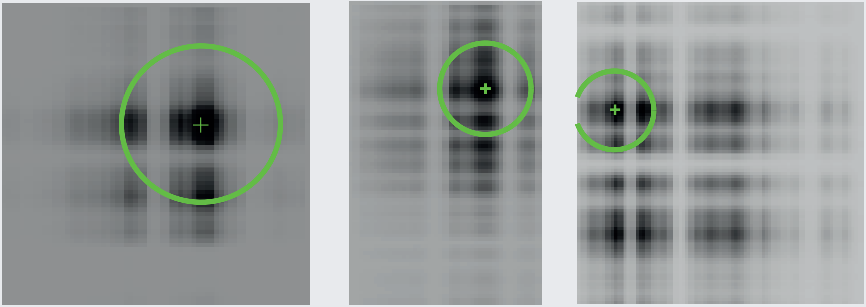


pvalue$(= \sum(dhyper(pos_hit : total_hit, \#pos_sample, \#neg_sample, total_hit))) < 0.05$ and FC$>$2,
#pos_features in each marker:

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

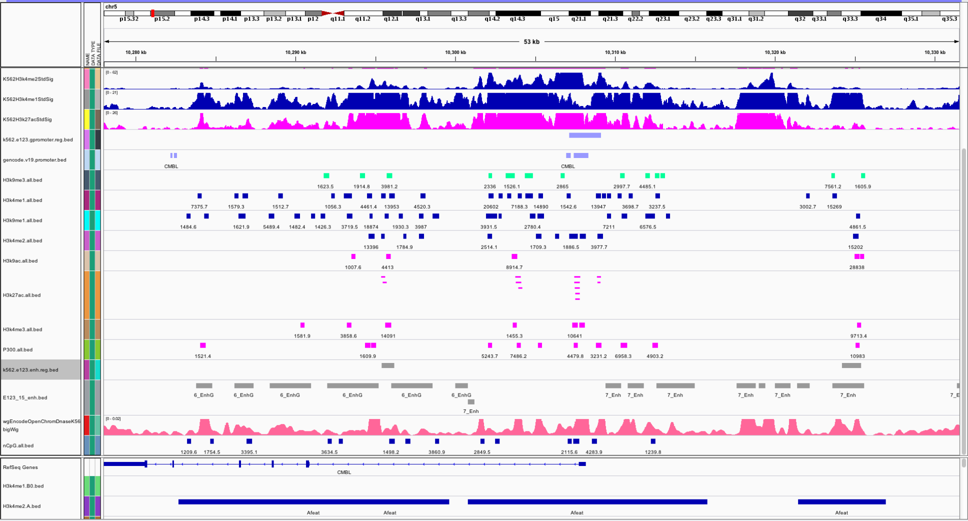
More #sig_features $\neq$ high importance;

Feature visualization



Example for top H3K27ac features

Feature visualization



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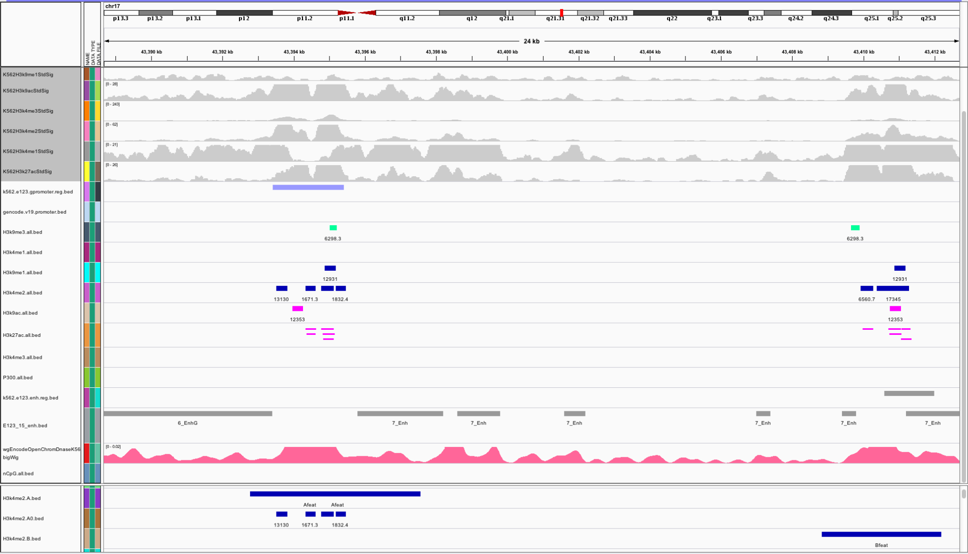

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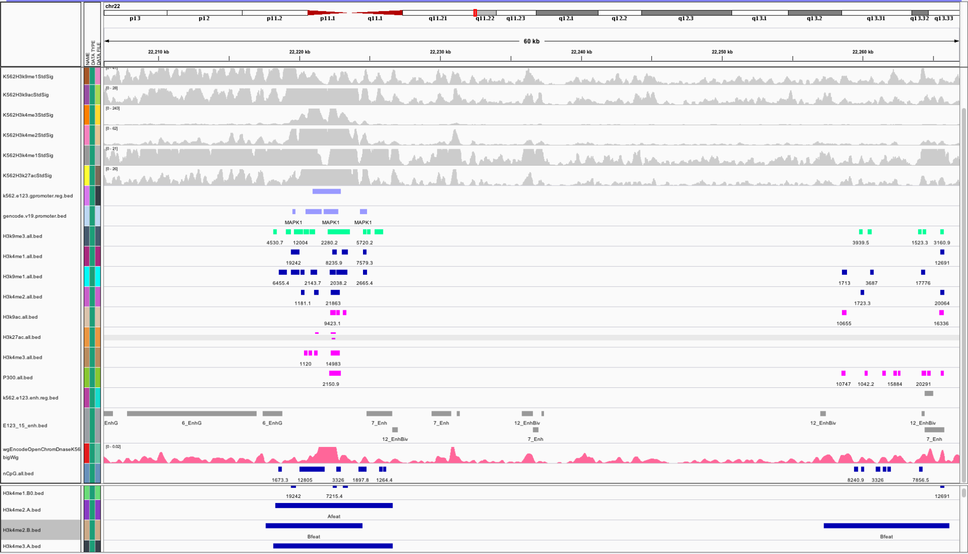
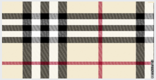
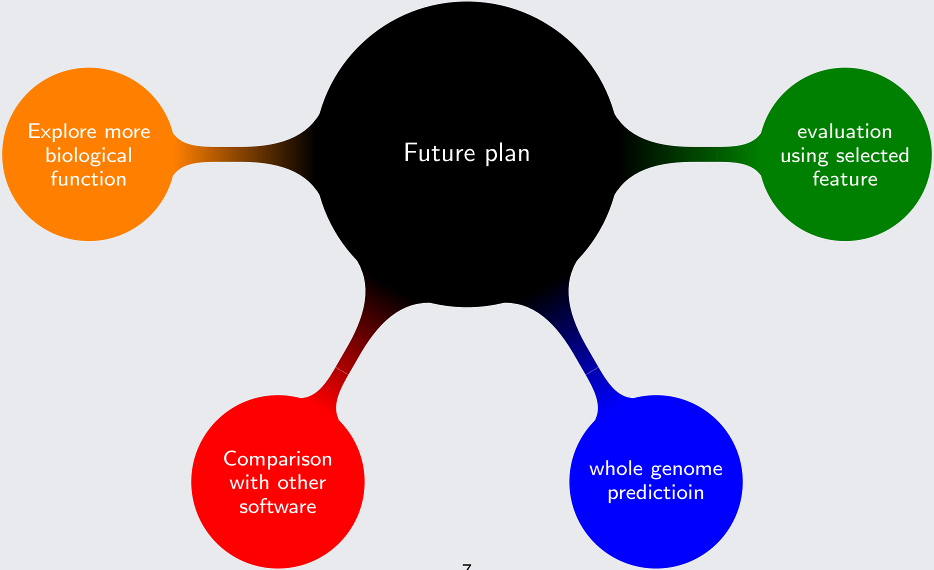


Pattern





Future plan

Explore more biological function

evaluation using selected feature

Comparison with other software

whole genome predictioin