Improving CLIP-seq data analysis by incorporating transcript information

Supplementary Material

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Supplementary tables

Table 1: Exon overlap statistics of ENCODE eCLIP datasets (see Additional File 1 in .xlsx format).

Table 2: Peak length statistics for CLIPper (replicate 1), CLIPper IDR, PEAKachu, and PureCLIP on YBX3 K562 replicate 1 eCLIP data. Peaks were called as described in supplementary methods section "Peak caller setup". Introns for determining overlapping sites were selected based on the set of exons extracted, as described in methods section "Data preparation and exon overlap statistics". A site is counted as intron-spanning if it completely overlaps with an intronic region.

Metric	CLIPper	CLIPper IDR	PEAKachu	PureCLIP
# sites	132,842	17,982	11,537	54,308
# sites > 500 nt	0	0	471	0
# intron-spanning sites	4	2	1,096	0
Minimum length	1	1	18	1
Maximum length	263	217	22,875	25
Mean length	37.9	28.0	112.4	1.6
Median length	34	27	48	1
25th percentile	19	13	42	1
75th percentile	51	50	64	2

Table 3: Dataset statistics for the 6 eCLIP sets used for genomic and transcript context comparison. A minimum log_2 fold change (LFC) of 3 and a maximum p-value (PV) of 0.01 was used for filtering initial CLIPper replicate 1 peak sites. Moreover, only exonic sites (overlapping $\geq 90\%$ with exons) near exon borders (≤ 10 nt away) were selected. In case of overlapping sites (≤ 10 nt distance), only the site with the highest LFC was kept. Positives: number of positive training instances. Negatives: number of negative training instances.

RBP	Cell type	LFC	PV	Positives	Negatives
FMR1	K562	3	0.01	2569	2569
FXR2	K562	3	0.01	3166	3166
IGF2BP1	K562	3	0.01	2199	2199
PUM2	K562	3	0.01	1136	1136
SRSF1	K562	3	0.01	1049	1049
YBX3	K562	3	0.01	4370	4370

Table 4: Performance results for 6 RBP eCLIP sets with genomic and transcript context. We report average accuracies obtained by 10-fold cross validation together with standard deviations (apart from GraphProt).

Methods	RBP	Cell line	Genomic context	Transcript context
DeepBind	FMR1	K562	80.63±1.58	88.22±1.99
	FXR2	K562	76.93±2.66	86.93±1.18
	IGF2BP1	K562	75.72±2.59	83.90±2.08
	PUM2	K562	70.05±2.94	80.69±2.31
	SRSF1	K562	79.39±4.64	85.98±3.07
	YBX3	K562	76.63±2.73	87.32±1.24
GraphProt	FMR1	K562	78.47	88.50
	FXR2	K562	75.71	86.73
	IGF2BP1	K562	66.24	84.18
	PUM2	K562	64.88	79.58
	SRSF1	K562	76.41	86.61
	YBX3	K562	71.63	86.61
GraphProt2	FMR1	K562	80.95±1.50	89.39±1.38
	FXR2	K562	77.04±1.20	88.55±1.34
	IGF2BP1	K562	74.31±2.27	85.38±1.47
	PUM2	K562	70.07±2.64	81.25±2.54
	SRSF1	K562	79.65±4.62	87.94±3.11
	YBX3	K562	77.94±1.27	88.99±0.86

Table 5: Motif search results for 9 RBPs and 28 binding motifs collected from various sources (see Additional File 3 in .xlsx format).

Supplementary figures

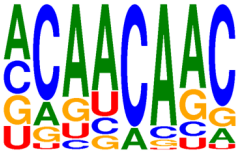
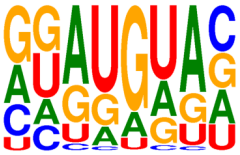
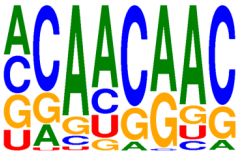
RBP	Literature knowledge	GraphProt sequence logo	
		Genomic context	Transcript context
FMR1	GAC-containing sites Similar to FXR1 and FXR2		
FXR2	GAC-containing sites Similar to FMR1 and FXR1		
IGF2BP1	CA(U)-rich sites*		
PUM2	UGUANAUA dominant motif		
SRSF1	GA(C)-containing sites		
YBX3	CA(U)-containing sites		

Figure 1: GraphProt sequence logos generated from models trained on the 6 eCLIP sets with genomic and transcript context (resulting in 12 models and 12 logos). Literature knowledge regarding RBP binding preferences was obtained from the ATtRACT database [1]. A logo is constructed for each RBP-context combination from the top 200 scoring sites (taking highest scoring 8-mer sequence for each site) of the positive set. *: note that IGF2BP1 binding sites are comprised of several parts, of which one dominant part are CA(U) rich sites.

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References

[1] Giudice, G., Sánchez-Cabo, F., Torroja, C., Lara-Pezzi, E.: Attract—a database of rna-binding proteins and associated motifs. Database **2016** (2016)