K-mer Analysis on Developmental and Housekeeping Enhancer Peaks

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Abstract

The regulation of gene expression involves interaction between transcriptional enhancers and core promoters. However, the separation between developmental and housekeeping gene regulation remains unknown. Here, we present a method to detect if different core promoters exhibit specificity to certain enhancers within massively parallel assays for enhancer detection. We use k-mers of various length (3-8bp) as sequence features and compare k-mer frequencies between developmental and housekeeping enhancers. This method shows promoter specificity of enhancers in *D. melanogaster*.

Background

- A promoter located in the upstream of protein-coding gene initiates transcription. An Enhancer located in non-coding DNA and far from its promoter activates gene transcription.
- Housekeeping enhancers are active among cells, while developmental enhancers exist in specific cell.
- K-mer is the subsequence of length k in DNA sequence.

Data Description

- STARR-seq, a method for enhancer detection, identifies thousands of cell-type-specific enhancers in Drosophila melanogaster S2 cell.
- Housekeeping core promoter (hkCP): RpS12, eEF1δ, NipB, x16
- Developmental core promoter (dCP): DSCP, eve, evelong, pnr, Hsp70
- Length of each enhancer peak is 500bp.

Methods

Step 1: For each enhancer peak, count all k-mers (k=3…8) to get k-mer frequency

Step 2: For each pair of promoters, run ANOVA test on each k-mer to detect if there is significant difference in means of frequency

Step 3: Narrow down significant k-mers

Results

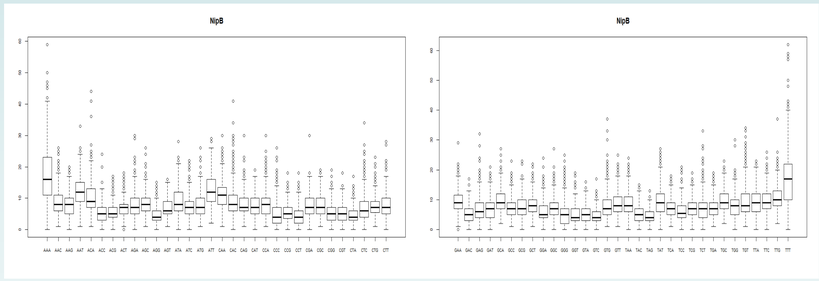


Figure 1: Frequency of 3-mers in enhancer peaks of NipB

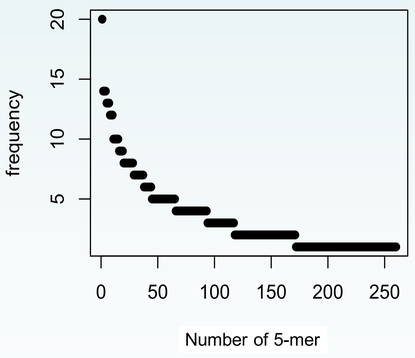
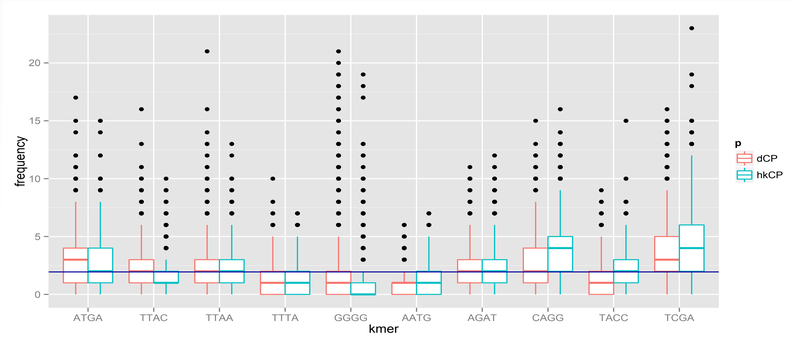


Figure 2 (left): Frequency distribution of 5-mers appearing significant in all pairs

Figure 3 (bottom): Compare frequency of significant 4-mers between merged dCP and hkCP enhancers



Conclusion

Kmer sequence features exhibit a specificity to developmental and housekeeping enhancers

3-mer	ATG AGA TTA
4-mer	ATGA TTAC TTAA TTTA GGGG AATG AGAT CAGG TACC TCGA
5-mer	AGATA CACTG TCGAT ATCGA TATCG TTTAA AATGA GGCGC TTACC AGCTG CATTC TGACC TGGGG TTTAC
6-mer	TATCGA ATCGAT CAGCTG ACAGCT CTATCG TCGATA GTGACC AGATAA CGATAG TTTAAA ATTTAA GGTCAC
7-mer	TATCGAT GGTCACA ATCGATA ACAGCTG ACTATCG TGTGACC CTATCGA GTGTGAC TCGATAG TTATCGA ATATCGA ATCGATT GTTATCG GTCACAC TCACACT
8-mer	GGTCACAC GTCACACT ATATCGAT CGGTCACA AACAGCTG CTATCGAT TATCGATA ACAGCTGA ATCGATAG GTGTGACC TATCGATG TCGATTGT ACTATCGA GTTATCGA TATCGATT

Future Research

- Compare result of significant k-mers with known DNA sequence motifs
- Build machine learning model to classify developmental and housekeeping enhancers

References

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