

MAAPER: model-based analysis of alternative polyadenylation using 3' end-linked reads

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Manuscript Source: <https://www.biorxiv.org/content/10.1101/2021.03.21.436343v1>

Manuscript Authors: Wei Vivian Li, Dinghai Zheng, Ruijia Wang & Bin Tian

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

Contact Information:

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title **MAAPER: model-based analysis of alternative polyadenylation using 3' end-linked reads**

S1 [001] Abstract

S1 [002] Most eukaryotic genes harbor multiple cleavage and polyadenylation sites (PASs), leading to expression of alternative polyadenylation (APA) isoforms.

Most eukaryotic genes harbor multiple cleavage ...
... and polyadenylation sites ...
... (PASs), ...
... leading ...
... to expression ...
... of alternative polyadenylation ...
... (APA) ...
... isoforms.

S1 [003] APA regulation has been implicated in a diverse array of physiological and pathological conditions.

APA regulation has been implicated ...
... in a diverse array ...
... of physiological ...
... and pathological conditions.

S1 [004] While RNA sequencing tools that generate reads containing the PAS, named onSite reads, have been instrumental in identifying PASs, they have not been widely used.

While RNA sequencing tools ...
... that generate reads containing the PAS, ...
... named onSite reads, ...
... have been instrumental ...
... in identifying PASs, ...
... they have not been widely used.

S1 [005] By contrast, a growing number of methods generate reads that are close to the PAS, named nearSite reads, including the 3' end counting strategy commonly used in single cell analysis.

By contrast, ...
... a growing number ...
... of methods generate reads ...
... that are close ...
... to the PAS, ...
... named nearSite reads, ...
... including the 3' end counting strategy commonly used ...
... in single cell analysis.

- S1 [006]** How these nearSite reads can be used for APA analysis, however, is poorly studied.
- How these nearSite reads can be used ...
... for APA analysis, ...
... however, ...
... is poorly studied.
- S1 [007]** Here, we present a computational method, named model-based analysis of alternative polyadenylation using 3' end-linked reads (MAAPER), to examine APA using nearSite reads.
- Here, ...
... we present a computational method, ...
... named model-based analysis ...
... of alternative polyadenylation ...
... using 3' end-linked reads ...
... (MAAPER), ...
... to examine APA ...
... using nearSite reads.
- S1 [008]** MAAPER uses a probabilistic model to predict PASs for nearSite reads with high accuracy and sensitivity, and examines different types of APA events, including those in 3'UTRs and introns, with robust statistics.
- MAAPER uses a probabilistic model ...
... to predict PASs ...
... for nearSite reads ...
... with high accuracy ...
... and sensitivity, ...
... and examines different types ...
... of APA events, ...
... including those ...
... in 3'UTRs ...
... and introns, ...
... with robust statistics.
- S1 [009]** We show MAAPER's accuracy with data from both bulk and single cell RNA samples and its applicability in unpaired or paired experimental designs.
- We show MAAPER's accuracy ...
... with data ...
... from both bulk ...
... and single cell RNA samples ...
... and its applicability ...
... in unpaired ...
... or paired experimental designs.
- S1 [010]** Our result also highlights the importance of using well annotated PASs for nearSite read analysis.
- Our result also highlights the importance ...
... of using well annotated PASs ...
... for nearSite read analysis.

S2 [011] Introduction

S2 [012] Almost all eukaryotic mRNA genes employ cleavage and polyadenylation (CPA) for 3' end processing (Proudfoot, 2016).

Almost all eukaryotic mRNA genes employ cleavage ...
... and polyadenylation ...
... (CPA) ...
... for 3' end processing ...
... (Proudfoot, 2016).

S2 [013] Well over half of the genes harbor multiple PASs, resulting in expression of alternative polyadenylation (APA) isoforms (Gruber and Zavolan, 2019; Tian and Manley, 2017).

Well ...
... over half ...
... of the genes harbor multiple PASs, ...
... resulting ...
... in expression ...
... of alternative polyadenylation ...
... (APA) ...
... isoforms ...
... (Gruber ...
... and Zavolan, 2019; ...
... Tian ...
... and Manley, 2017).

S2 [014] While most of the APA events occur in the 3'-most exon of genes, leading to isoforms with variable 3' untranslated regions (3'UTRs), a sizable fraction of APA sites, e.g., ~20% in the human genome, are located in introns, the usage of which additionally leads to alternation of coding sequence (CDS).

While most of the APA events occur ...
... in the 3'-most exon ...
... of genes, ...
... leading ...
... to isoforms ...
... with variable 3' untranslated regions ...
... (3'UTRs), ...
... a sizable fraction ...
... of APA sites, ...
... e.g., ...
... ~20% ...
... in the human genome, ...
... are located ...
... in introns, ...
... the usage ...
... of which additionally leads ...
... to alternation ...
... of coding sequence ...
... (CDS).

- S2 [015]** APA is increasingly being appreciated as a major mechanism for gene regulation (Gruber and Zavolan, 2019; Tian and Manley, 2017), diversifying the transcriptome in different cell types and under various pathological and physiological conditions.
- APA is increasingly being appreciated ...
... as a major mechanism ...
... for gene regulation ...
... (Gruber ...
... and Zavolan, 2019; ...
... Tian ...
... and Manley, 2017), ...
... diversifying the transcriptome ...
... in different cell types ...
... and ...
... under various pathological ...
... and physiological conditions.
- S2 [016]** To accurately profile APA isoforms is of great importance in understanding the mechanisms and consequences of APA.
- To accurately profile APA isoforms is ...
... of great importance ...
... in understanding the mechanisms ...
... and consequences ...
... of APA.
- S2 [017]** The advent of RNA-seq technologies has enabled comprehensive transcriptome analysis.
- The advent ...
... of RNA-seq technologies has enabled comprehensive transcriptome analysis.
- S2 [018]** RNA-seq data have also been used to examine APA isoform profiles, either by taking advantage of drop of RNA-seq read coverage at the PAS (Xia et al., 2014) or by using annotated PASs (Grassi et al., 2016; Ha et al., 2018; Wang and Tian, 2020).
- RNA-seq data have also been used ...
... to examine APA isoform profiles, ...
... either ...
... by taking advantage ...
... of drop ...
... of RNA-seq read coverage ...
... at the PAS ...
... (Xia et al., 2014) ...
... or by using annotated PASs ...
... (Grassi et al., 2016; ...
... Ha et al., 2018; ...
... Wang ...
... and Tian, 2020).
- S2 [019]** However, because RNA-seq data are not designed to identify PASs, these approaches lack high accuracy and sensitivity for PAS identification and APA profiling.
- However, ...

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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