

BRAKER1: Unsupervised RNA-Seq-Based Genome Annotation with GeneMark-ET and AUGUSTUS

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ABSTRACT

Motivation: Many genome sequencing projects are accompanied by transcriptome sequencing. GeneMark-ET is a gene prediction tool that incorporates unassembled RNA-Seq reads into unsupervised training and subsequently generates *ab initio* gene predictions. AUGUSTUS is a gene finder that usually requires supervised training and uses information from unassembled RNA-Seq reads in the prediction step.

Results: We present BRAKER1, a pipeline for unsupervised RNA-Seq-based genome annotation that combines the advantages of GeneMark-ET and AUGUSTUS. BRAKER1 requires an RNA-Seq read alignment file and a genome file as input. First, GeneMark-ET performs iterative training and generates initial gene structures. Second, AUGUSTUS uses predicted genes for training and then integrates RNA-Seq read information into final gene predictions. In our experiments, we observed that BRAKER1 was more accurate than MAKER2 when it is using RNA-Seq as sole source for training and prediction. BRAKER1 does not require pre-trained parameters or a separate training step.

Availability: BRAKER1 is available for download at <http://bioinf.uni-greifswald.de/downloads/> and <http://exon.gatech.edu/>.

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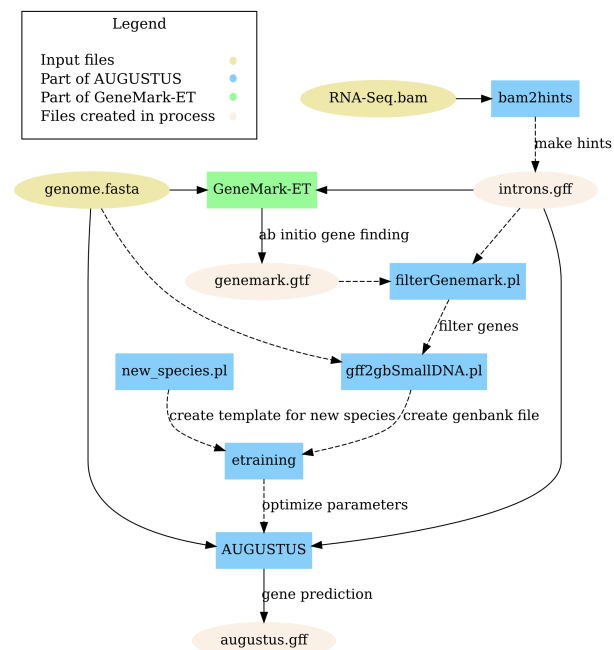


Fig. 1. Schematic view of the BRAKER1 pipeline.

1 INTRODUCTION

2 PIPELINE DESCRIPTION

BRAKER1 is implemented in Perl and requires two input files: an RNA-Seq alignment file in bam-format, and a corresponding genome file in fasta-format. Spliced alignment information is extracted from the RNA-Seq file and stored in gff-format. GeneMark-ET uses the genome file and the spliced alignment gff-file for RNA-Seq supported unsupervised

training. After training, GeneMark-ET creates an *ab initio* gene set. Those gene structures that have support by RNA-Seq alignments in all introns are selected for automated training of AUGUSTUS. After training, AUGUSTUS predicts genes in the input genome file using spliced alignment information from RNA-Seq as extrinsic evidence. The pipeline is illustrated in figure 1.

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Table 1. Accuracy results of BRAKER1 and MAKER2 in genomes of four model organisms. For BRAKER1, accuracy is shown for the GeneMark-ET *ab initio* predictions as well as for the AUGUSTUS predictions with hints from RNA-Seq.

	<i>Arabidopsis thaliana</i>			<i>Caenorhabditis elegans</i>			<i>Drosophila melanogaster</i>			<i>Schizosaccharomyces pombe</i>		
	BRAKER1- GeneMark	BRAKER1- AUGUSTUS	MAKER2	BRAKER1- GeneMark	BRAKER1- AUGUSTUS	MAKER2	BRAKER1- GeneMark	BRAKER1- AUGUSTUS	MAKER2	BRAKER1- GeneMark	BRAKER1- AUGUSTUS	MAKER2
Gene sensitivity	53.9	63.2	51.3	43.0	55.1	41.0	58.5	70.23	58.0	80.0	77.3	42.7
Gene specificity	46.1	51.3	52.5	41.7	56.1	30.8	49.9	59.0	46.9	84.9	81.2	68.6
Transcript sensitivity	45.4	53.9	43.5	32.9	43.2	31.3	42.3	52.0	42.3	80.0	77.3	42.7
Transcript specificity	46.1	50.0	52.5	41.7	54.0	30.8	49.9	57.8	47.9	84.9	77.4	68.6
Exon sensitivity	81.1	83.0	76.1	79.9	80.9	69.4	68.5	75.1	64.9	85.2	84.2	50.1
Exon specificity	72.4	78.5	76.1	78.2	85.4	62.3	57.9	66.2	55.0	89.0	82.6	71.4

3 TEST DATA

In order to demonstrate prediction accuracy, genomes, reference annotations and RNA-Seq libraries were retrieved for four model organisms from the respective databases: for *Arabidopsis thaliana*, TAIR 10 was downloaded from <http://arabidopsis.org/>; for *Caenorhabditis elegans*, WS240 was downloaded from <http://www.wormbase.org/>; for *Drosophila melanogaster*, R5 was downloaded from <http://flybase.org/>; for *Schizosaccharomyces pombe*, ASM294v2.23 was downloaded from <http://www.pombase.org/>. The following RNA-Seq libraries were retrieved from the short read archive at NCBI: SRR934391 (for *A. thaliana*); SRR065719 (for *C. elegans*); SRR023505, SRR023546, SRR023608, SRR026433, SRR027108 (for *D. melanogaster*); SRR097898, SRR097899, SRR097900, SRR097902, SRR097903, SRR097905, SRR097906, SRR097907, SRR097908, SRR097909, SRR097912, SRR097915, SRR097917, SRR097921, SRR097922, SRR097925, SRR402833 (for *S. pombe*).

4 ACCURACY RESULTS

5 CONCLUSION

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