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Databases and ontologies

FoldAtlas: a repository for genome-wide RNA structure probing data

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Abstract

Summary: Most RNA molecules form internal base pairs, leading to a folded secondary structure. Some of these structures have been demonstrated to be functionally significant. High-throughput RNA structure chemical probing methods generate millions of sequencing reads to provide structural constraints for RNA secondary structure prediction. At present, processed data from these experiments are difficult to access without computational expertise. Here we present FoldAtlas, a web interface for accessing raw and processed structural data across thousands of transcripts. FoldAtlas allows a researcher to easily locate, view, and retrieve probing data for a given RNA molecule. We also provide in silico and in vivo secondary structure predictions for comparison, visualized in the browser as circle plots and topology diagrams. Data currently integrated into FoldAtlas are from a new high-depth Structure-seq data analysis in Arabidopsis thaliana, released with this work.

Availability and Implementation: The FoldAtlas website can be accessed at www.foldatlas.com. Source code is freely available at github.com/mnori/foldatlas under the MIT license. Raw reads data are available under the NCBI SRA accession SRP066985.

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Supplementary information: Supplementary data are available at Bioinformatics online.

1 Introduction

RNA structure plays an important role in all steps of gene expression and regulation (Mortimer et al., 2014; Sharp, 2009). Earlier studies inferred the secondary structures of individual RNA sequences using low throughput in vitro probing or in silico prediction approaches. More recently, genome-wide in vivo structure probing methods have emerged, allowing structures to be determined across the transcriptomes of living cells (Ding et al., 2014; Rouskin et al., 2014; Spitale et al., 2013; Talkish et al., 2014; Tang et al., 2015).

Chemical probing methods can be used to determine RNA secondary structure in living cells (Kwok et al., 2013; McGinnis and Weeks, 2014; Spitale et al., 2013). These methods include dimethyl sulfate (DMS) probing and selective 2′-hydroxyl acylation analyzed by primer extension (SHAPE). In DMS probing, the N1 position of adenine and the N3 position of cytosine are methylated when the base is not involved in Watson–Crick base pairing. In SHAPE, all unpaired bases are modified.

Chemically modified bases lead to stalling of reverse transcriptase. With reverse transcription, PCR, deep sequencing and normalization, reactivities can be assigned to individual RNA sequence positions. These reactivities describe the extent of exposure of a nucleotide to solution, and can be exploited as pseudo-free energy constraints for
along with alternative splice isoforms, where relevant. An overview work, displays the splicing configuration of the selected transcript, loaded, the functionality across the genome. When a transcript is selected and processed structure probing data, along with pre-generated RNA allows a researcher without computational expertise to se-FoldAtlas

2 Results

FoldAtlas provides convenient access to in vivo RNA structure probing data across thousands of transcripts. The current release, 1.1, includes data from a high depth genome-scale probing experiment in Arabidopsis thaliana. To predict structure for a transcript, we generated up to 20 secondary structures using the RNAstructure Fold tool, and visualized the structure ensemble using PCA plots. In this work, our preference to use RNAstructure is due to the ability to specify experimental constraints, and is consistent with the approach taken in our earlier work (Ding et al., 2014). In future versions of FoldAtlas, we plan to also provide options to visualize structure predictions made using other methods, including SeaFold (Ouyang et al., 2013), and Vienna RNAfold, which now allows experimental constraints (Lorenz et al., 2011, 2015). We are also considering including SHAPE probing data, in vitro data, reactivities calculated using alternative normalization methods, data from other organisms, and data from other studies.

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References