FoldAtlas
a repository for genome-wide RNA structure probing data
Norris, Matthew; KWOK, Chun Kit; Cheema, Jitender; Hartley, Matthew; Morris, Richard J.; Aviran, Sharon; Ding, Yiliang

Published in:
Bioinformatics

Published: 15/01/2017

Document Version:
Final Published version, also known as Publisher's PDF, Publisher's Final version or Version of Record

License:
CC BY-NC

Publication record in CityU Scholars:
Go to record

Published version (DOI):
10.1093/bioinformatics/btw611

Publication details:

Citing this paper
Please note that where the full-text provided on CityU Scholars is the Post-print version (also known as Accepted Author Manuscript, Peer-reviewed or Author Final version), it may differ from the Final Published version. When citing, ensure that you check and use the publisher's definitive version for pagination and other details.

General rights
Copyright for the publications made accessible via the CityU Scholars portal is retained by the author(s) and/or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights. Users may not further distribute the material or use it for any profit-making activity or commercial gain.

Publisher permission
Permission for previously published items are in accordance with publisher's copyright policies sourced from the SHERPA RoMEO database. Links to full text versions (either Published or Post-print) are only available if corresponding publishers allow open access.

Take down policy
Contact lbscholars@cityu.edu.hk if you believe that this document breaches copyright and provide us with details. We will remove access to the work immediately and investigate your claim.
Databases and ontologies

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

Matthew Norris1,*, Chun Kit Kwok2, Jitender Cheema1, Matthew Hartley1, Richard J. Morris1, Sharon Aviran3 and Yiliang Ding1,*

1John Innes Centre, Norwich Research Park, Norwich, UK, 2Department of Biology and Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong SAR, China and 3Department of Biomedical Engineering and Genome Center, UC Davis, Davis, CA, USA

*To whom correspondence should be addressed.

Associate Editor: Ivo Hofacker

Received on December 21, 2015; revised on August 5, 2016; accepted on September 20, 2016

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. Contact: yiliang.ding@jic.ac.uk or matthew.norris@jic.ac.uk.

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., 2015; 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

© The Author 2016. Published by Oxford University Press. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
are visualized using a Principal Components Analysis (PCA) view (Fig. 1C). PCA plots were generated using a previously described method (Halvorsen et al., 2010). Each structure can also be visualized using both circle plots (Fig. 1D) and structure diagrams (Fig. 1E) generated using the ViennaRNA package (Hofacker, 2013; Kerpedjiev et al., 2015, Lorenz et al., 2011). The corresponding MFE structures can be downloaded as tab-delimited text files.

The FoldAtlas chemical reactivity data are from a DMS chemical modification experiment in Arabidopsis thaliana. These data were generated by using a previously established Structure-seq method (Ding et al., 2014, 2015), but with two rounds of poly-A selection to enrich the proportion of mRNA. Detailed analysis of this experiment is provided in the Supplementary Results section of the Supplementary Material.

3 Conclusions and future work

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 SeqFold (Ouyang et al., 2013), and ViennaRNAfold, 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.

Acknowledgements

This research was supported in part by the NBIP Computing infrastructure for Science (CGS) group through the provision of a High Performance Computing Cluster.

Funding

This work was supported by the Biotechnology and Biological Sciences Research Council (BBSRC) [BB/L025000/1 to M.N. and Y.D. and BB/N022572/1 to M.N. Y.D and S.A.]; and the National Institutes of Health [HG006860 to S.A.].

Conflict of Interest: none declared.

References


