Chromatin interactions predict co-expression in the mouse cortex

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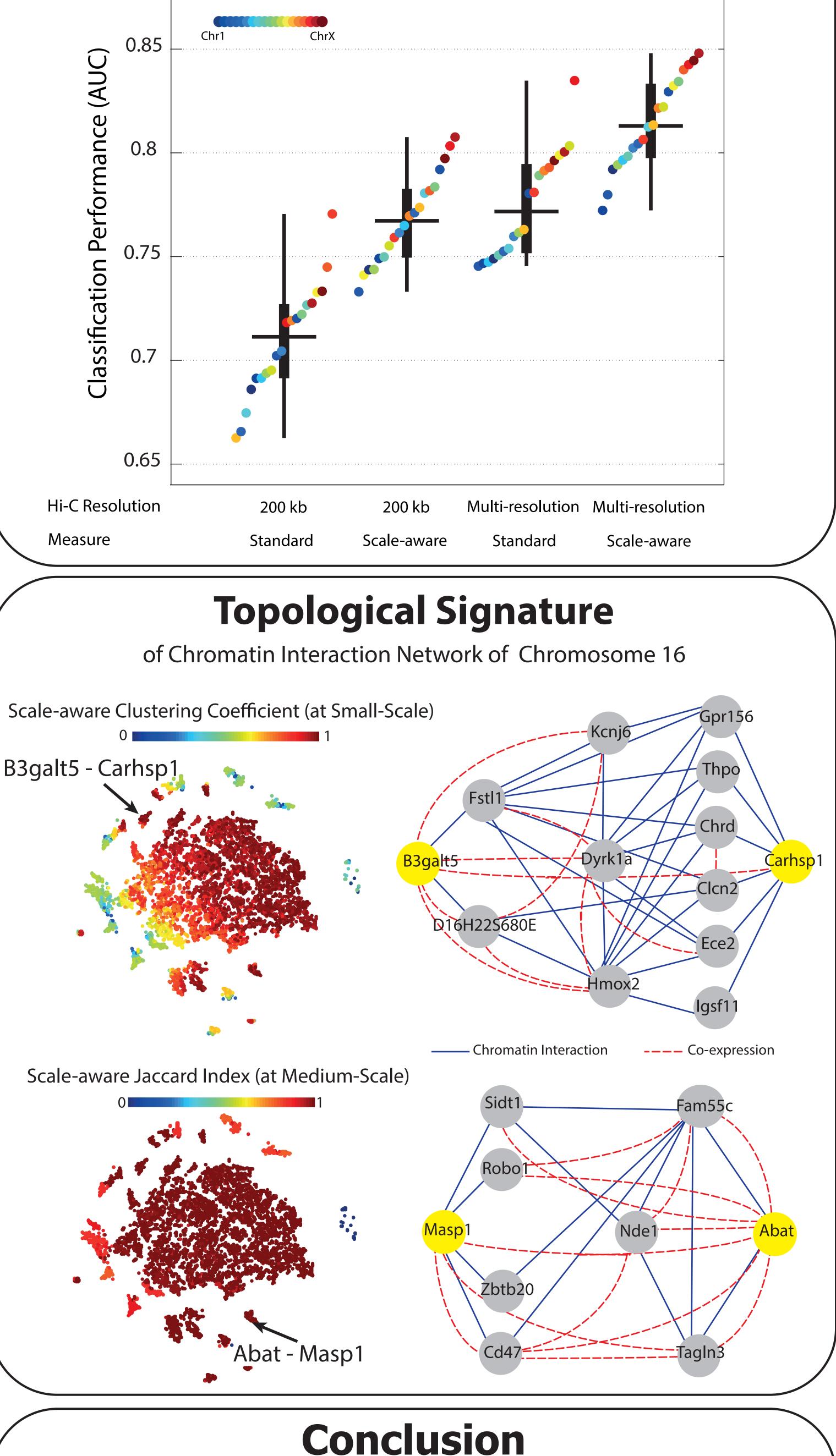
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Summary

The 3D conformation of the genome in the cell nucleus influences important biological processes such as gene expression. Predicting gene co-expression from frequent long-range chromatin interactions is a challenging task. We address this by characterizing the topology of the cortical chromatin interaction network using scale-aware topological measures¹. We demonstrate that based on these characterizations it is possible to accurately predict spatial co-expression between genes in the mouse cortex.

Classification Performance

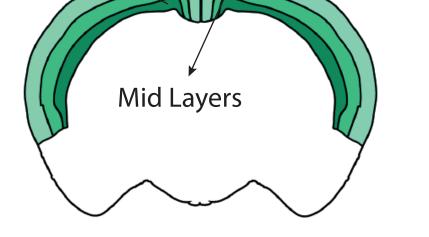
RNN classifier is trained on topological measures

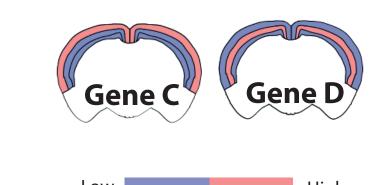


Co-expression Prediction

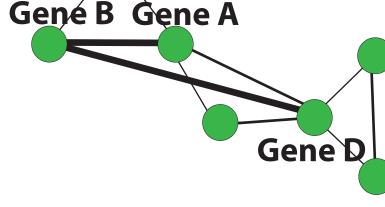
Using interaction profile between a gene-pair encoded in interaction network

Chromatin Interaction Profile 3D Structure of Genome Gene D Gene D Gene D Gene D Gene D Gene D Chromatin Interaction Network Gene D Coronal View of Cortical Layers Deep Layer Superficial Layers Gene D Gene C Gene C Gene D Co-expression Network Gene C





Expression Level



Chromatin Interaction Network:

Intrachromosomal Hi-C contacts from mouse cortical cells²

Co-expression Network:

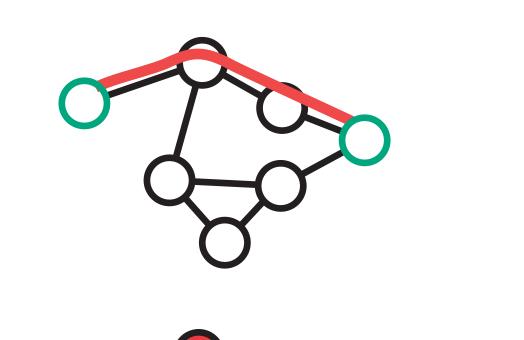
Spatial co-expression between genes from Allen Mouse Brain Atlas (ABA)³

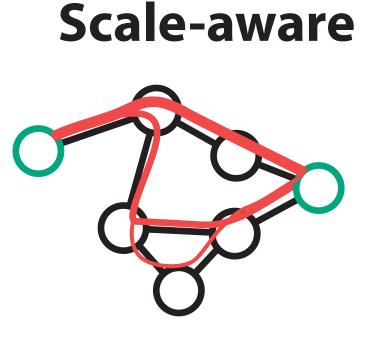
Topological Measures

Scale-aware topological measures are calculated based on diffusion kernels

Standard

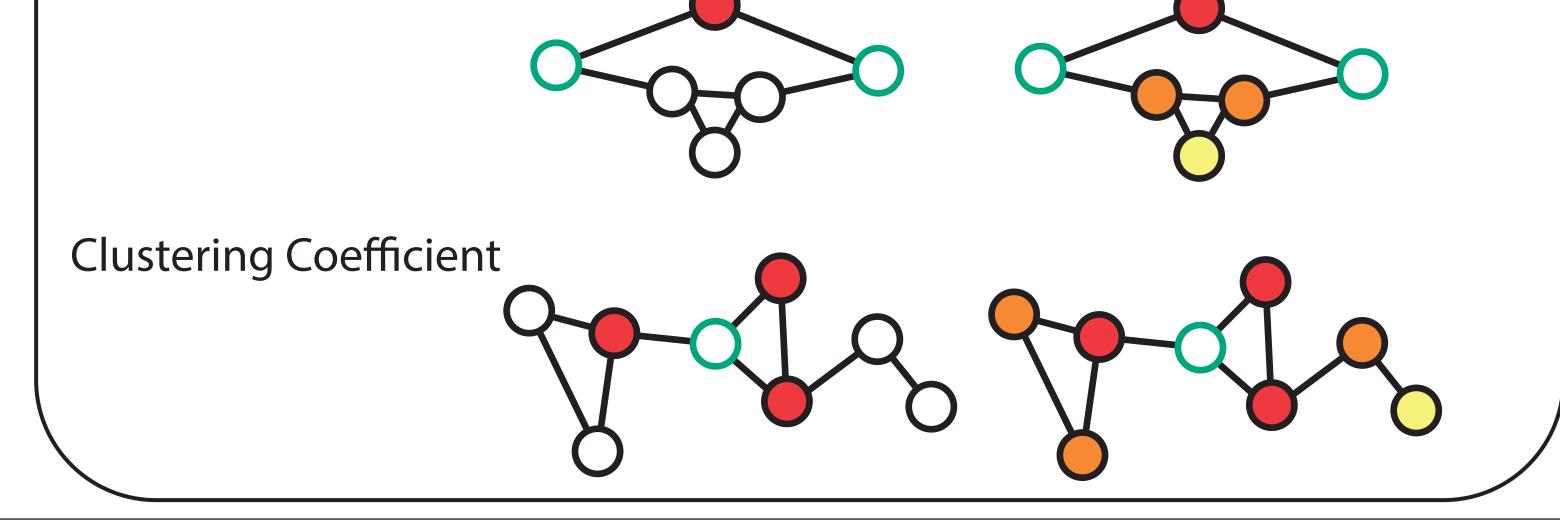
Shortest Path





Jaccard Index

We find that the chromatin interaction profile of a gene-pair is a good predictor of their spatial co-expression. The accuracy of the prediction substantially improves when chromatin interactions are described by scale-aware topological measures of the multi-resolution chromatin interaction network. For co-expression prediction, it is necessary to take into account different levels of chromatin interactions from direct interaction between genes (i.e. small-scale) to chromatin compartment interactions (i.e. large-scale).



Reference

[1] M. Hulsman, et al., Graph-topological scale-spaces reveal functional information in physical protein interaction networks, Bioinformatics (2014)
[2] Y. Shen, et al., A map of the cis-regulatory sequences in the mouse genome. Nature (2012)
[3] E. Lein, et al., Genome-wide atlas of gene expression in the adult mouse brain. Nature (2007)

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