

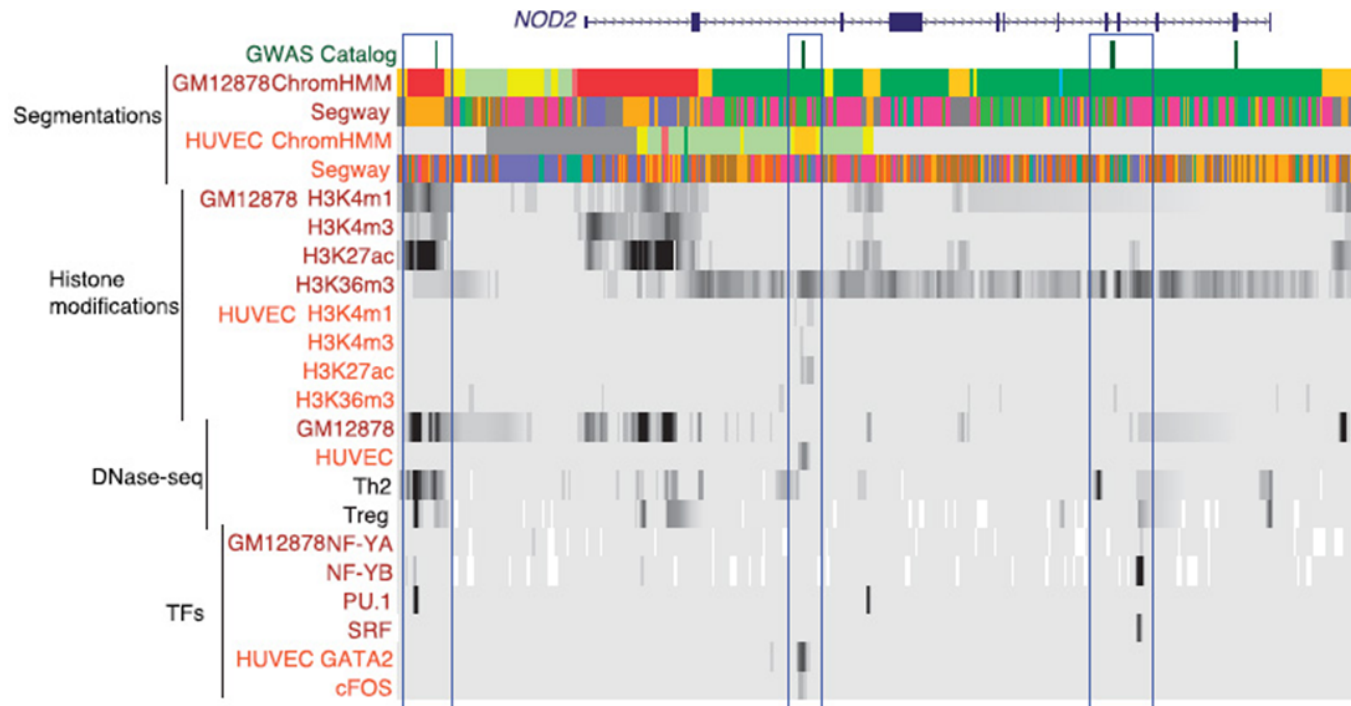
Spectacle: fast chromatin state annotation using spectral learning

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Chromatin State Annotation via HMMs

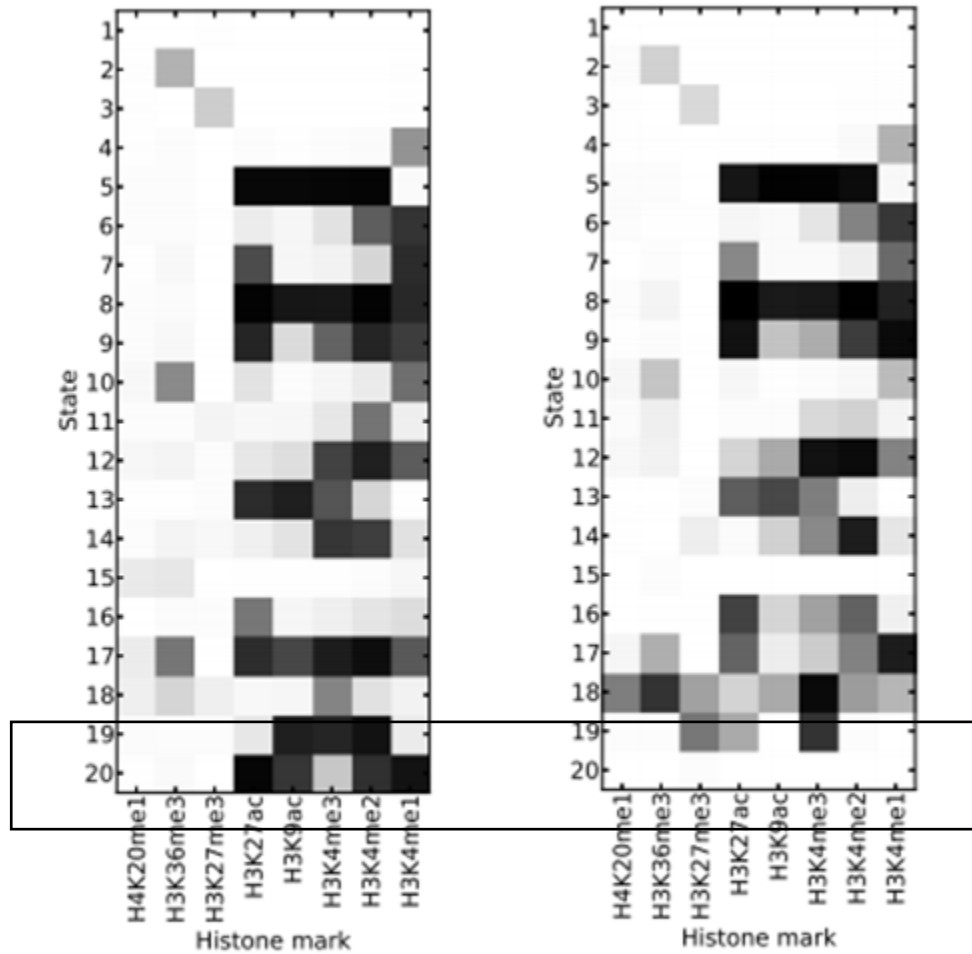
- Input: a set of chromatin marks in a cell type
- Output: chromatin states (i.e. colors) representing biological features such as enhancers, promoters, *etc.*



Overview

- Spectacle: predicting chromatin states for a single cell type
 - **Song and Chen, Genome Biology, 2015**
- Spectacle-Tree: joint analysis of multiple samples
 - **Zhang, Song, Chaudhuri, Chen, NIPS 2015**
 - **Song, Zhang, Chaudhuri, Chen, in review**
- **Main idea:** Expectation-Maximization is slow and only finds a local optimum, so we use Spectral Learning instead
- Spectacle learns the model ~100 times faster than ChromHMM

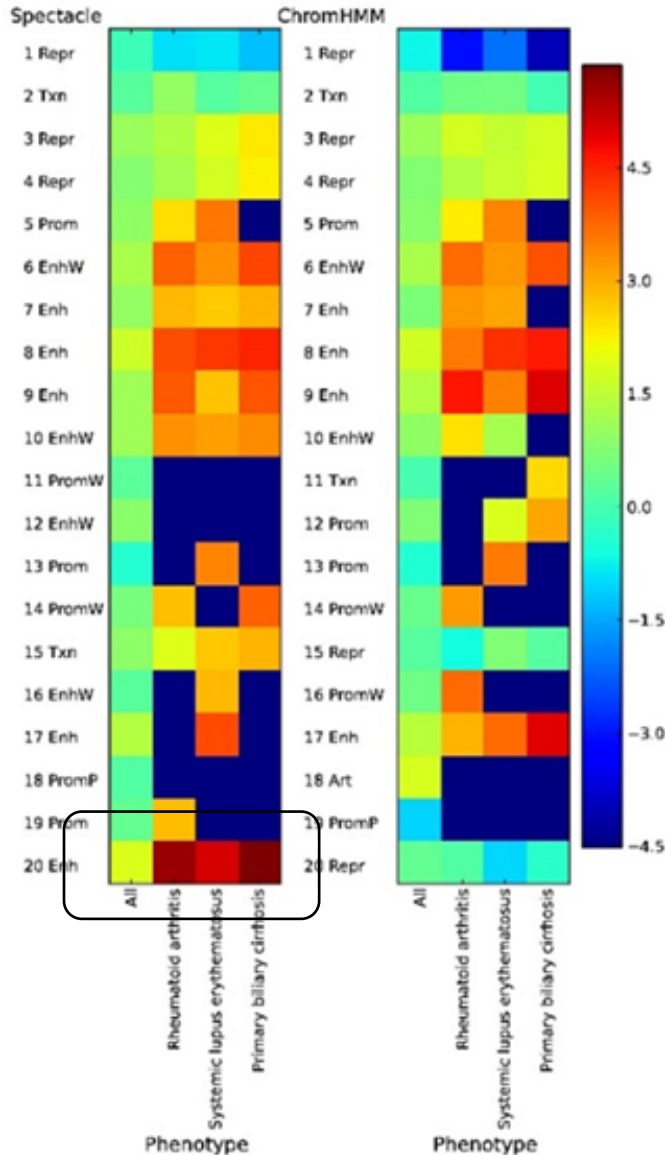
Comparison of Chromatin States



(b) Spectacle

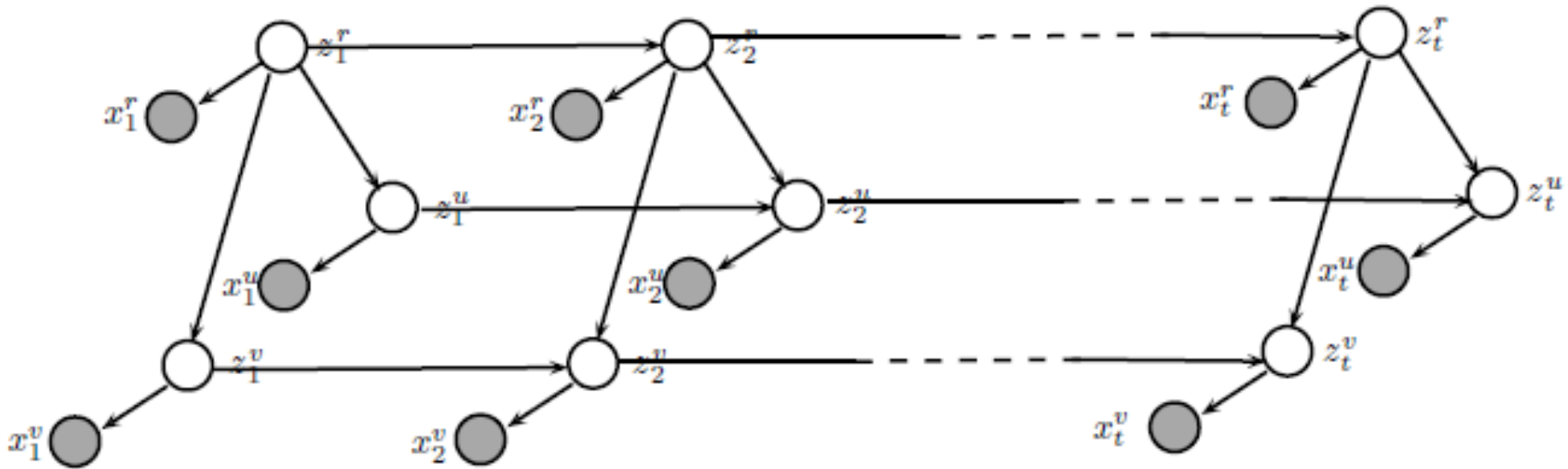
(a) ChromHMM

Enrichment of Disease-Associated Variants



- There is higher enrichment of disease SNPs in chromatin state 20 which was found only by Spectacle

Spectacle-Tree: analyzing multiple cell types



Summary of Spectacle-Tree Results

- Tree-HMM took 13 hours
- Spectacle-Tree took 22 min

- Tree-HMM found many null chromatin states
- Spectacle-Tree found biologically significant chromatin states (enhancers, promoters etc.)

- Spectacle-Tree had higher prediction accuracy for promoters than Tree-HMM or Spectacle

- Tree-HMM finds the same chromatin state in all samples
- Spectacle-Tree found poised enhancers in ES cells

Conclusions

- Spectacle analyzes a single cell type or tissue
- Spectacle-Tree analyzes multiple related samples

- Main advantages over ChromHMM and Segway are
 - Faster speed
 - Ability to jointly analyze multiple samples
 - Higher accuracy when a lot of the genome has no biochemical signal

- Software and chromatin state annotations for ENCODE and Roadmap Epigenomics samples are available on Kevin Chen's web page

- For any questions, please email kcchen@dls.rutgers.edu