

Multiple Logistic Regression Model Pipeline for MRE

Prediction Task for Dosage Compensation in Drosophila

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PHP1560 Final Project



School of
Public Health

Outline

- **Motivation and Background**

- Data and Metrics

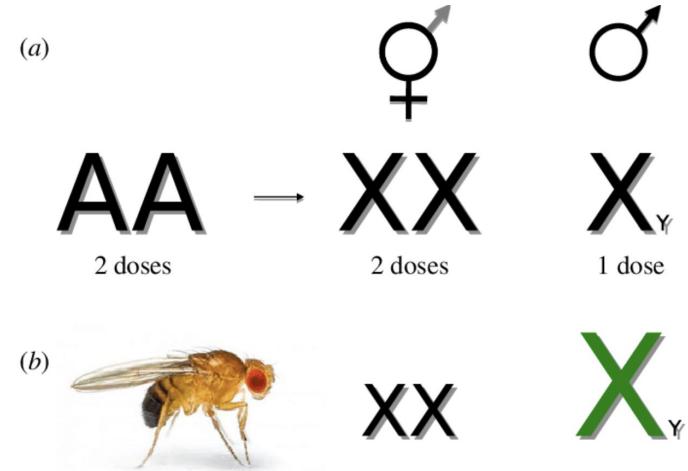
- Program Design

- Results and Interpretation

- Reflection and Conclusion

Dosage Compensation in Drosophila

- **Dosage Compensation (DC)** equalizes gene expression in sex chromosomes
 - In Drosophila, DC upregulates single X chromosome in males (XY) to match females (XX)
- A transcription factor CLAMP binds to **MRE (Male-Specific Lethal) motif** to start DC machinery
 - However, MRE motif is not a strict sequence, making it difficult to locate.
- Certain **epigenetic markers** are markers of MREs
 - **Histone modifications** control chromatin environment → impacts where MRE can exist
 - **ChIP-seq** data reveals amount of histone modifications across all chromosomes



Research Question

Research Question:

Are epigenetic features, specifically histone modifications, accurate predictors of the presence of the MRE motif in Drosophila chromosomes?

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Data

- Epigenetic factors collected from ChIP-Seq data
 - 8 Histone modifications:
h3k27ac, h3k27me3, h3k36me3, h3k4me1, h3k4me2, h3k4me3, h3k9me3, h4k16ac
- Data organized by **1 kilobase pair bins** each with values for epigenetic factors and labels
 - Label 0: No MRE
 - Label 1: MRE
- Labeled data is heavily **imbalanced** (80% 0s and 20% 1s)

Model and Metrics

- Multiple Logistic Regression model used for **binary classification** of the MRE labels
- **Recall:** proportion of positive samples that were correctly classified
- **Precision:** proportion of positive-predicted samples that were actually positive samples
- Main metrics used to evaluate model performance:
 - **AUROC:** how well the model separates the two classes (Recall / False Positive Rate)
 - **AUPRC:** how well the model balances precision and recall with changing the decision threshold (Precision / Recall)

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Workflow and Organization

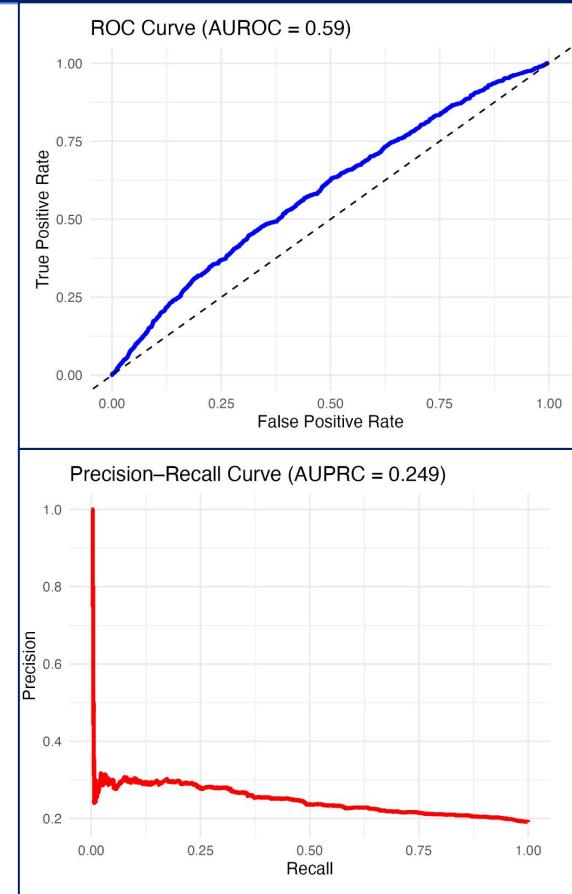
- preprocess.R
 - preprocess_data () - loads the dataset and cleans it
 - filter_chromosome_data () - keeps only the rows of the selected chromosome
- split_data.R
- train_model.R
 - integrates downsampling of the unbalanced dataset
- evaluate_model.R
- plotting.R
 - plot_curves () - ROC and Precision-Recall curves
 - plot_metric_cross_model () - barplots for a given metric for the cross evaluated model
- cross_chromosome.R

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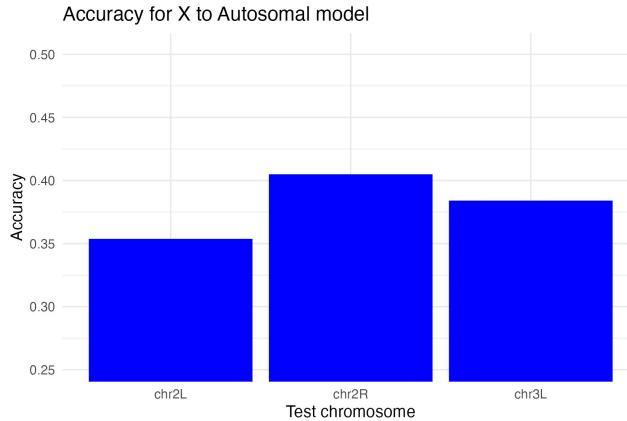
Results

- AUROC: 0.59
 - Baseline: 0.5 - **So our model performs better than random guessing**
- AUPRC: 0.249
 - Not very good at balancing recall and precision

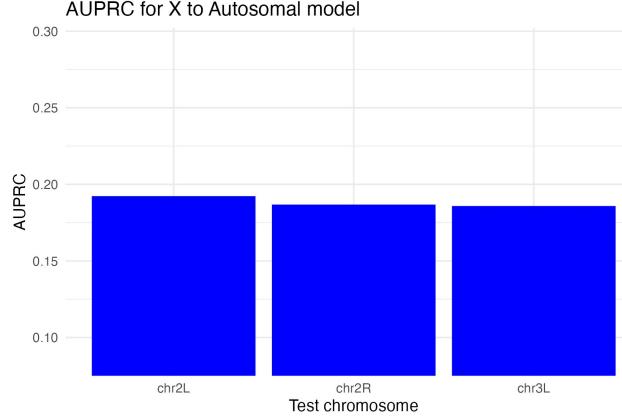


Cross Chromosome Experiments

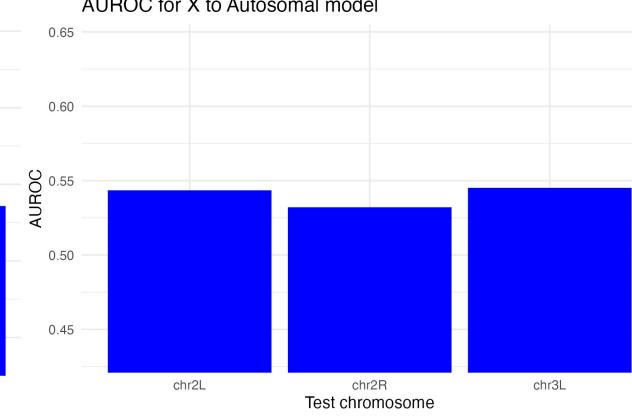
Accuracy for X to Autosomal model



AUPRC for X to Autosomal model



AUROC for X to Autosomal model



- Ran our X-trained model on 3 autosomal chromosomes to test whether X-linked MRE epigenetic patterns also appear on autosomes
- Results:
 - Accuracy is lower than 50% (baseline) for all the autosomal chromosomes
 - AUPRC is also low
 - AUROC near 0.5 means model cannot differentiate between MRE/non-MRE bins in autosomes

Outline

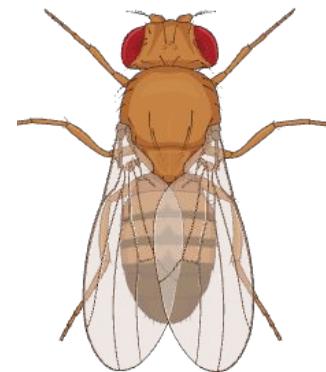
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Conclusion

- Results may indicate the histone modifications alone may not be the best predictors
 - **Future steps:** incorporate different data modalities (3D chromatin organization) or more complex models (neural networks)
 - More experiments: perturbations and examining coefficients
- Pipeline is **fully flexible** for any binary classification task on any ChIP-seq dataset!

References:

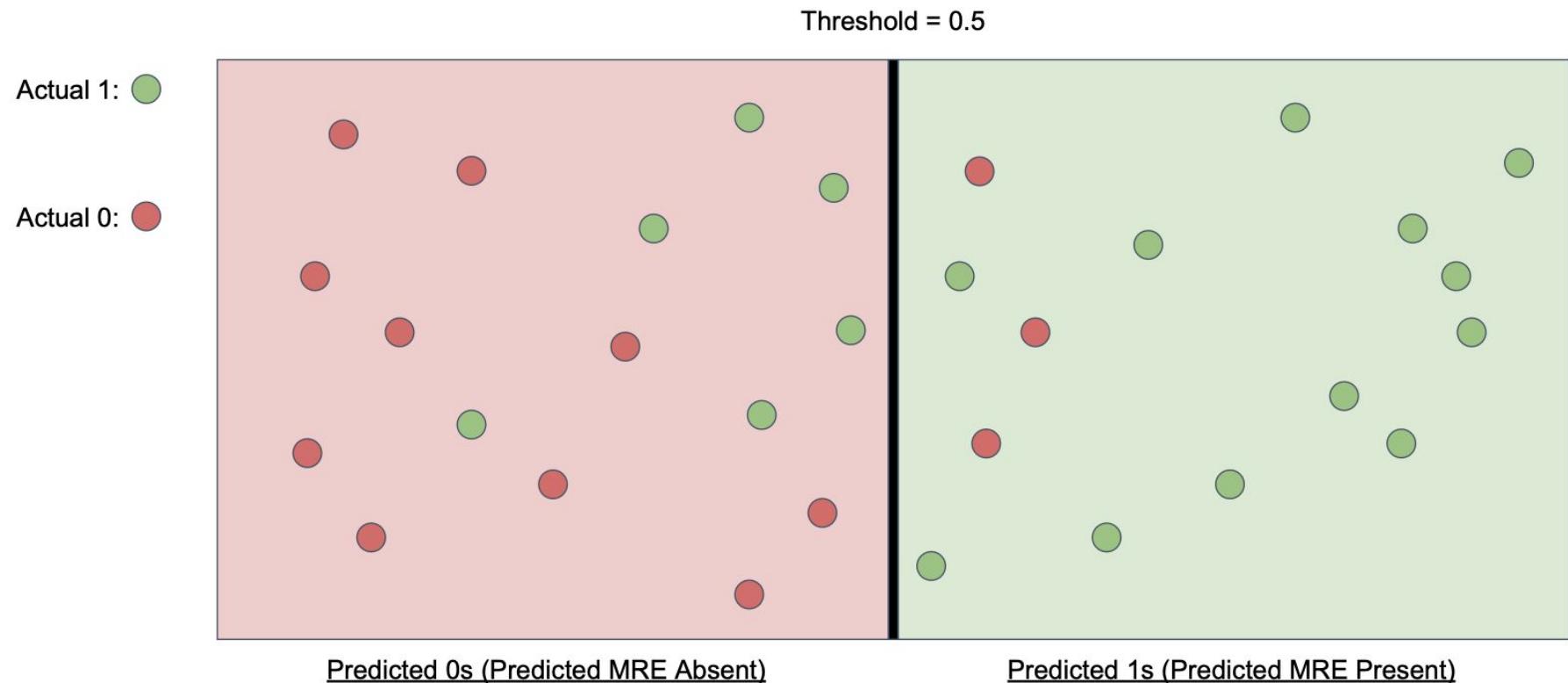
1. Duan, J., & Larschan, E. N. (2019). Dosage compensation: How to be compensated... or not? *Current Biology*, 29(23), R1229–R1231.
<https://doi.org/10.1016/j.cub.2019.09.065>
2. <https://medium.com/the-researchers-guide/modelling-binary-logistic-regression-using-tidymodels-library-in-r-part-1-c1bdce0ac055>



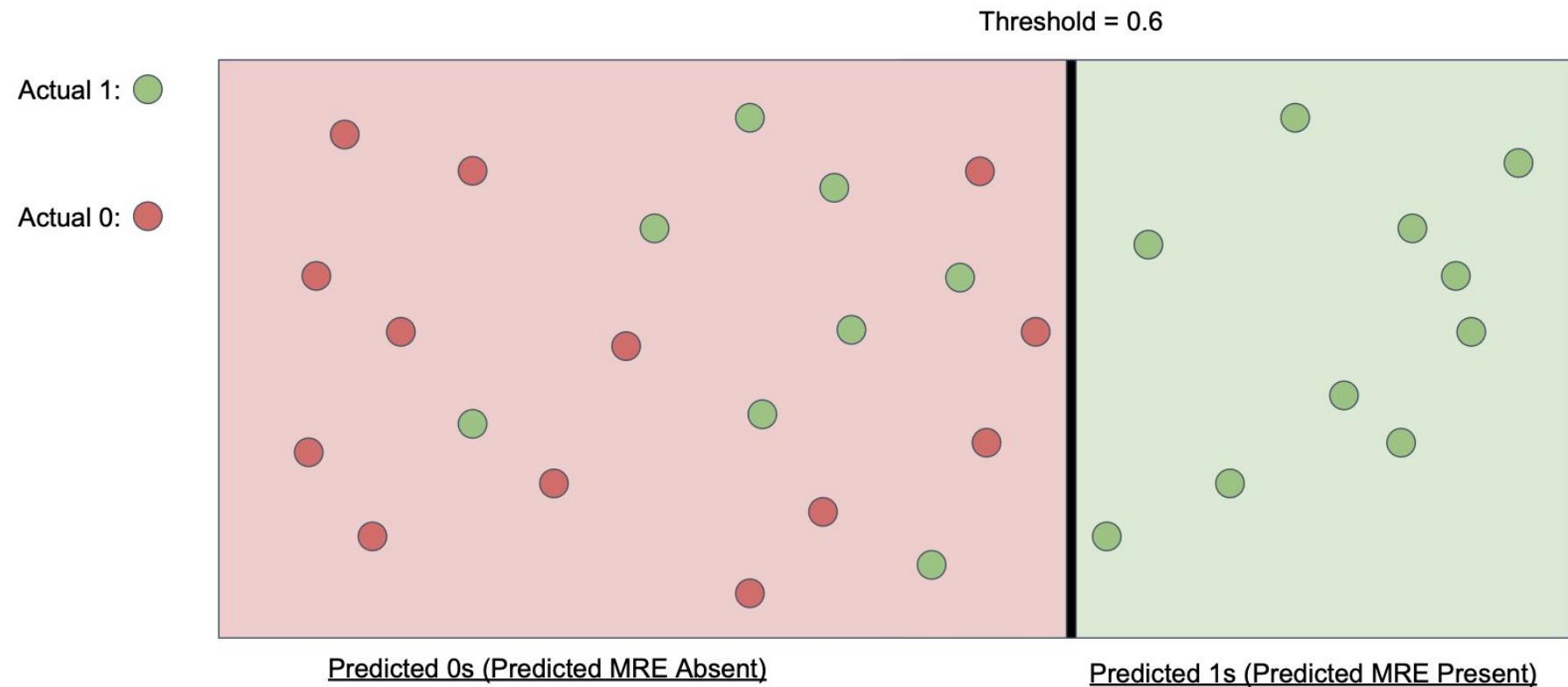
Thank You!

Questions?

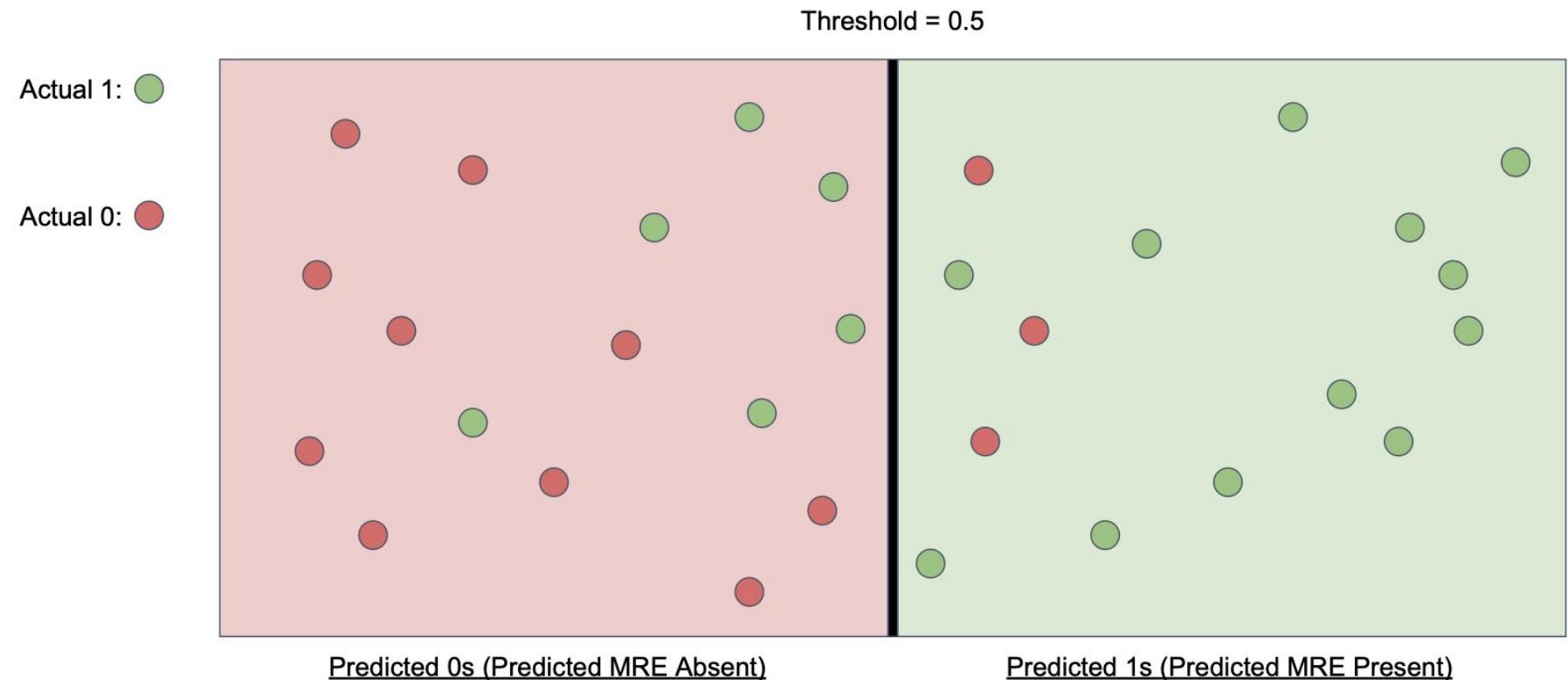
Supplementary Figures



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