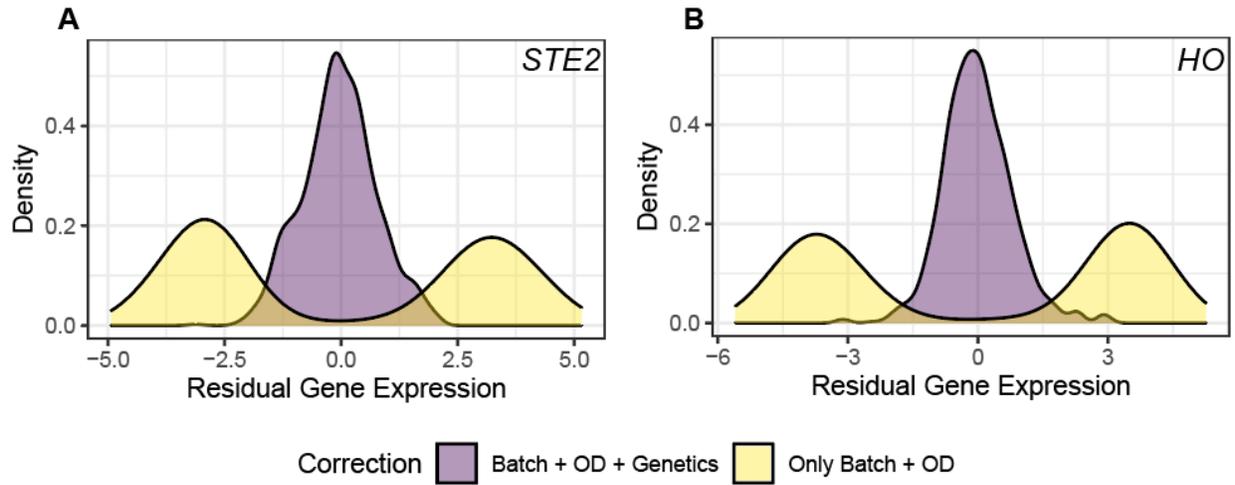
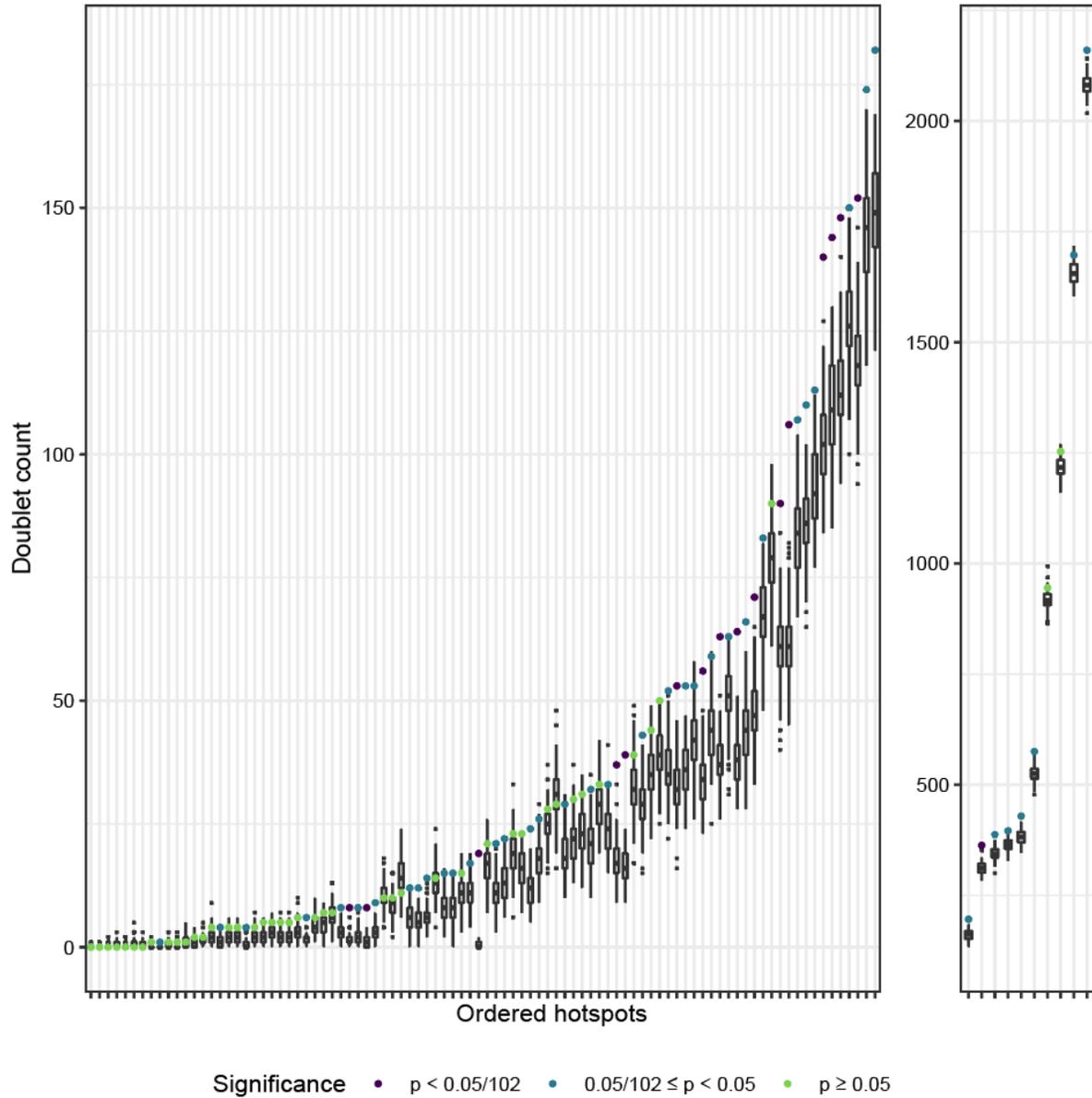


## SUPPLEMENTARY FIGURES



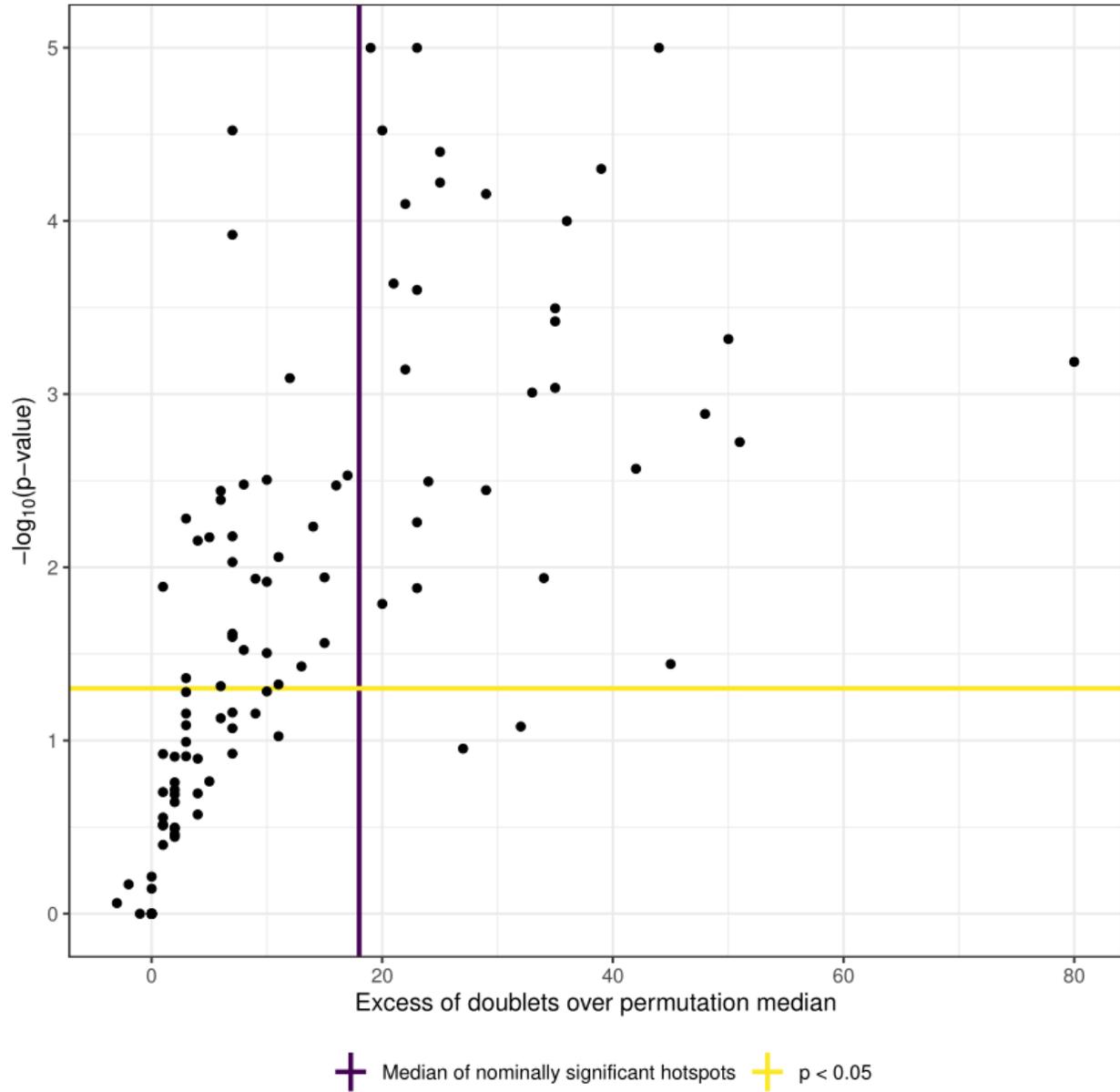
2

3 Figure S1: Distribution of residual gene expression for two genes after correction for either only  
4 batch and optical density (OD) or batch, OD, and genetic variation (A) Residuals for *STE2*,  
5 whose expression is strongly affected by the mating type locus before correction for genetic  
6 variation. (B) Residuals for *HO*, which is deleted in the RM but not the BY strain used in Albert  
7 *et al.*, 2018, resulting in a strong local eQTL in the BY / RM progeny.



8

9 Figure S2: The number of doublets in real data (colored circles) are plotted against the number  
 10 of doublets in permuted data (white boxes). Boxes extend from the 25th to 75th percentile.  
 11 Whiskers extend from each box to the largest or smallest values within 1.5 times the difference  
 12 in the 25th to 75th percentile. Data beyond the whiskers are considered outliers and plotted as  
 13 small black squares. Circles are colored by the number of permutations in which a number of  
 14 doublets was counted that was greater than or equal to the number observed in the real data.  
 15 Hotspots are ordered along the x-axis based on the value of the doublet count in the real data.  
 16 For clarity, the ten hotspots with the largest number of doublets are shown with a different scale.

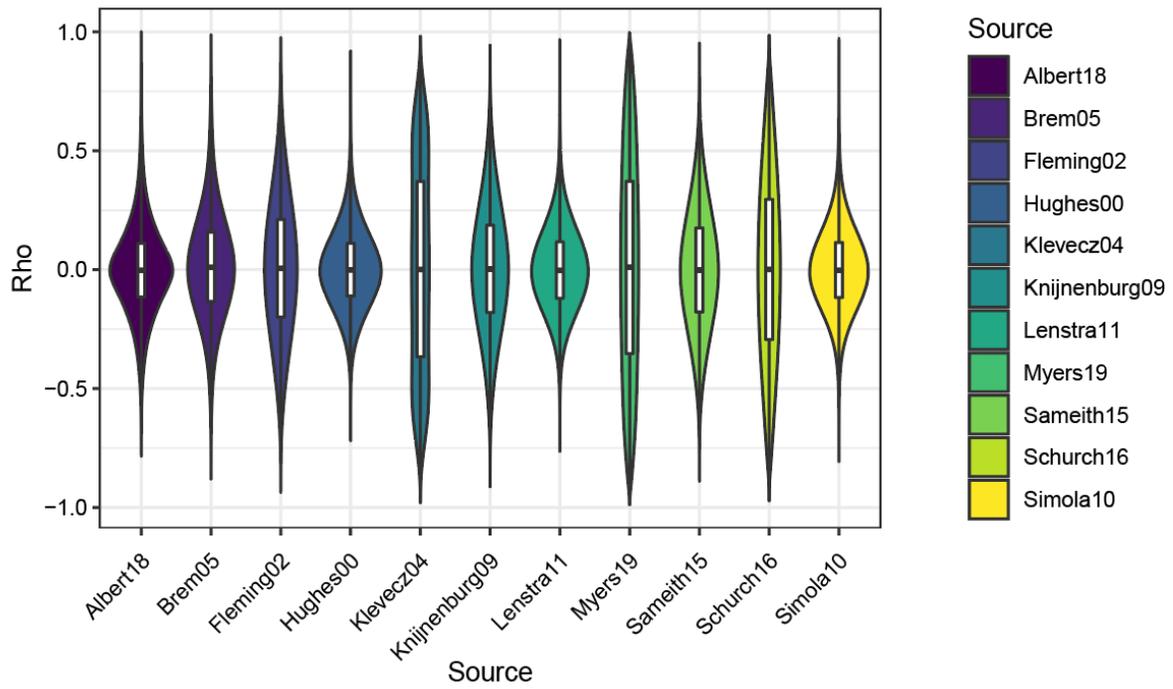


17

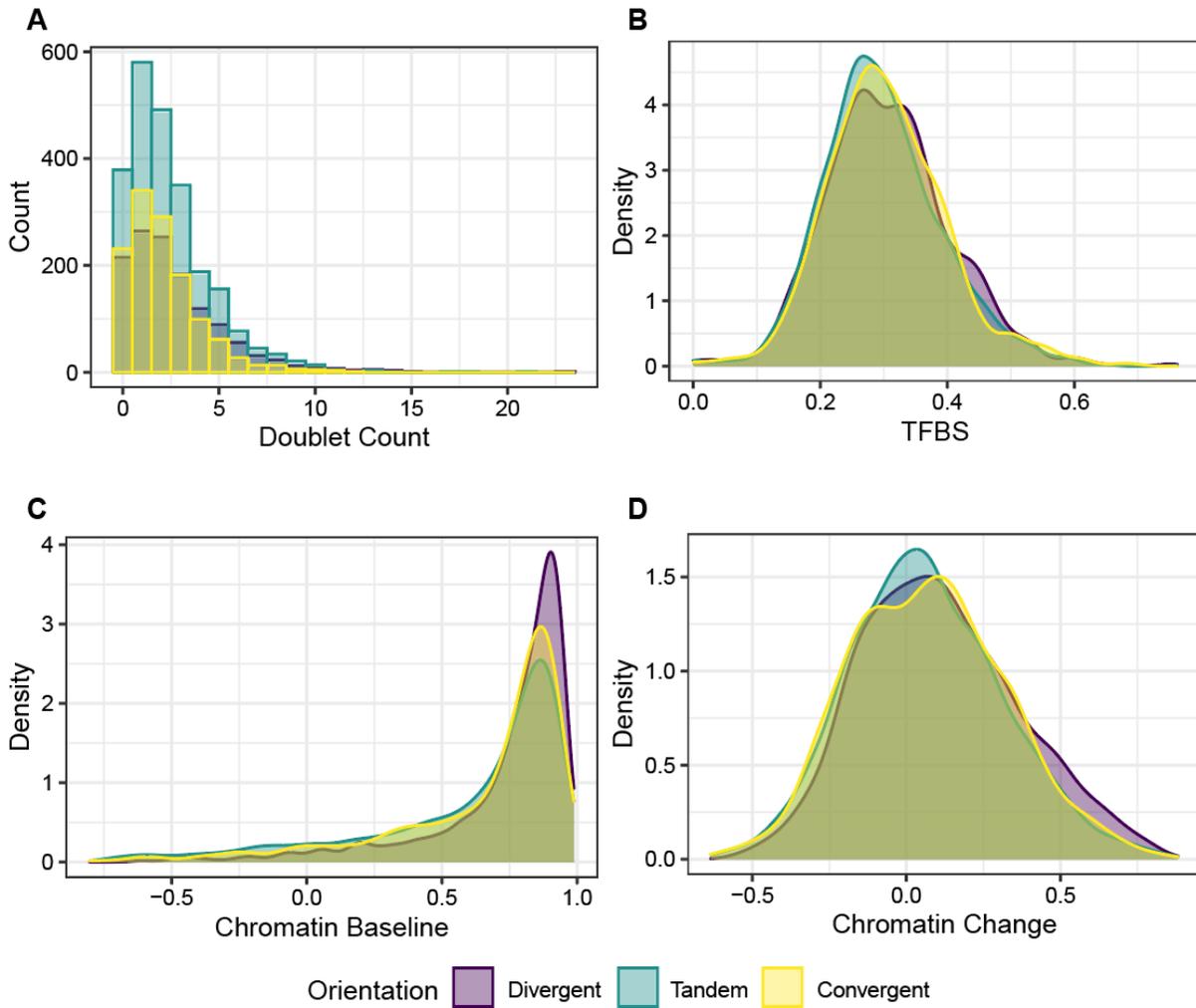
18 Figure S3: The excess number of doublets by which hotspots exceed their permutation medians

19 plotted against the significance of the excess. Hotspots with a  $-\log_{10}(p\text{-value})$  equal to 5 have

20 the lowest possible p-value given the number of permutations performed.



23 Figure S4: The distribution of Rho values for each coexpression matrix generated from the 11  
24 expression datasets.



25

26 Figure S5: Distributions of doublet counts per neighboring gene pair and predictor variables,  
 27 separated by gene pair orientation. Distance is shown in Figure 4A. (A) Number of times gene  
 28 pairs were targeted by the same hotspot. (B) Similarity in regulation by transcription factors. (C)  
 29 Correlation between marks on +1 nucleosomes without perturbation. (D) Correlation in change  
 30 in marks in response to cell stress on +1 nucleosomes.