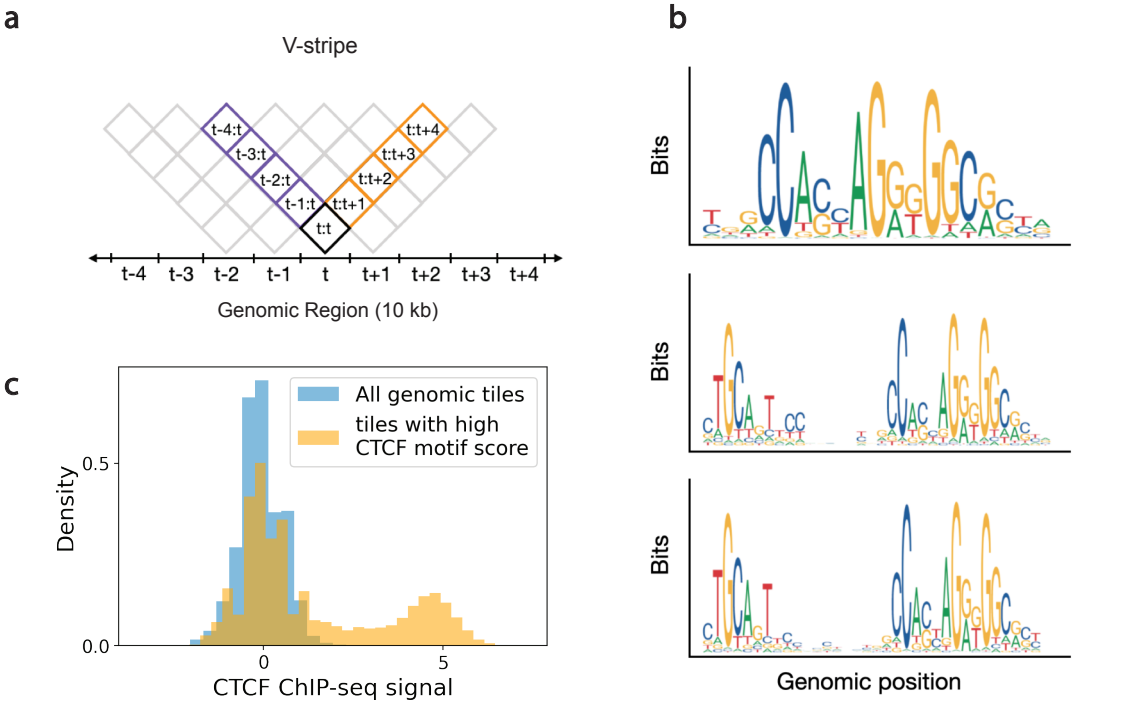
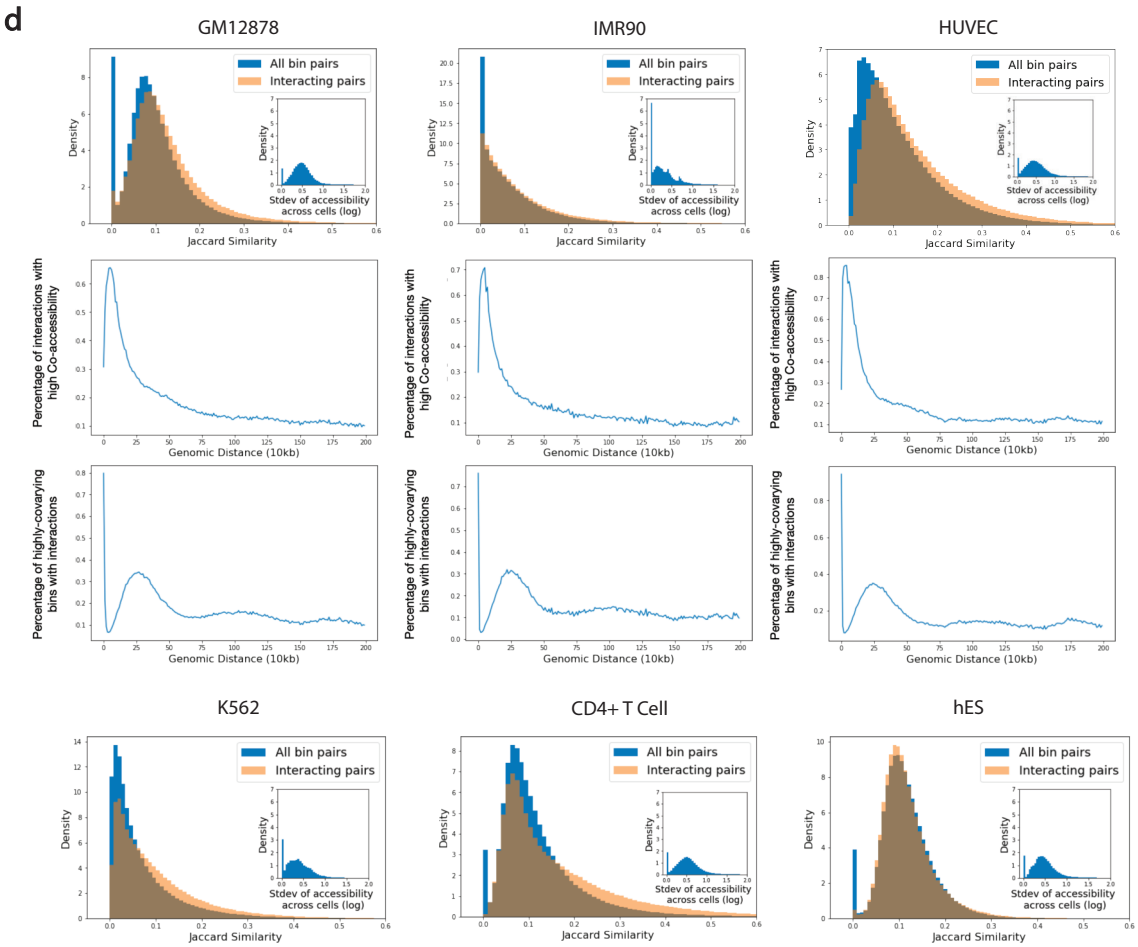
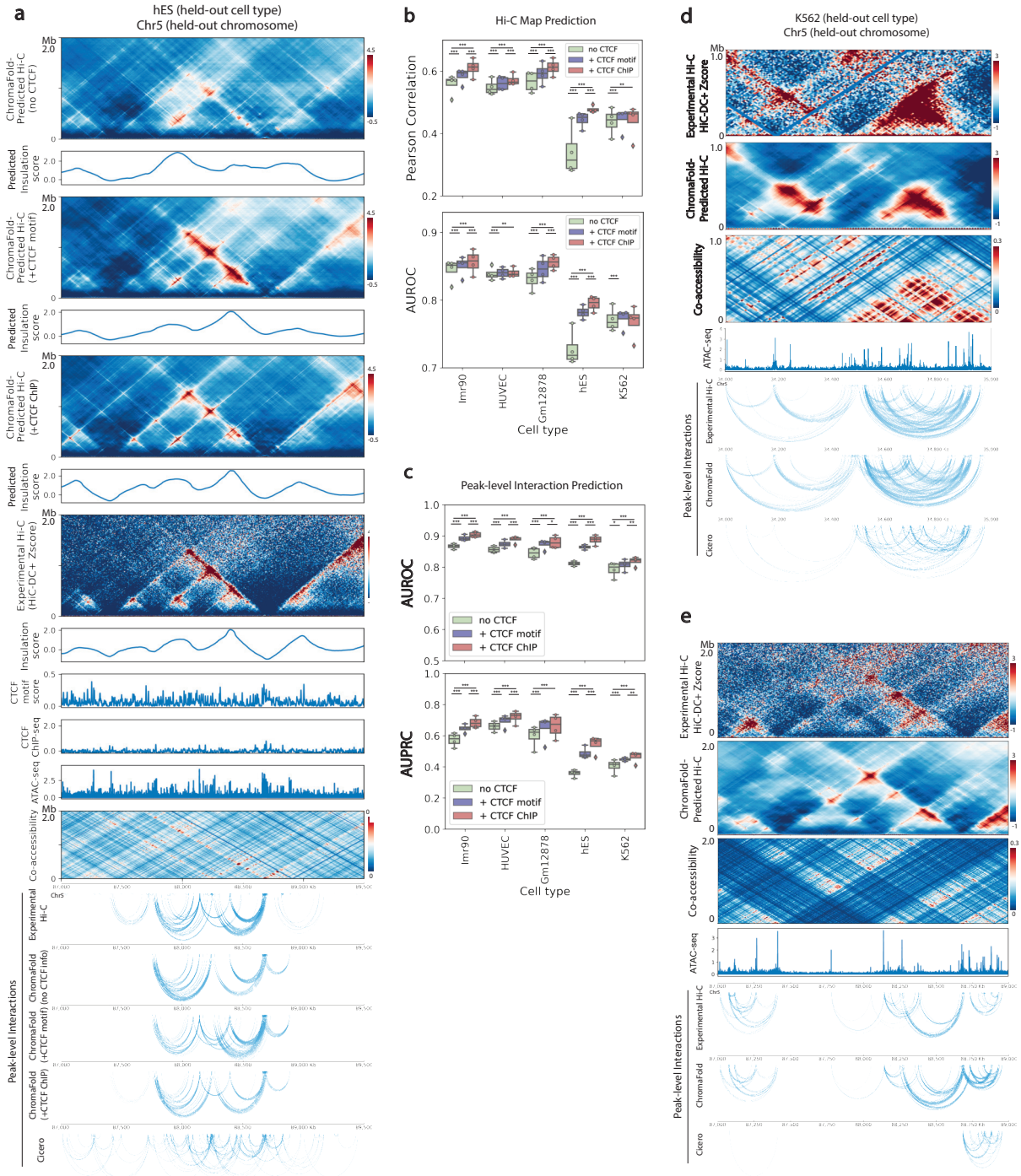


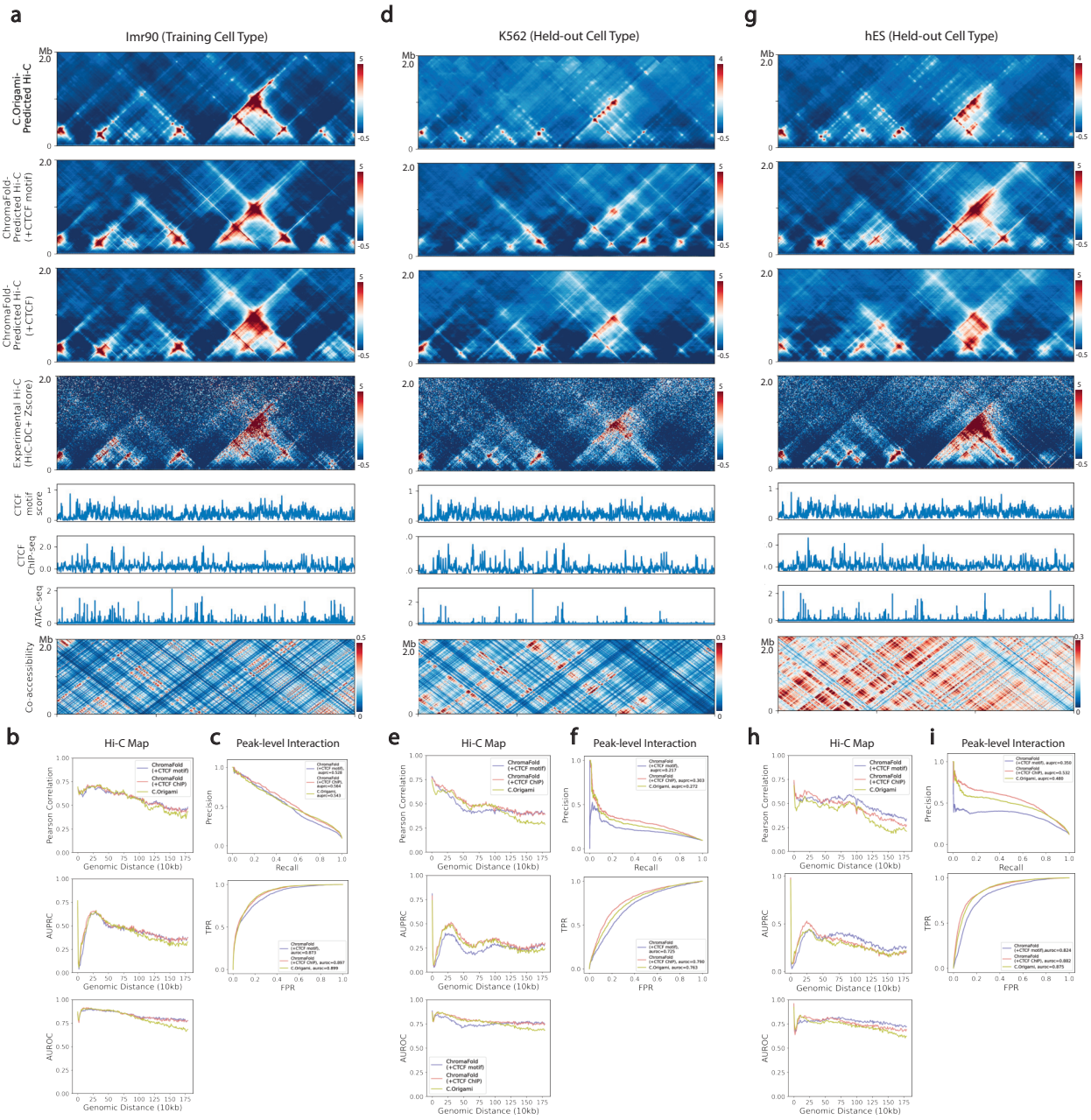


Supplementary Figure 1. ChromaFold model choices and input analysis. a. ChromaFold's prediction scheme for the chromatin interaction map. Each diamond *t_i*:*t_j* represents the interaction between genomic bins *t_i* and *t_j*. For each input centered around tile *t*, ChromaFold predicts the interaction between tile *t* and its neighboring bins within 2Mb. **b.** CTCF motif PWMs used for CTCF motif scoring. **c.** Histogram shows the distribution of CTCF ChIP-seq signal in genomic bins with top 0.1% CTCF motif score (yellow) and in all genomic bins (blue). **d.** Analysis of the extent of overlap between Hi-C interaction and Jaccard similarity in training cell types. (Top) Histogram show the distribution of Jaccard similarity between interacting bin pairs (top 10% HiC-DC+ Zscore; orange) and all tile pairs within a 2Mb distance (blue). The embedded histogram shows the variability of ATAC-seq accessibility across cells. (Middle) The line plot shows the percentage of interacting bin pairs with high Jaccard similarity (top 10%) at each genomic distance. (Bottom) The line plot shows the percentage of bins with high Jaccard similarity that are interacting at each genomic distance.

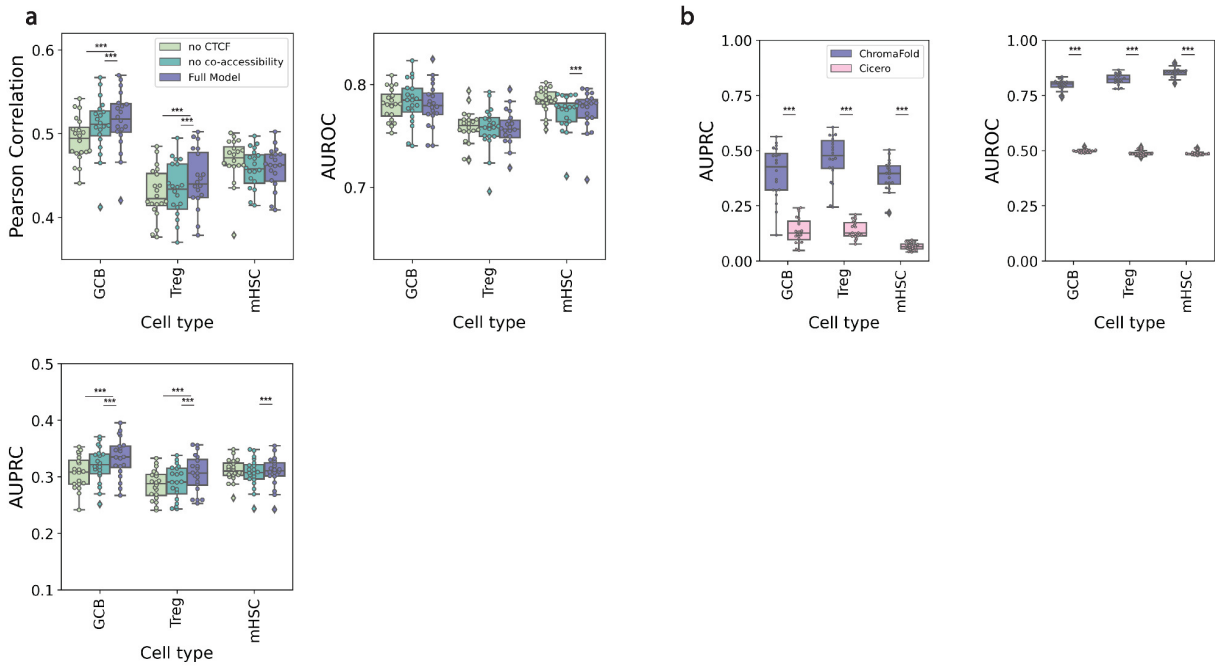


Supplementary Figure 2. CTCF information is crucial for accurate prediction of Hi-C interactions. a. Visualization of Hi-C contact maps, insulation scores and peak-level interactions predicted by ChromaFold using no CTCF information, CTCF motif score and CTCF ChIP-seq data as input in held-out cell type hESC on held-out chromosome 5. **b.** Box plots show (top) the averaged distance-stratified Pearson correlation between the experimental and predicted contact

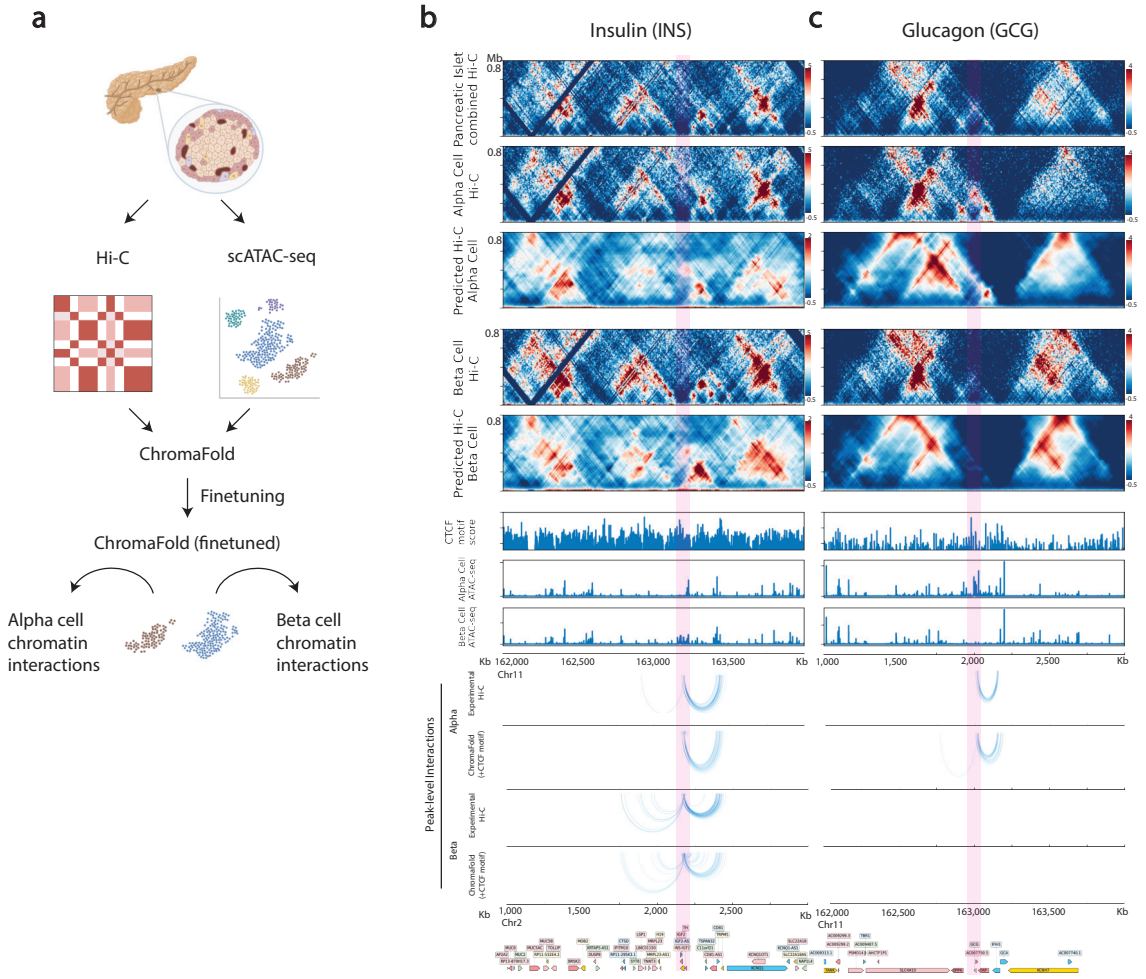
map and (bottom) the averaged distance-stratified AUROC of significant interactions (top 10% in Z-score), per held-out chromosome. Paired t-test is performed on the distance-stratified person correlation across test chromosomes (P-value *: <0.05, **: < 0.01, ***: < 0.001). **c.** Box plots show the AUPRC (top) and AUROC (bottom) of significant peak-level interaction prediction per held-out chromosome. Statistical test is the same as above. **d, e.** Additional visualization of ChromaFold-predicted Hi-C contact map and significant peak-level interactions and Cicero-predicted peak-level interactions in held-out cell type K562 on held-out chromosomes.



Supplementary Figure 3. ChromaFold outperforms C.Origami at prediction of HiC-DC+ normalized contact maps in held-out cell types. Visualization of C.Origami and ChromaFold predictions in training cell type IMR-90 (**a, b, c**), held-out cell type K562 (**d, e, f**) and hESC (**g, h, i**): HiC-DC+ normalized Hi-C contact maps (**a, d, g**); distance-stratified Pearson correlation for Hi-C contact map prediction, distance-stratified AUPRC and AUROC of significant interactions (top 10% in Z-score) (**b, e, h**); and PR and ROC curve for peak-level interaction prediction (**c, f, i**).



Supplementary Figure 4. Quantitative evaluation and mode comparison in mouse cell types. **a.** Comparison between ChromaFold model performance in the absence of CTCF motif score information and co-accessibility information. Box plots show the averaged distance-stratified Pearson correlation between the experimental and predicted contact map and the averaged distance-stratified AUPRC and AUROC of significant interactions (top 10% in Z-score), per chromosome. Paired t-test is performed on the distance-stratified person correlation across test chromosomes (P-value *: <0.05, **: < 0.01, ***: < 0.001). **b.** Comparison between ChromaFold and Cicero. Box plots show the AUPRC (top) and AUROC (bottom) of significant peak-level interaction prediction per held-out chromosome. Statistical test is the same as above.



Supplementary Figure 5. Deconvolution of pancreatic islet cell contact maps at additional loci. a. Schematic of ChromaFold applied to the task of deconvoluting chromatin interactions in a complex tissue. **b, c.** Visualization of deconvolved contact maps (top) and peak-level interactions (bottom) in alpha cells and beta cells near the TSS of (**b**) glucagon (*GCG*), and (**c**) insulin (*INS*).