A Setting hyperparameters

To identify optimum values for VSS-Hi-C's hyperparameters, we evaluated many possible combinations of values using the three evaluation measures including variance-instability, metrics of enrichment for structural proteins and histone modification in TAD boundaries and also signals variance-explained metric to quantify the agreement between epigenomic signals/replication timing signals and genome predicted subcompartments (Figure 3). The optimum set of parameters would minimize the variance-instability metric while maximizing the two other metrics. Based on all evaluations, we chose $\beta = Inf$ and $b = 100$ (Unweighted mean-variance relationship) as the optimal set of the parameters.

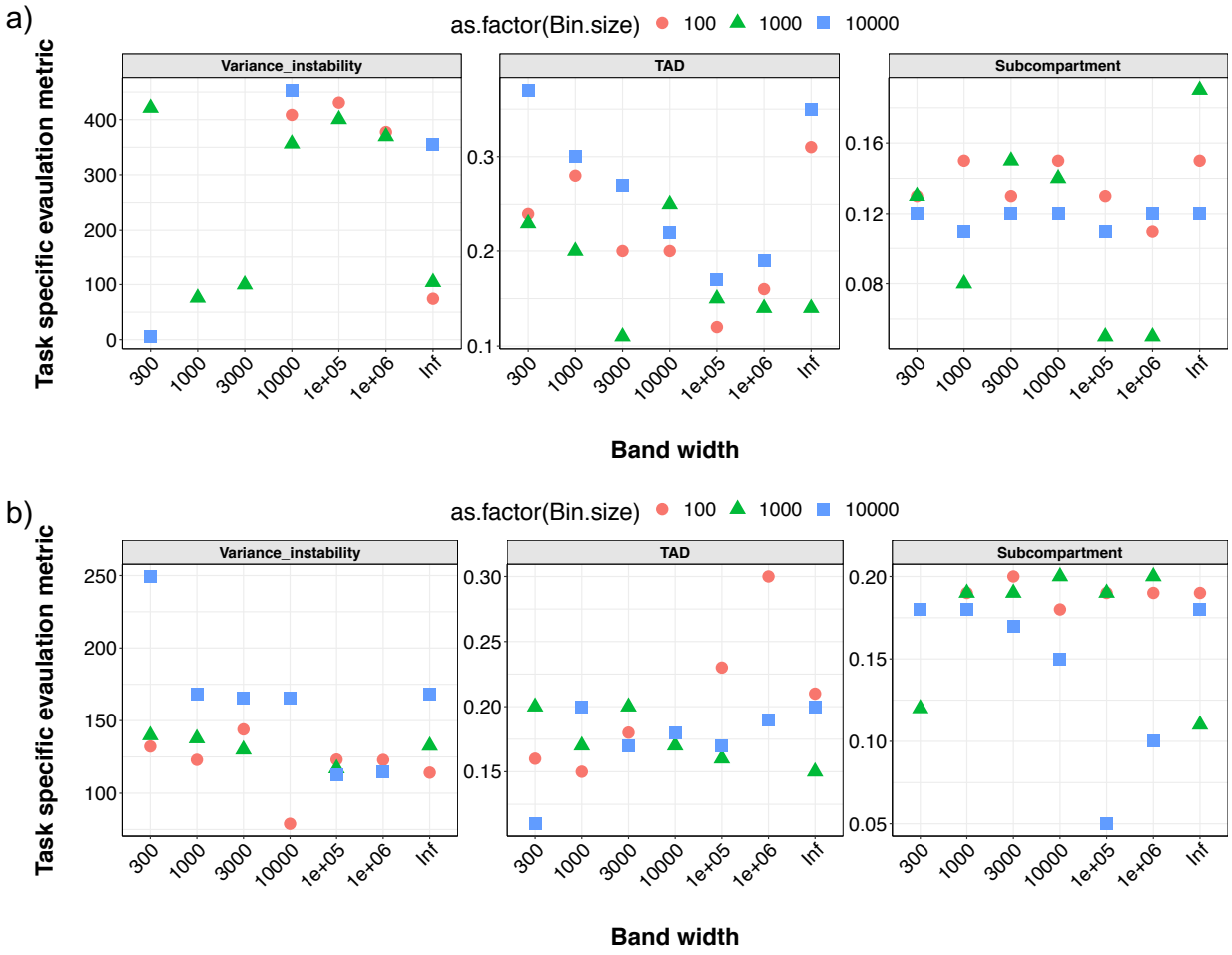

Figure 3: Relationship between bin size and bandwidth in variance instability analysis, Topological associating domains enrichment in histone modification/protein structure and signal variance explained in subcompartmentization analysis from left to right, respectively in a) observed b) observed over expected (O/E) contact matrix. Among the band width values, the value Inf indicates that we applied no smoothing on the curve (Unweighted mean-variance curve). Large variance-instability score indicates more unstabilized signals. Higher values for TAD enrichment and variance-explained in subcompartment analysis indicates better performance of transformation method.

B Transformed signals improve subcompartment calling

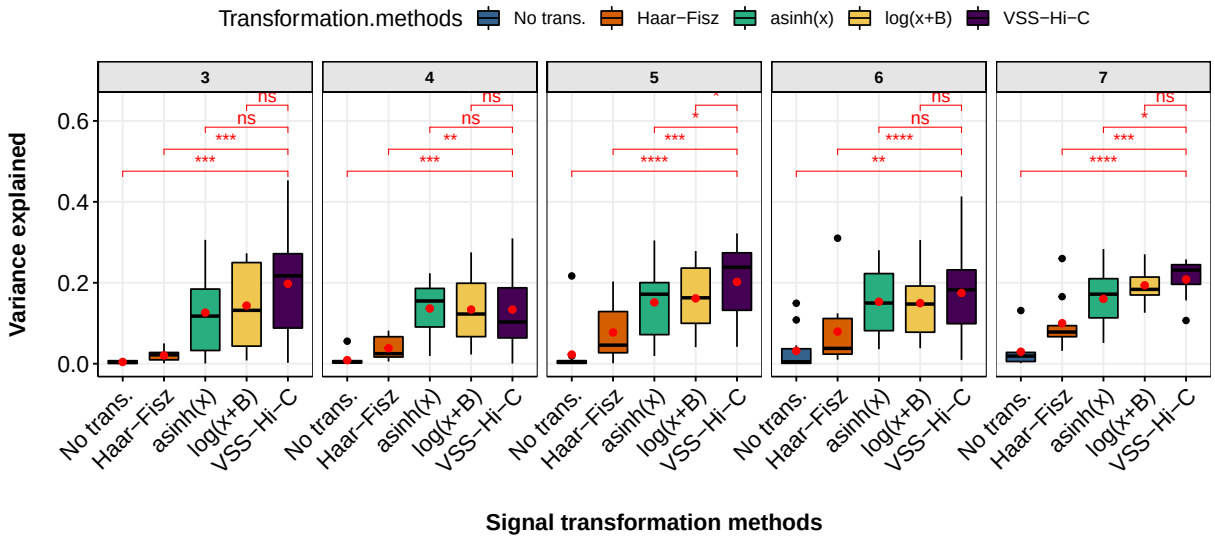

Figure 4: Signal variance-explained in subcompartment callers in Repli-seq data for O/E matrix

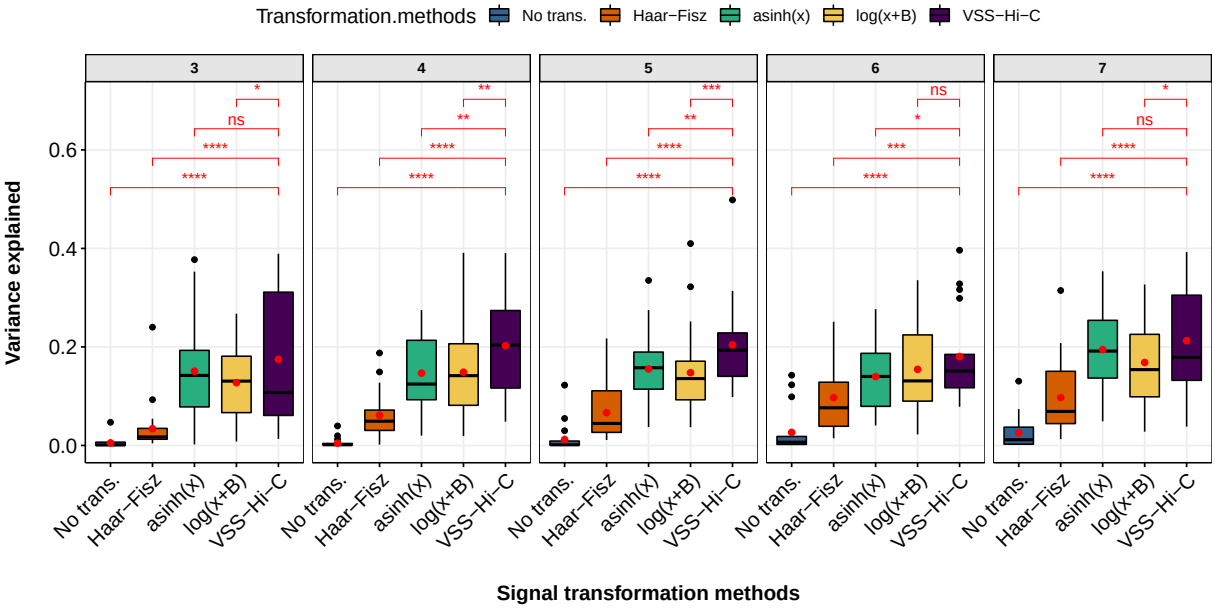

Figure 5: Signal variance-explained in subcompartment callers in ChIP-seq data for O/E matrix