

JMnorm: a novel method for Joint Multi-feature normalization of epigenomic data

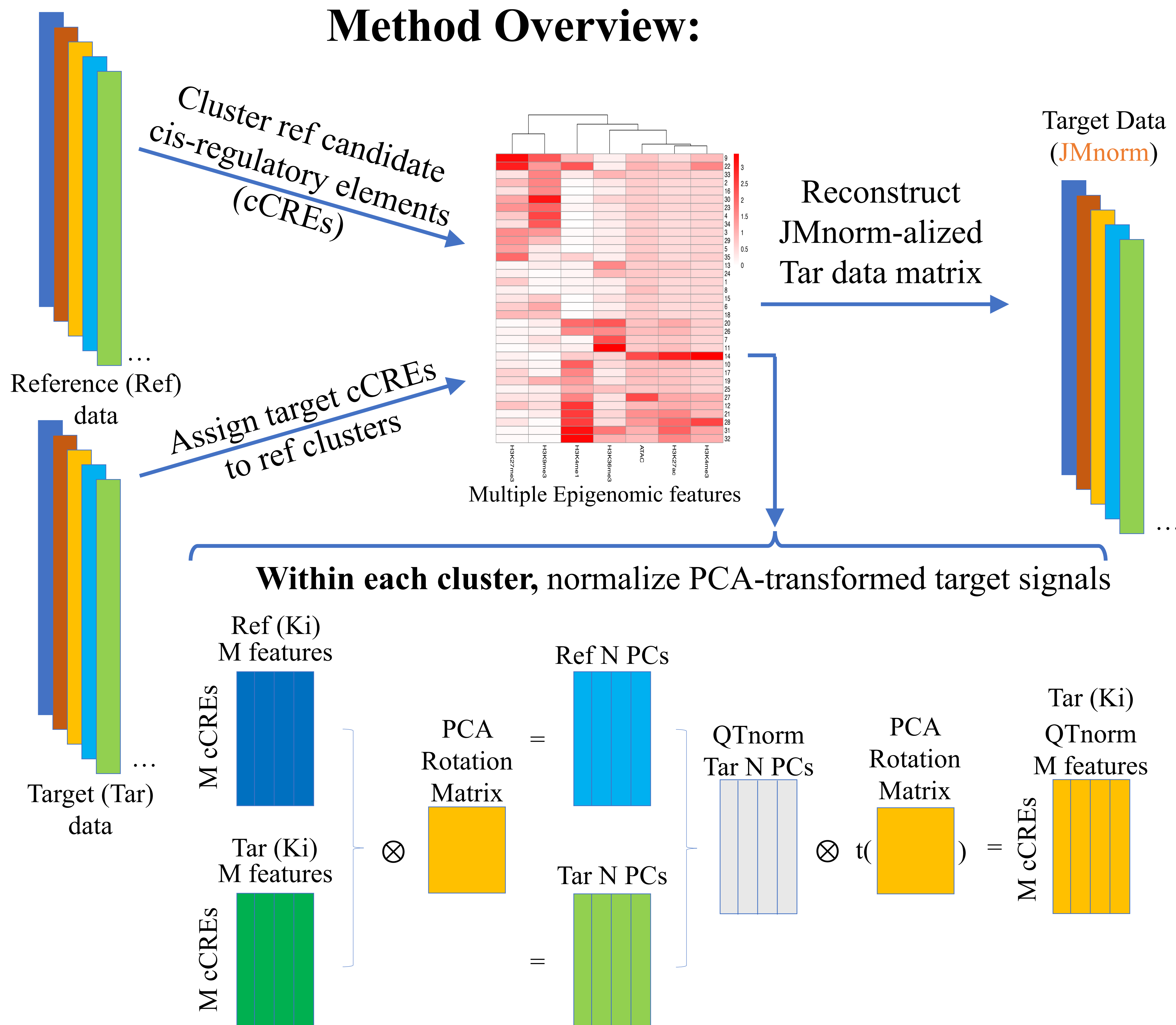
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Motivations:

1. Chromatin features provide important information in integrative and comparative epigenomic studies and exhibit correlated relationships.
2. Robust normalization methods are required for comparison of epigenomic data between replicates and different cell types.
3. Existing normalization methods ignore cross-feature correlations and are inadequate for highly variable signal distributions that exist in different cell types.

Method Overview:

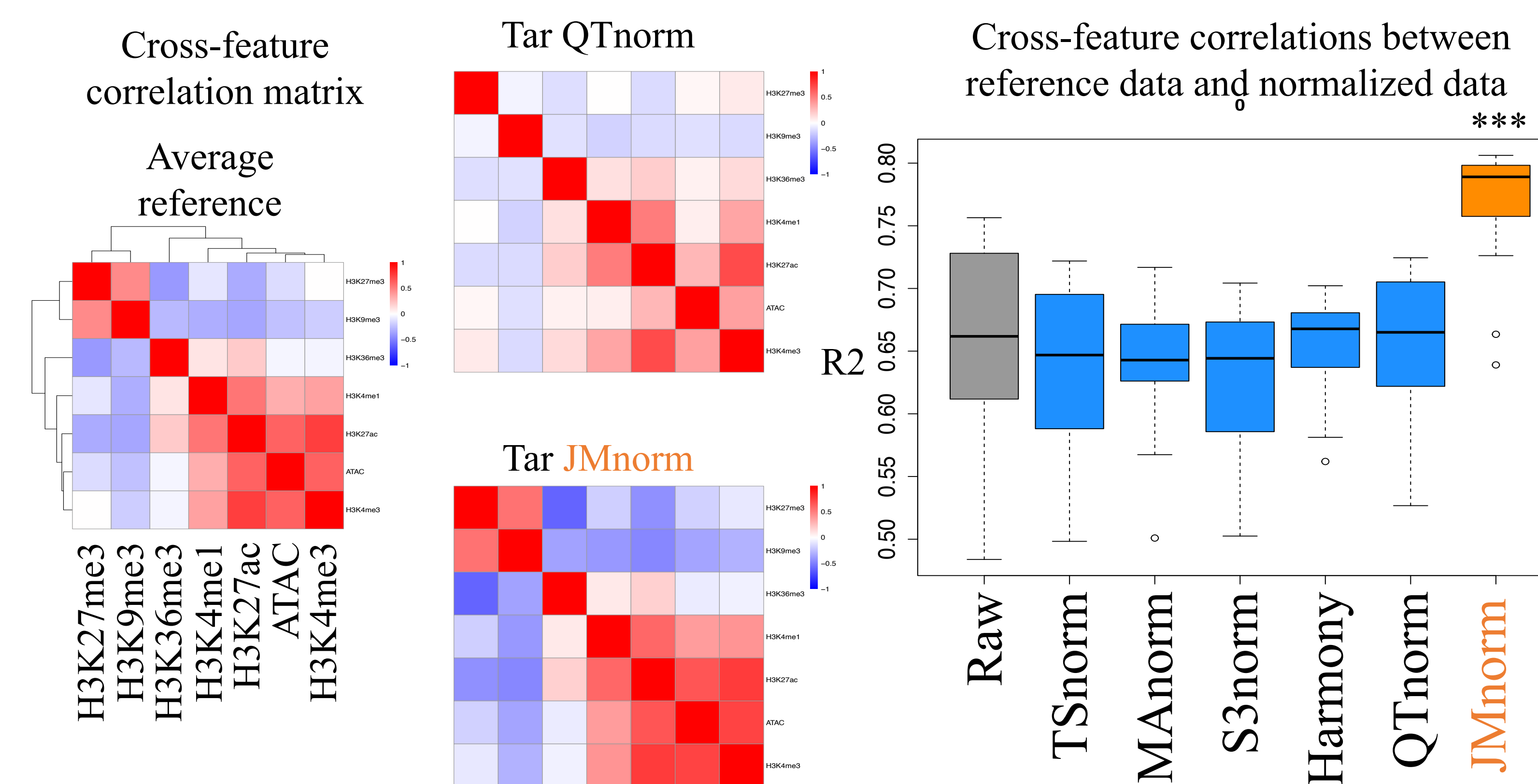


1. Transform multi-dimension epigenomic signal matrices into orthogonal Principal Component (PC) spaces
2. Generate reference cCRE clusters based on reference data in PC space
3. Assign target cCRE into reference clusters based on target data in PC space
4. Within each cluster in PC space, apply quantile normalization to normalize target data against reference data
5. Reconstruct JMnorm target signal matrix by transforming the normalized target signal in PC space back to the original signal space

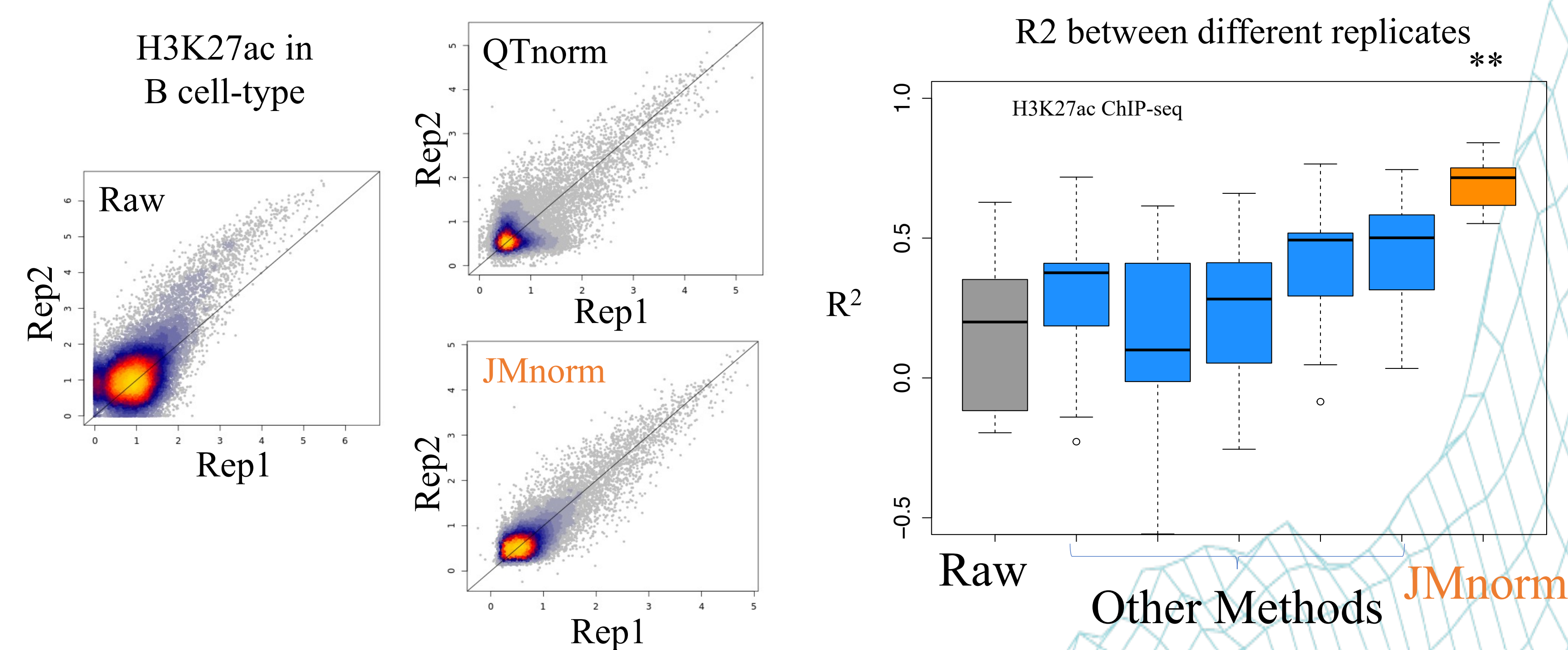
Performance evaluation relative to existing normalization methods:

- A. JMnorm better preserves cross-feature correlations
- B. JMnorm improves signal consistency between biological replicates
- C. JMnorm improves cross-cell RNA-seq predictions
- D. JMnorm allows different numbers of peaks across cell types and identifies CTCF peaks that are more enriched at topologically associating domain (TAD) boundaries and YY1 transcription factor binding sites

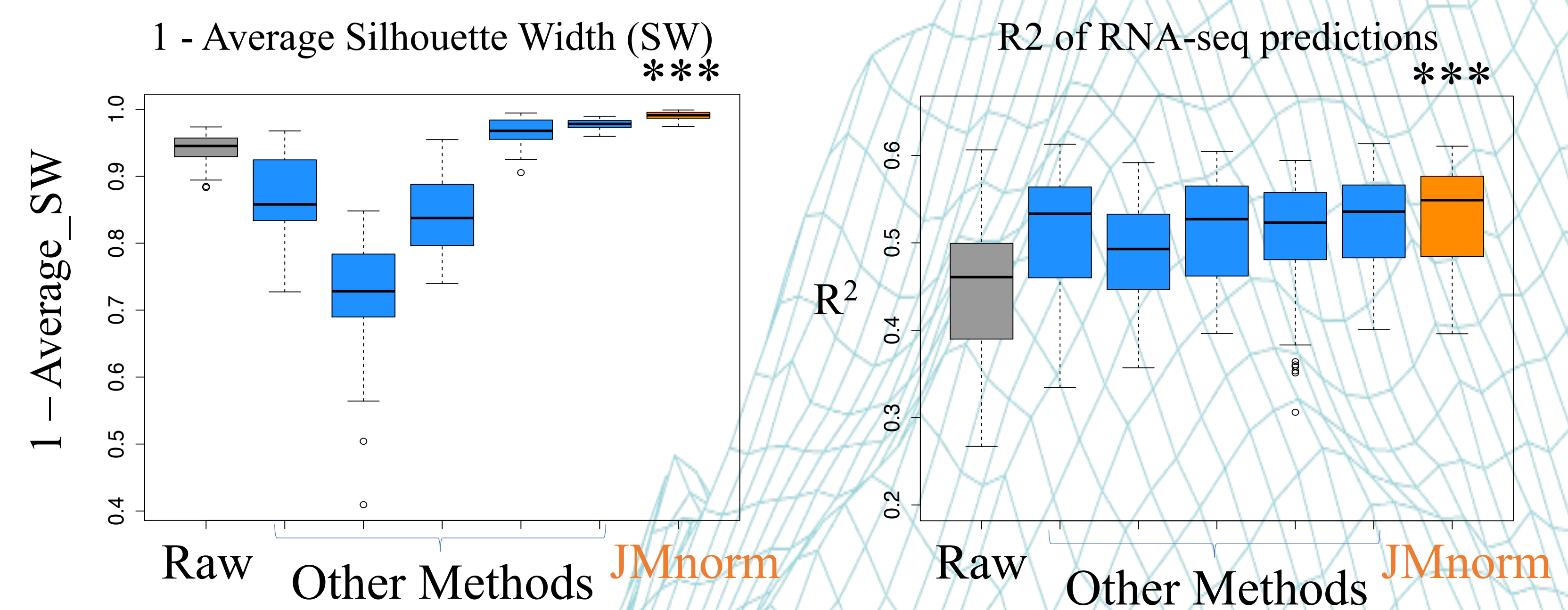
(A) JMnorm better preserves cross-feature correlations



(B) JMnorm improves signal consistency between biological replicates



(C) JMnorm improves combinatorial pattern transferring & RNA-seq predictions across cell types



(D) JMnorm allows different number of peaks across cell types and identifies CTCF peaks that are significantly enriched at TAD boundaries and YY1 peaks

