Chromatin loops are involved in spatial organization of replication in budding yeast

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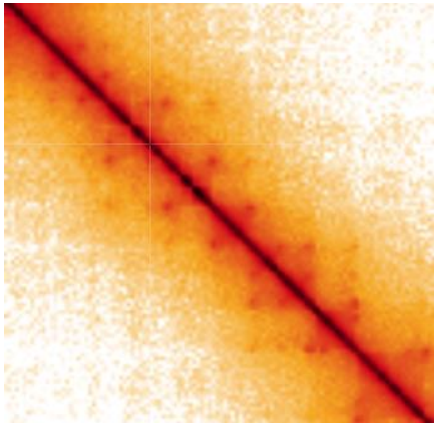
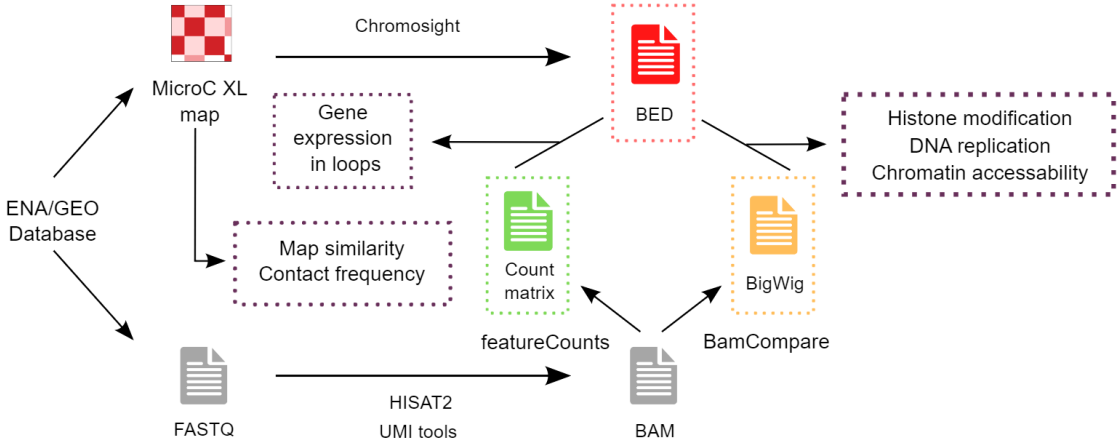
Introduction

Problem: The loop extrusion model explains well formation of chromatin loops via recruiting of cohesin and CTCF proteins in Mammals, but we still find loops in organisms lacking CTCF

Research aim: Conduct an analysis of chromatin loops in MicroC XL maps in tandem with multi-omics data to find features underlying the loop formation at different stages of the cell cycle in *Saccharomyces cerevisiae*.





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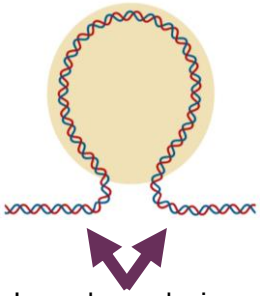
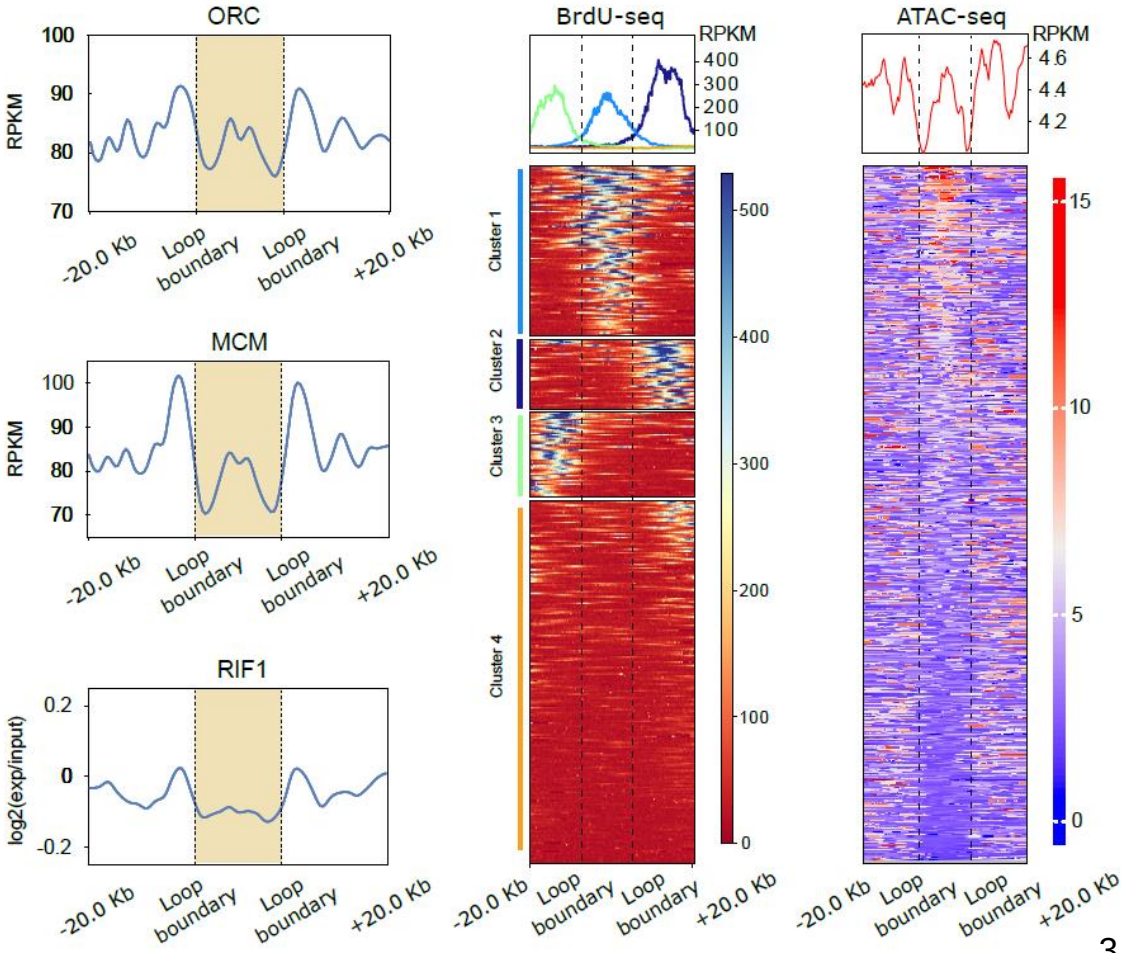
Results

The profiling of ChIP-seq signal revealed enrichment of Orc-6, Mcm-7, and Rif1 proteins near the loop boundaries. All three are known to be responsible for the initialization and/or maintenance of the replication process.

BrdU-seq data demonstrated that newly synthesized DNA is likely placed inside loops rather than at the loop boundaries.



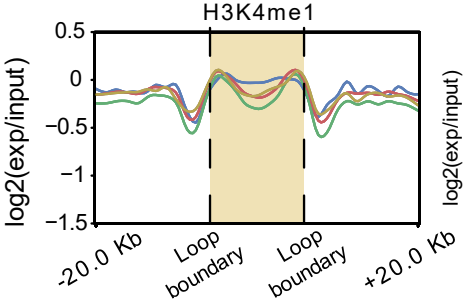
Loop boundaries

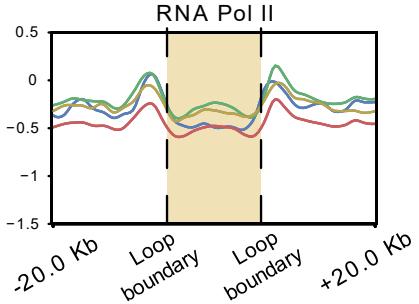


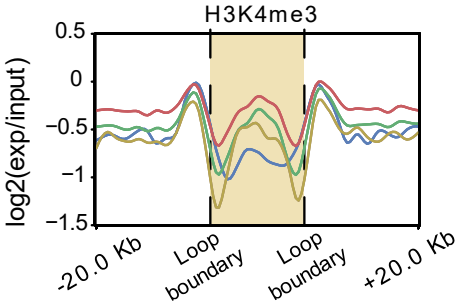
Results

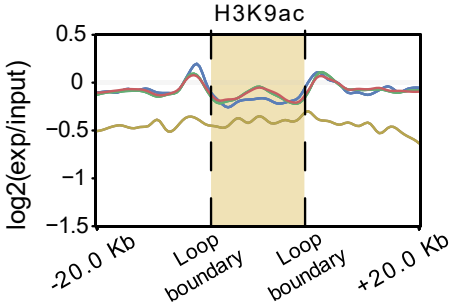
We found characteristic patterns near loop boundaries for active-chromatin histones modifications H3K4me1, H3K4me3, and H3K9ac.

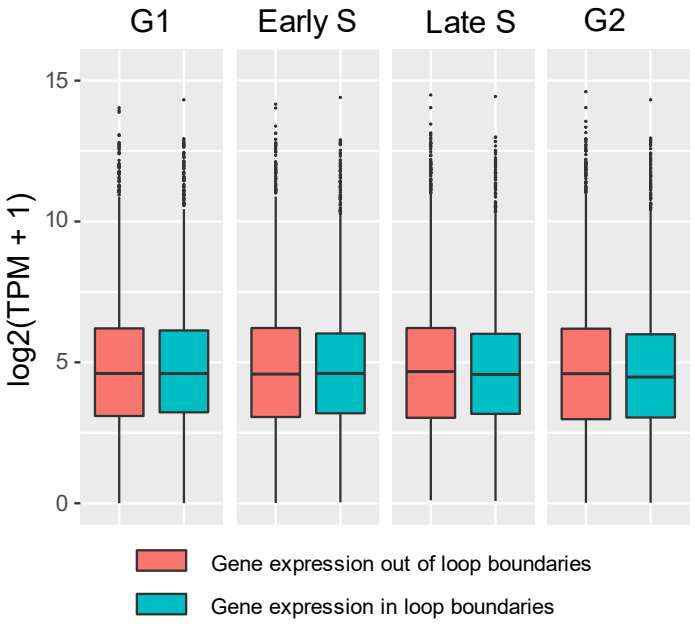
However, expression level of genes located in the boundary regions does not differ from the control group.











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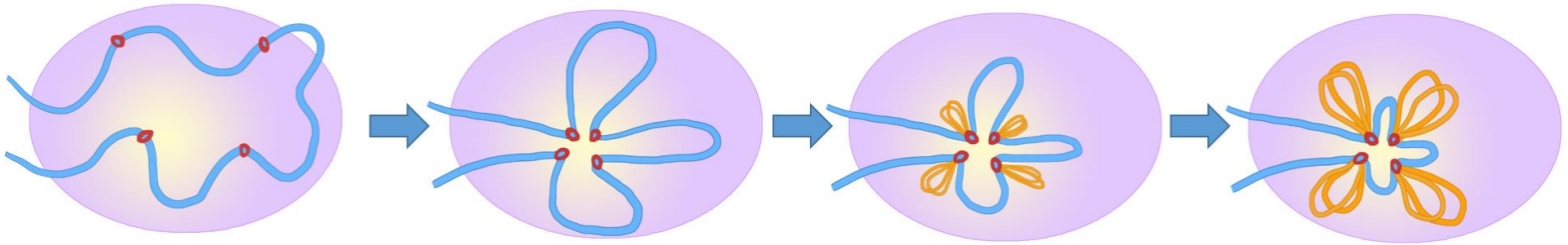
Conclusion

Based on gene expression analysis and ChIP-seq profiles, we concluded that observing loops are related to the cellular replication machinery rather than transcription regulation. We assume that the replication machinery might determine the positions of the loop boundaries. Our findings agree with the model of loop-mediated organization of replication foci in the nucleus proposed by Guillou et al.*



The model of replication foci structure: In the beginning, the replication origins with pre-assembled replication machinery (red circles) are brought together via cohesin-mediated loop formation (blue line). After replication is initialized, replisomes extrude loops of new DNA threads (orange lines).

* Guillou, E., Ibarra, A., Coulon, V., Casado-Vela, J., Rico, D., Casal, I., Schwob, E., Losada, A., & Méndez, J. (2010). Cohesin organizes chromatin loops at DNA replication factories. *Genes & development*, *24*(24), 2812–2822. https://doi.org/10.1101/gad.608210