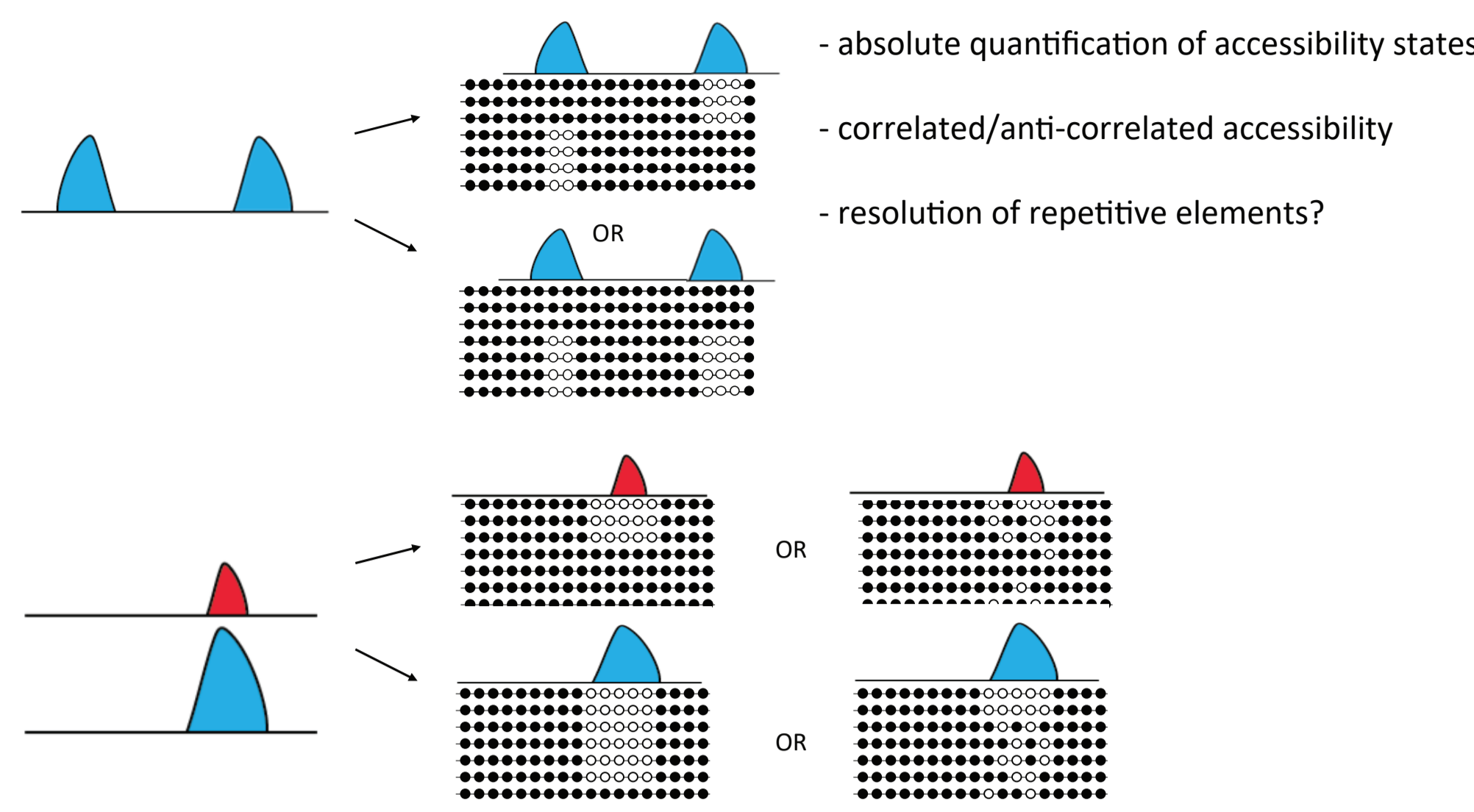


Georgi K. Marinov^{1,*}, Zohar Shiphony^{1,*}, Matthew P. Swaffer⁵, Nasa A. Sinott-Armstrong¹, Jan Skotheim⁵, Anshul Kundaje^{1,2}, William J. Greenleaf^{1,3,4}

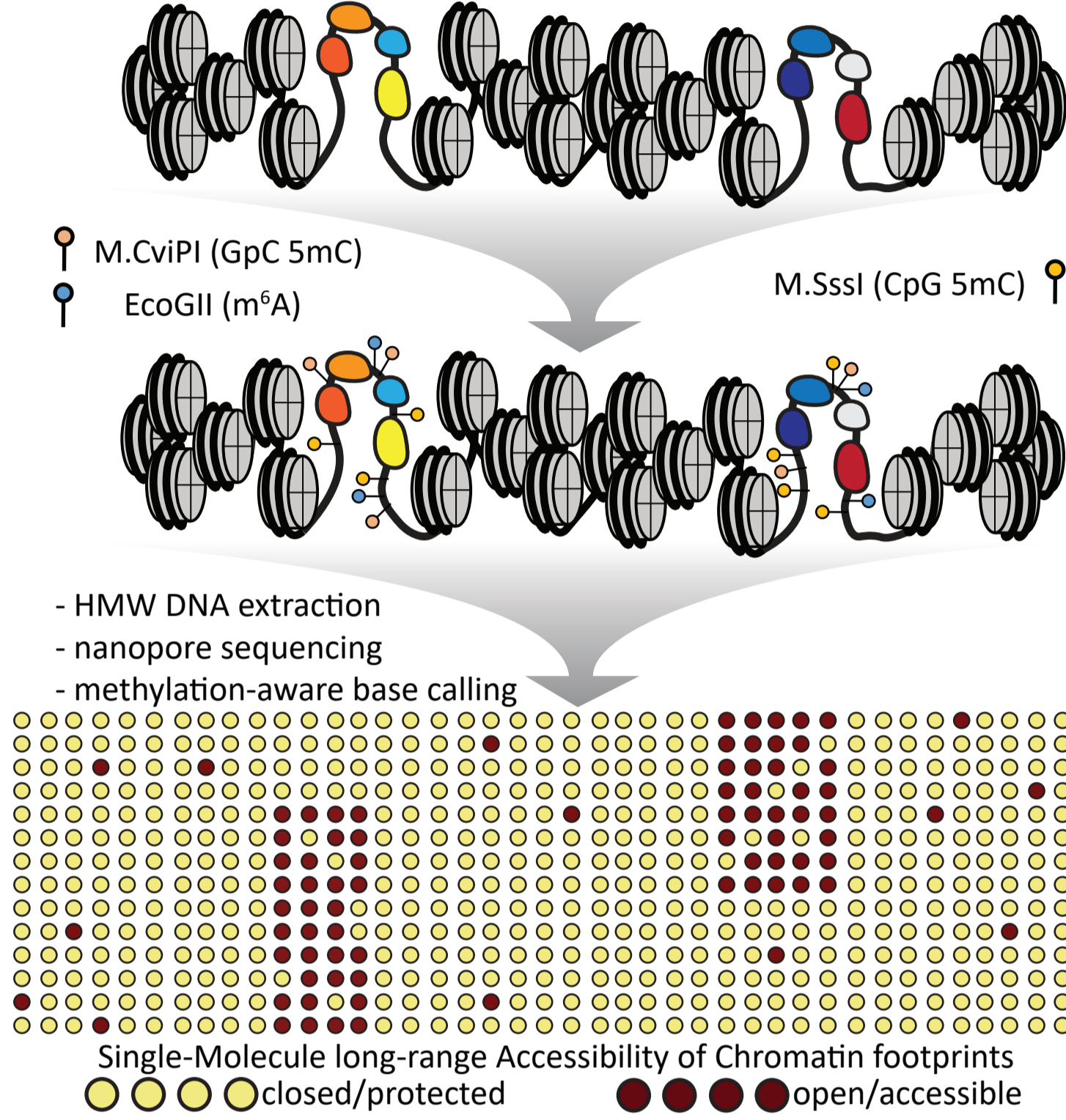
¹Department of Genetics, ²Department of Computer Science, ³Department of Applied Physics, ⁵Department of Biology, Stanford University, Stanford, CA 94305, USA;

⁴Chan Zuckerberg Biohub, San Francisco, California, USA; *These authors contributed equally to this work

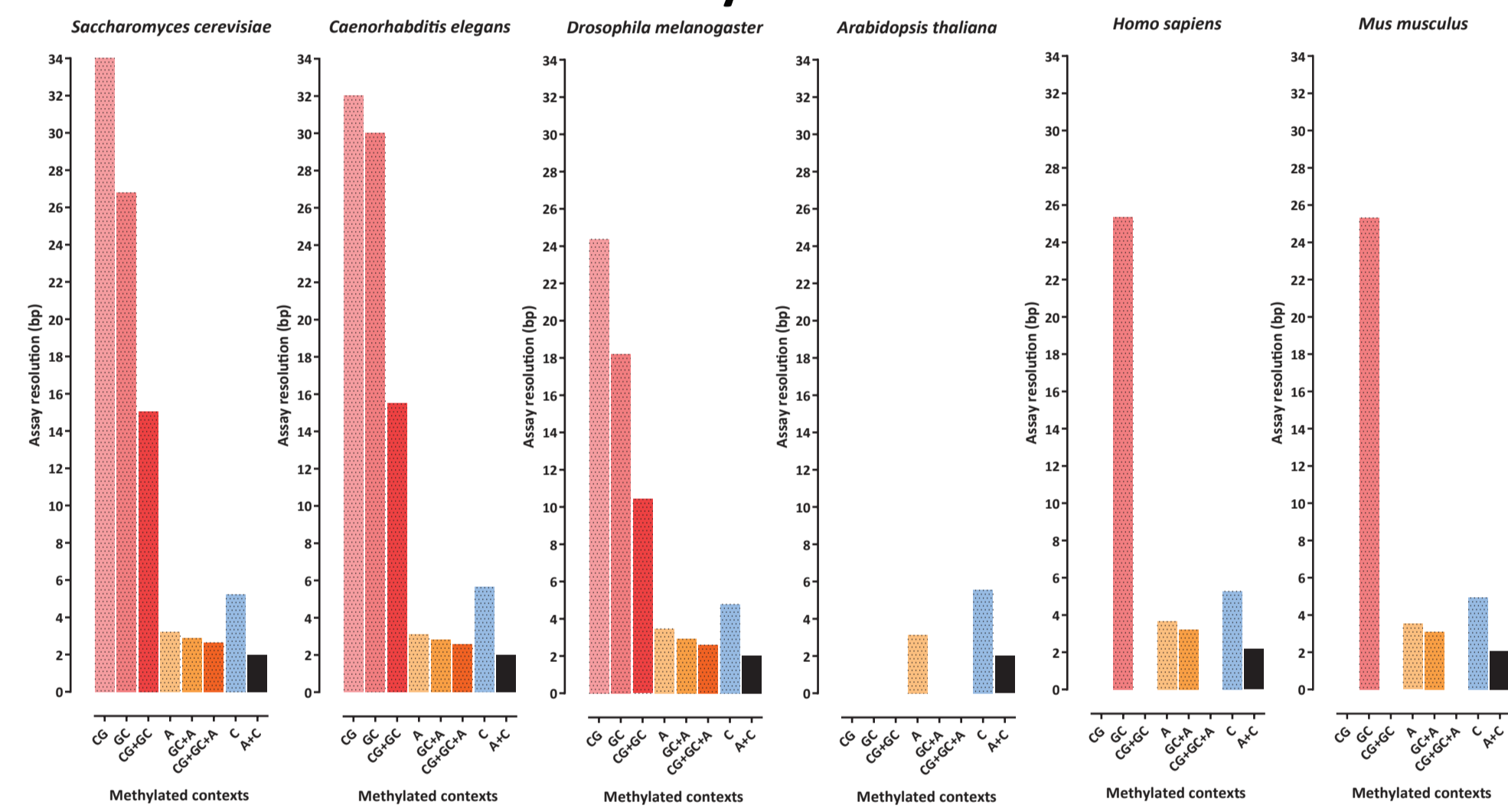
1. Why do we need a new method for mapping accessibility?



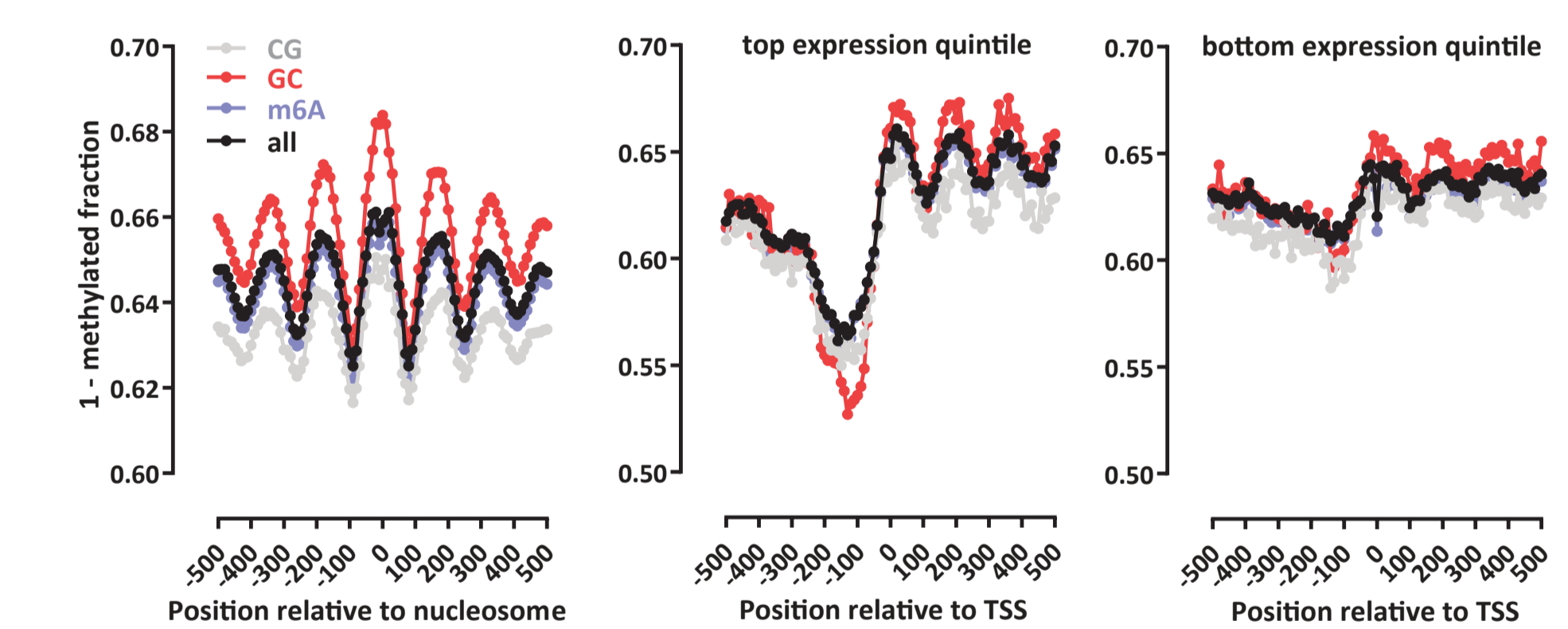
2. Single-molecule long read accessible chromatin mapping



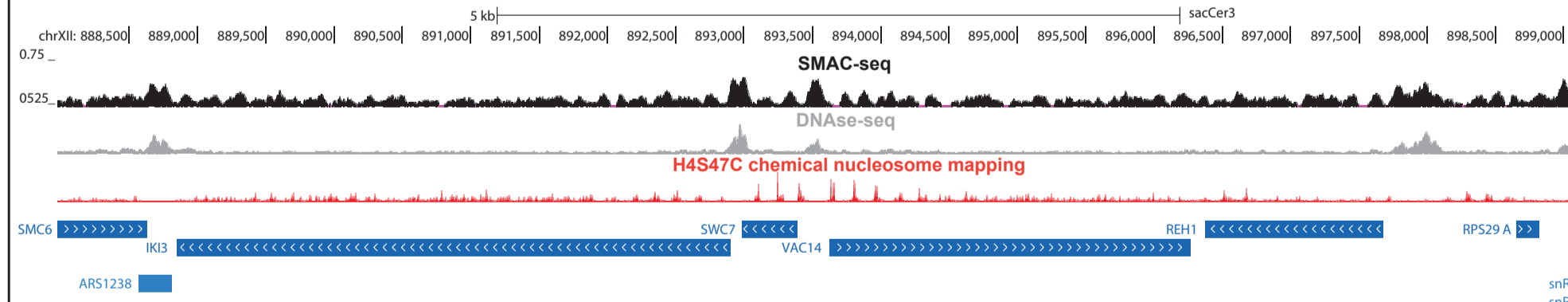
3. Assay resolution



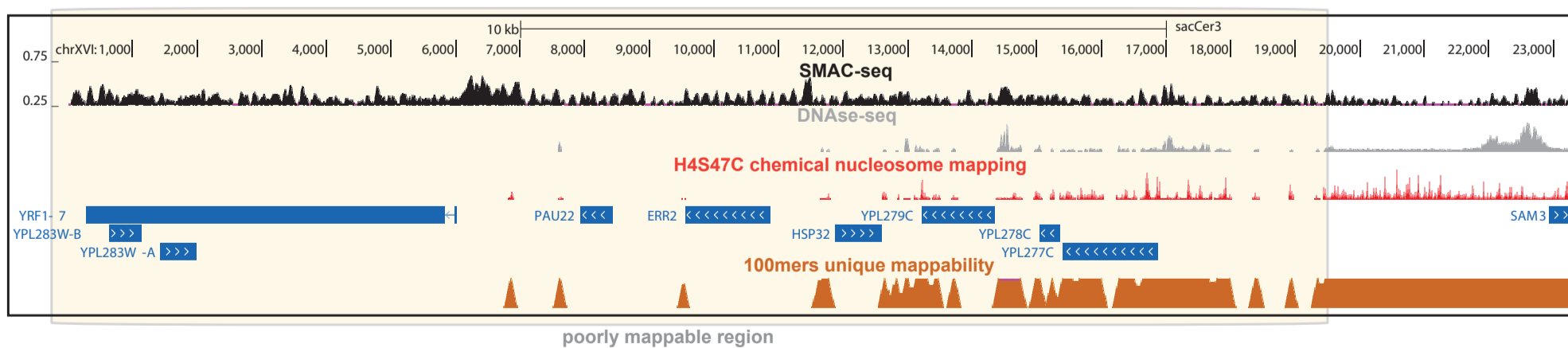
4. Known features of chromatin accessibility are reproduced



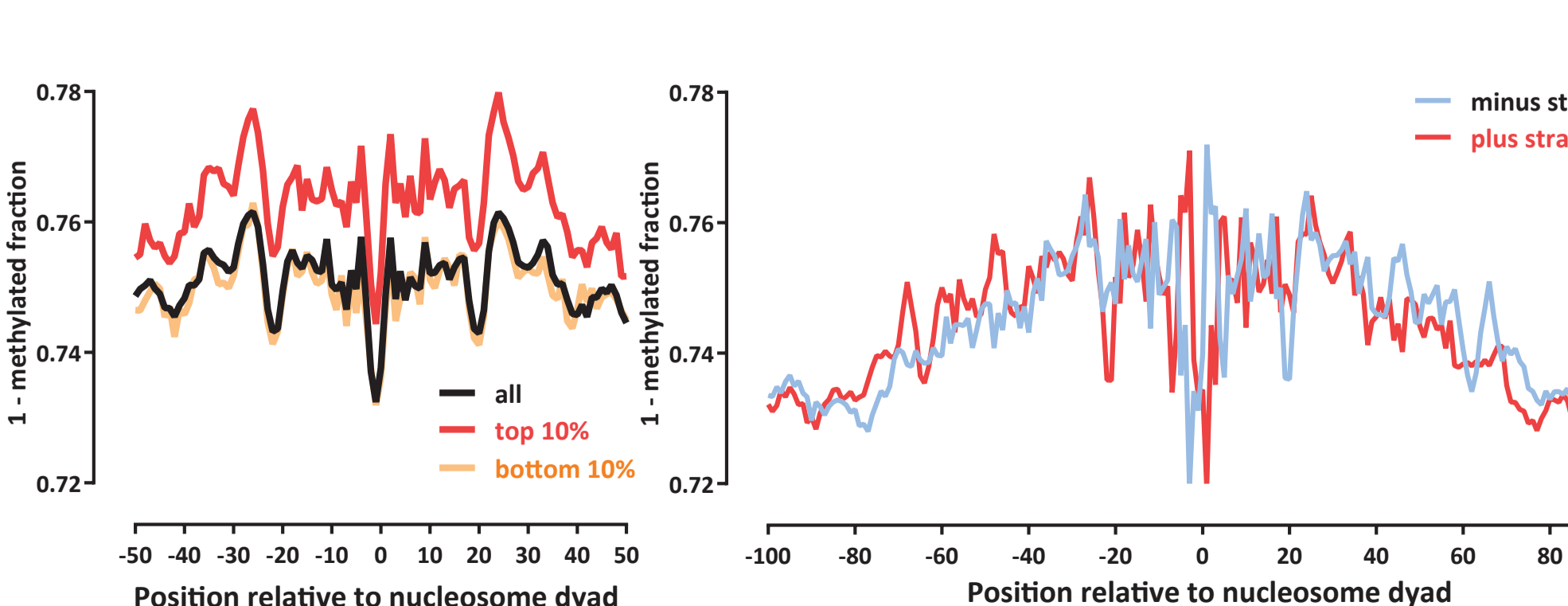
5. Simultaneous nucleosome and open chromatin mapping



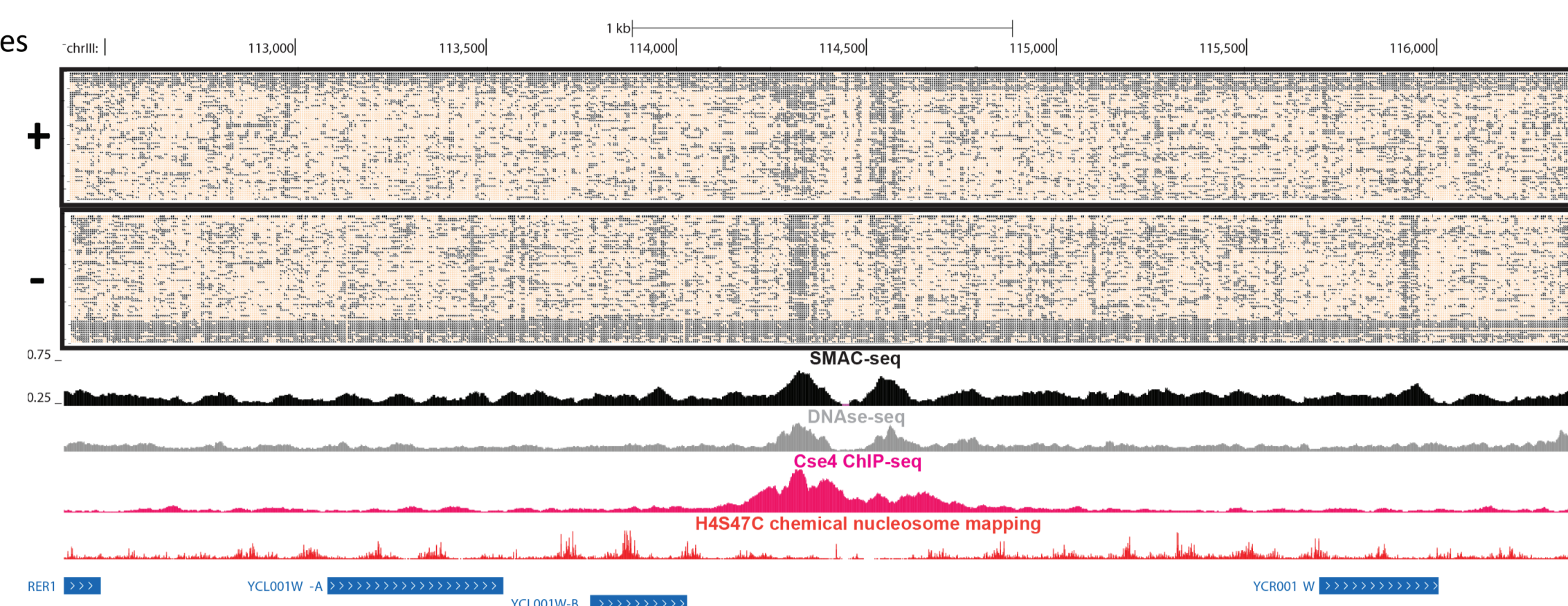
6. Accessibility and nucleosome mapping in repetitive regions



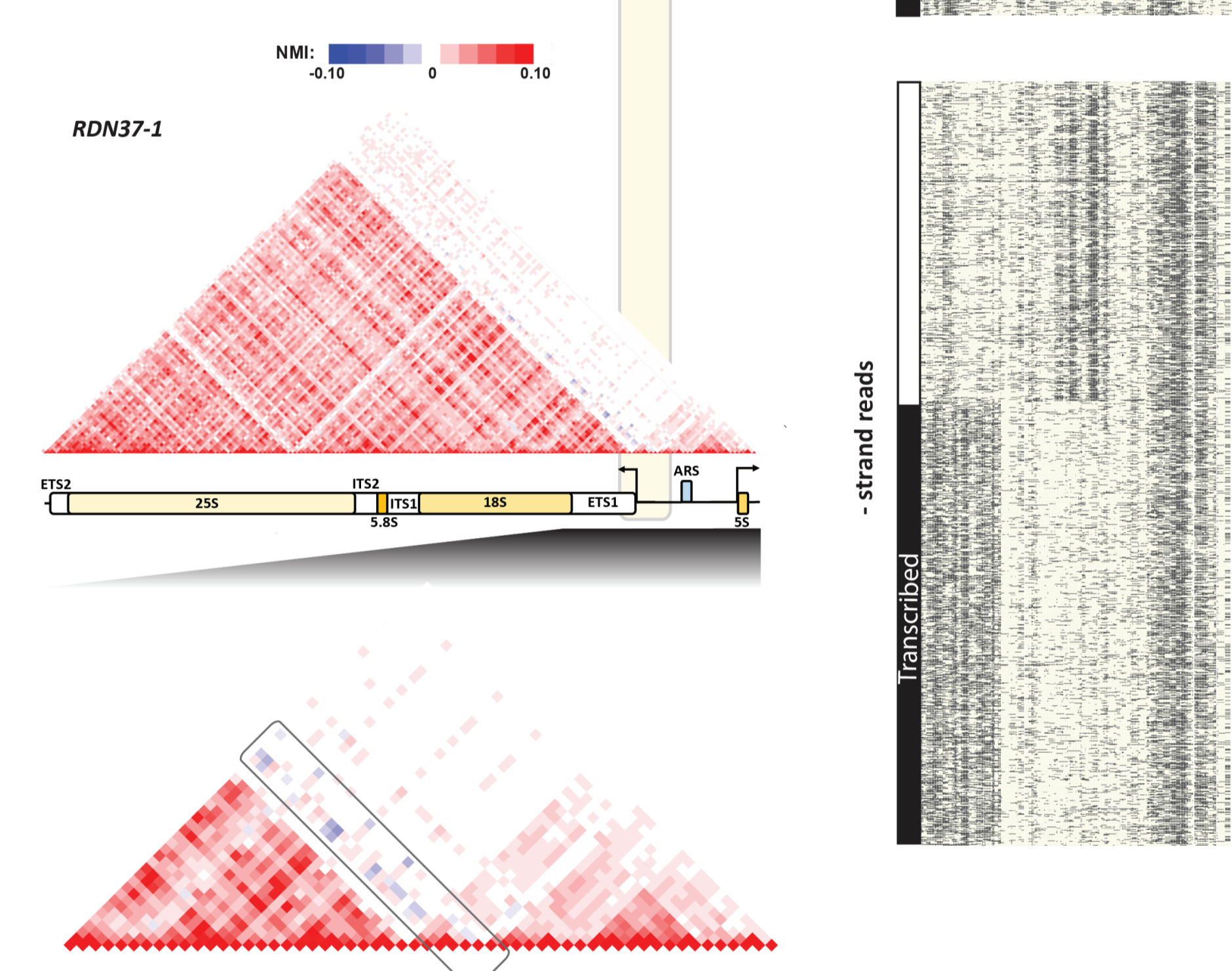
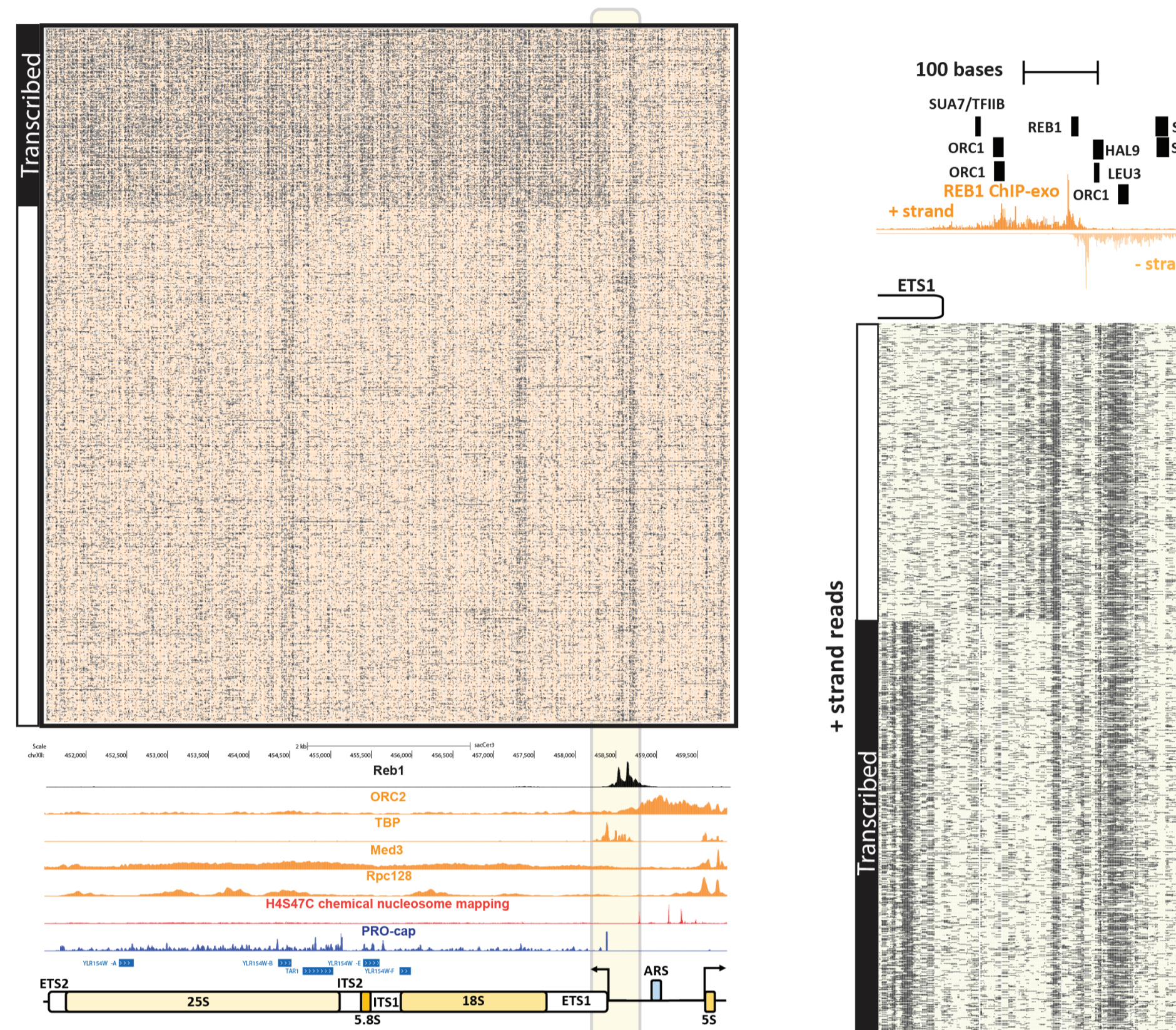
7. Fine-scale mapping of DNA exposure on the nucleosome



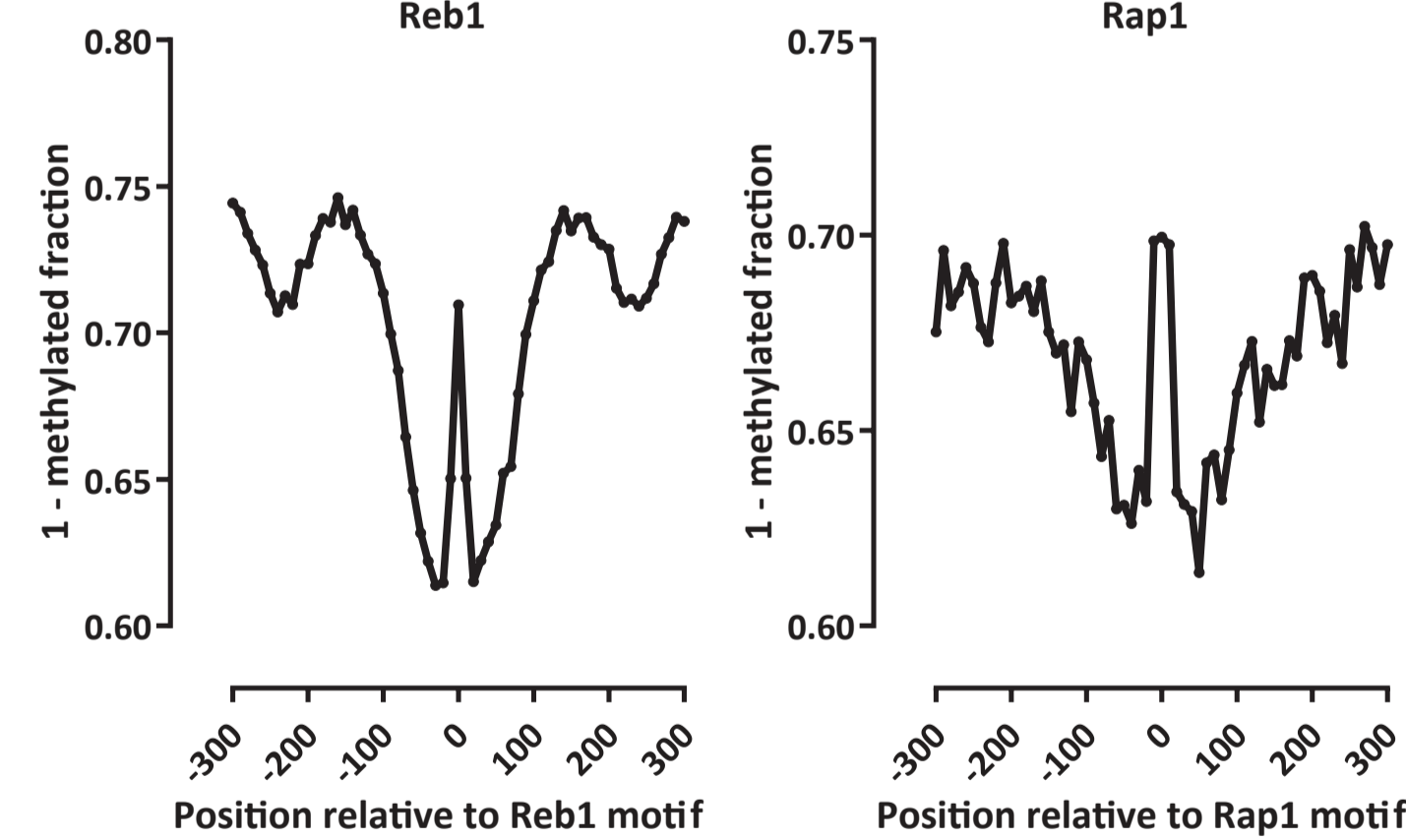
8. Single-molecule population scale view of chromatin accessibility



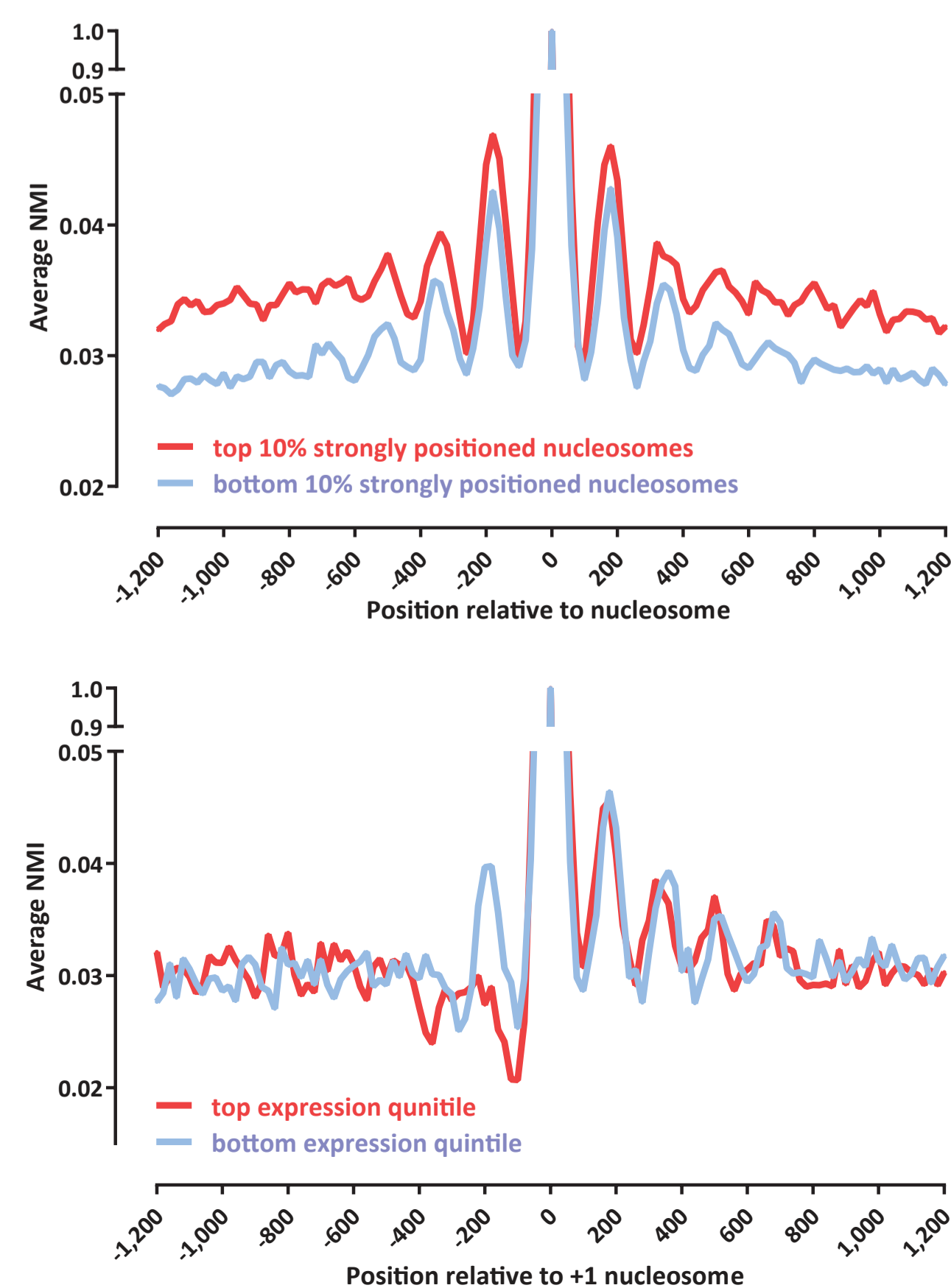
9. Quantification of chromatin states - rDNA locus case study



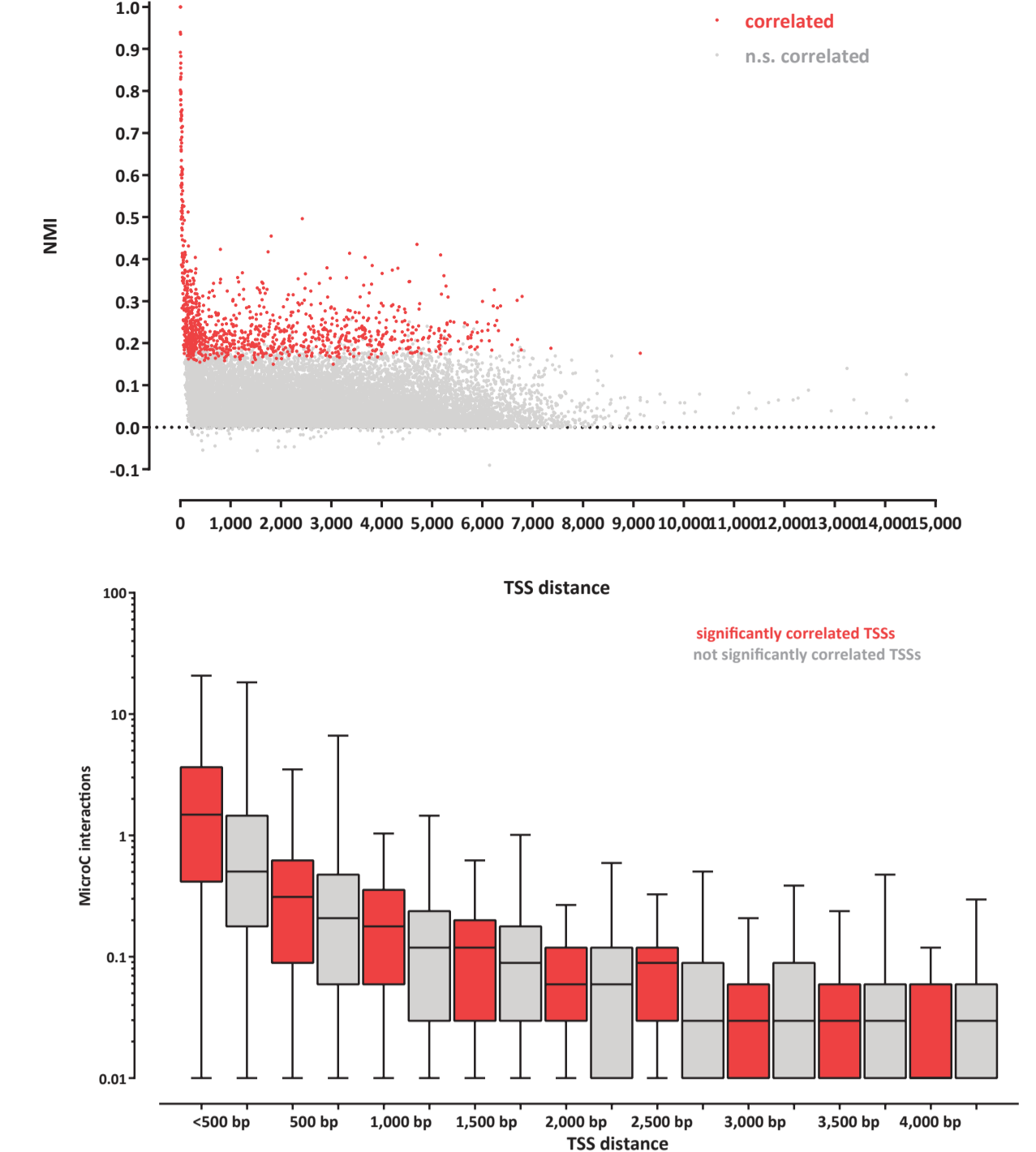
10. Transcription factor footprinting



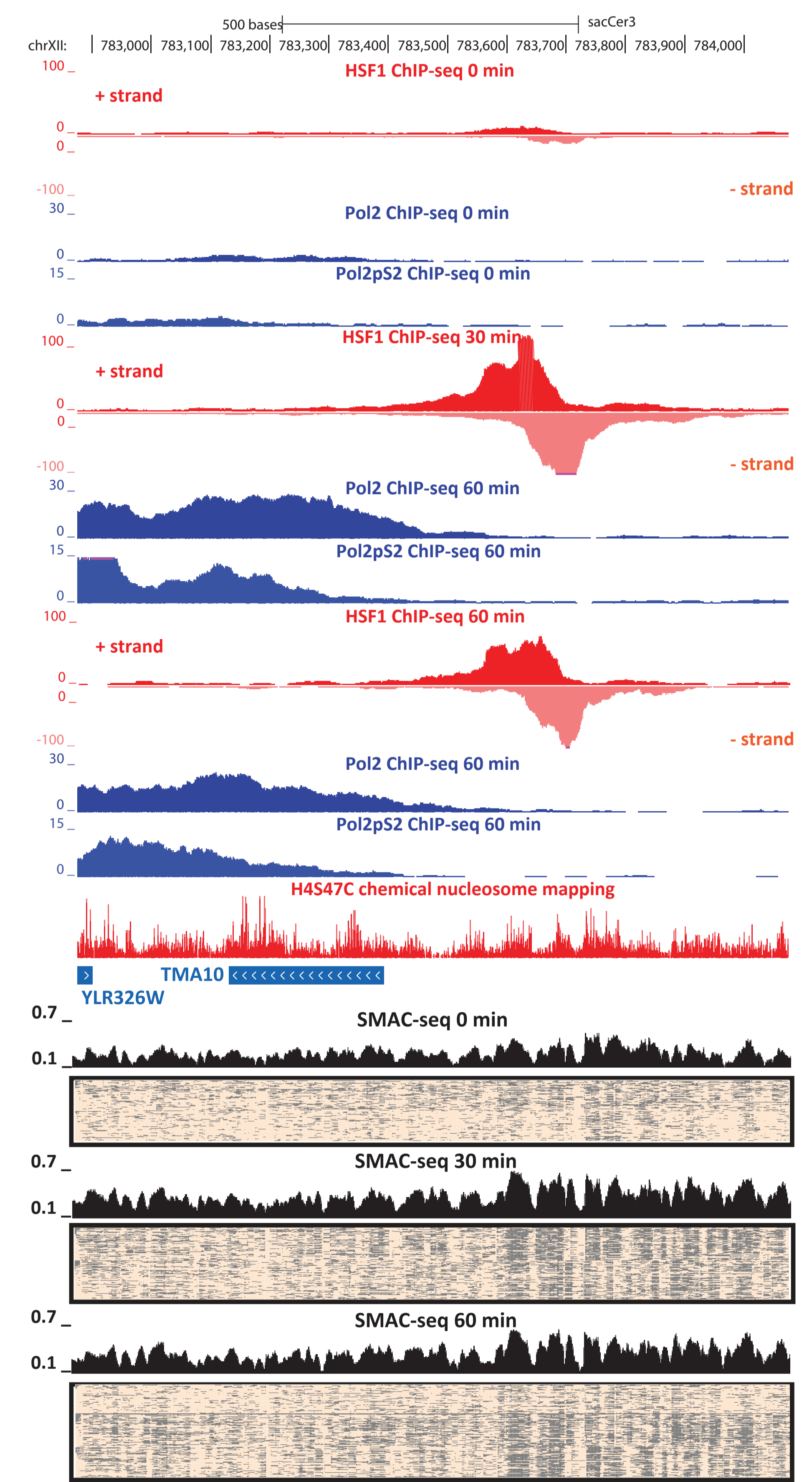
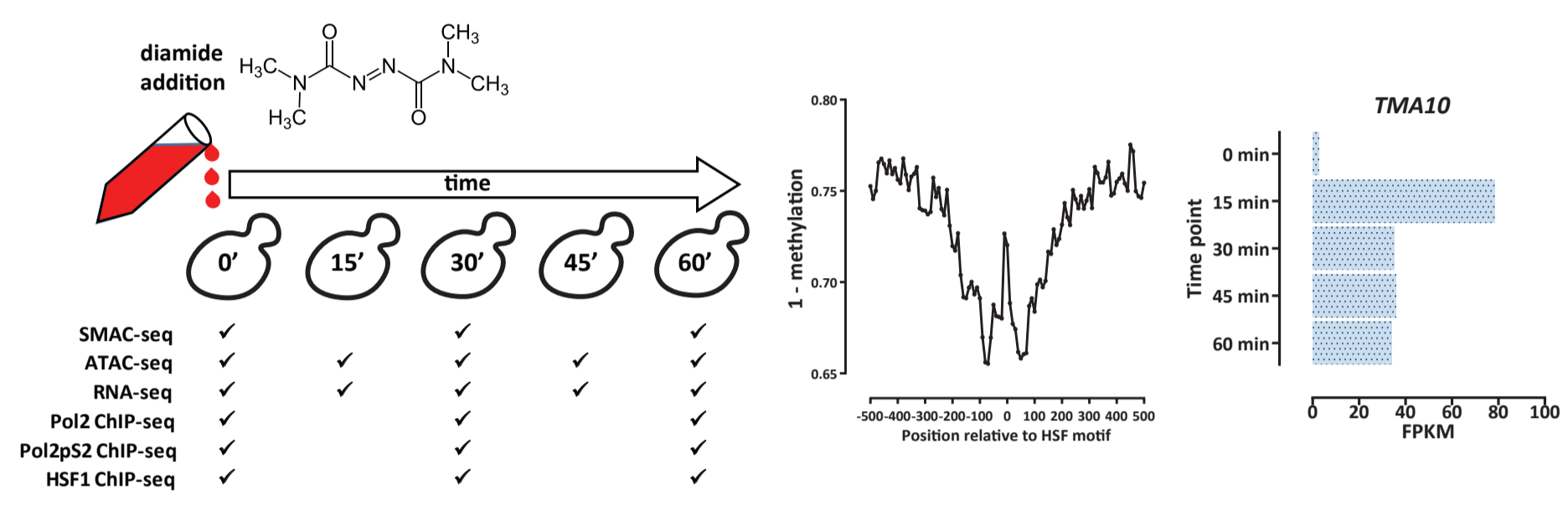
11. Local accessibility correlations



12. Global accessibility correlations



13. Chromatin dynamics during the yeast stress response



Ongoing efforts and future directions

- Methylated base calling improvement through development of defined sequence-context standards with modified bases
- Base calling improvements through the incorporation of bulkier tags (e.g. alkylation) rather than methyl groups
- Ongoing experiments in metazoans with smaller genomes (*Drosophila*, *C. elegans*)
- Adapting targeted Cas9-mediated enrichment approaches so that that large genomes (e.g. mammals) can be studied using the method
- Integration with other assays (Hi-C, ChIP, and others) for single-molecule simultaneous profiling of accessibility, nucleosome positioning and protein-DNA and chromatin interactions