



CHROMATIC reveals chromatin-associated factors contributing to genome topology

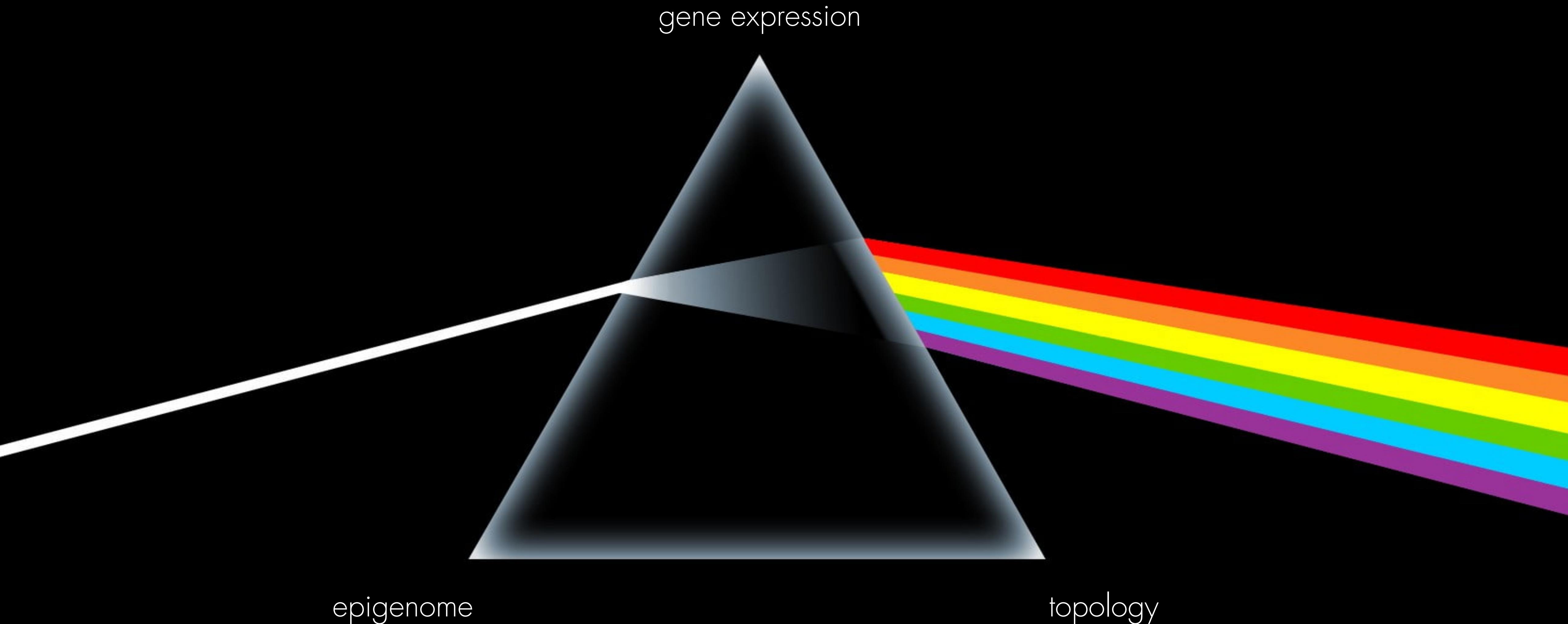
Marc A. Martí-Renom
CNAG-CRG · ICREA

<http://marciuslab.org>
<http://3DGenomes.org>
<http://cnag.crg.eu>

cnag CRG^R ICREA

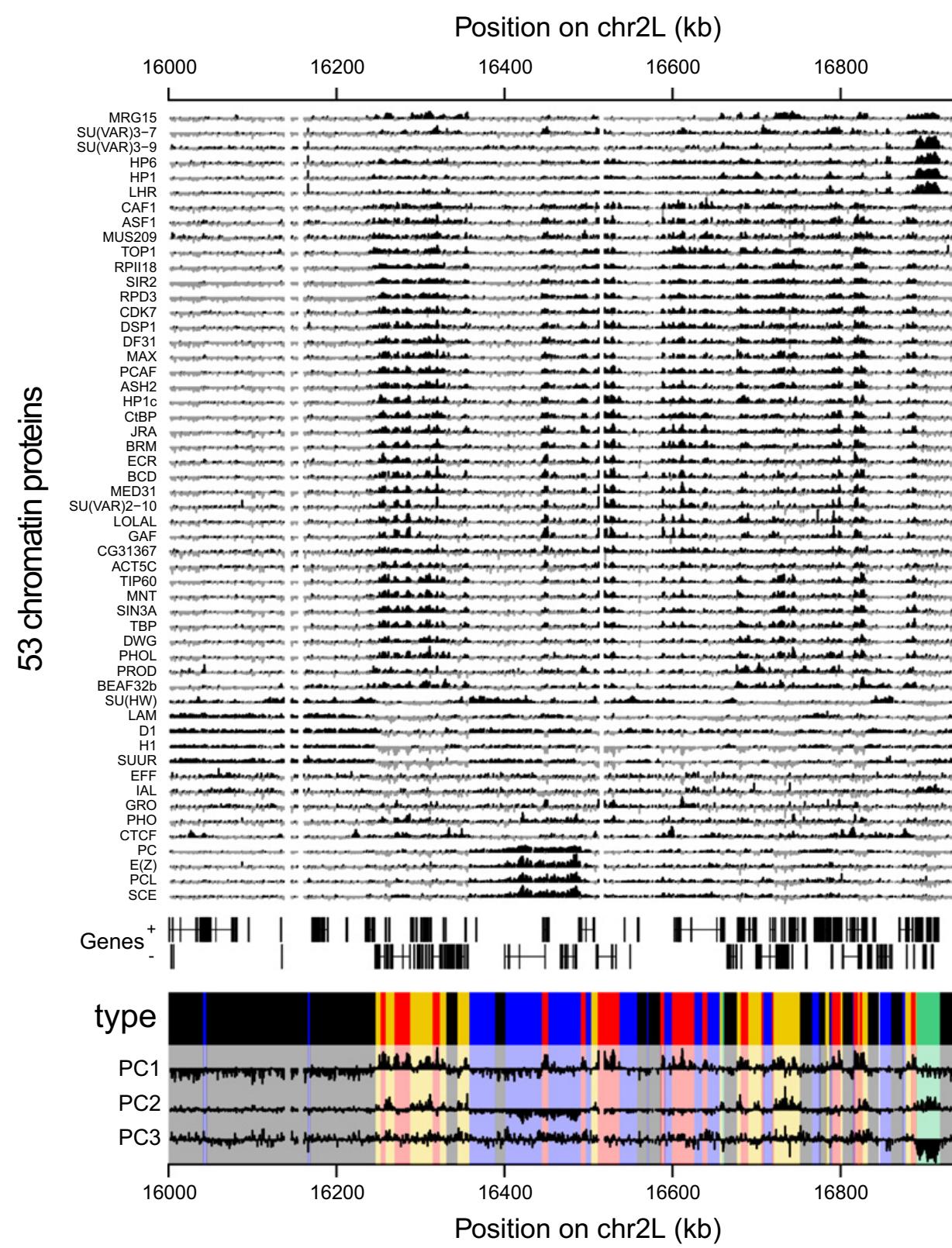
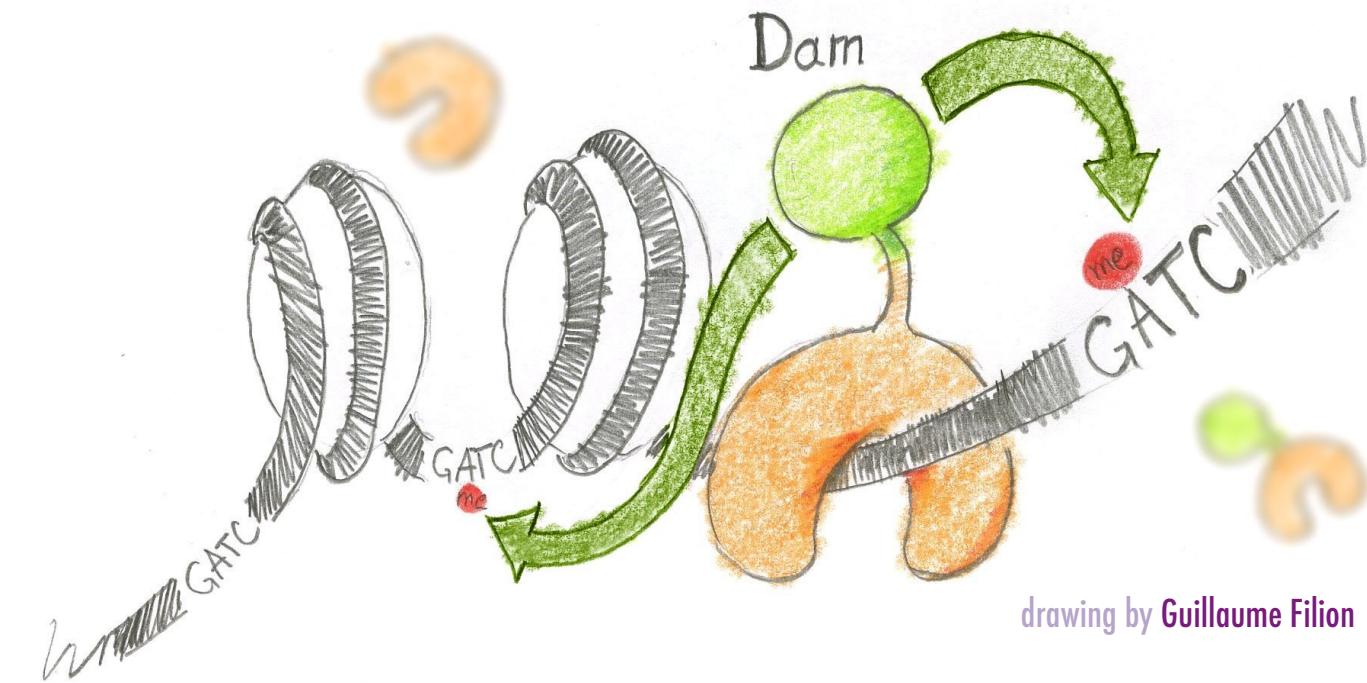
Photo by Laia Marín

The genome is a complex system

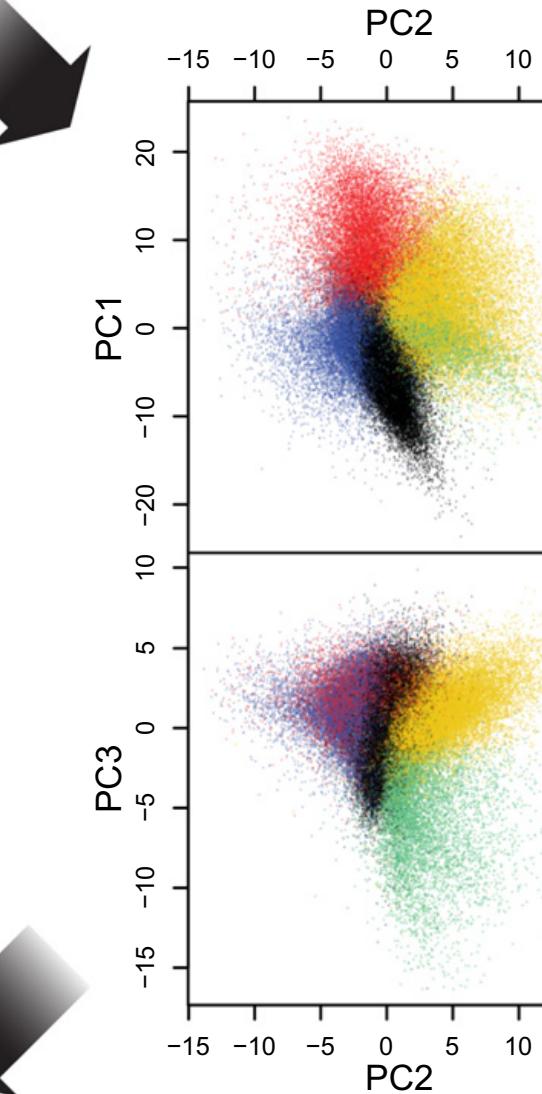


Fly Chromatin **COLORs**

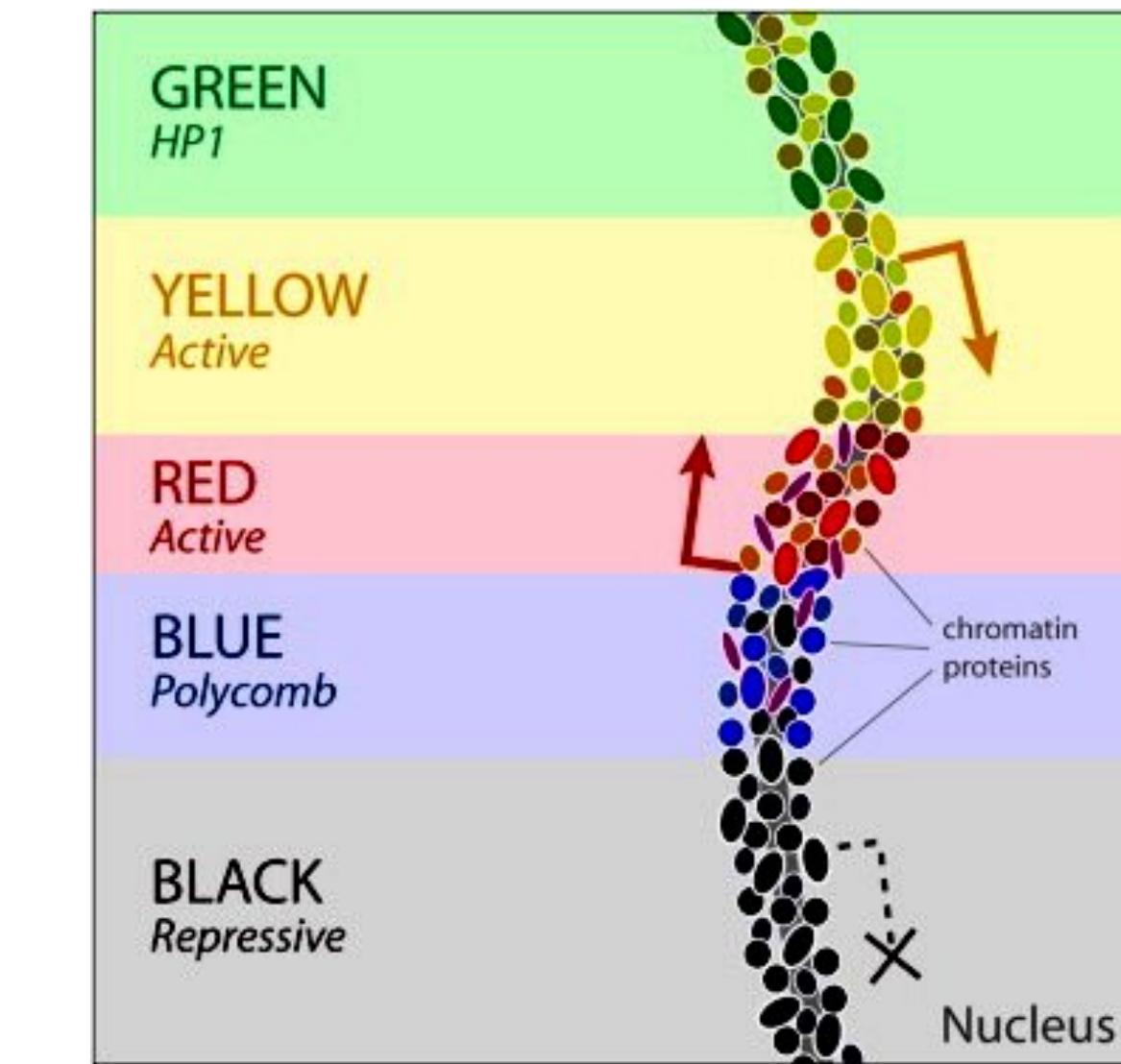
Filion et al. (2010). Cell, 143(2), 212–224.



Principal component analysis

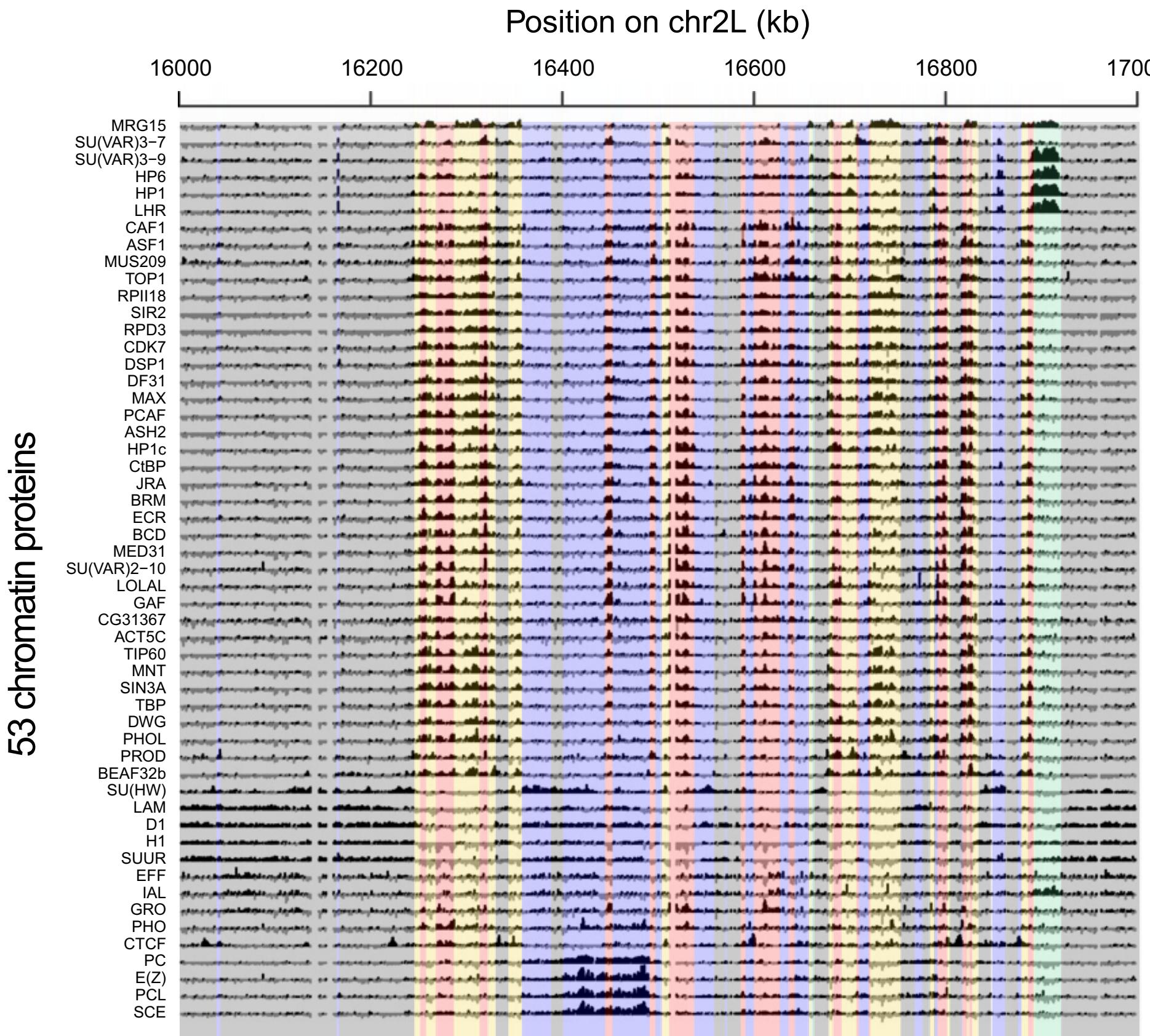
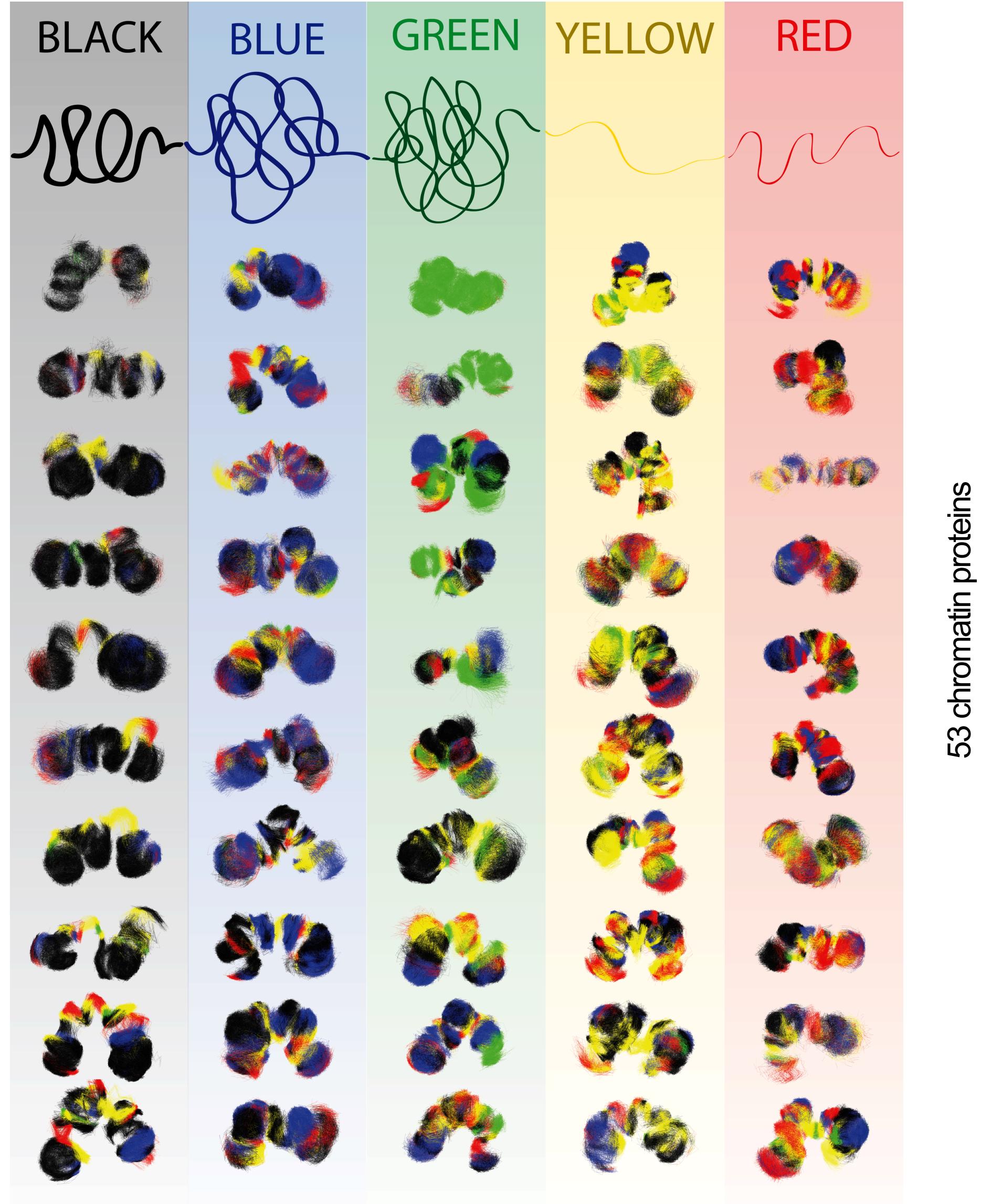


Hidden Markov model



Who “holds” the genome structure?

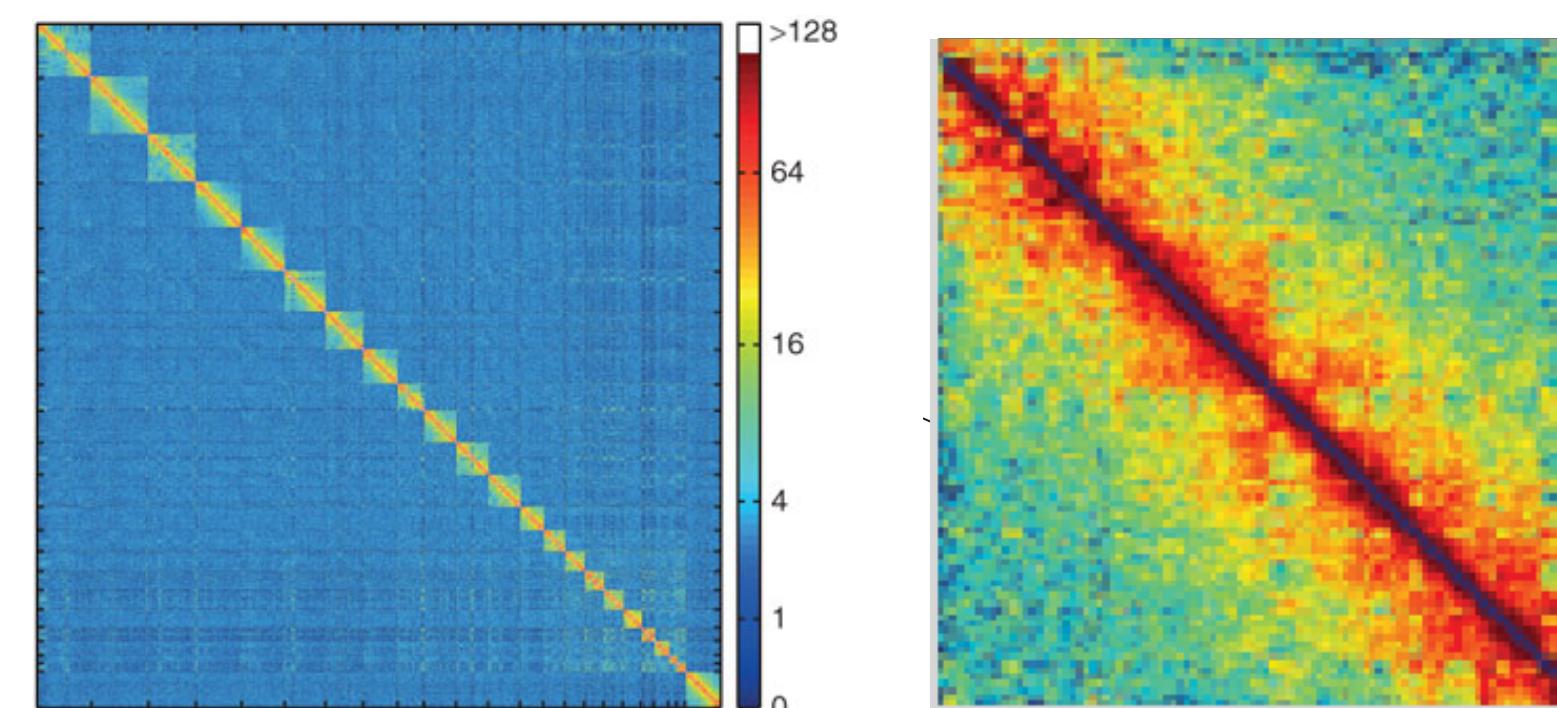
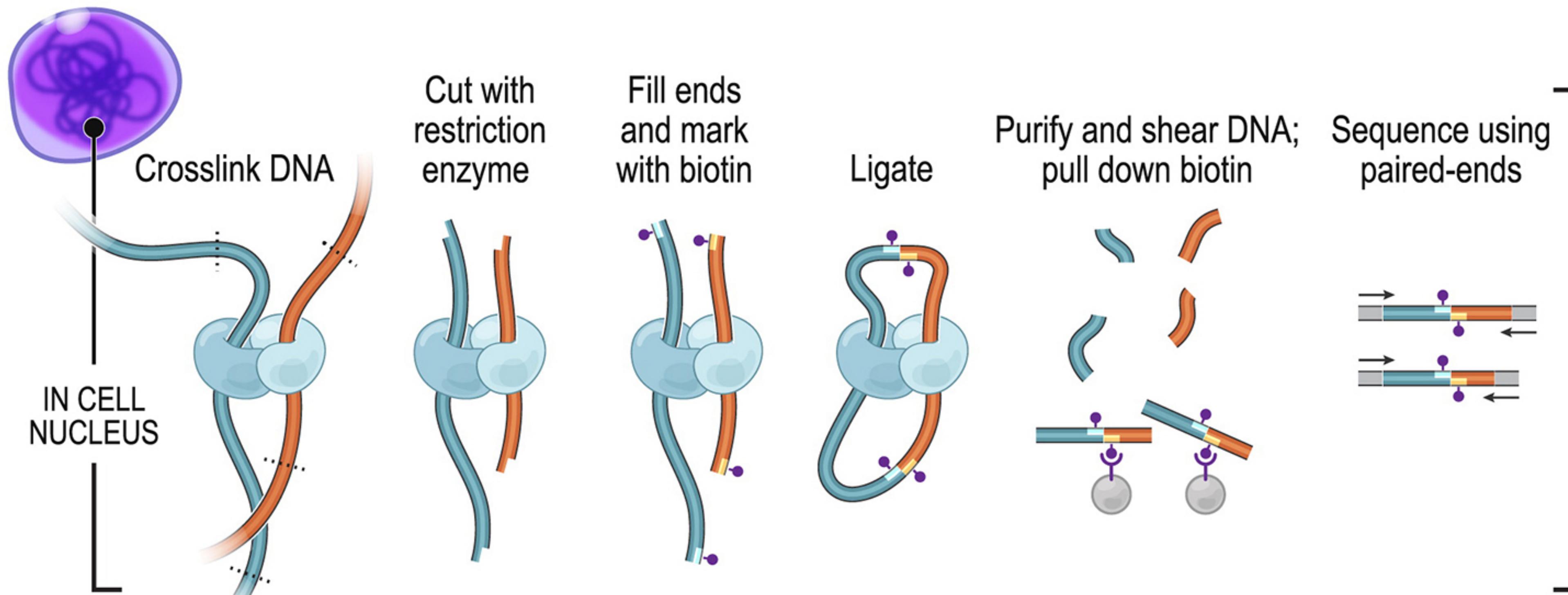
Serra et al. PLoS Comput Biol (2017) 13(7): e1005665



Chromosome Conformation Capture

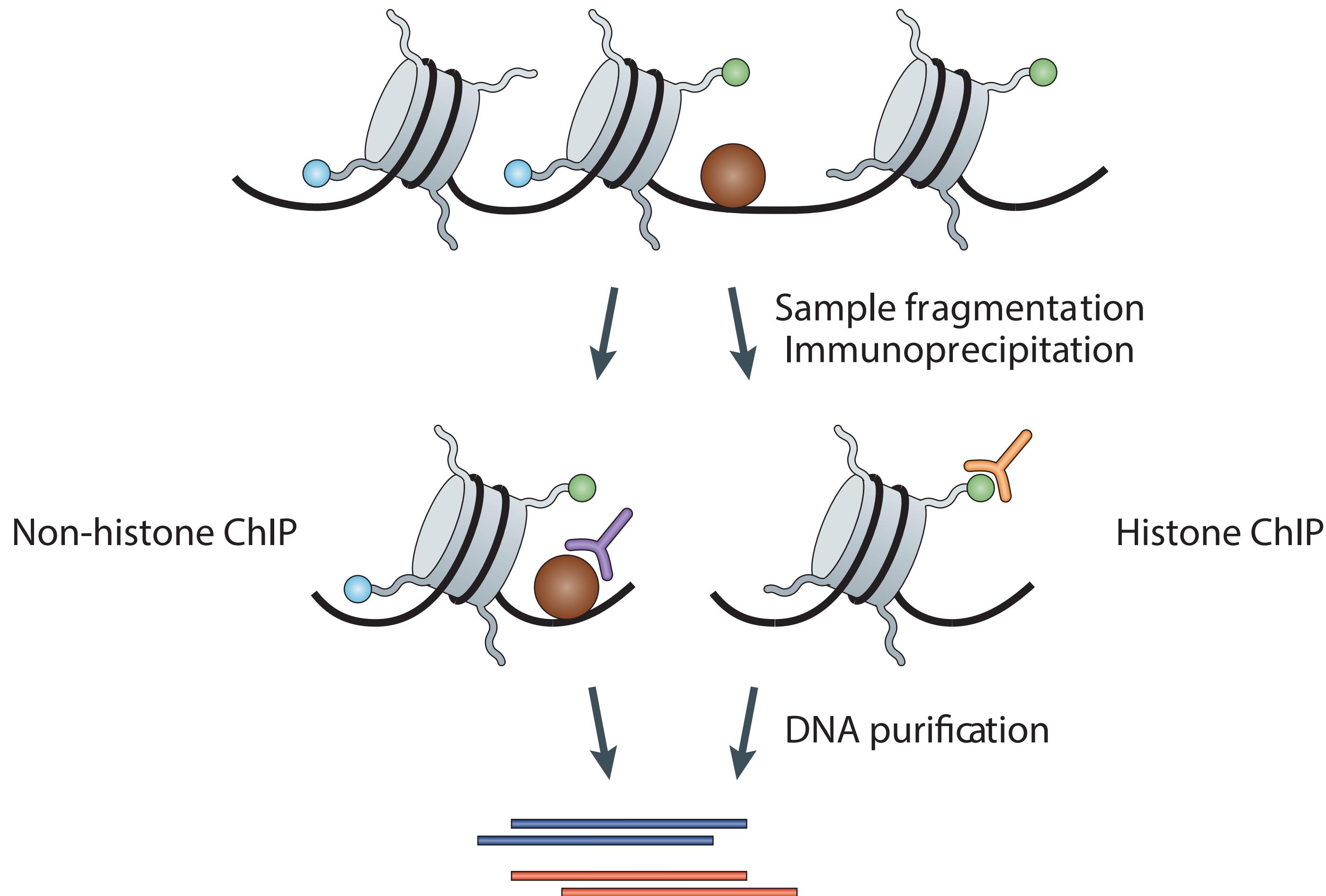
Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311.

Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.

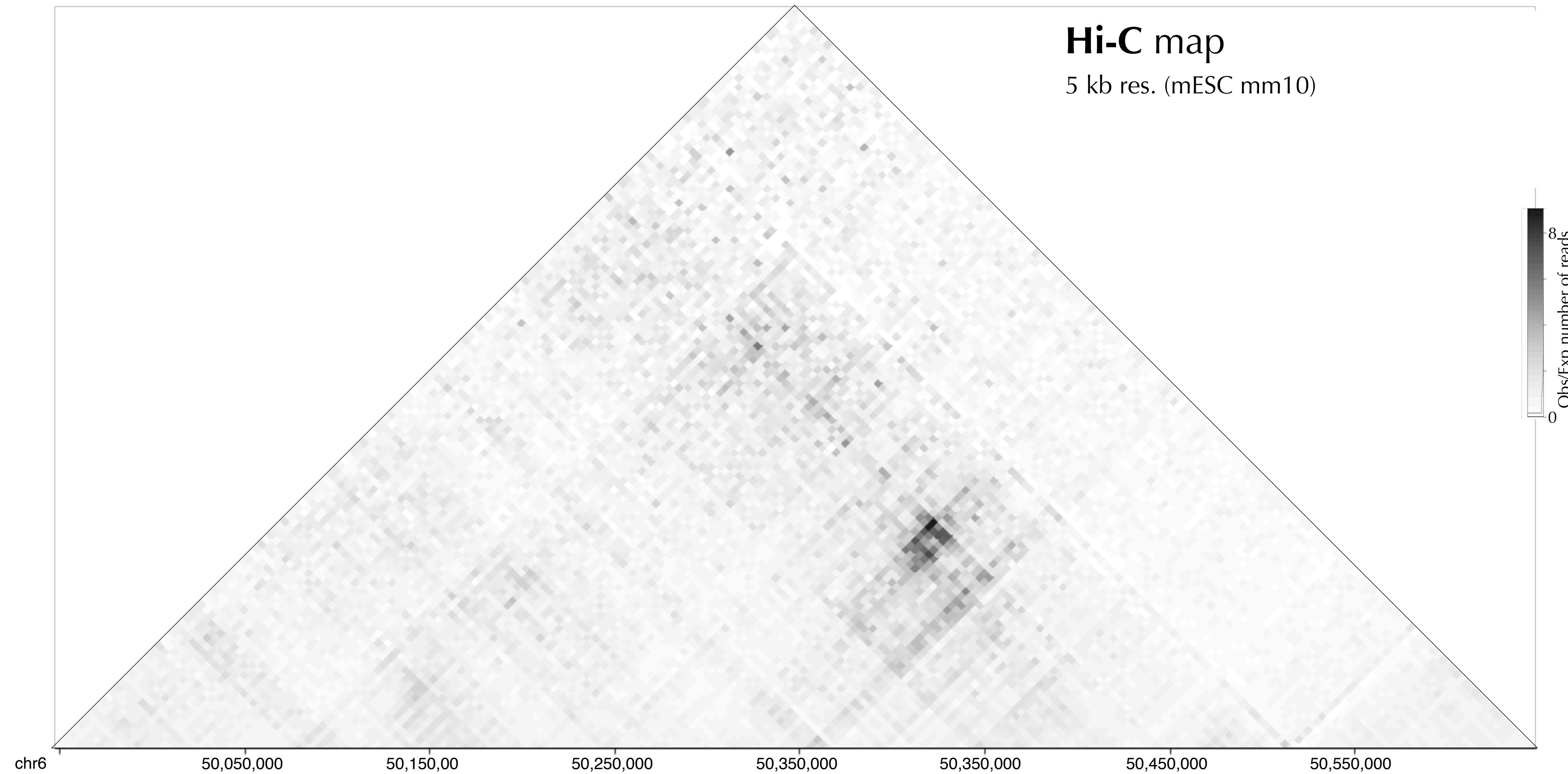


Chromatin Immunoprecipitation (ChIP)

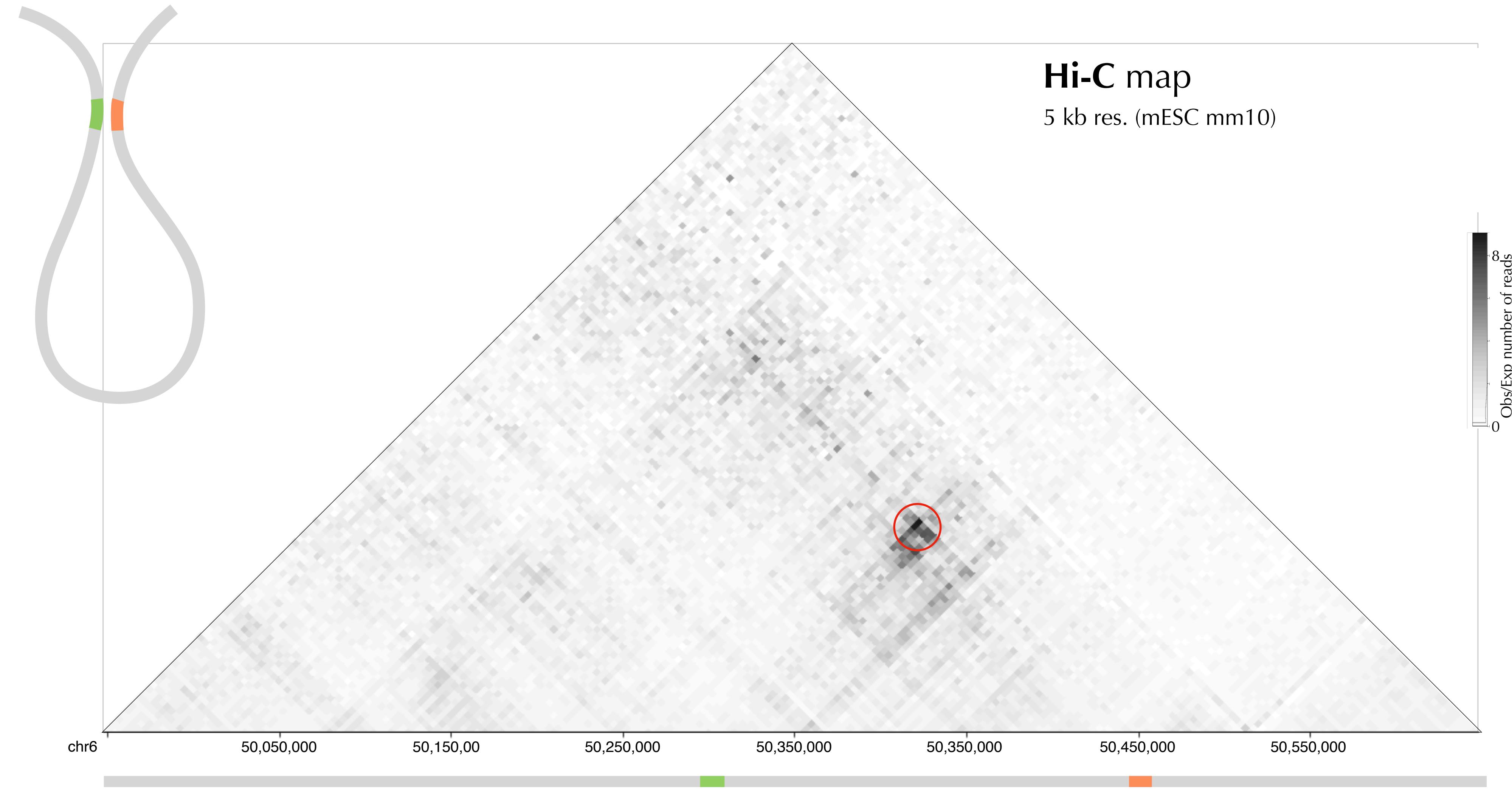
Solomon, M. J., Larsen, P. L. & Varshavsky, A. (1988) Cell 53, 937–947.
Park, P.J. (2009) Nature Reviews Genetics 10, 669–680.



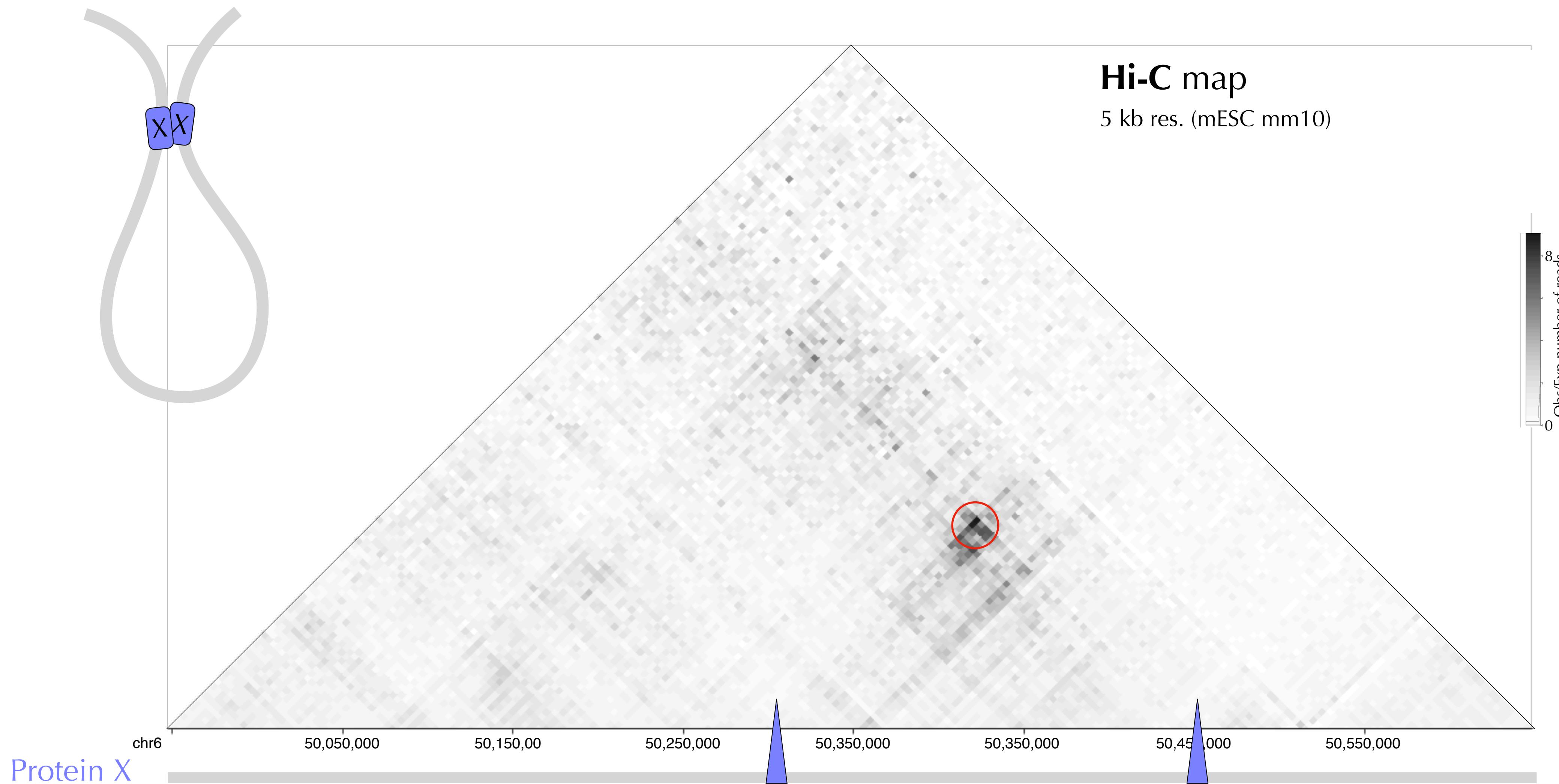
High-throughput Chromosome Conformation Capture (Hi-C)



Chromatin interaction on a Hi-C map

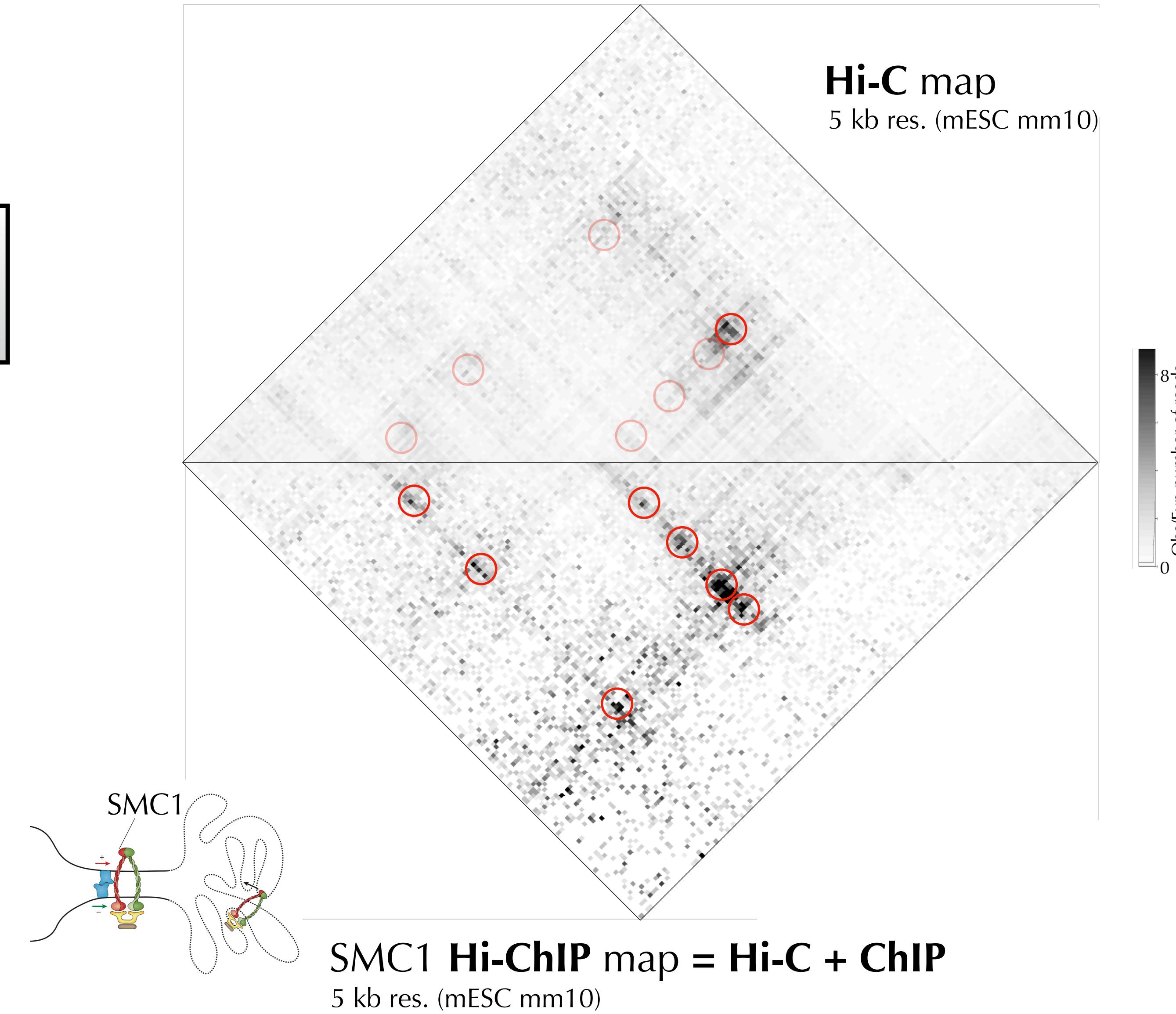
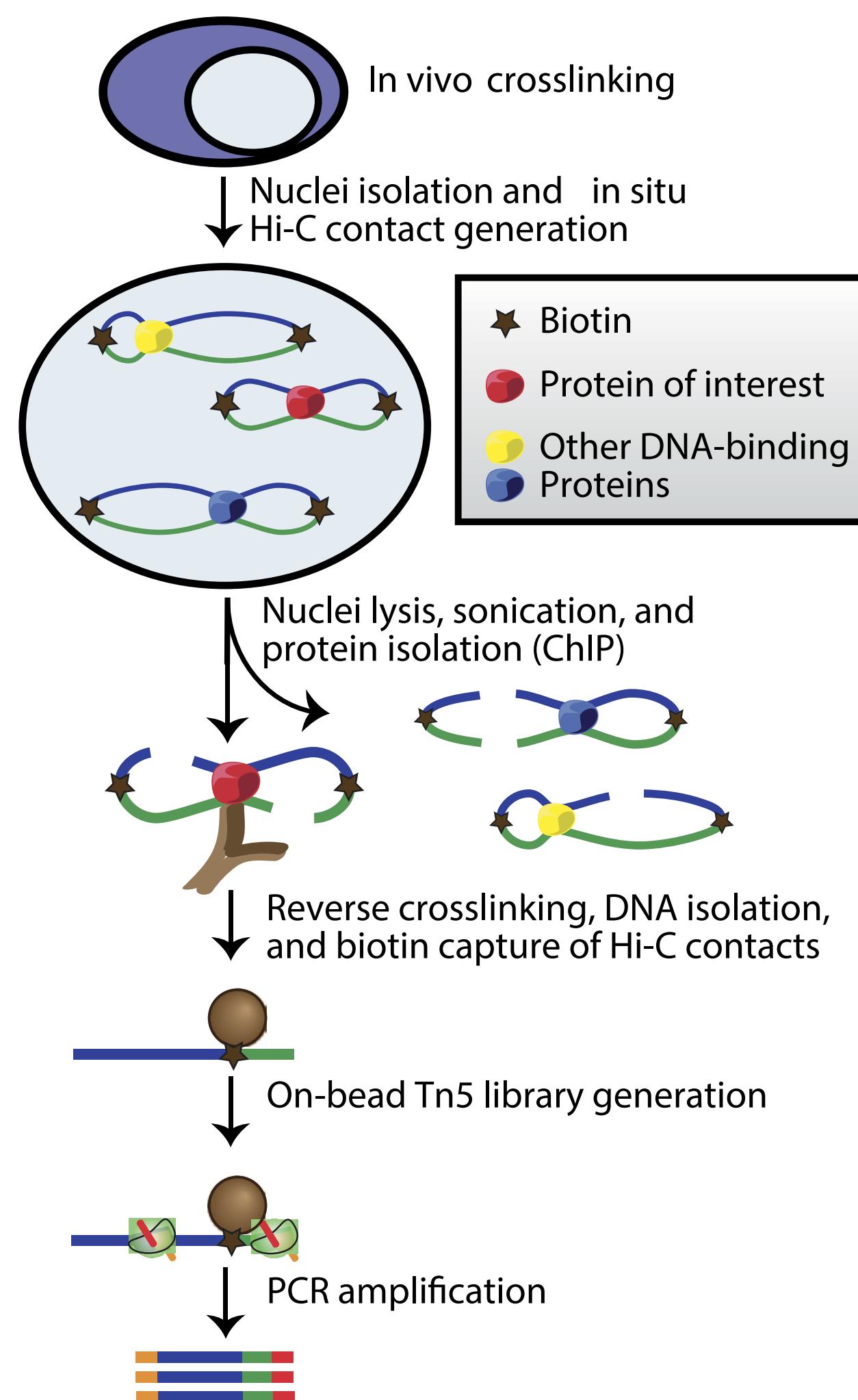


Chromatin interaction “mediated” by a protein

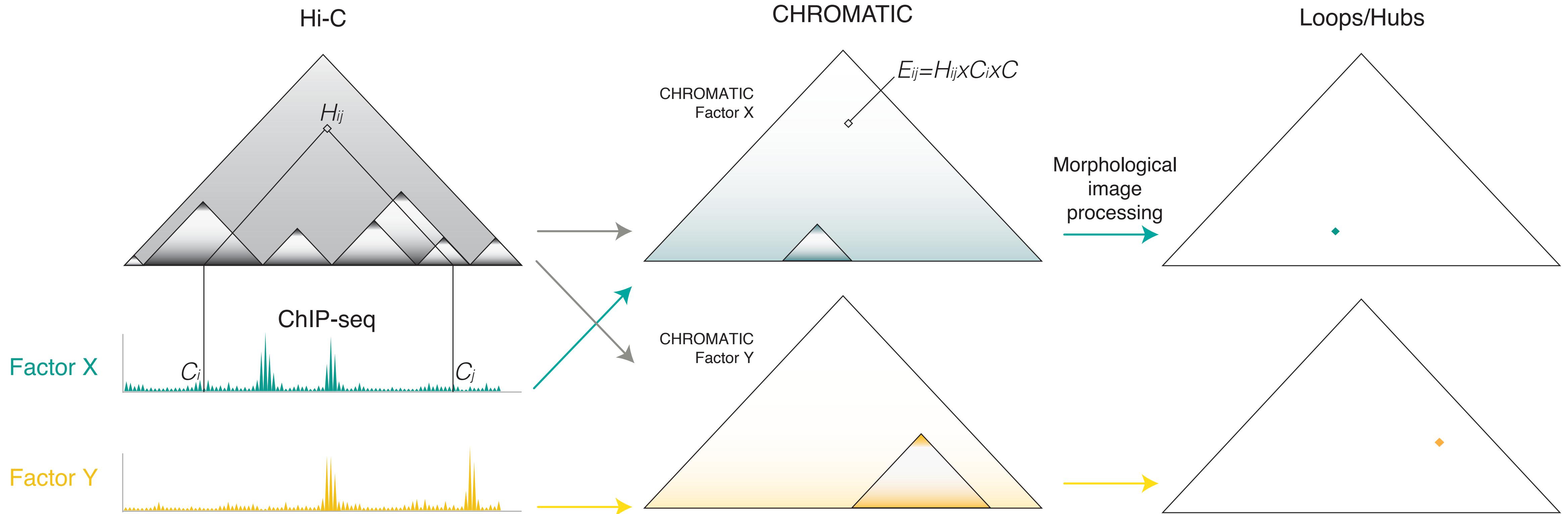


Hi-ChIP: capturing specific protein-mediated interactions

Mumbach, M.R. et al. (2016) Nature Methods 13(11) 919-922.

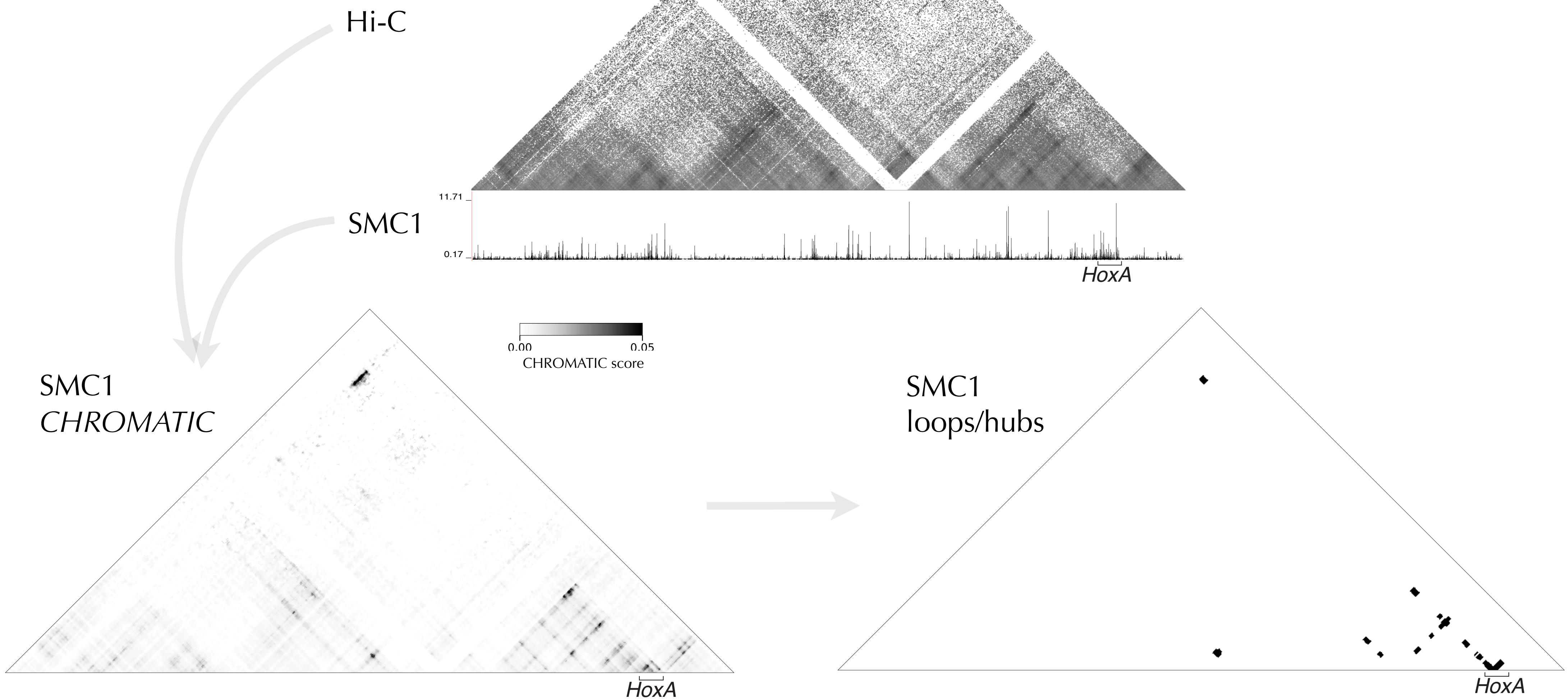
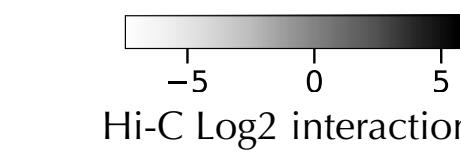


CHROMATIC



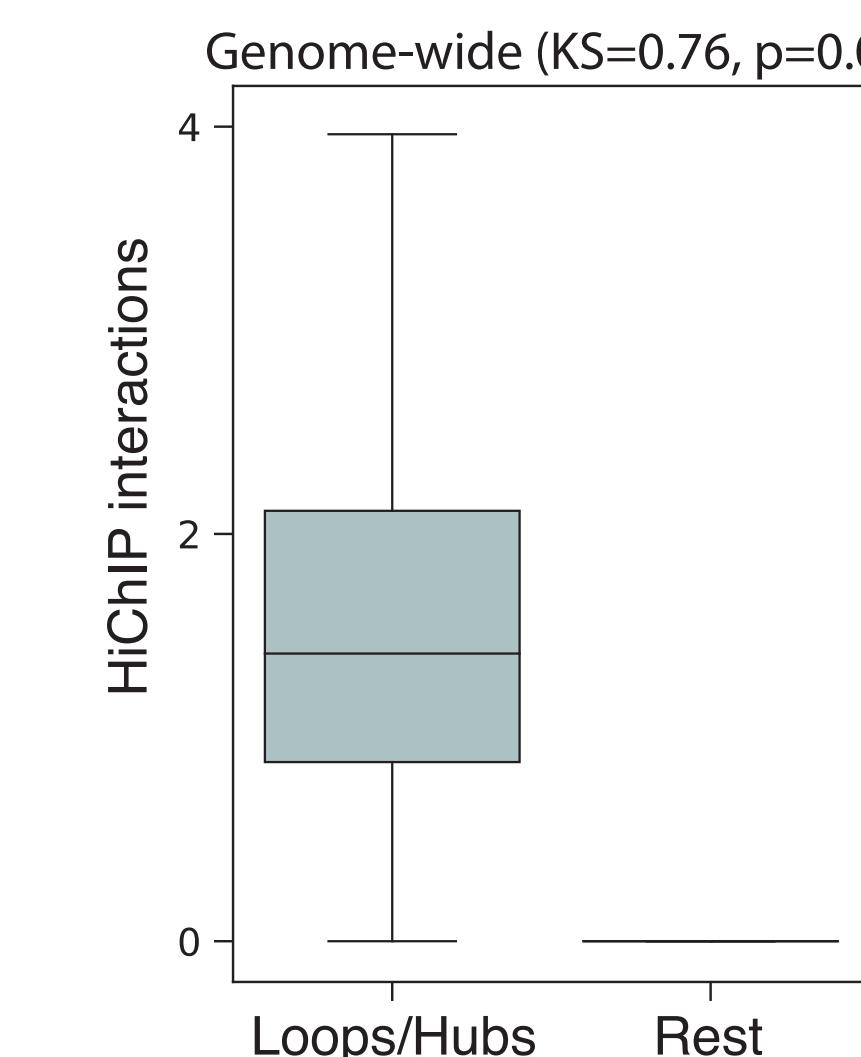
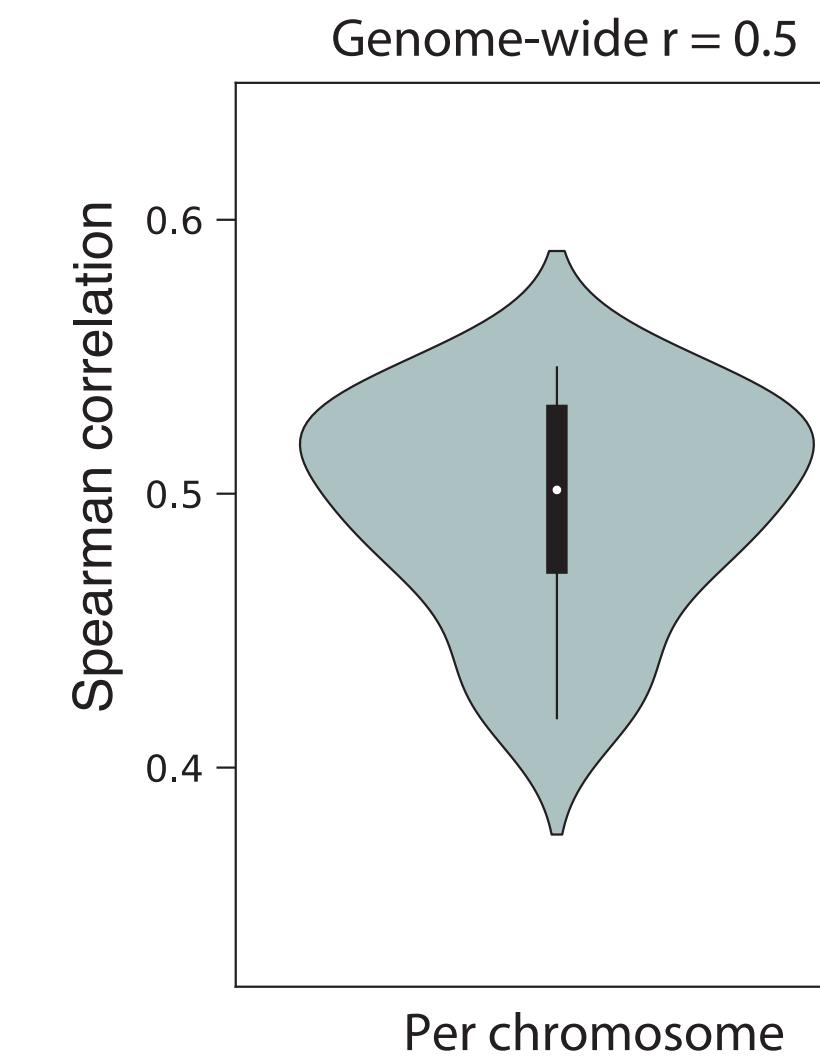
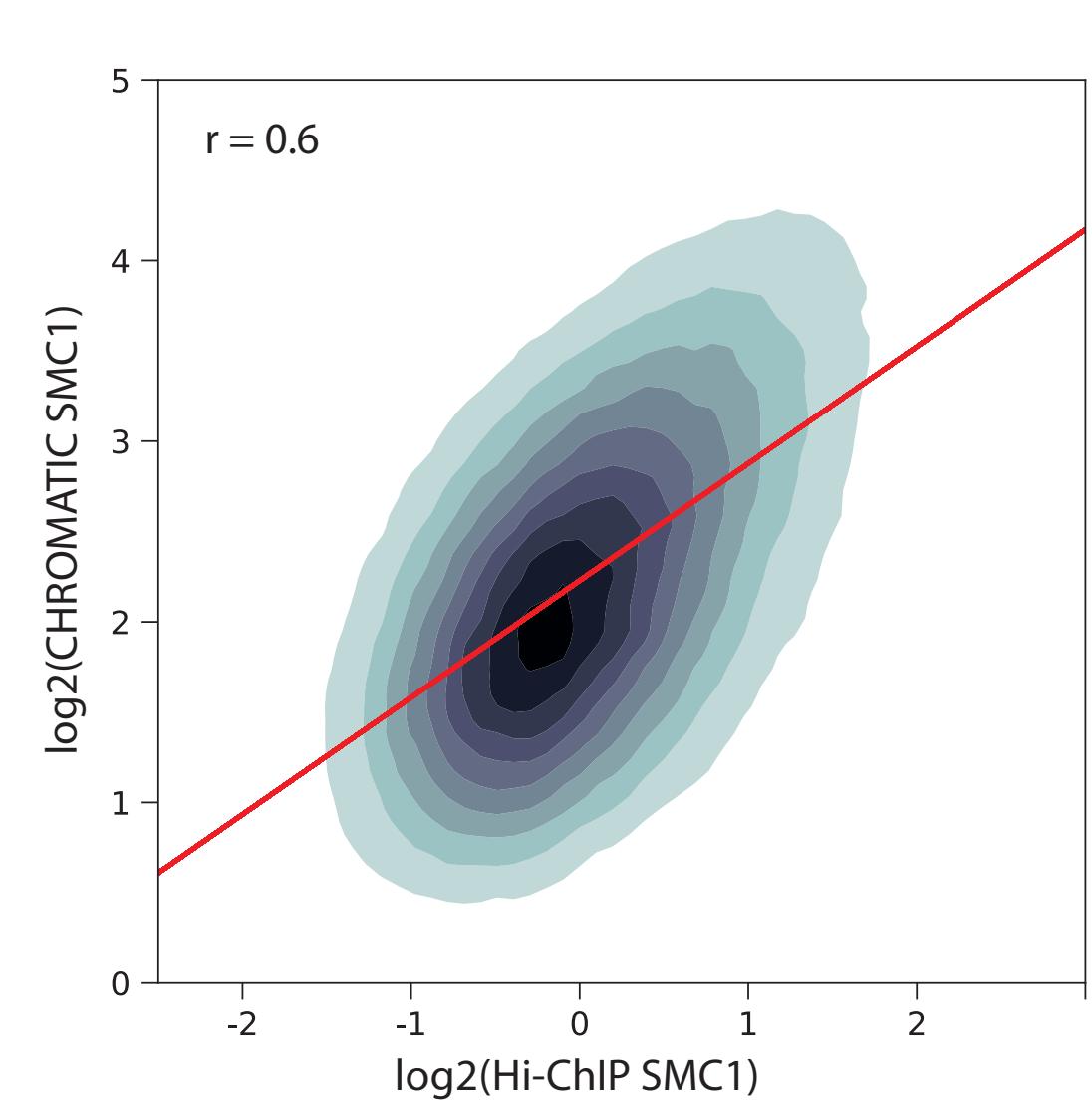
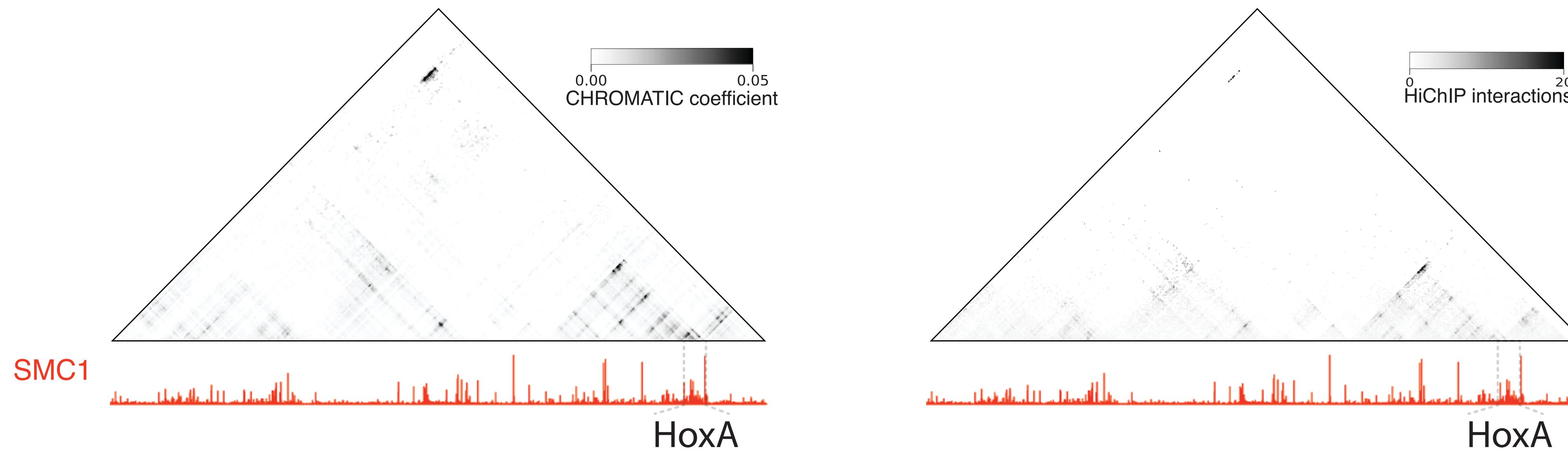
CHROMATIC example

mm10 chr6:48,050,001-52,750,006

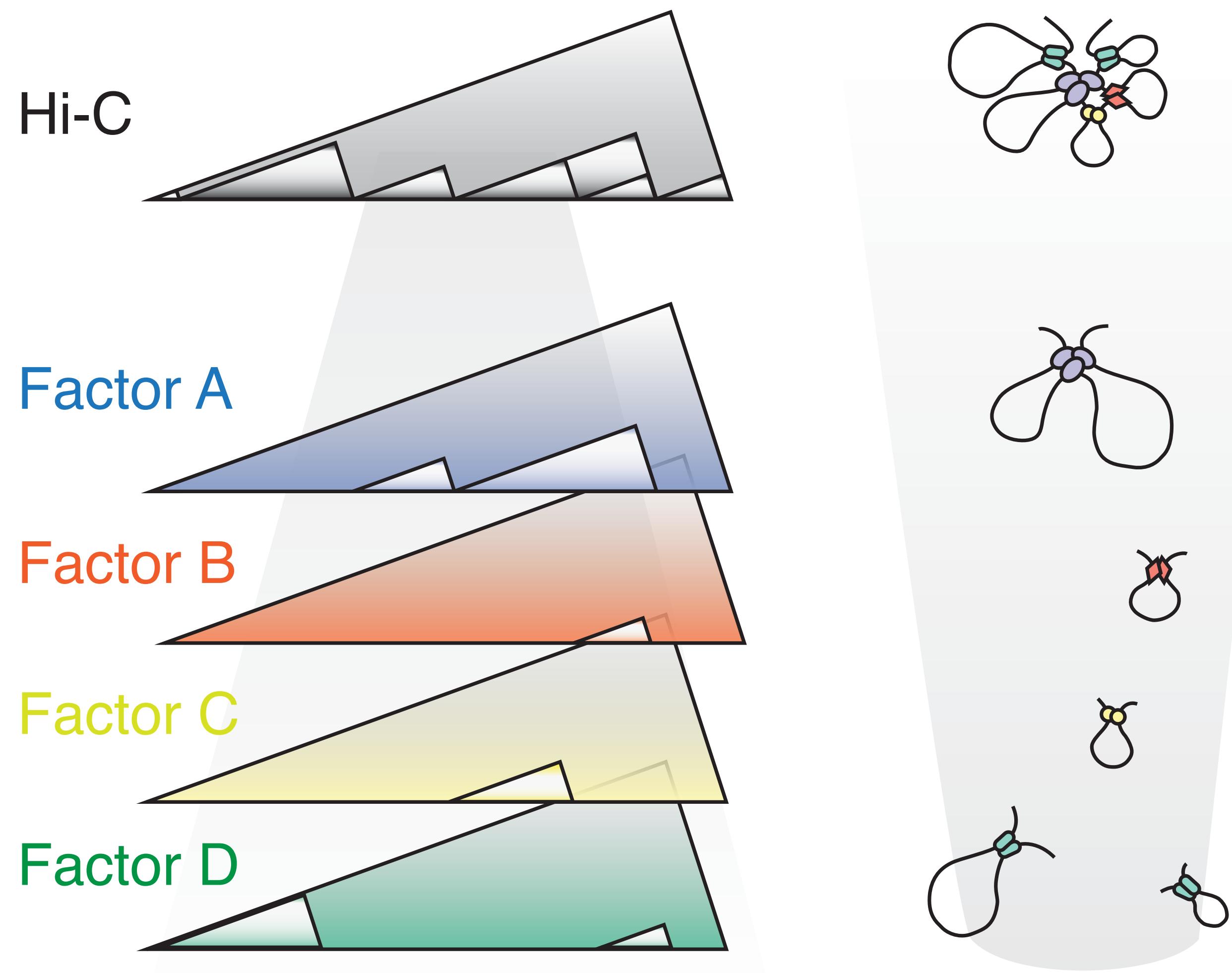


Validation with HiChIP as benchmark

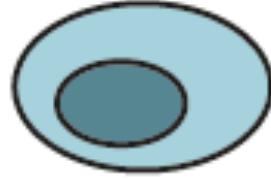
mm10 - mESC - 5kb - chr6:48,050,001-52,750,006



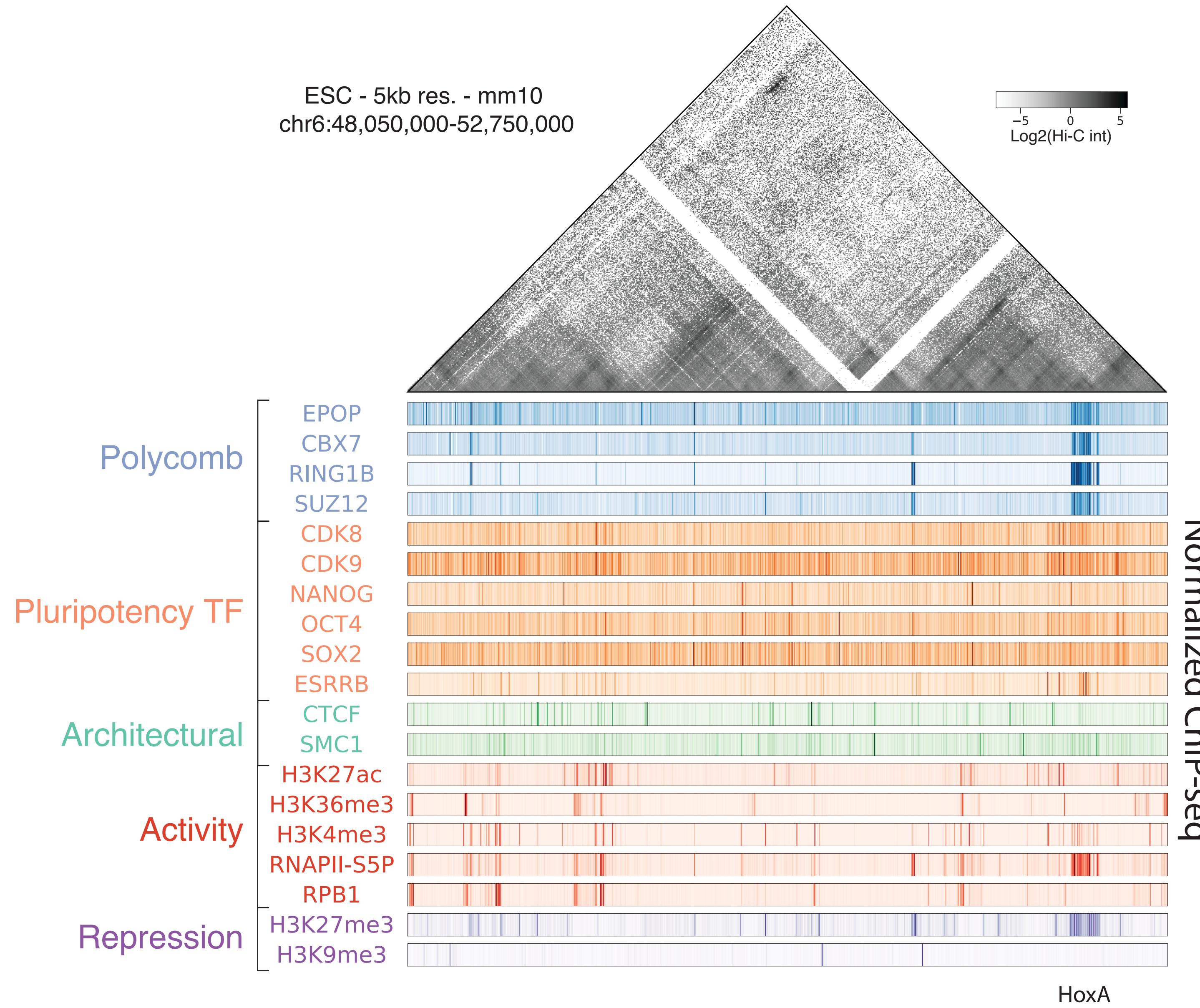
The role of chromatin factors in genome topology



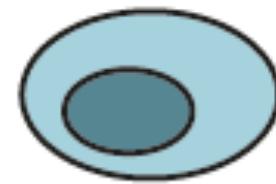
ESC



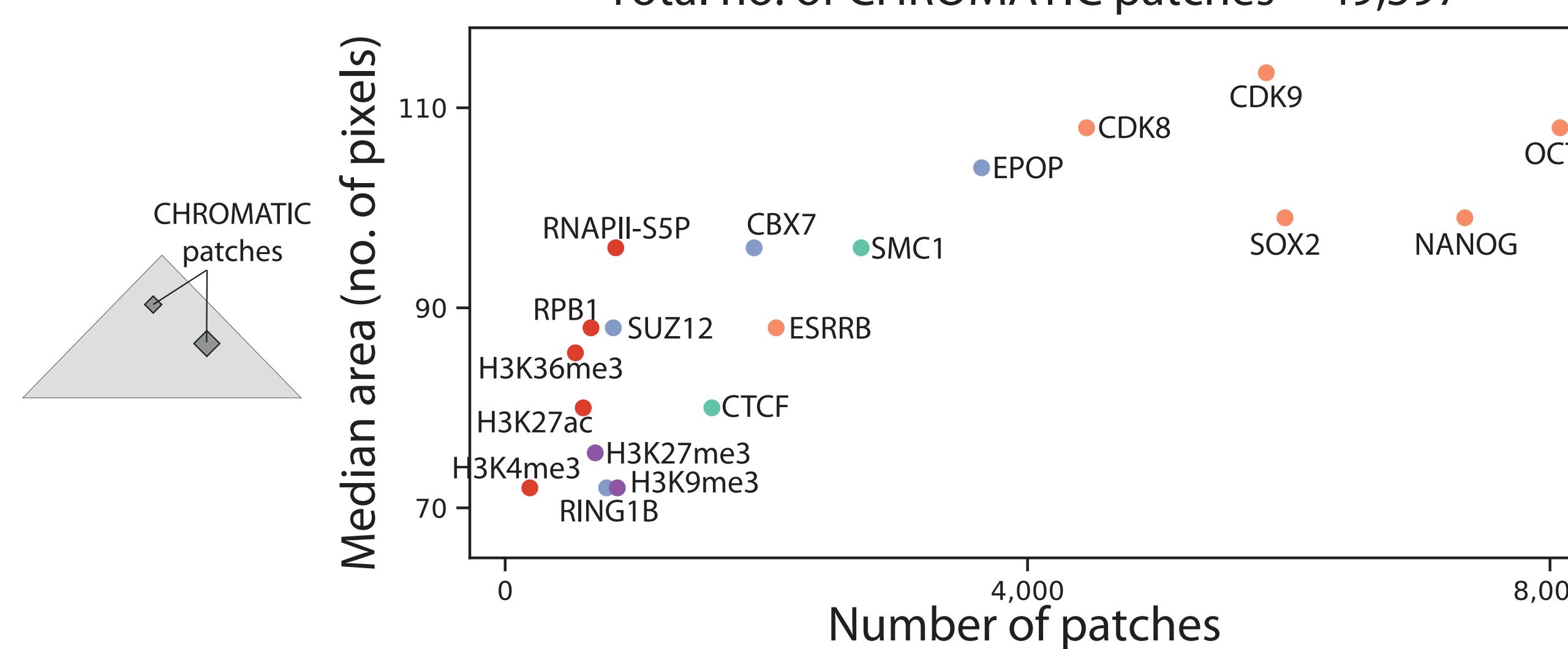
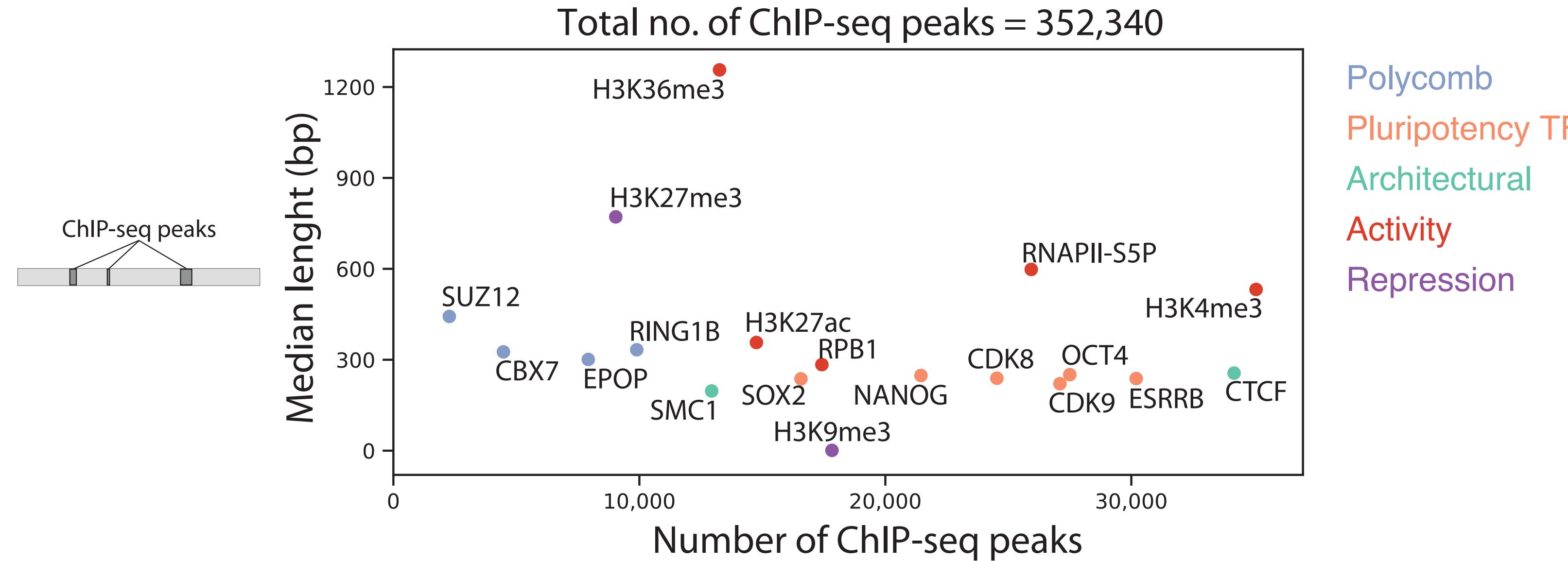
HoxA cluster (example in ESC)



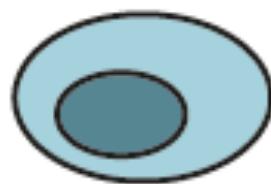
ESC



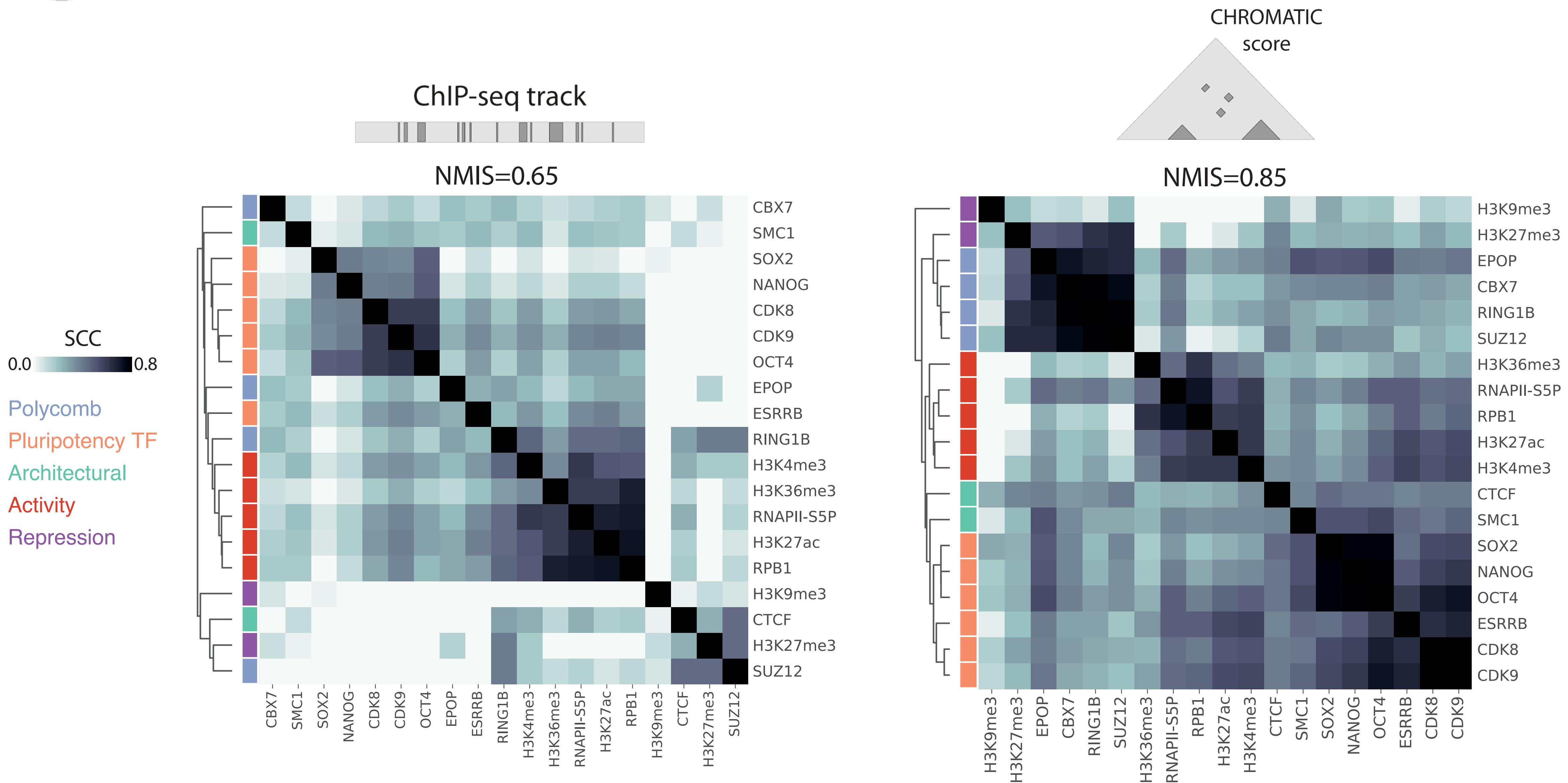
3D interactions are mostly associated with pluripotent TFs

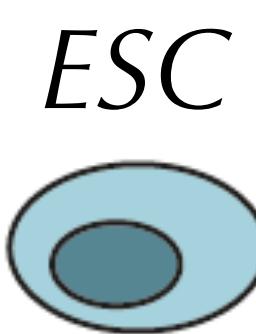


ESC

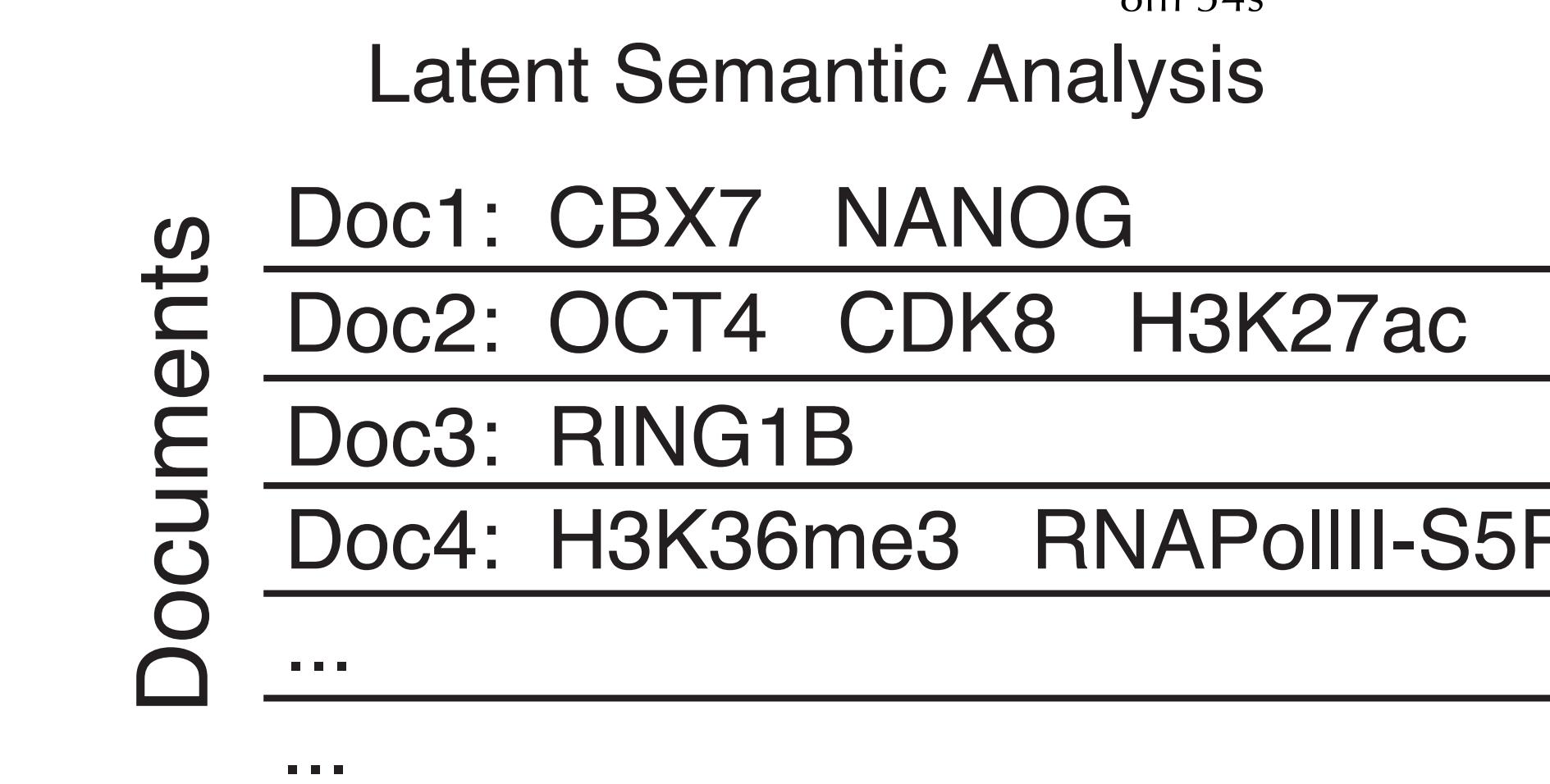
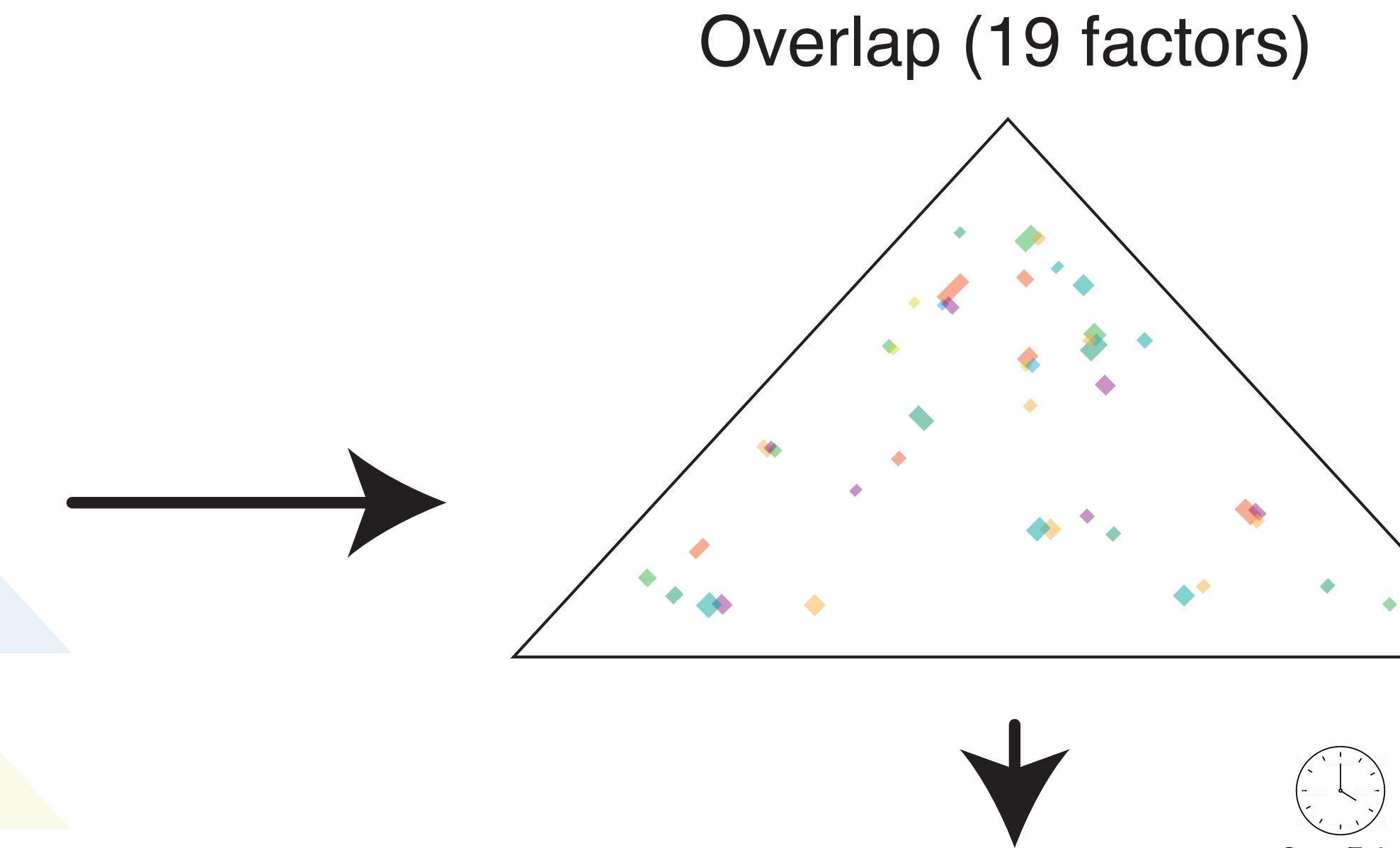
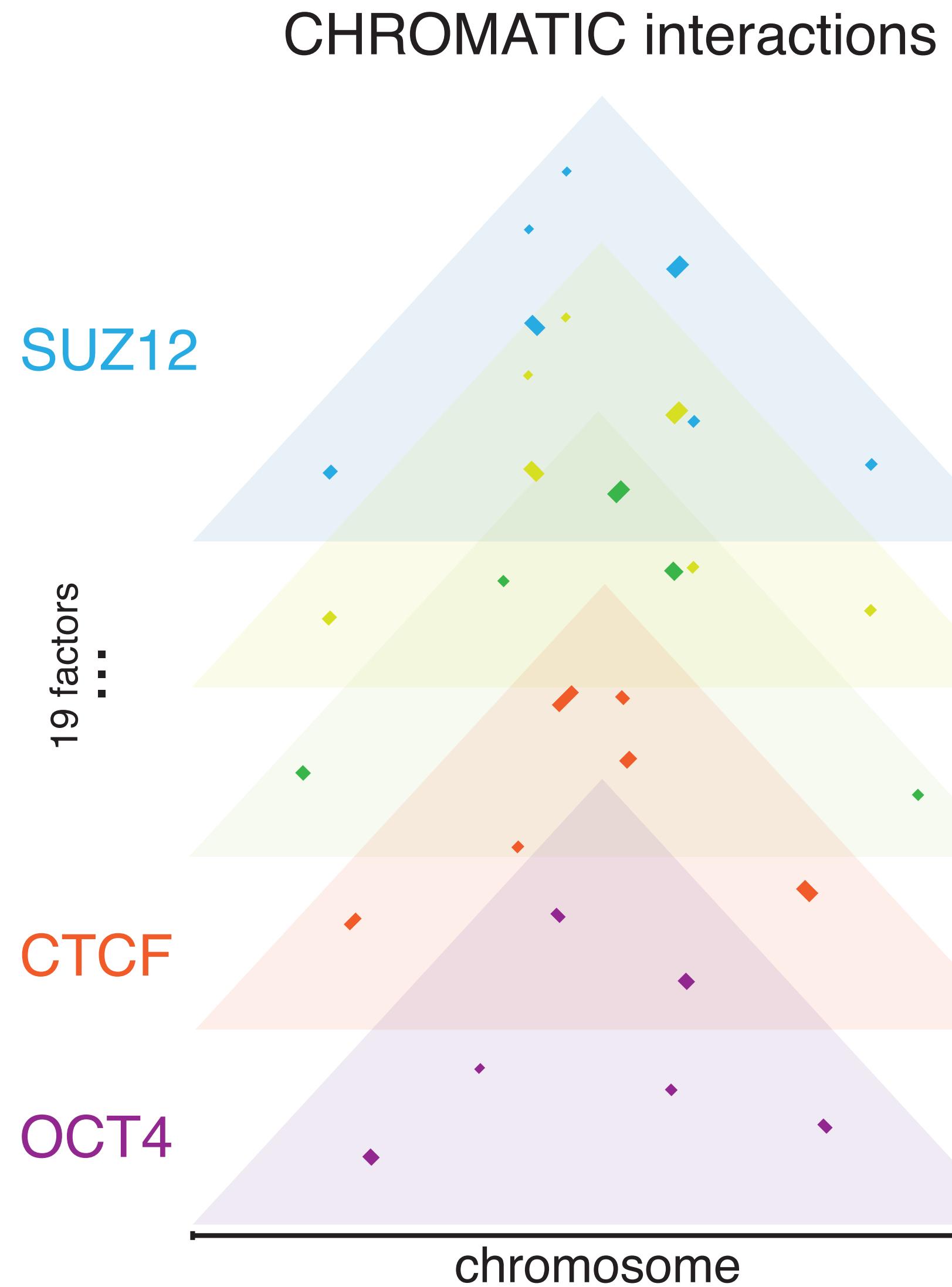


CHROMATIC better represents genome function than ChIP-seq alone





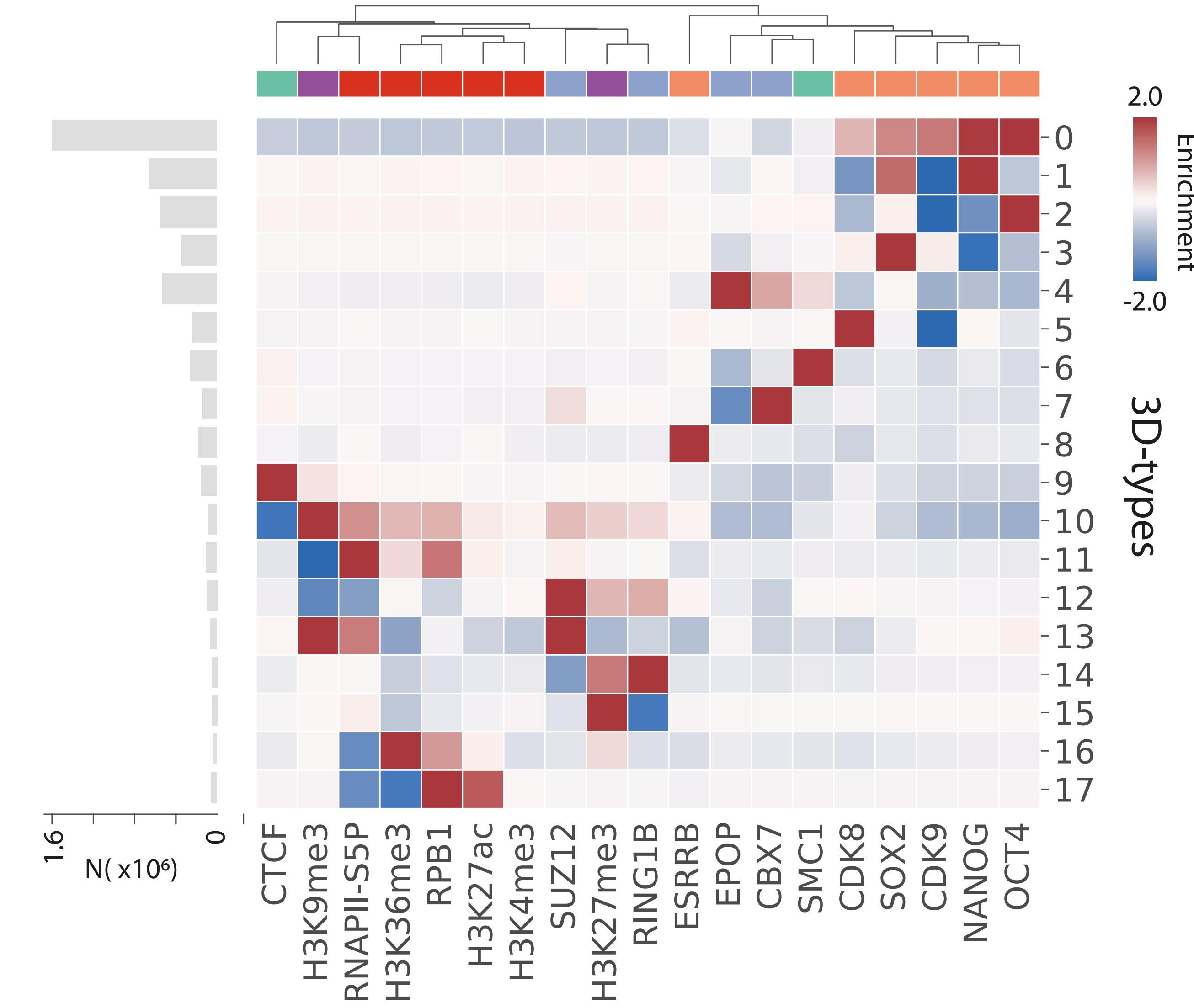
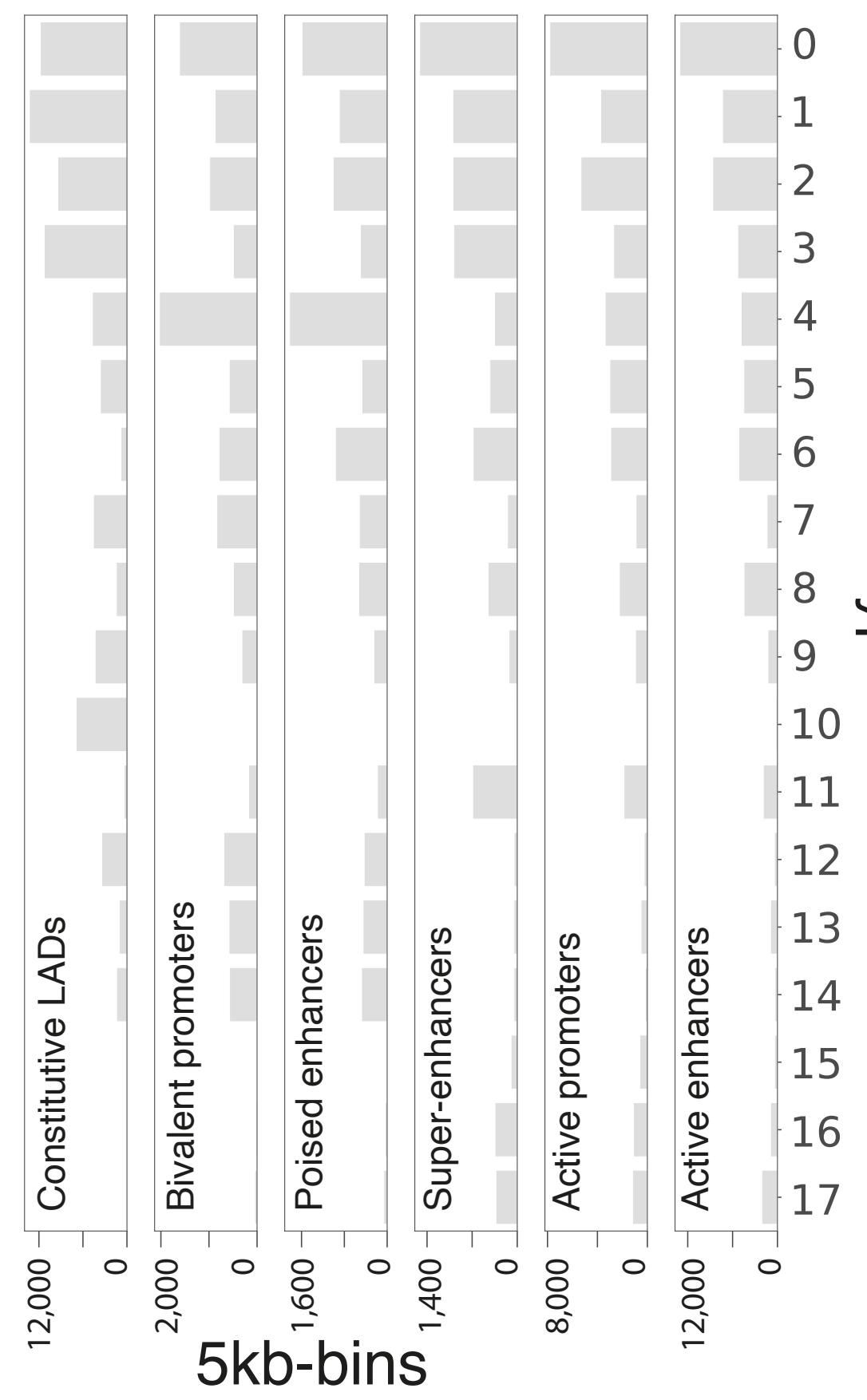
Measure the 3D co-localization of factors

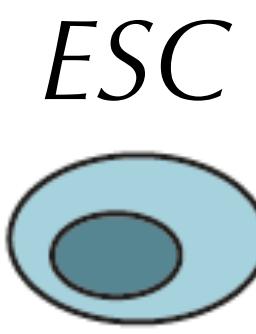


ESC
○

Types of 3D interactions with LSA in ESC

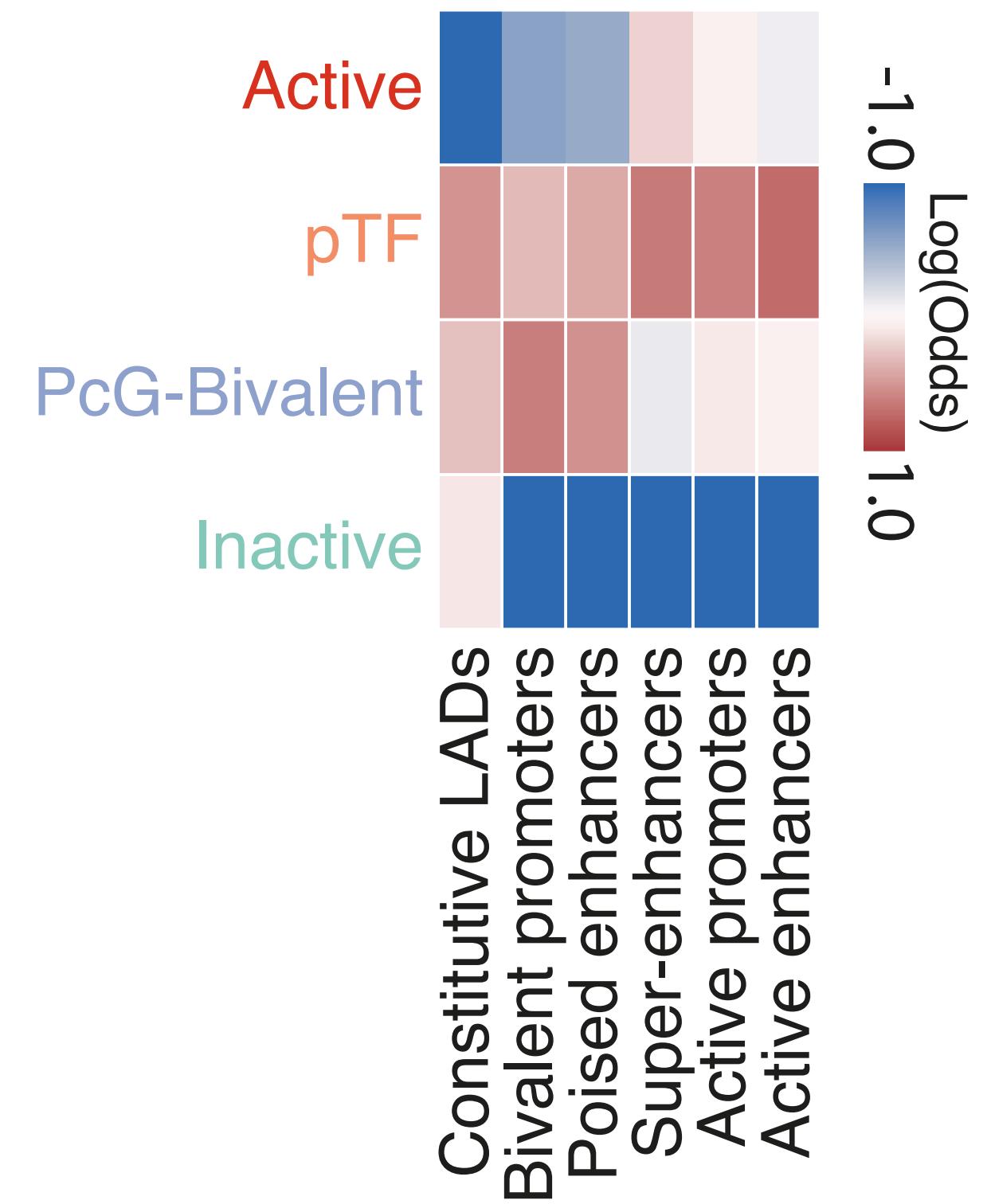
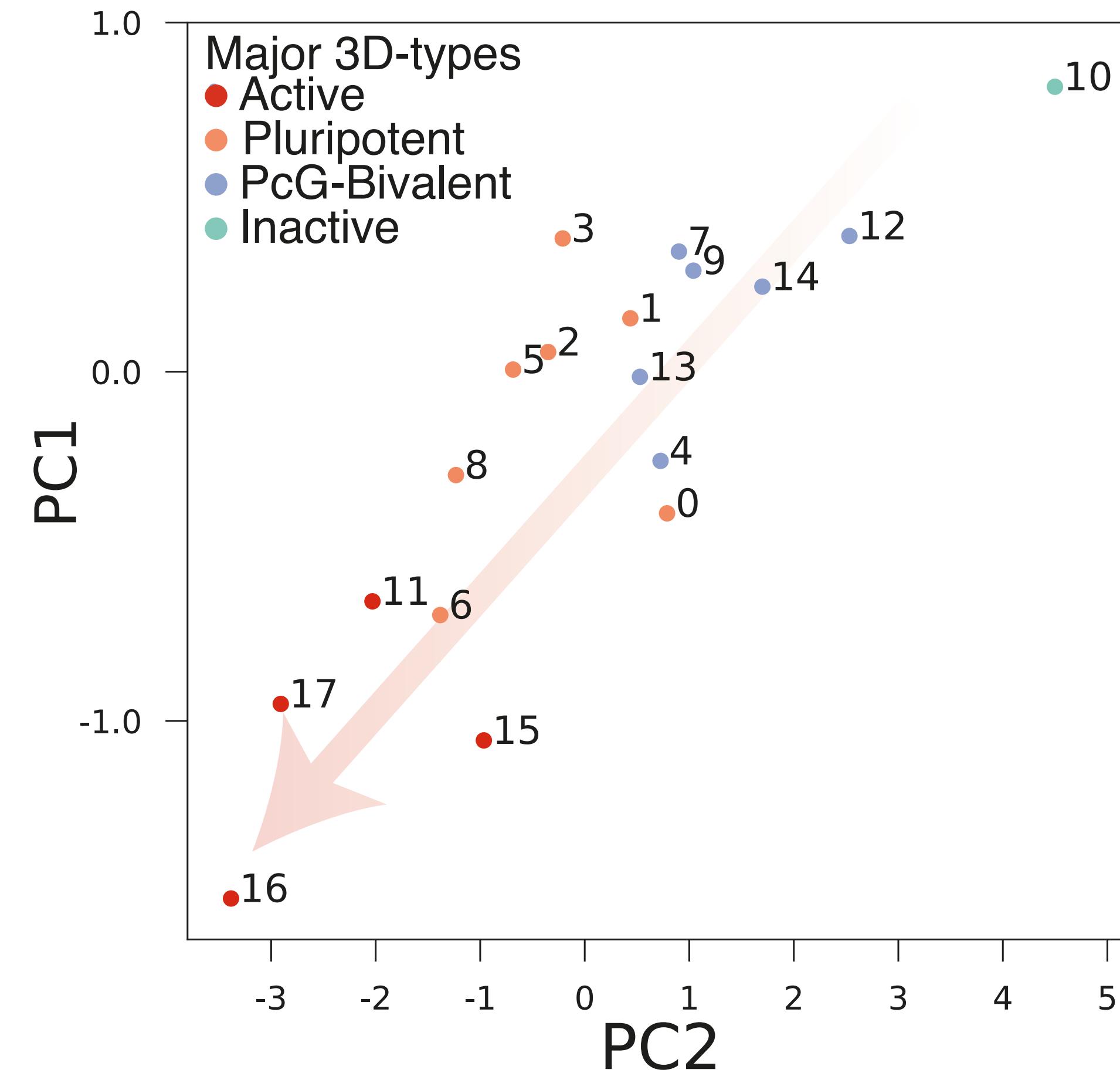
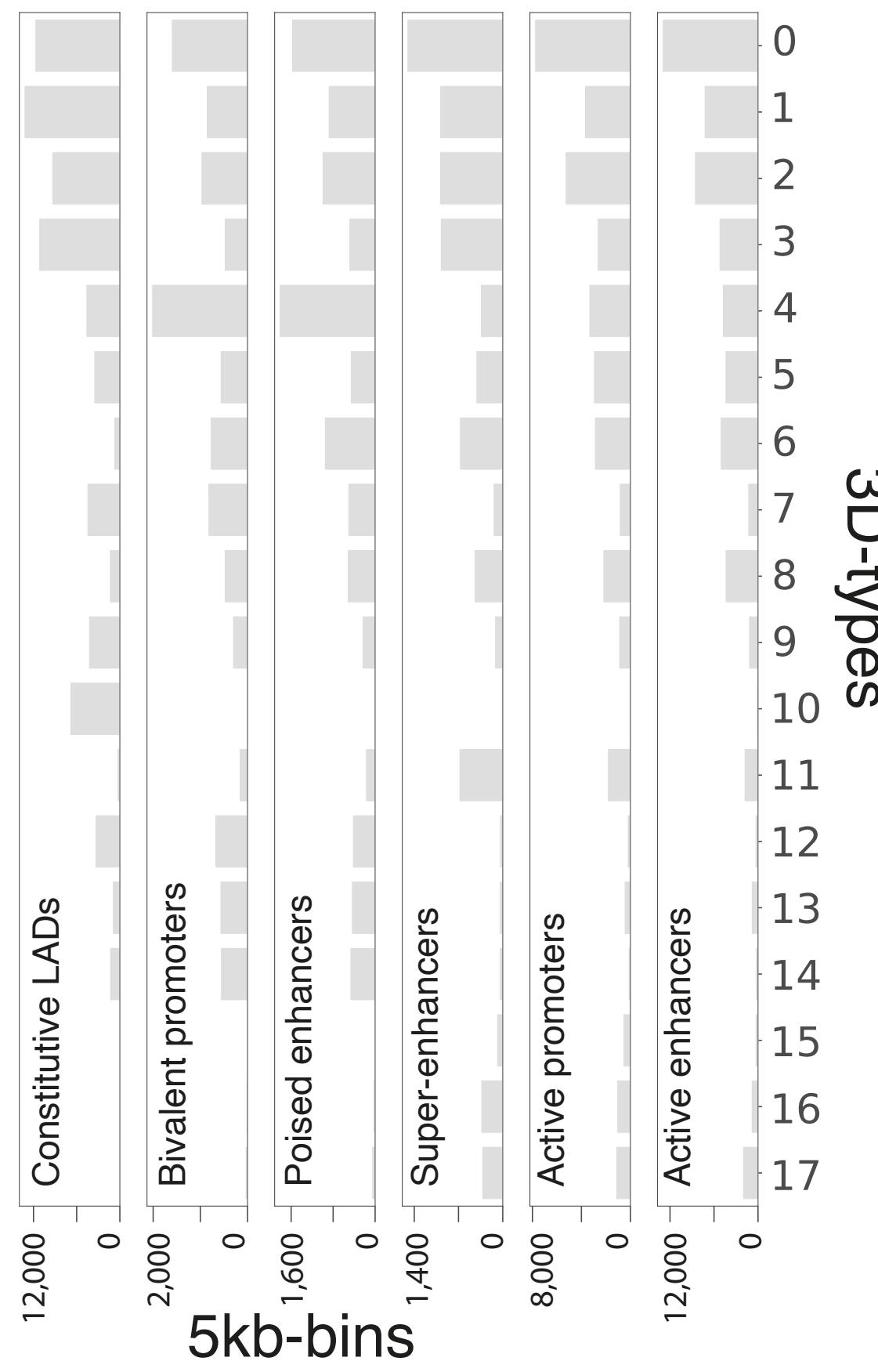
Annotated using ChIP-Seq and literature



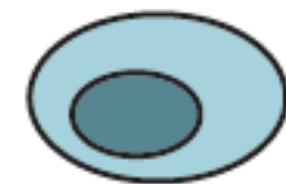


Types of 3D interactions with LSA in ESC

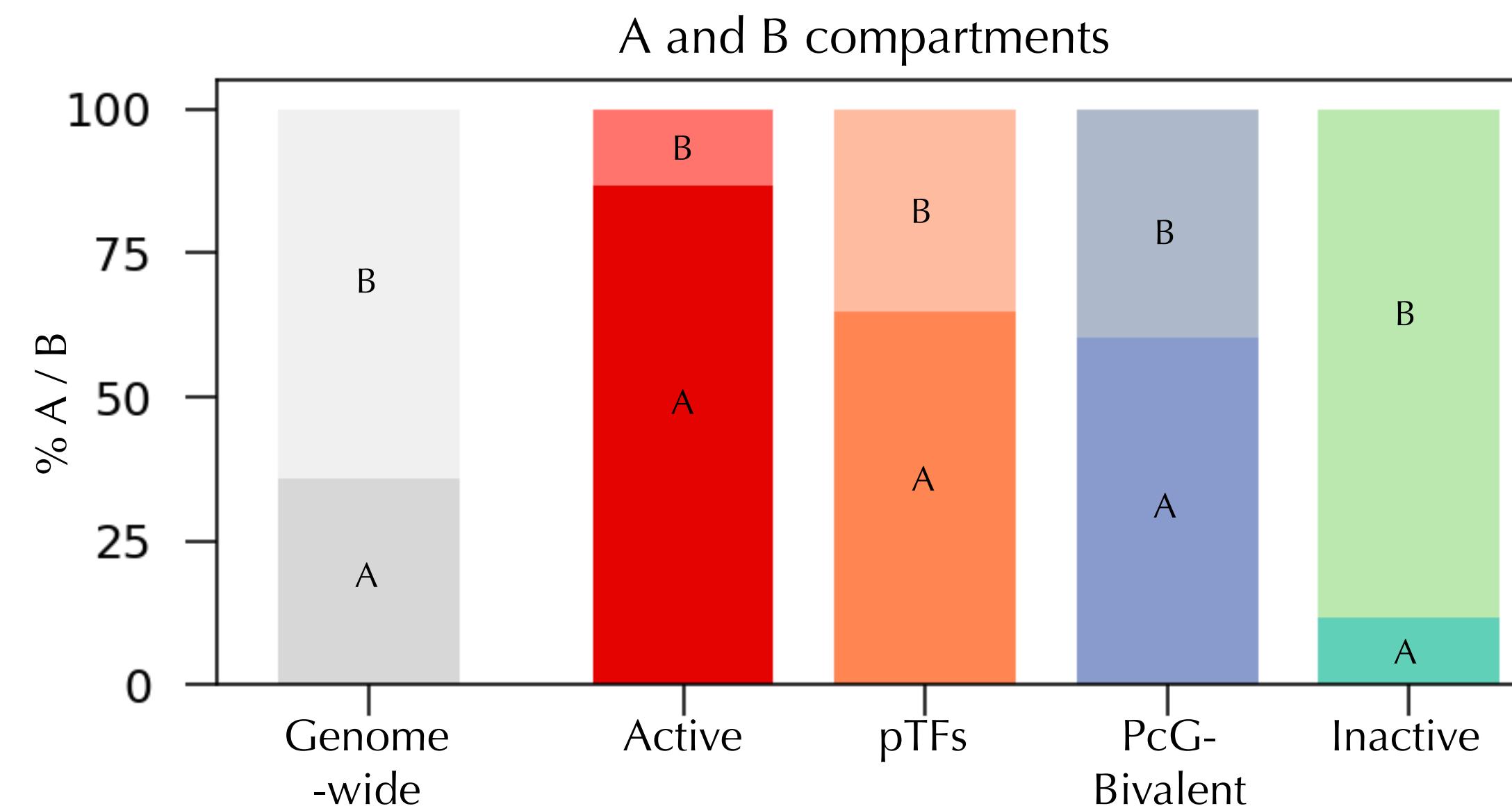
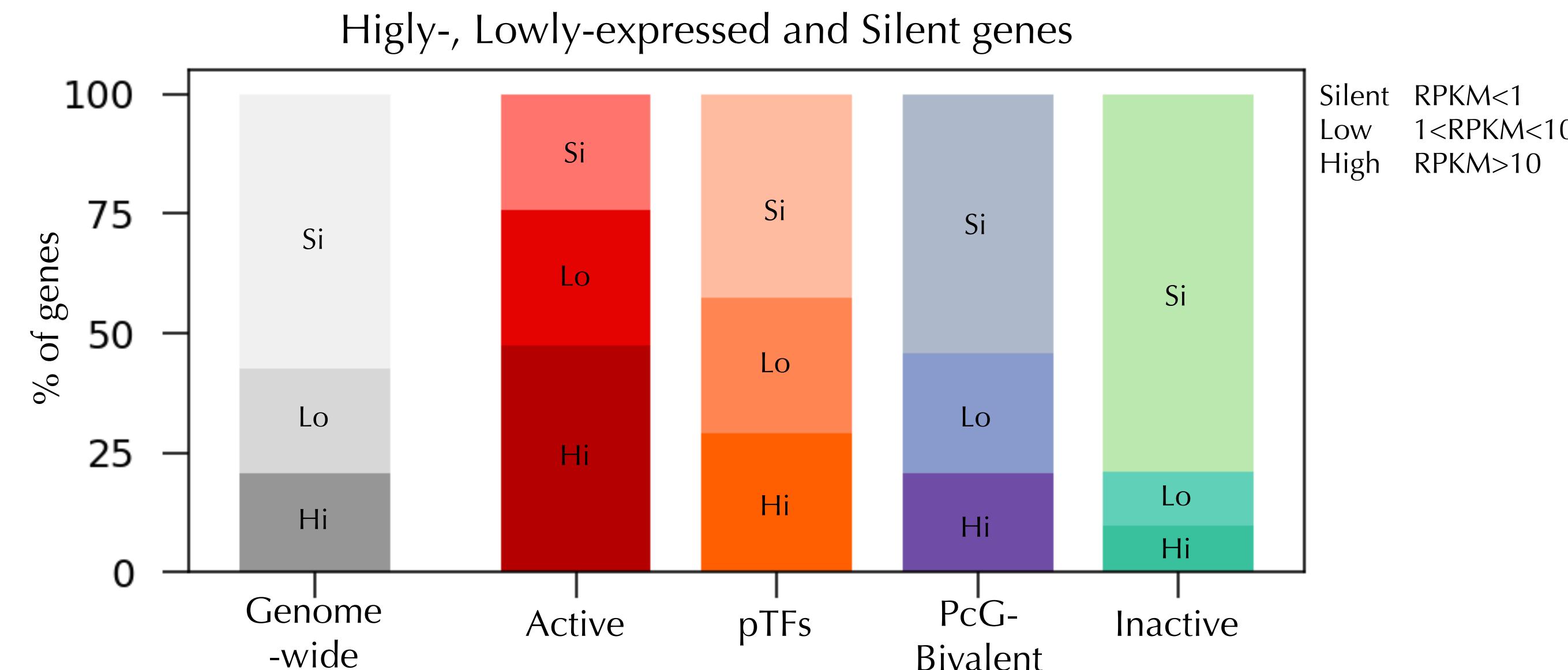
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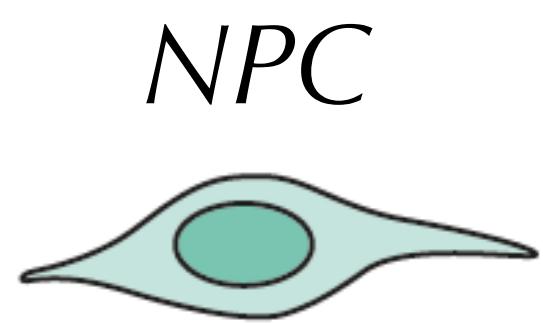


ESC

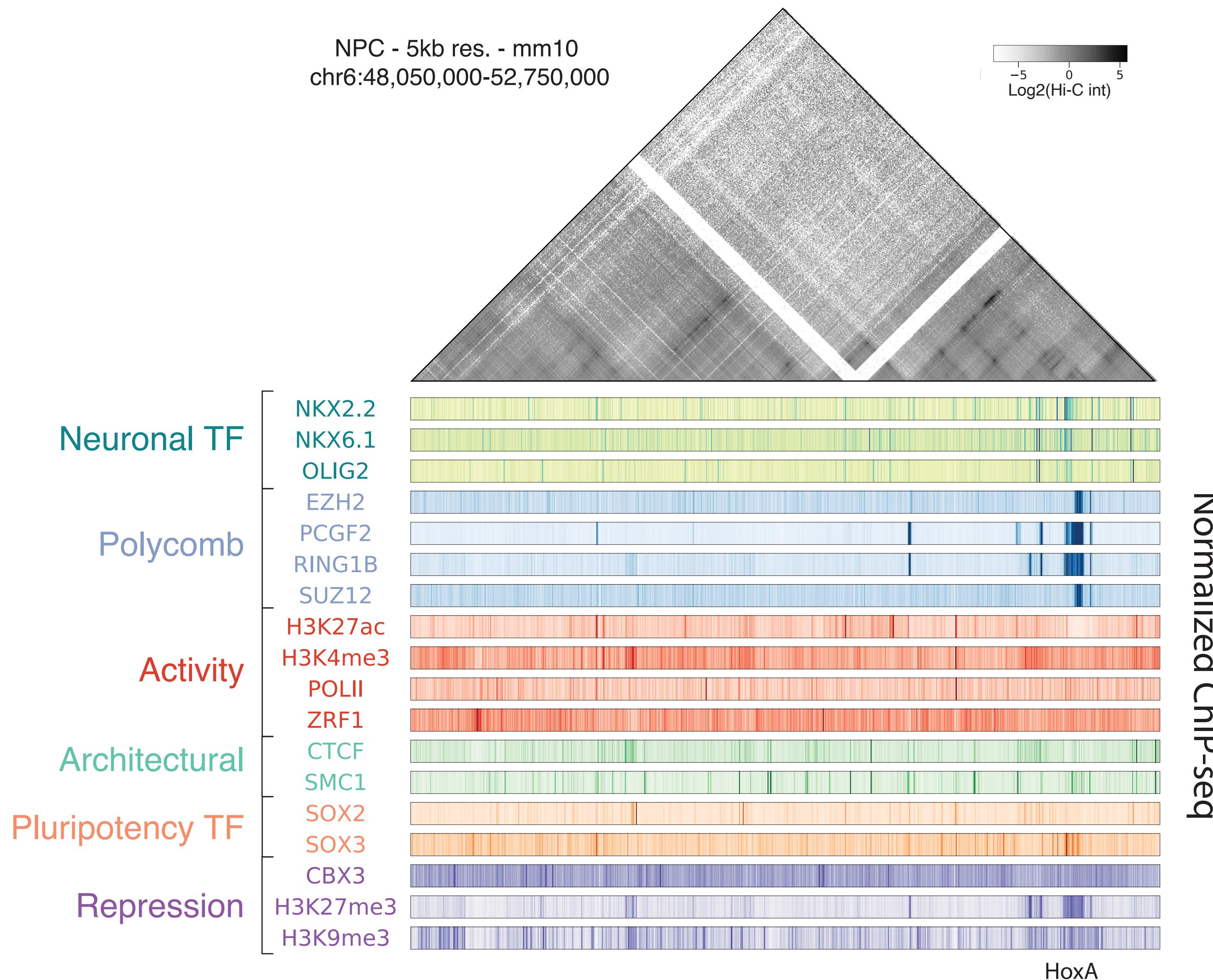


4 major types of 3D interactions in ESC

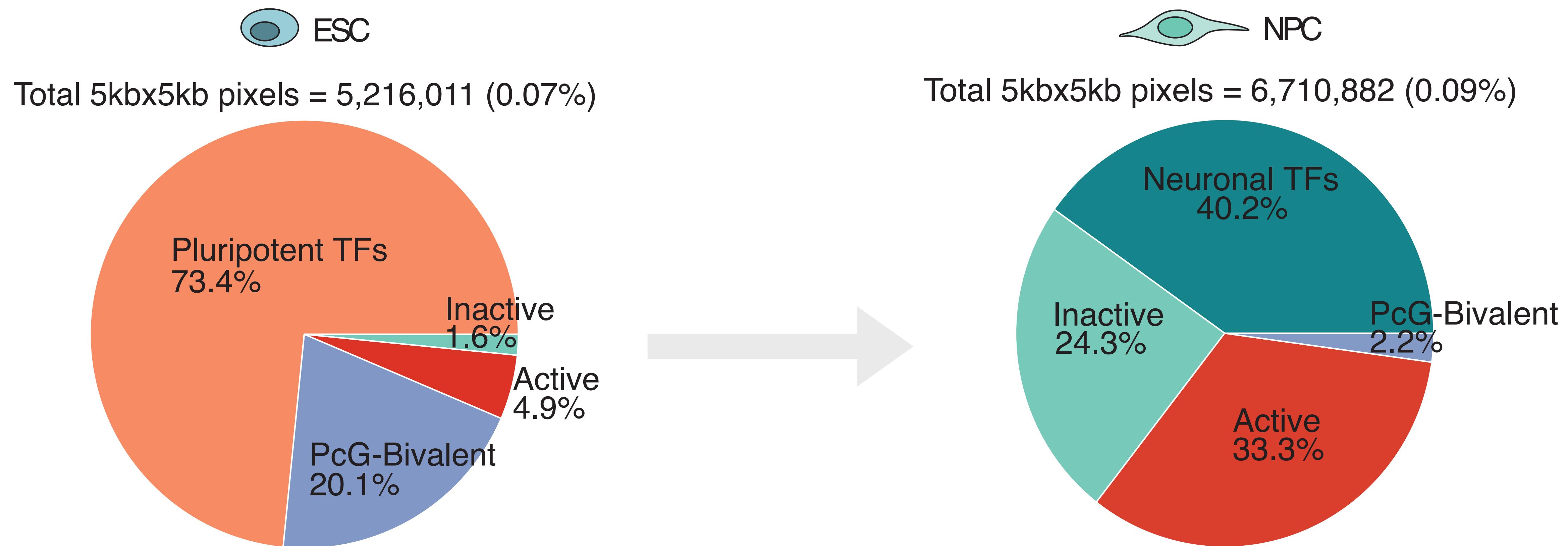




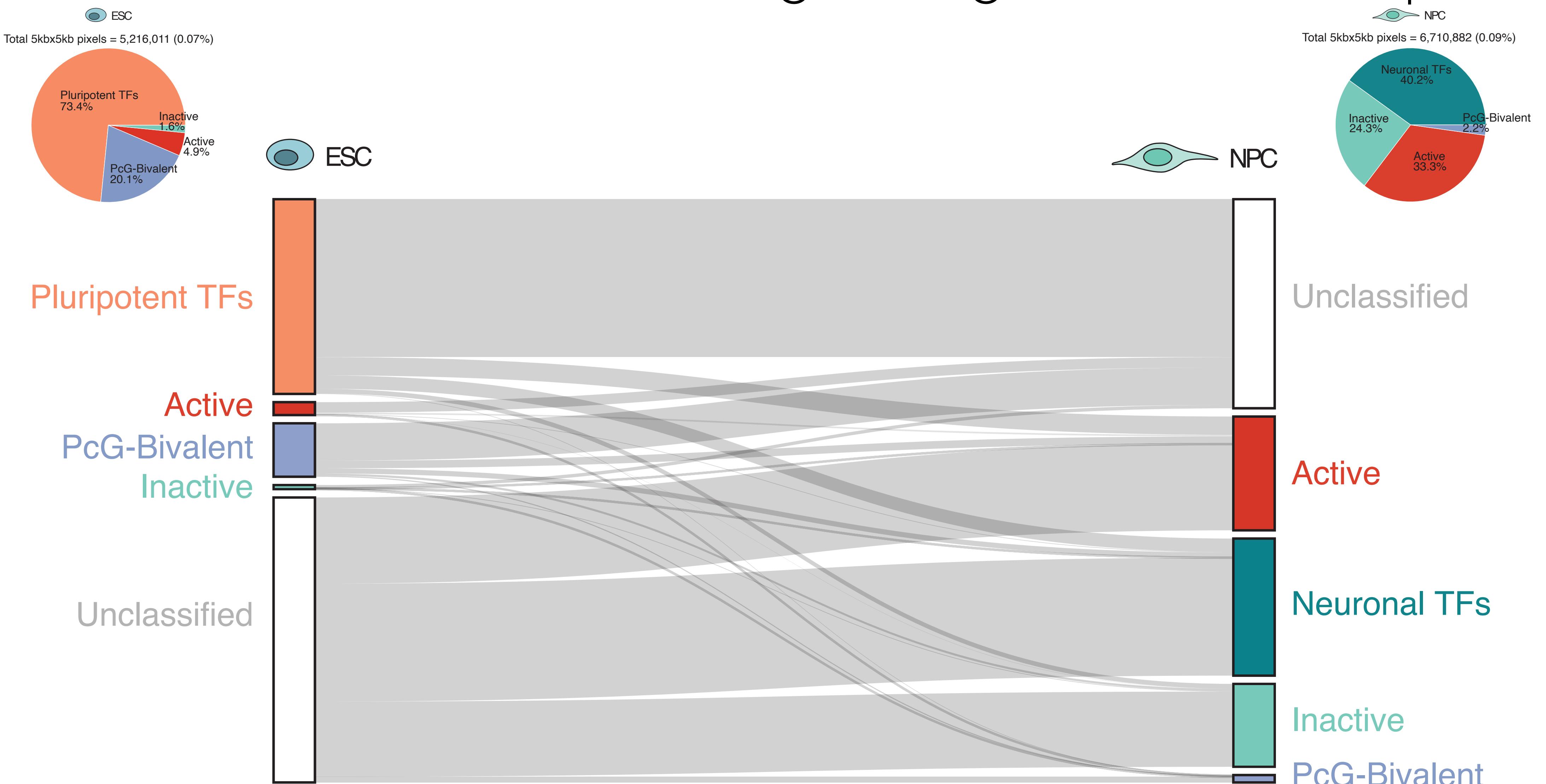
HoxA cluster (example in NPC)



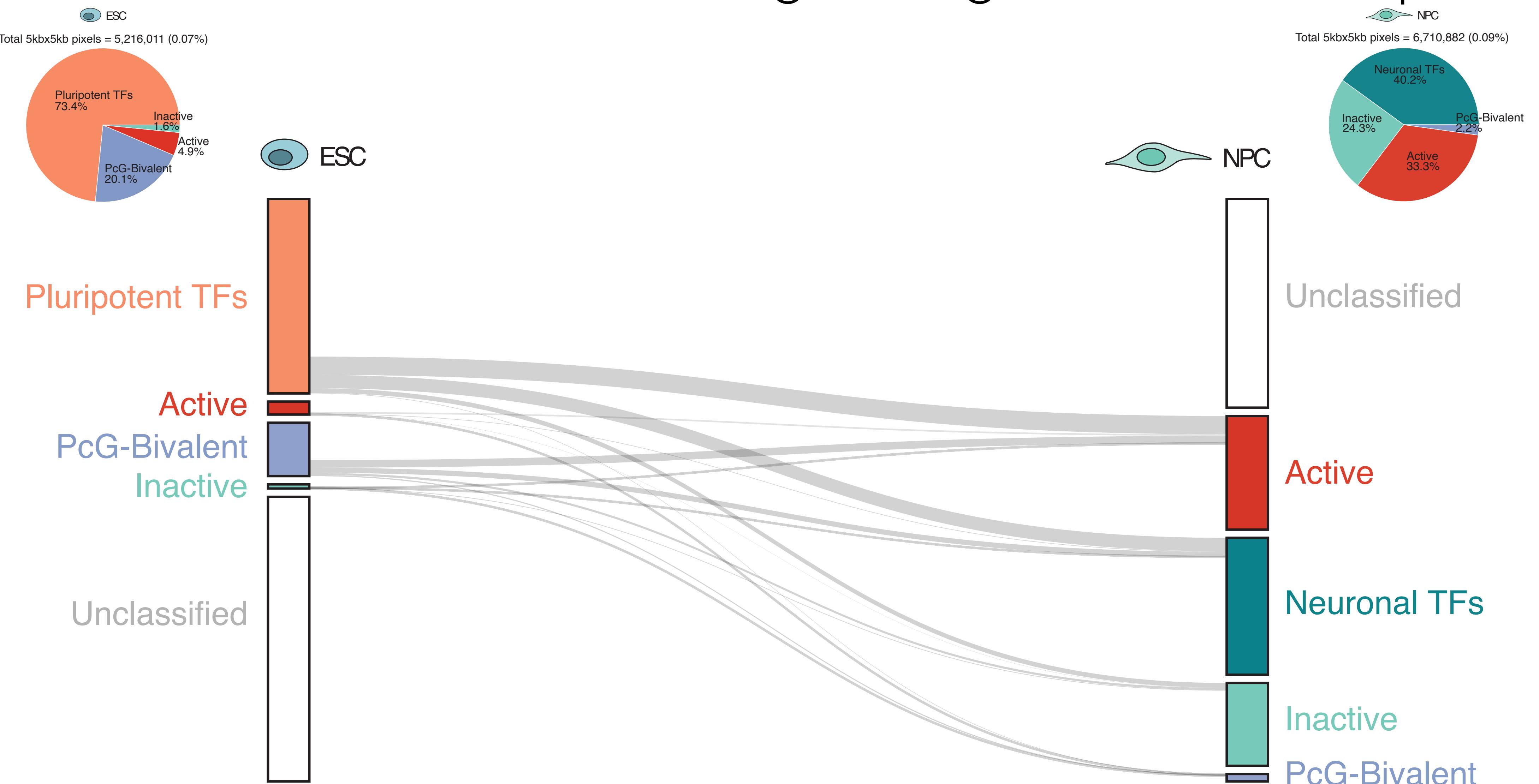
Global 3D interactions rewiring during mouse development



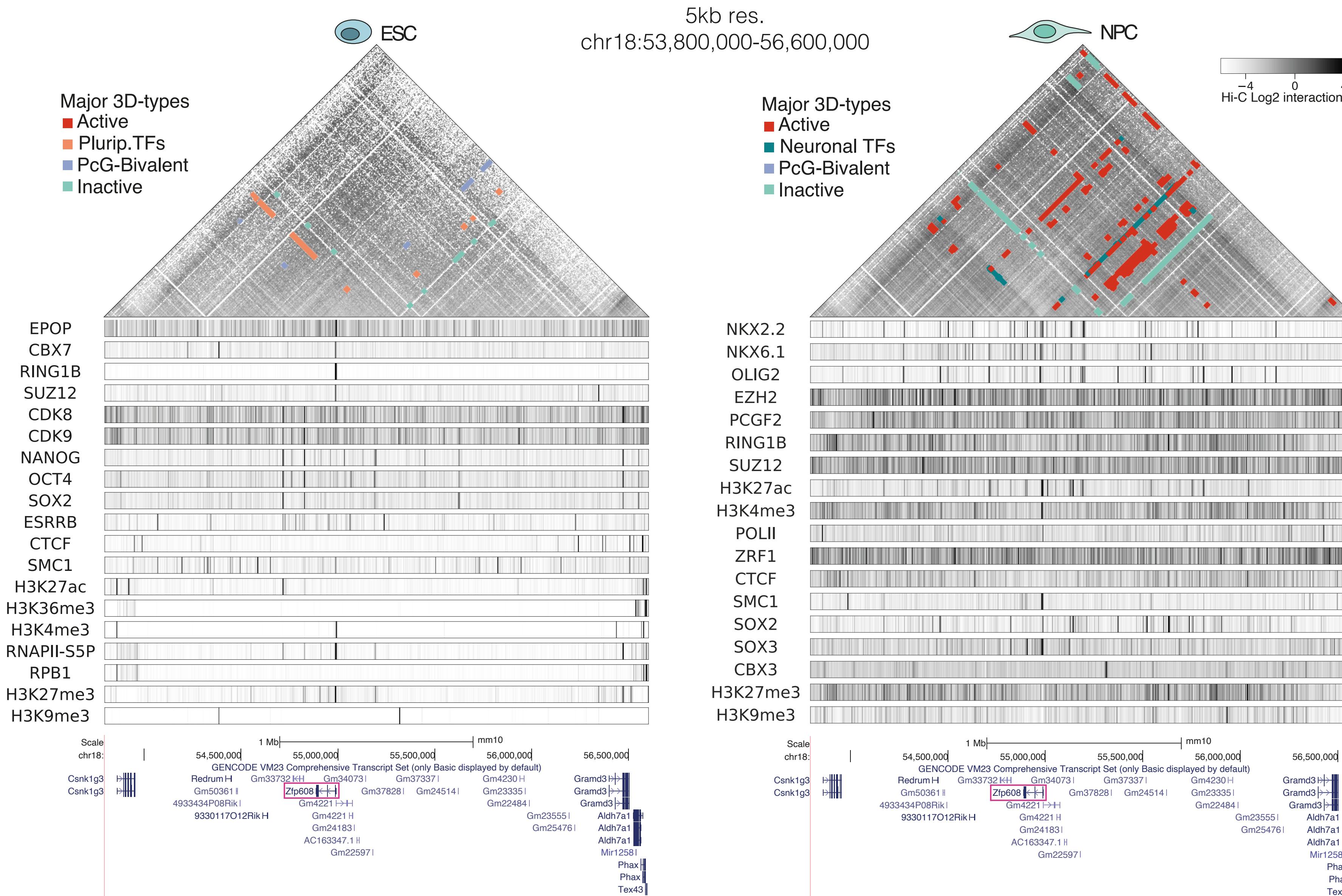
Global 3D interactions rewiring during mouse development



Global 3D interactions rewiring during mouse development



3D interactions rewiring at Zfp608 locus during mouse neural development



Take home message...

