



CHROMATIC reveals chromatin-associated factors contributing to genome topology

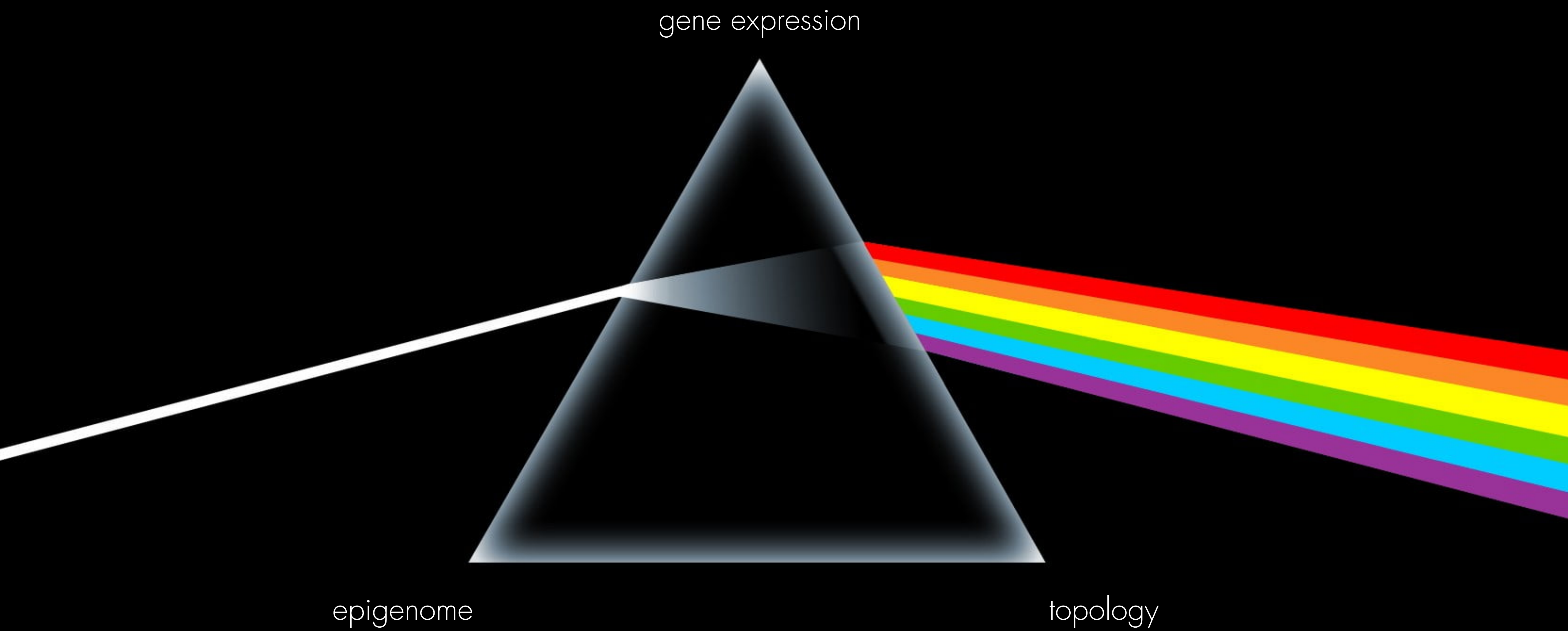
Marc A. Marti-Renom

CNAG-CRG · ICREA

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

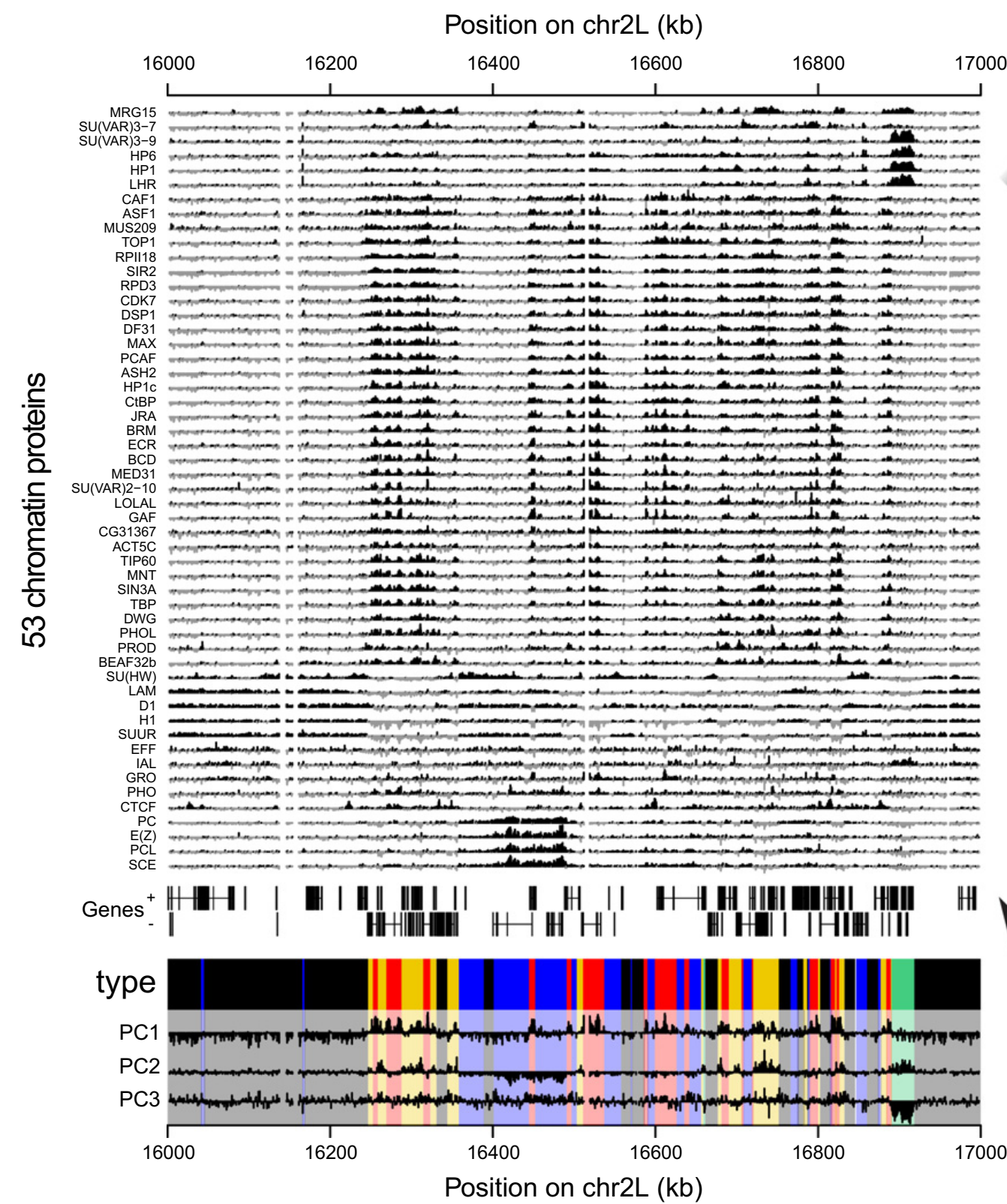
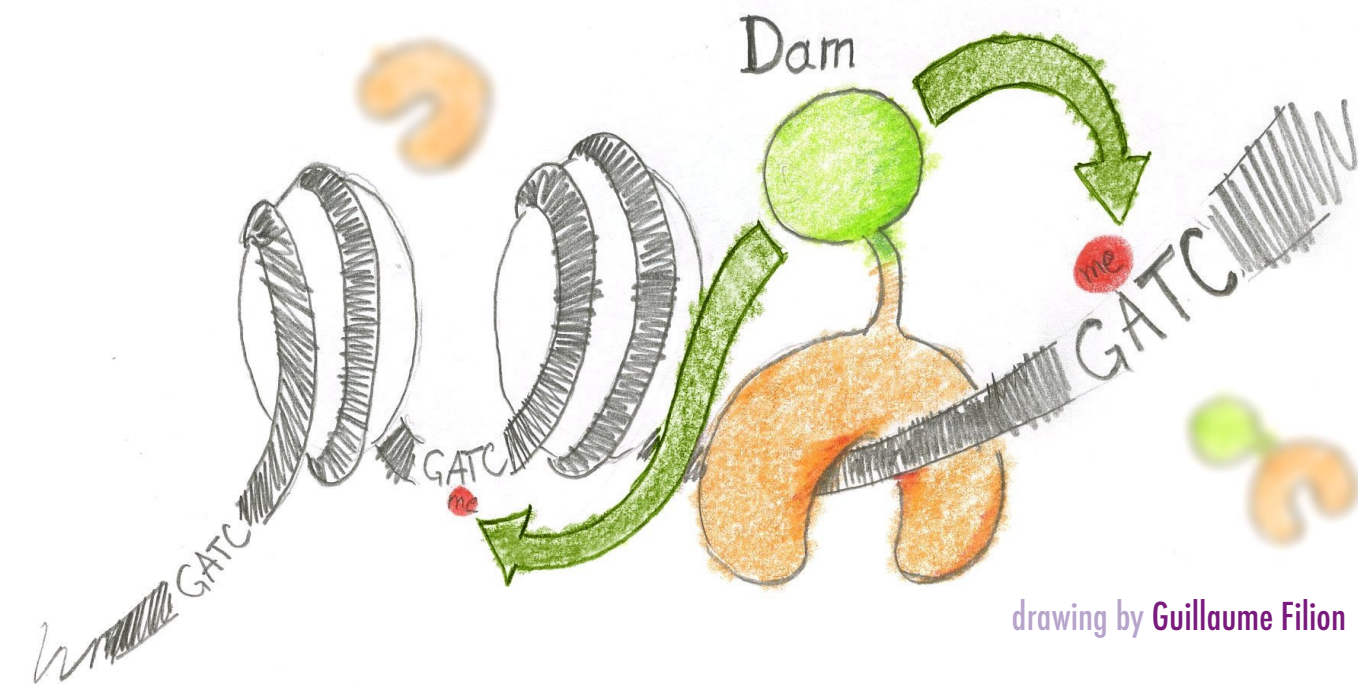
cnag CRG[®] ICREA

Photo by Laia Marín

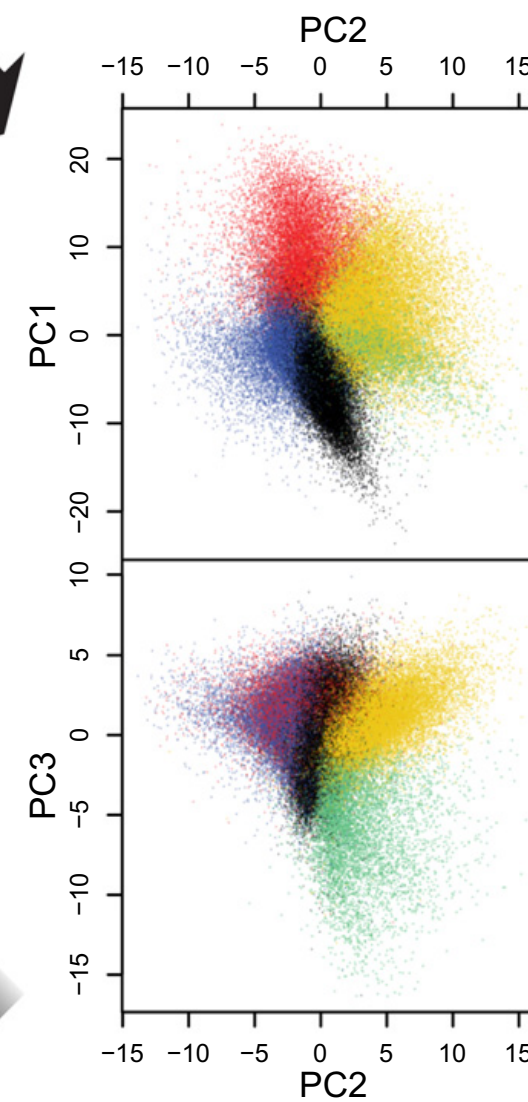


Fly Chromatin **COLORs**

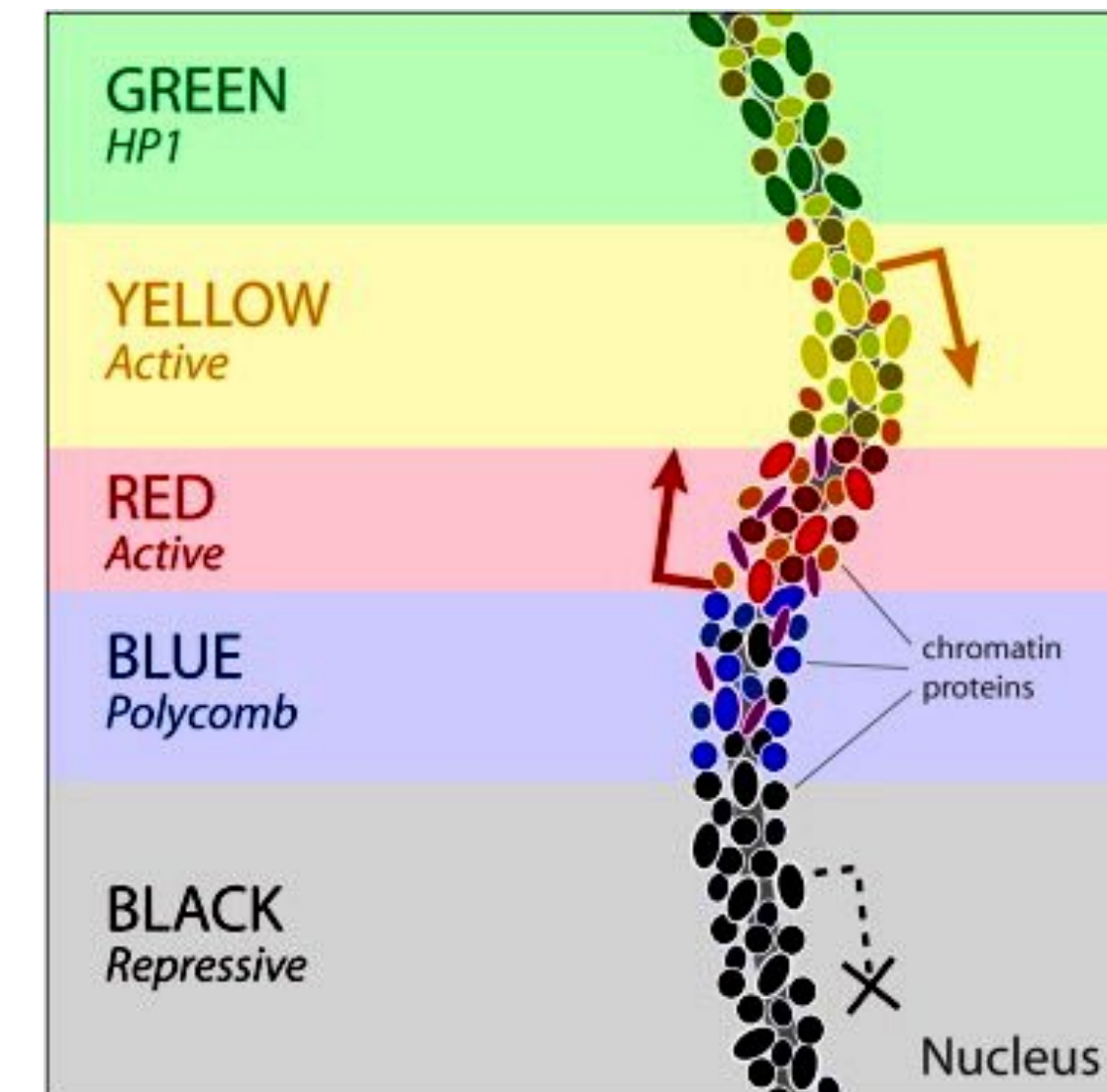
Filion et al. (2010). Cell, 143(2), 212–224.



Principal component analysis

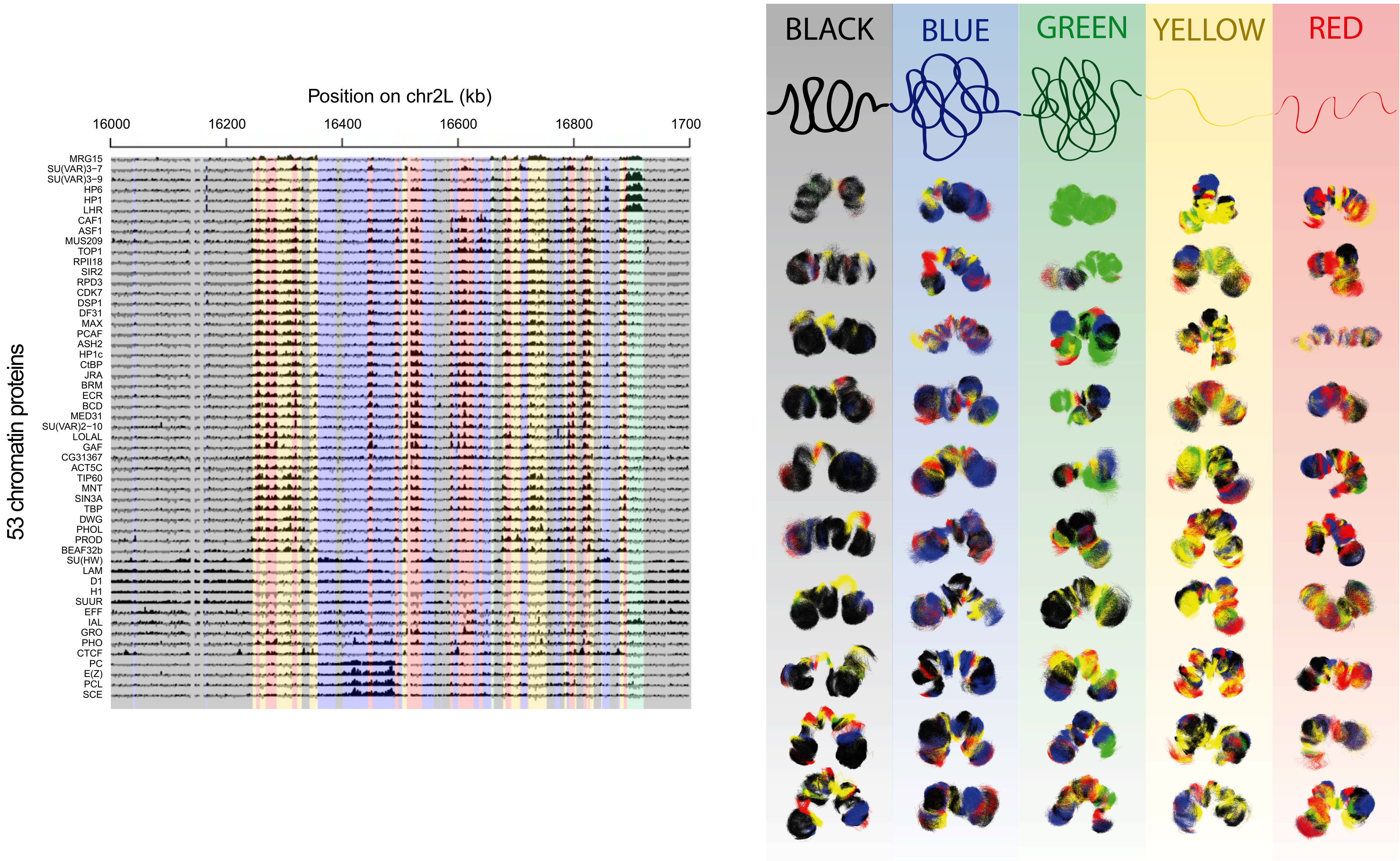


Hidden Markov model

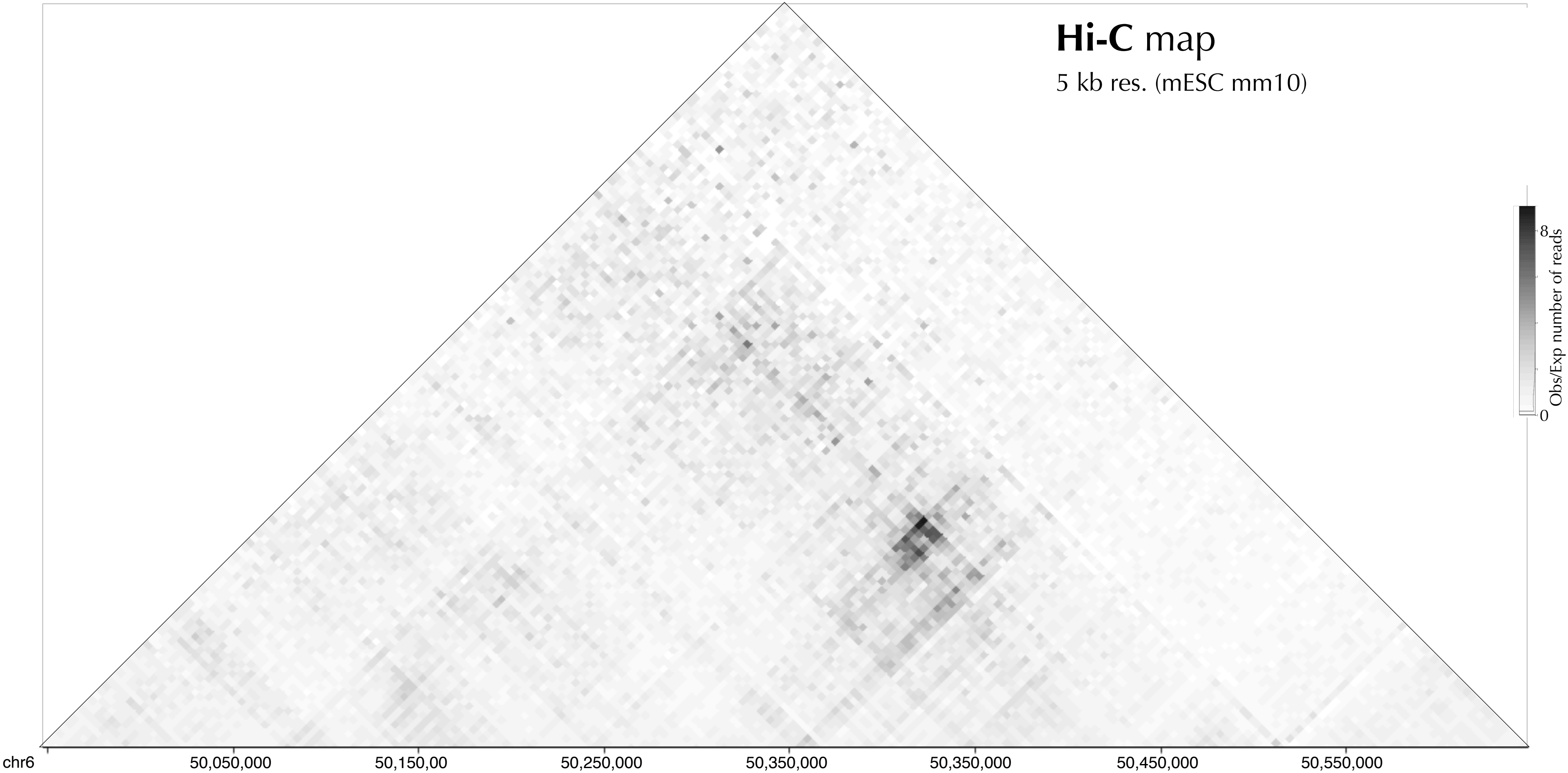


Who “holds” the genome structure?

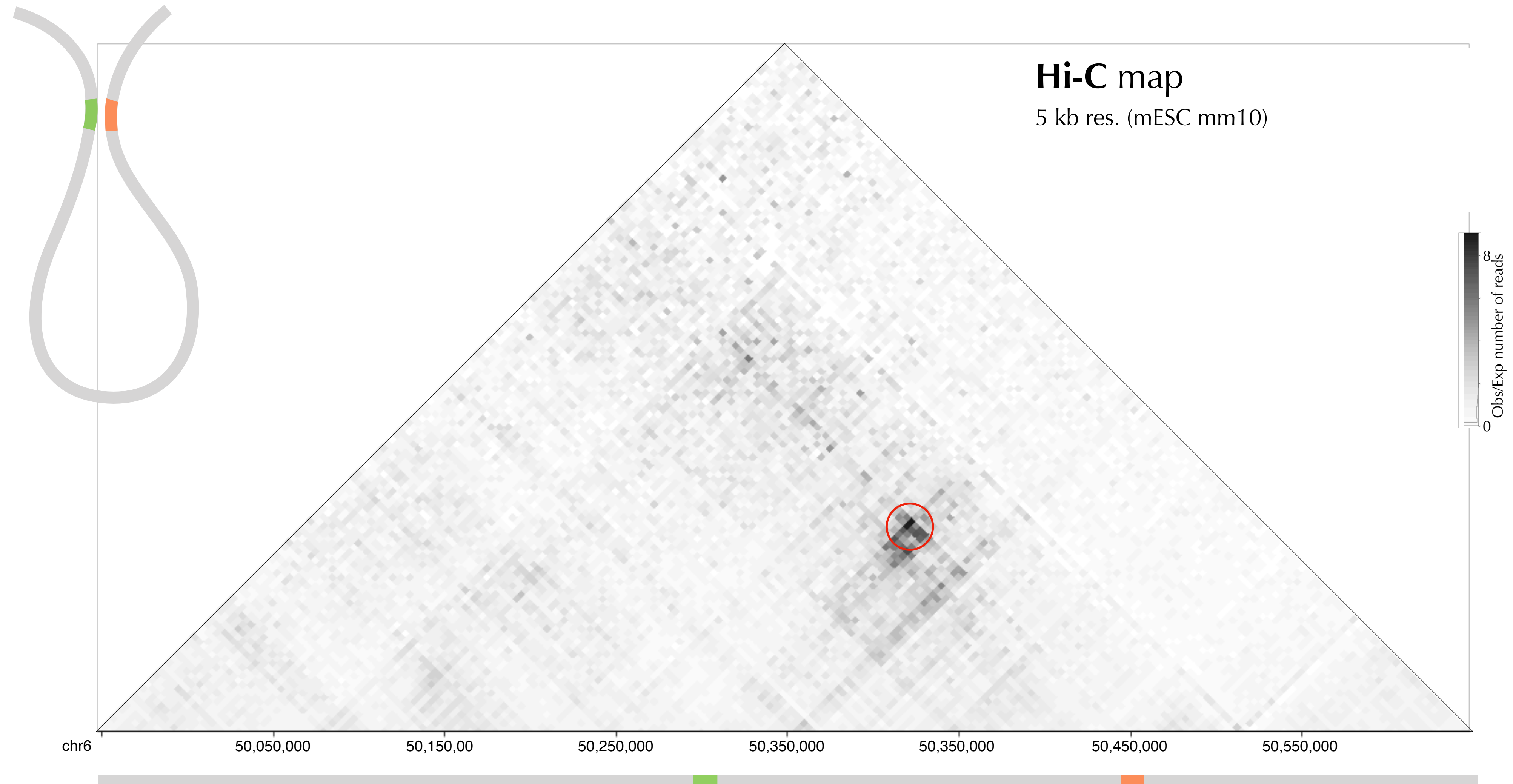
Serra et al. PLoS Comput Biol (2017) 13(7): e1005665



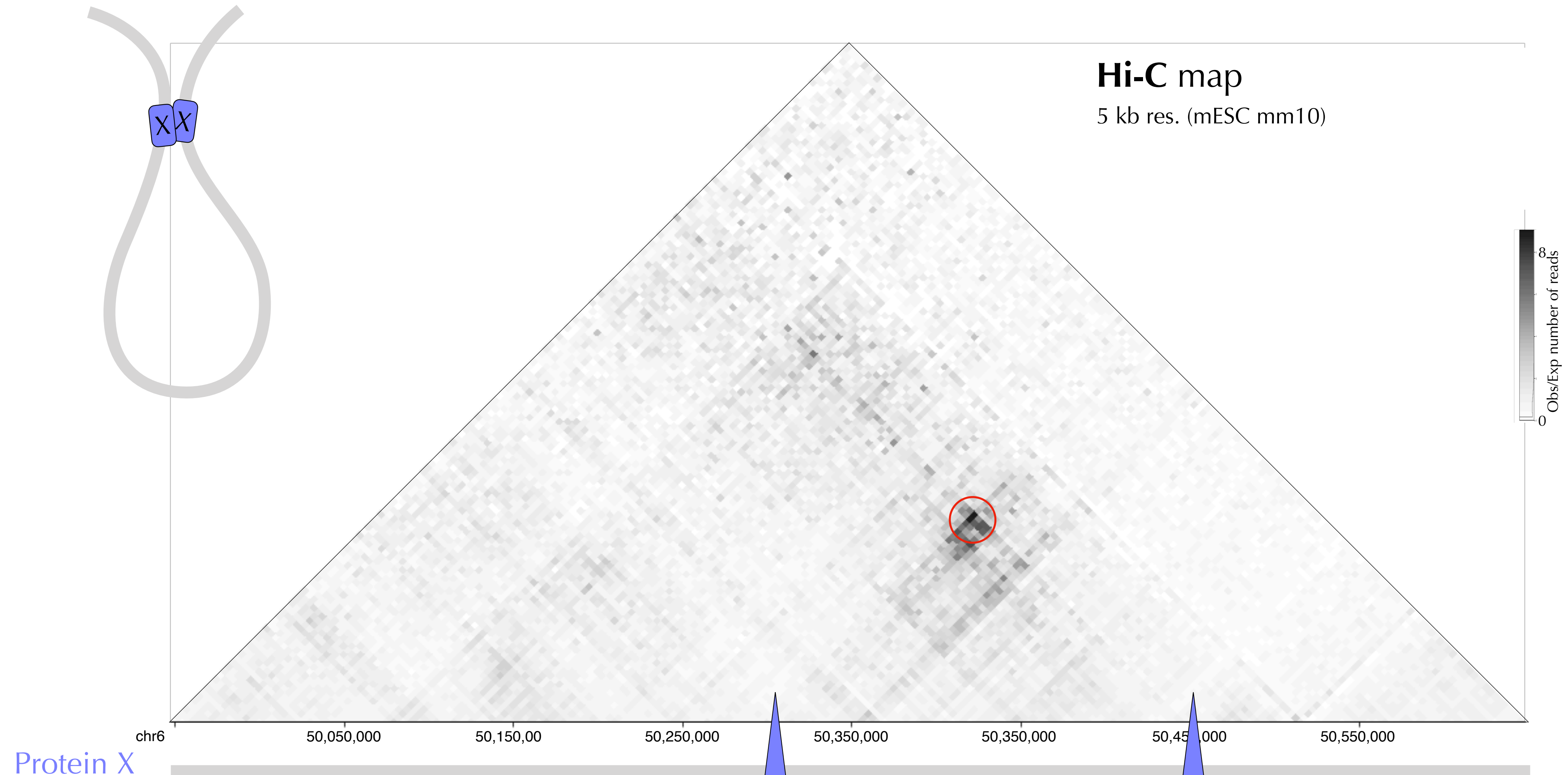
High-throughput Chromosome Conformation Capture (Hi-C)



Chromatin interaction on a Hi-C map

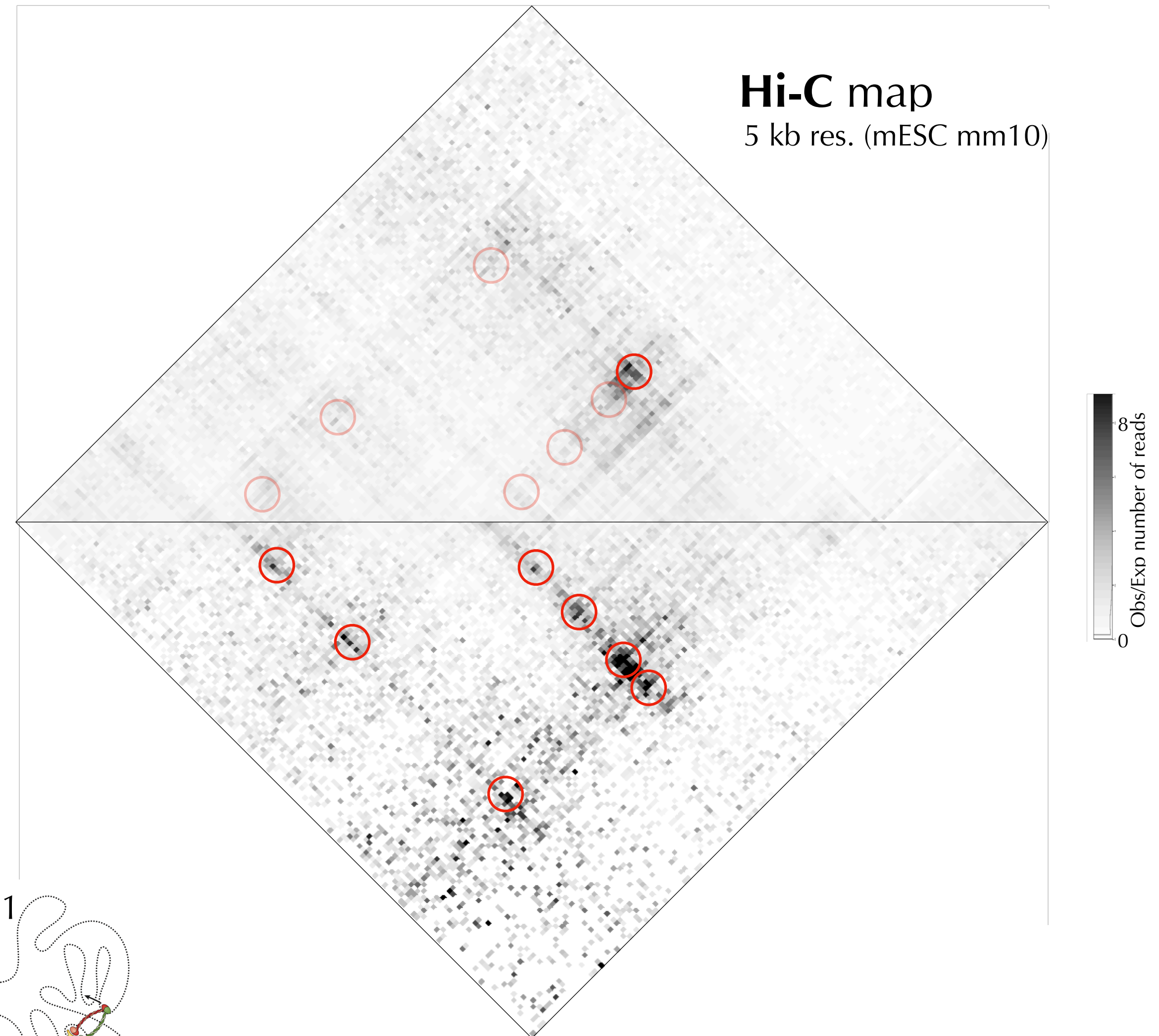
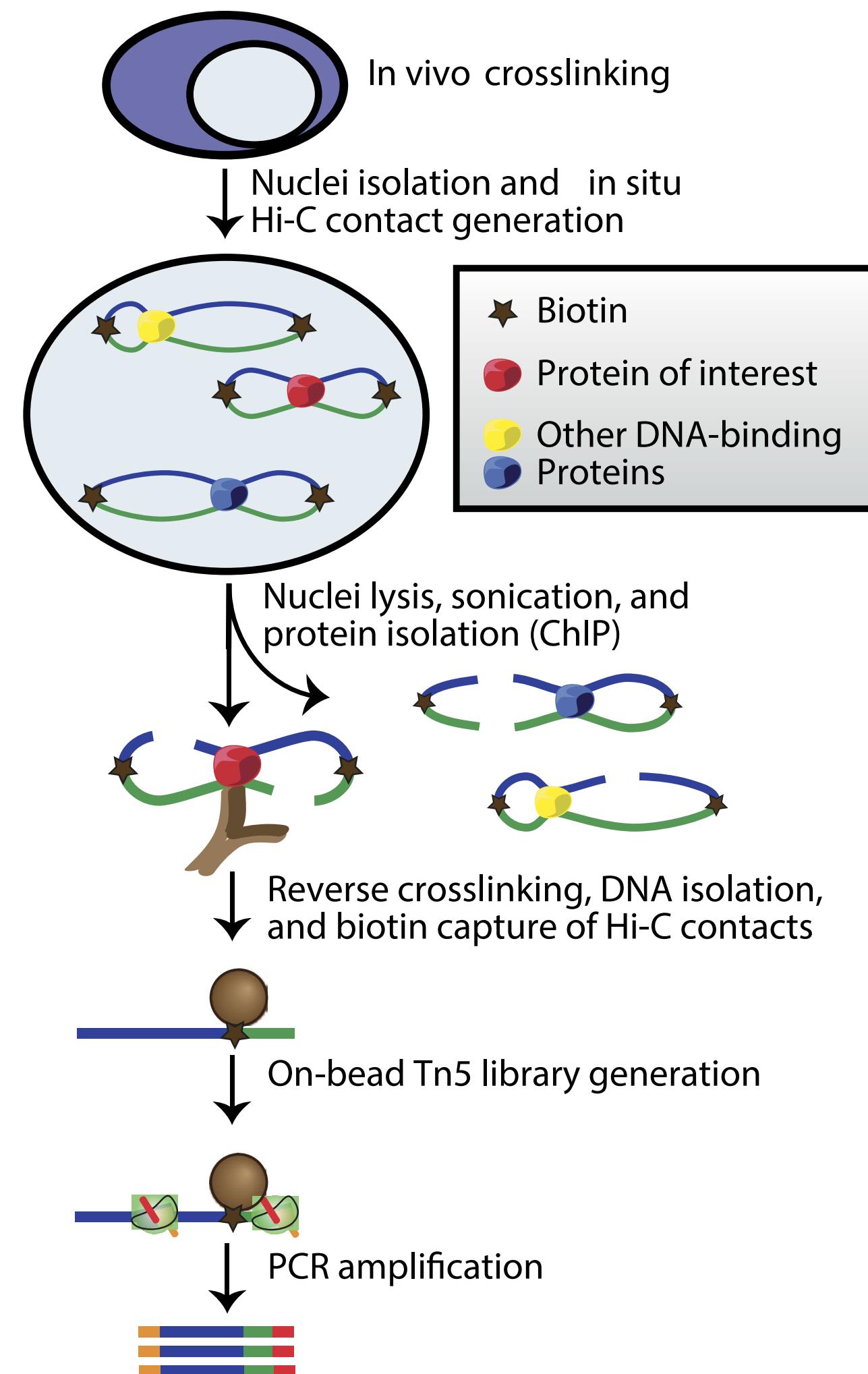


Chromatin interaction “mediated” by a protein



Hi-ChIP: capturing specific protein-mediated interactions

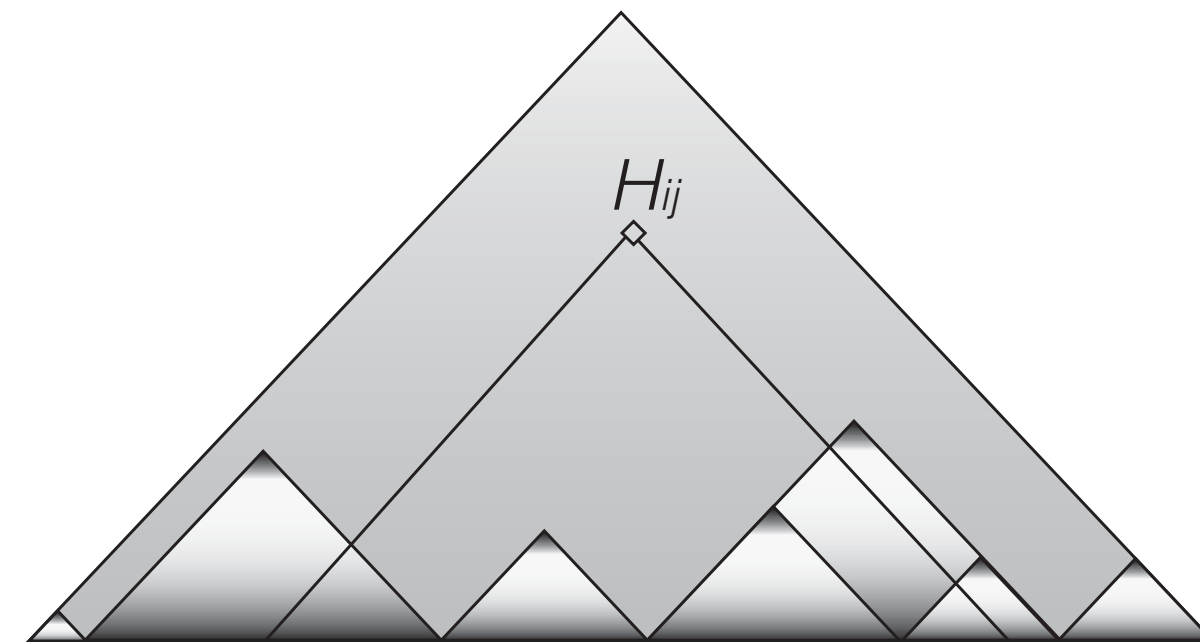
Mumbach, M.R. et al. (2016) Nature Methods 13(11) 919-922.



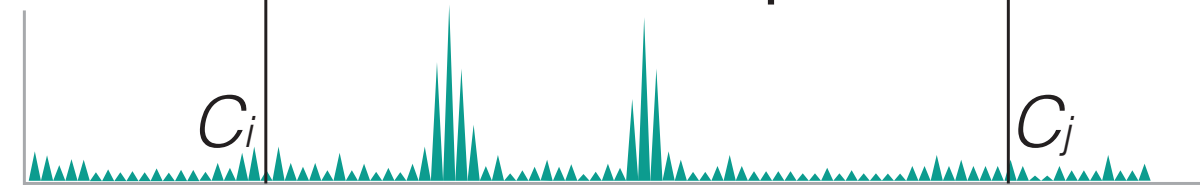
SMC1 Hi-ChIP map = Hi-C + ChIP
5 kb res. (mESC mm10)

CHROMATIC

Hi-C

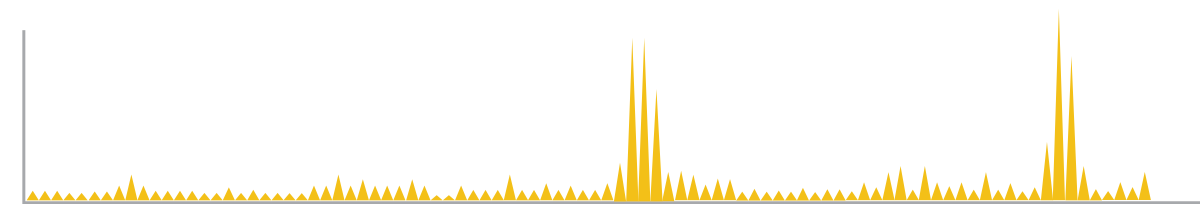


ChIP-seq

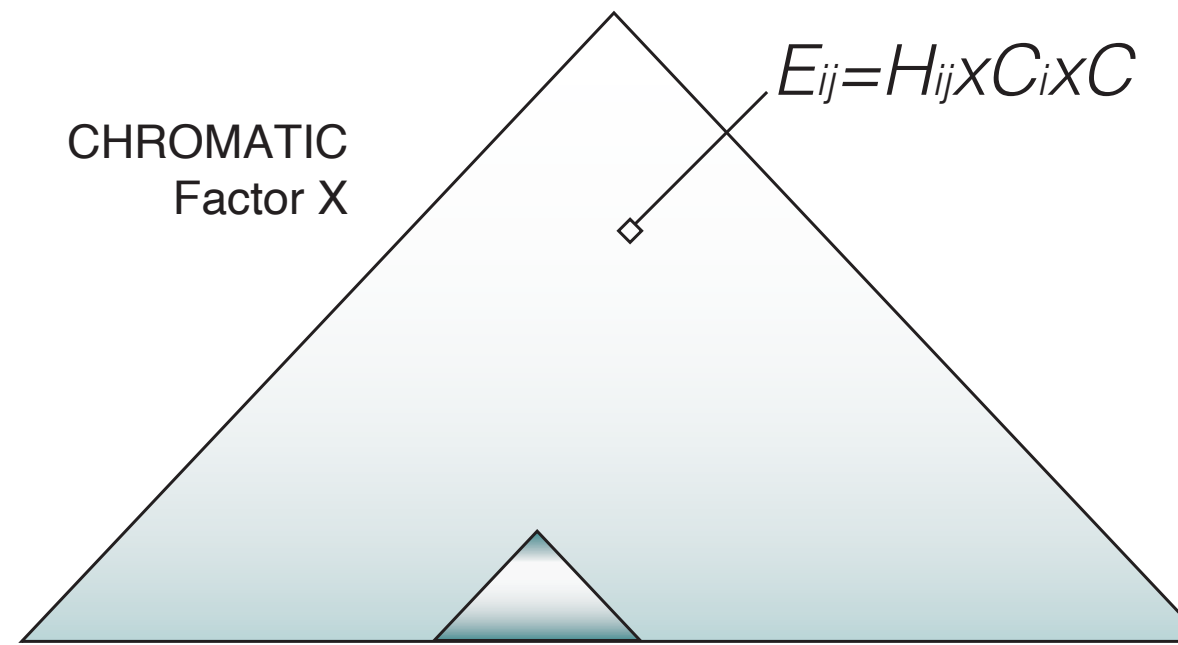


Factor X

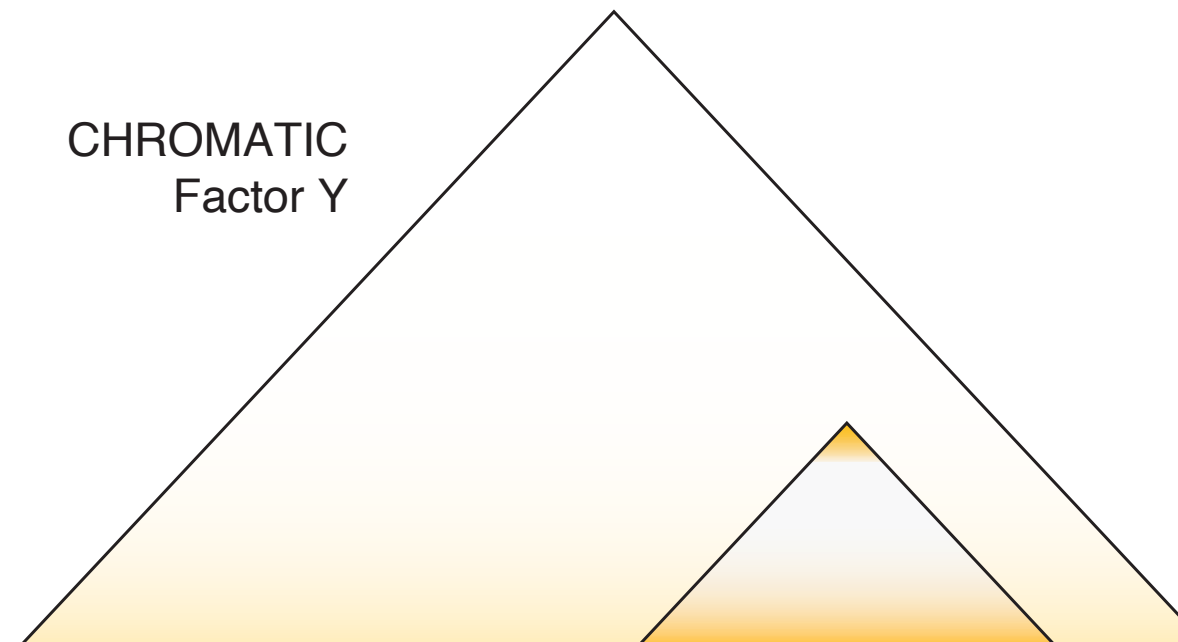
Factor Y



CHROMATIC

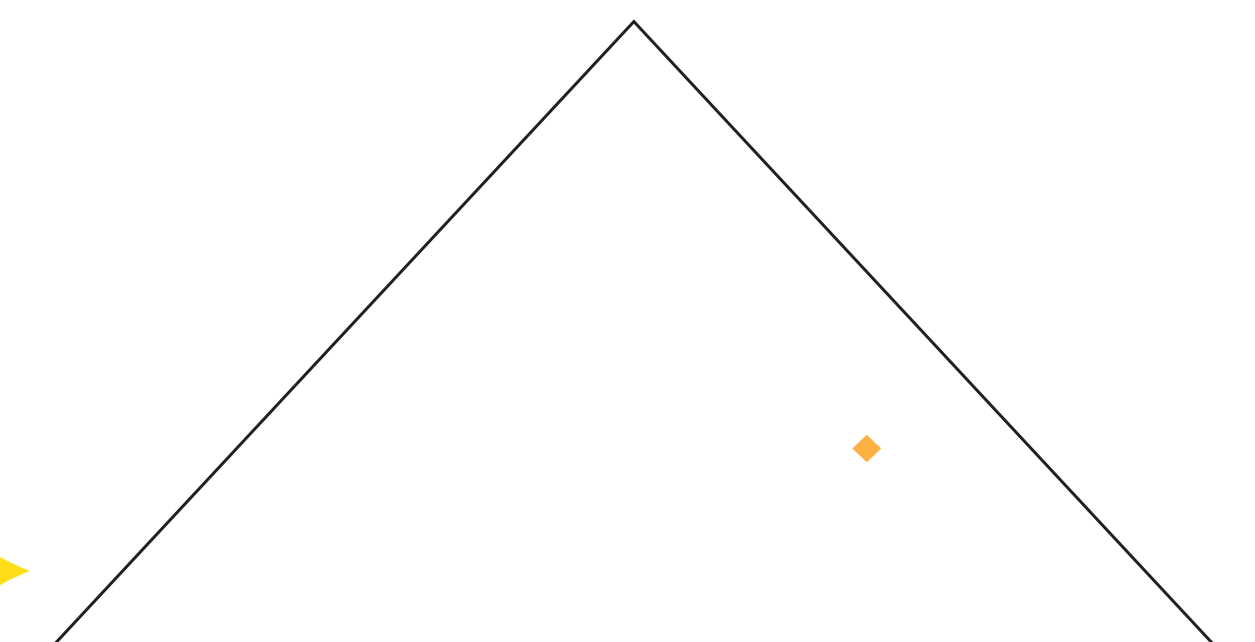
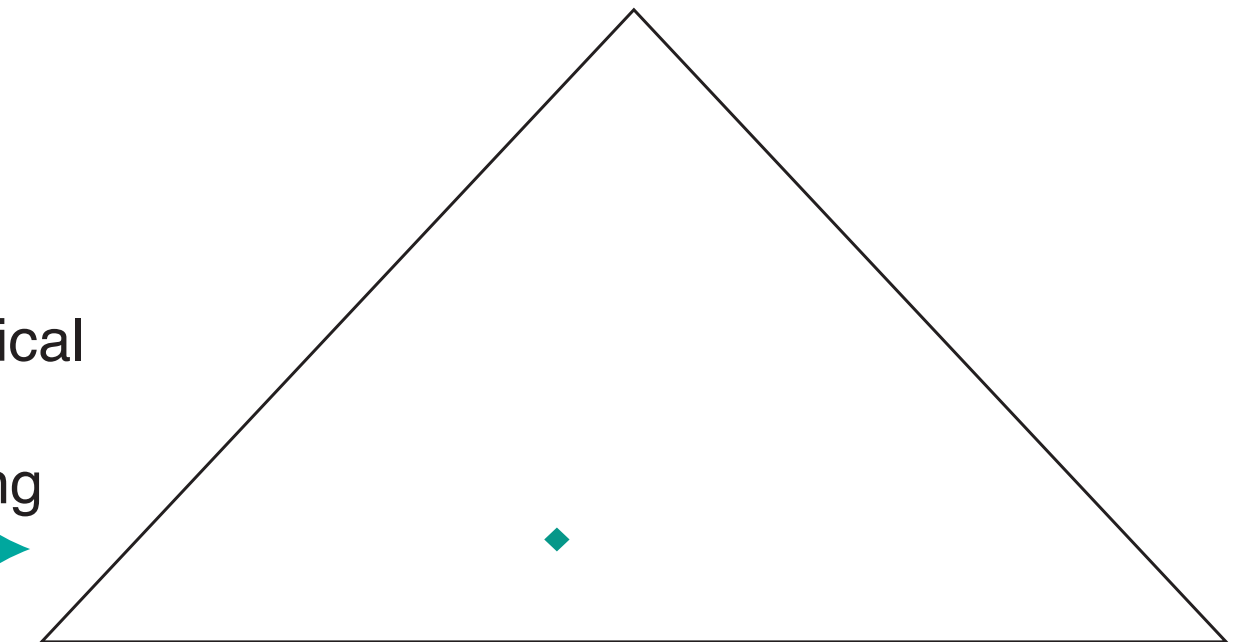


CHROMATIC
Factor Y



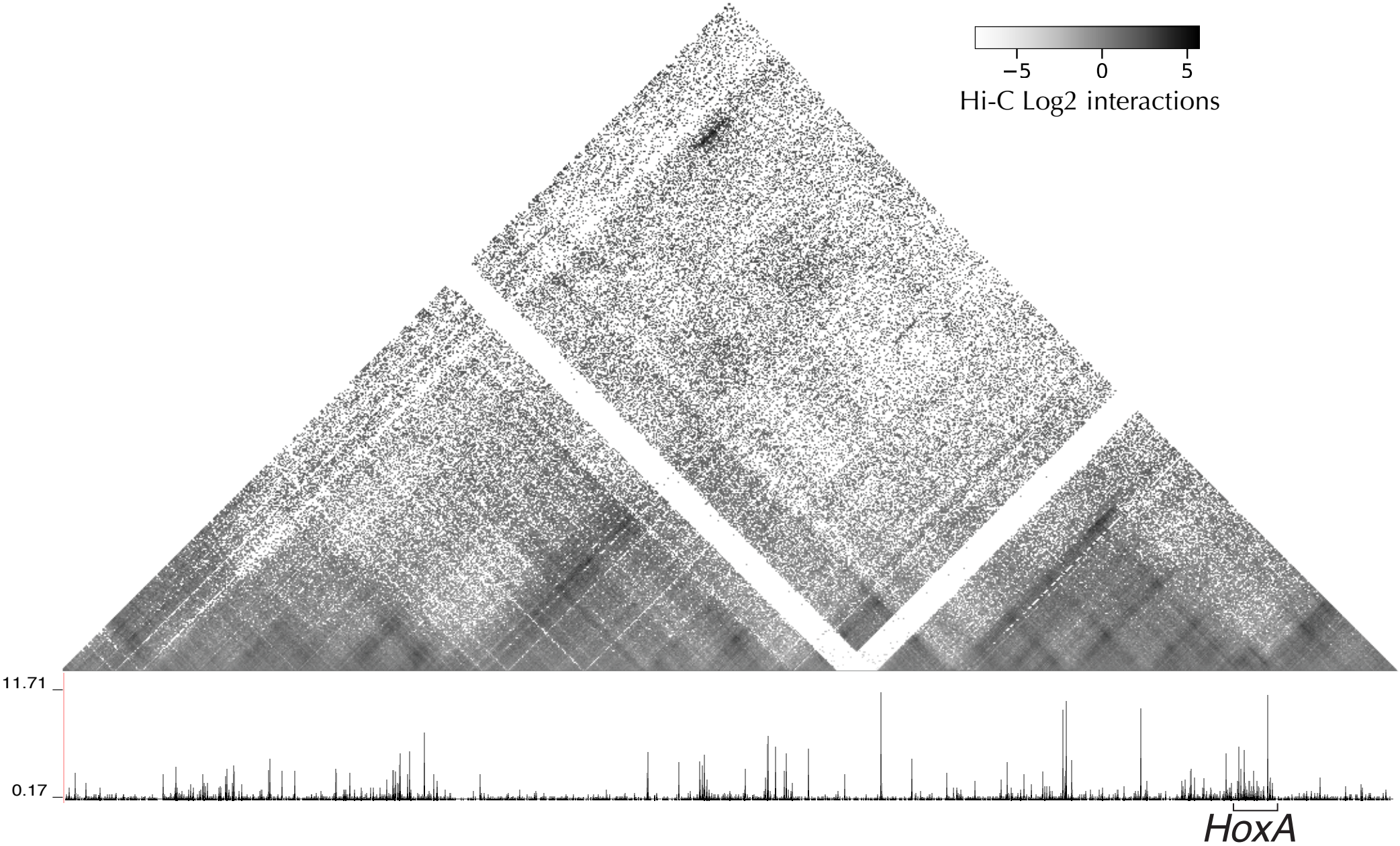
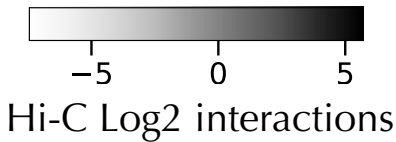
Morphological
image
processing

Loops/Hubs

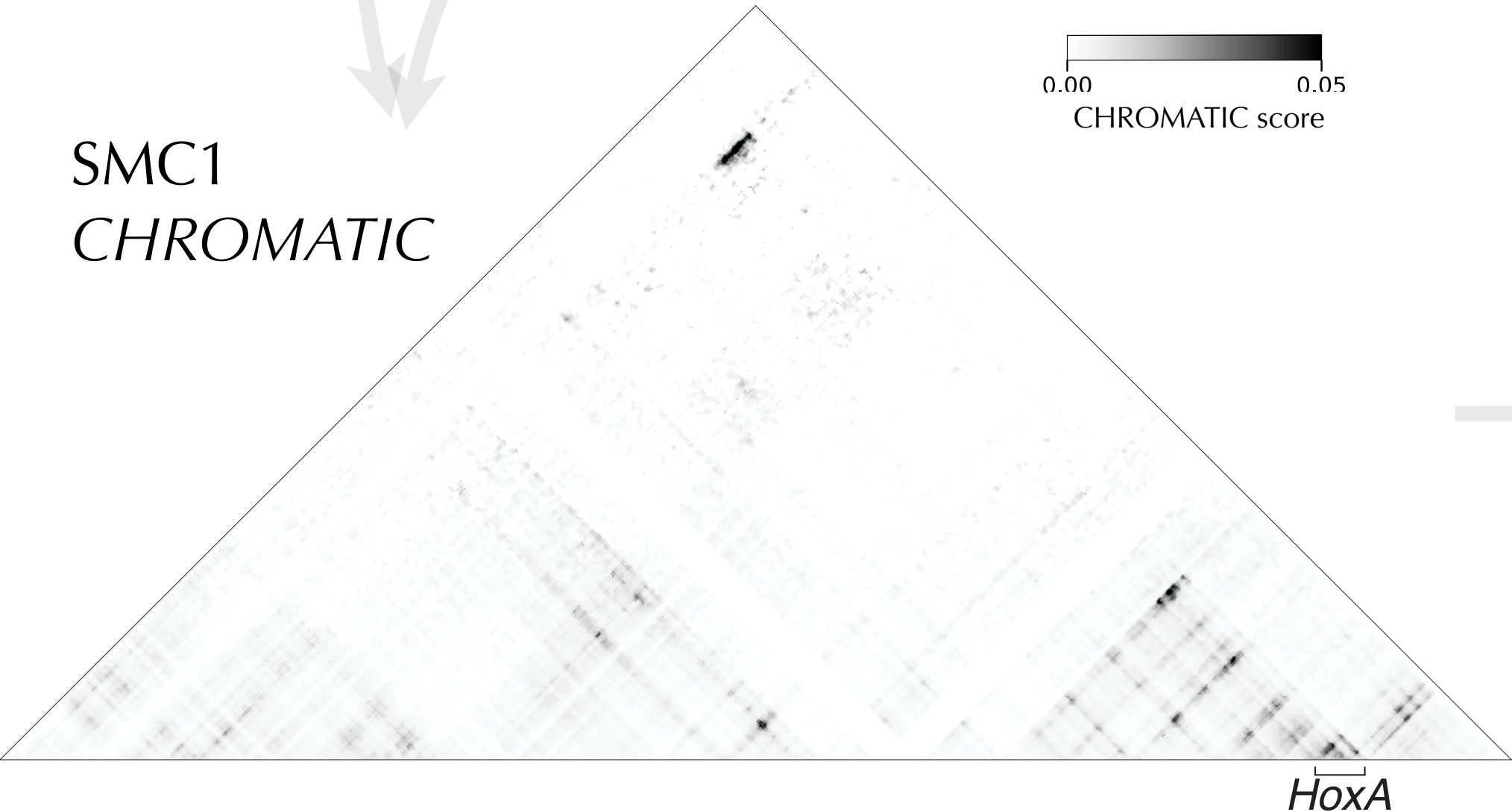
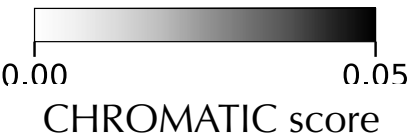


CHROMATIC example

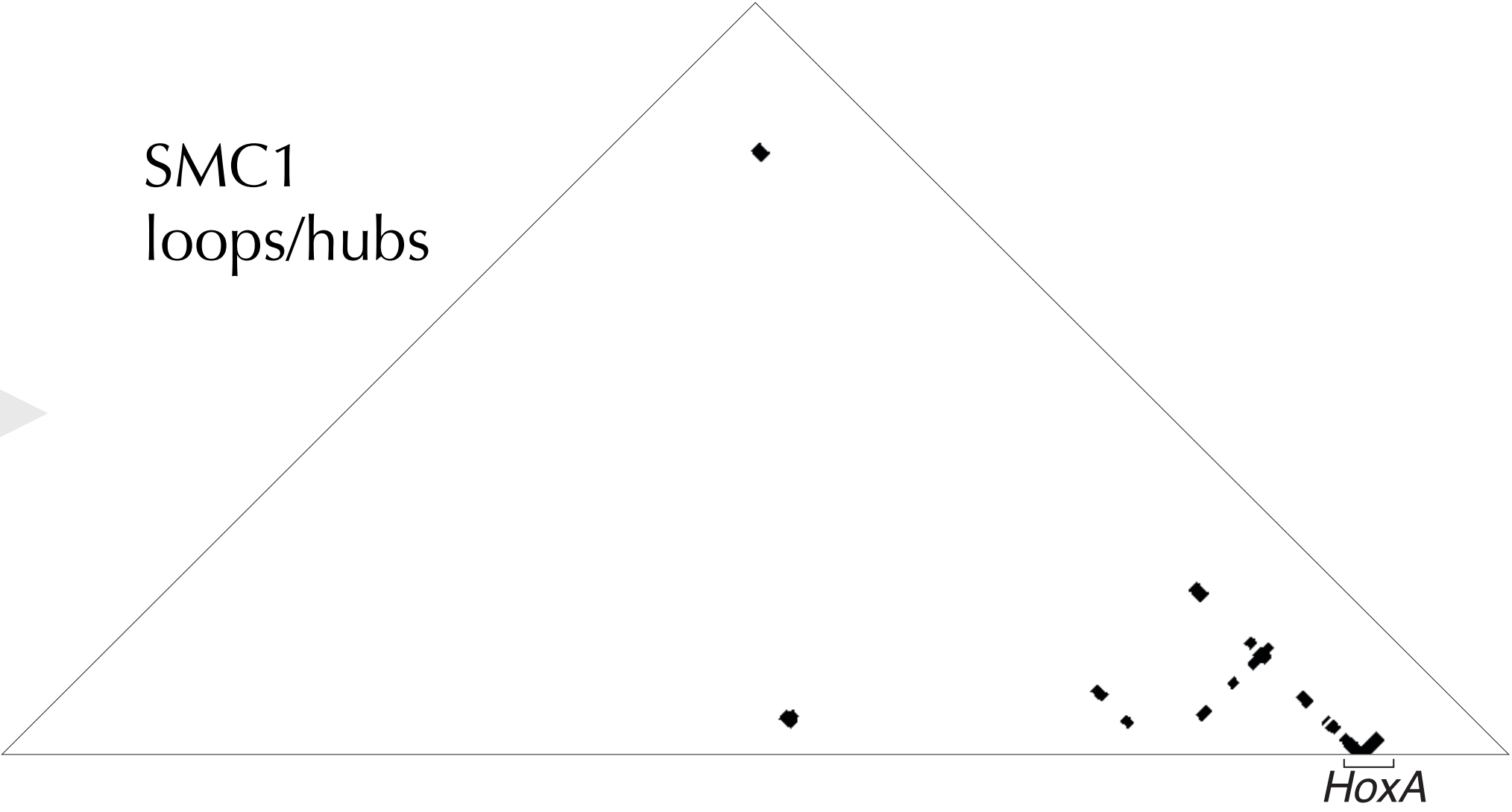
mm10 chr6:48,050,001-52,750,006



SMC1
CHROMATIC

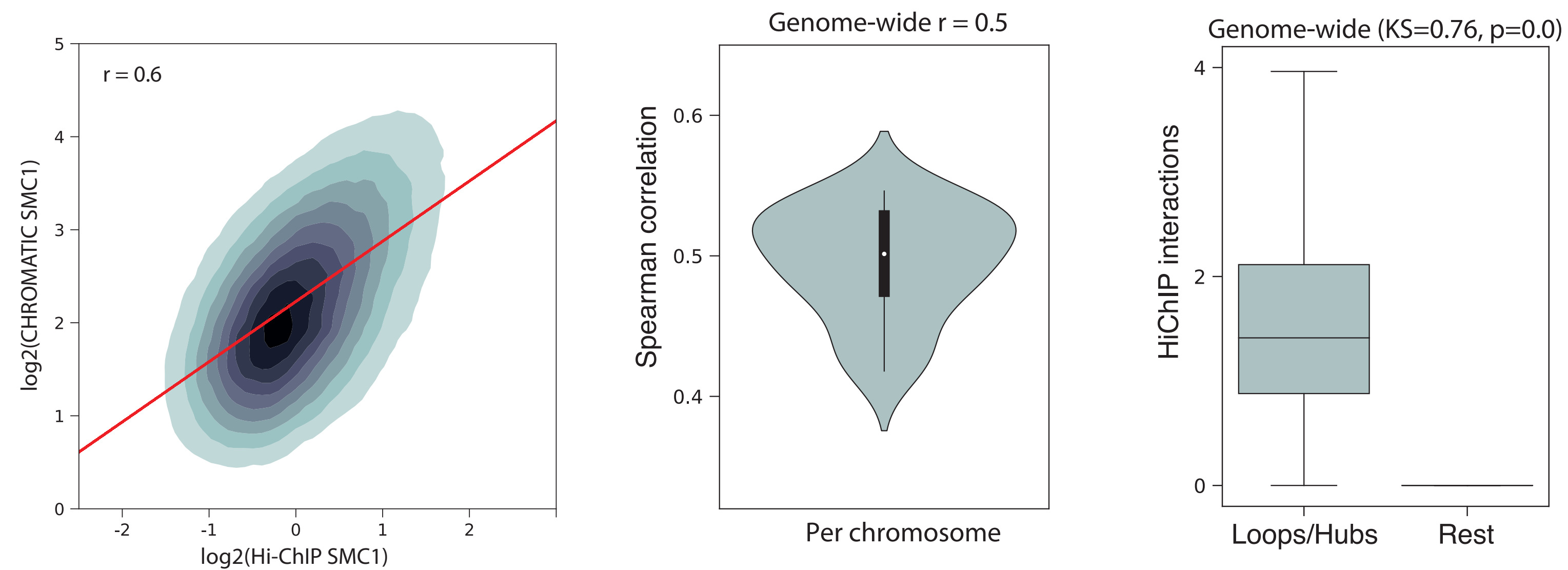
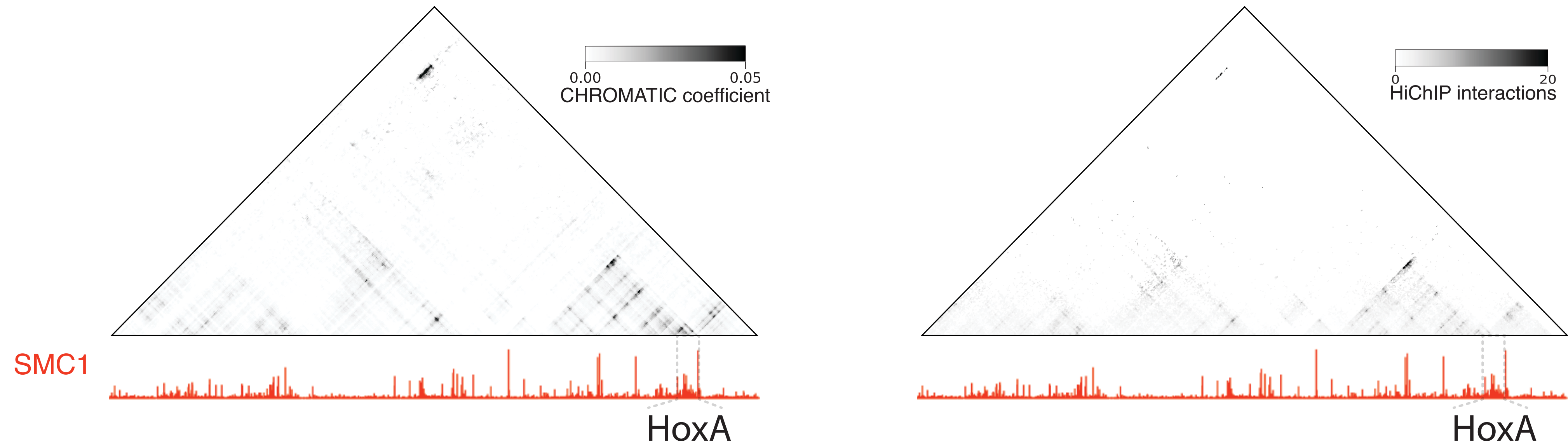


SMC1
loops/hubs

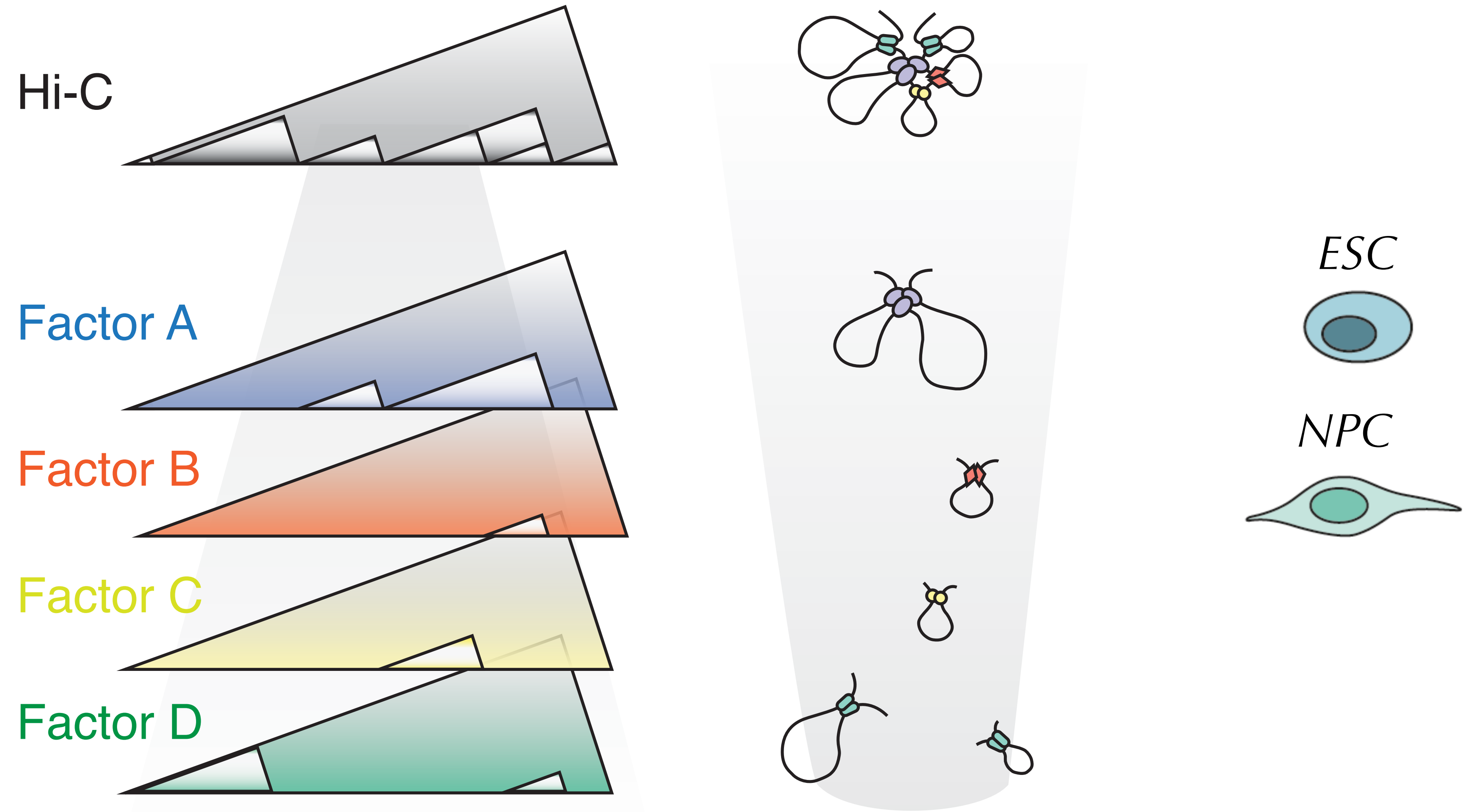


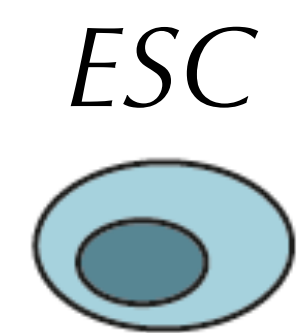
Validation with HiChIP as benchmark

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

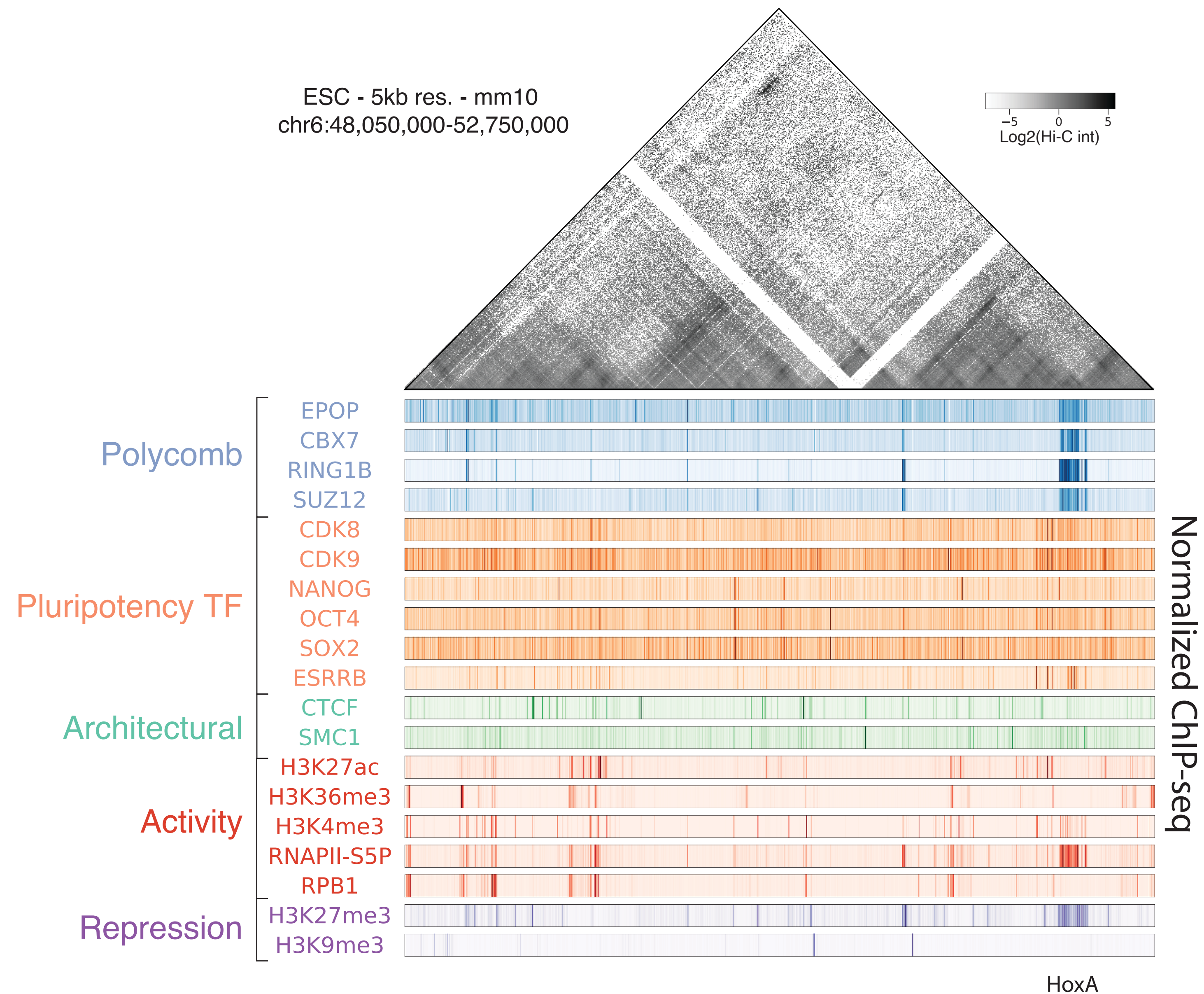


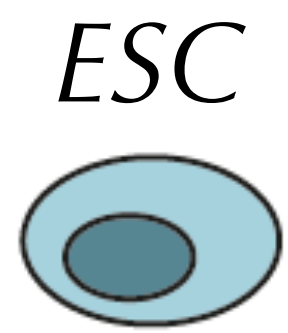
The role of chromatin factors in genome topology



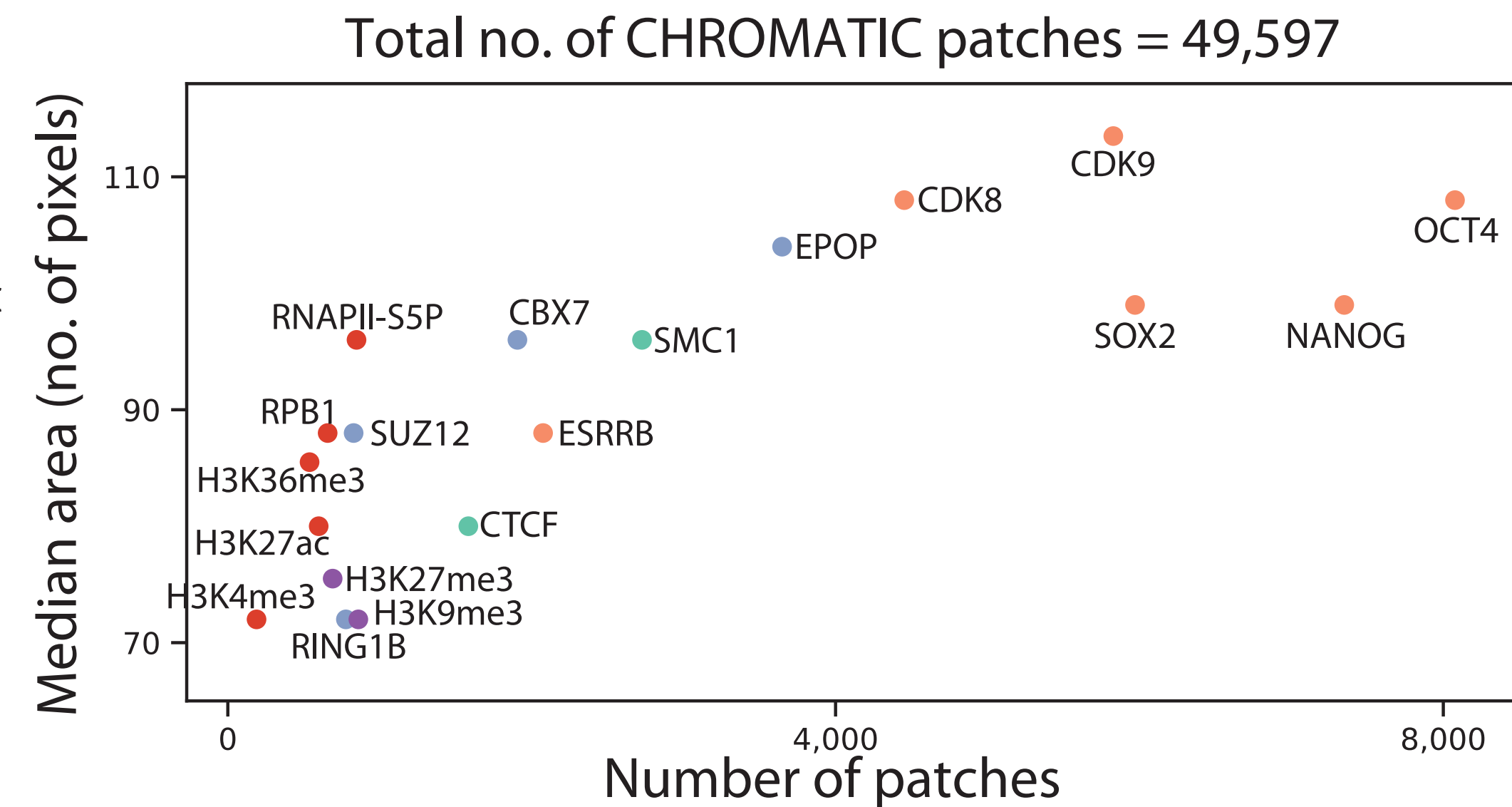
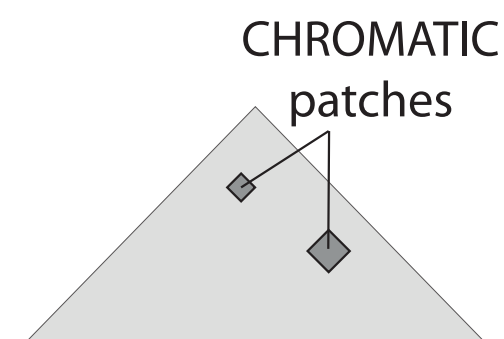
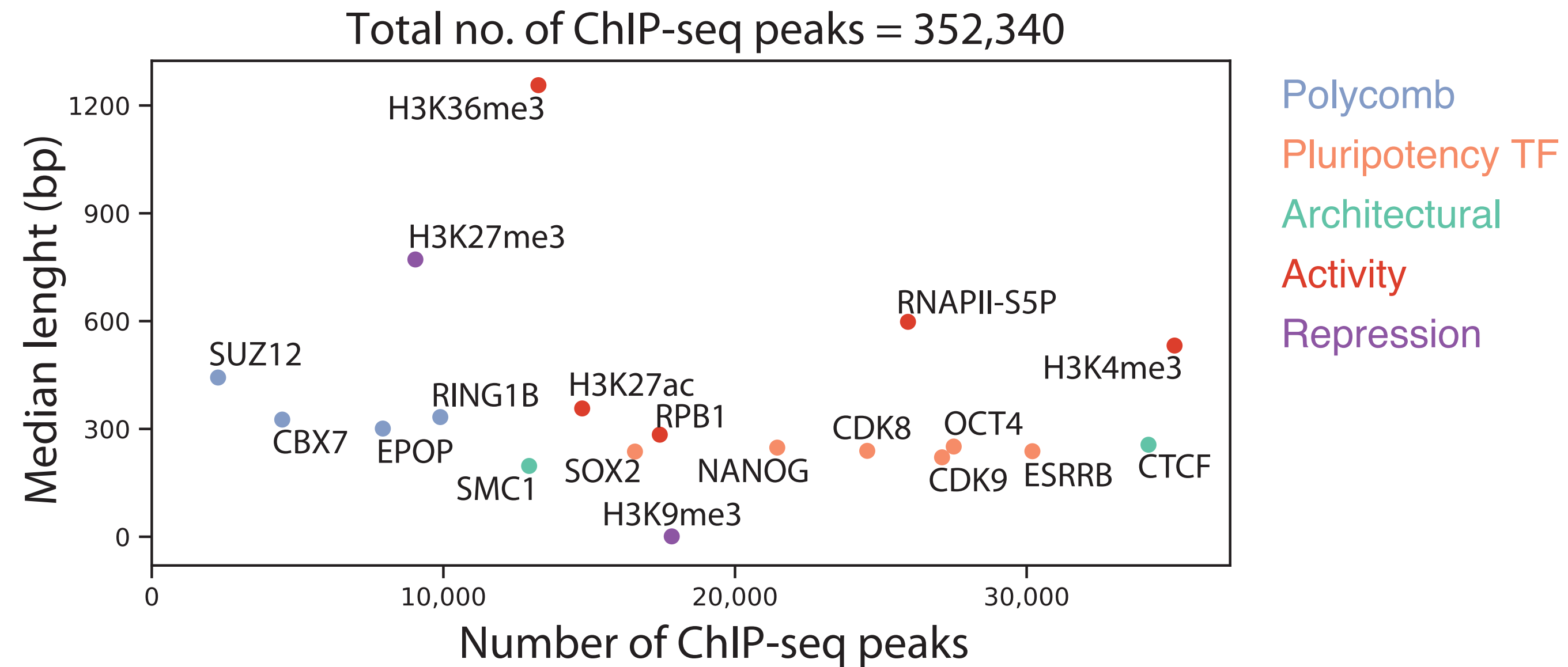
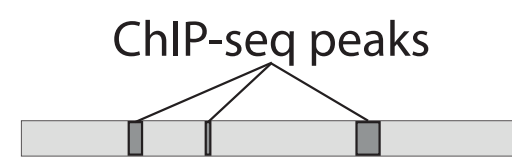


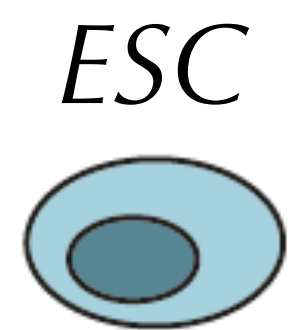
HoxA cluster (example in ESC)





3D interactions are mostly associated with pluripotent TFs



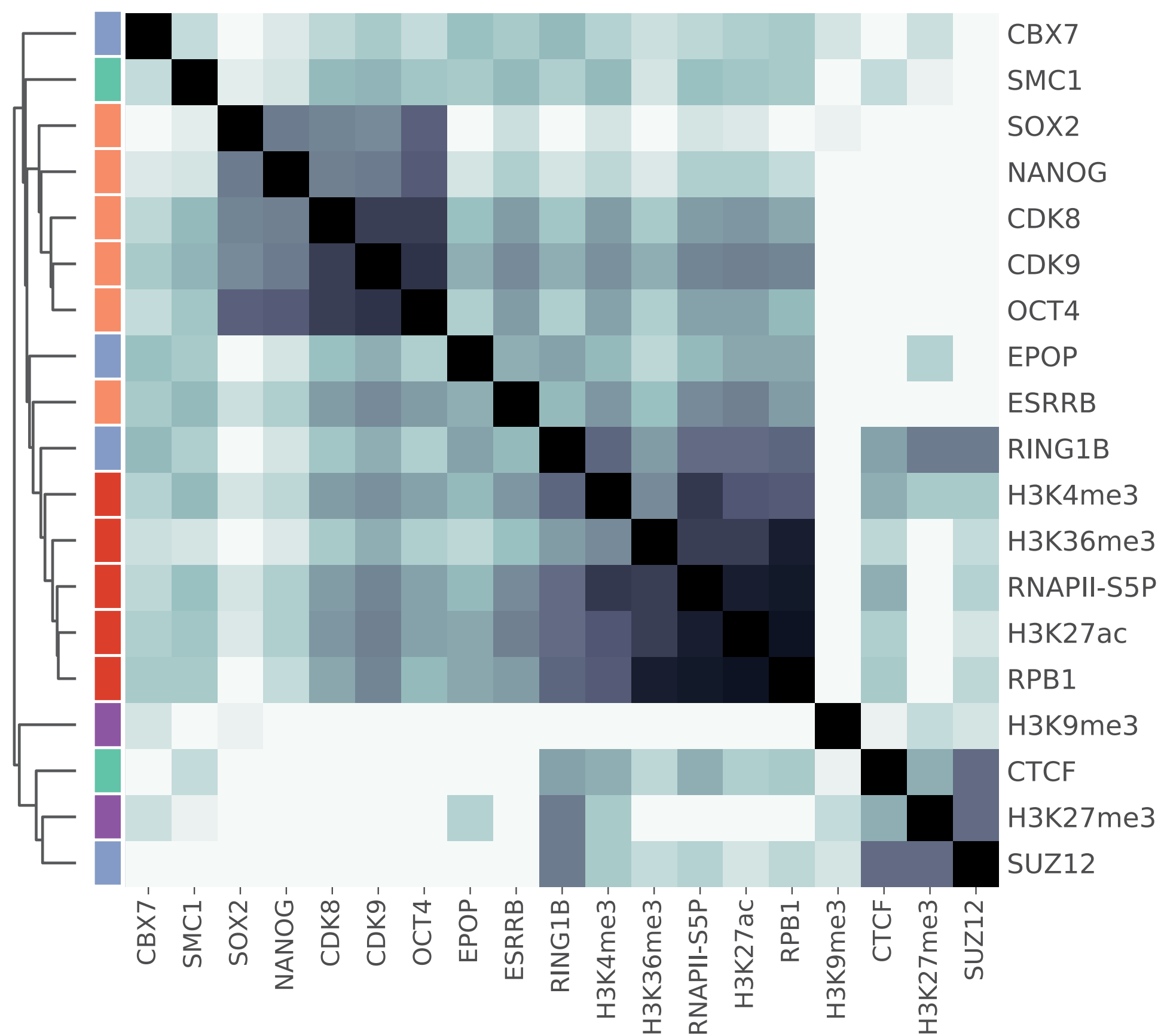


CHROMATIC better represents genome function than ChIP-seq alone

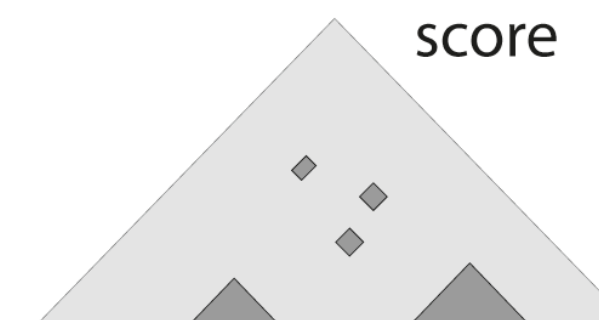
ChIP-seq track



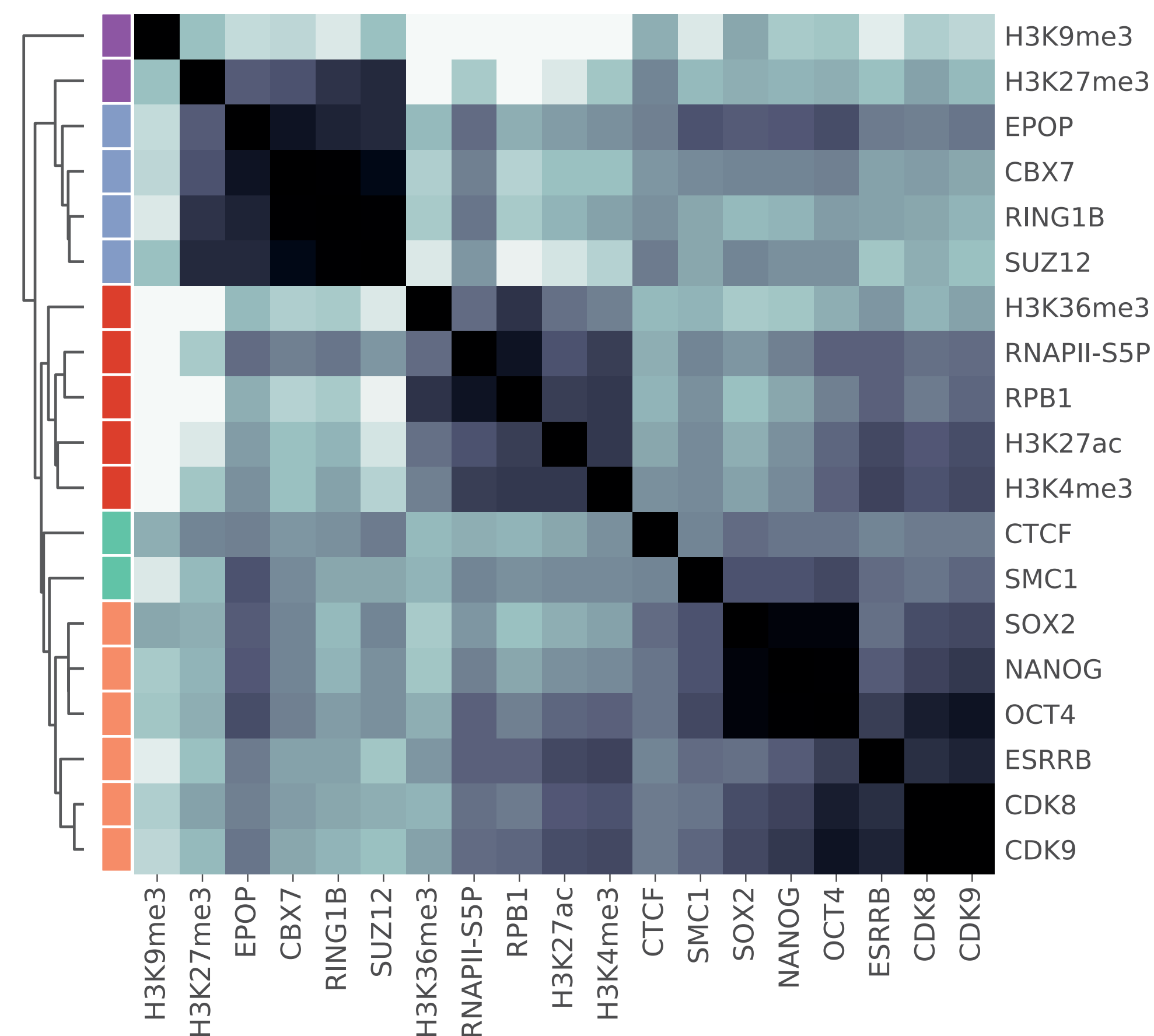
NMIS=0.65

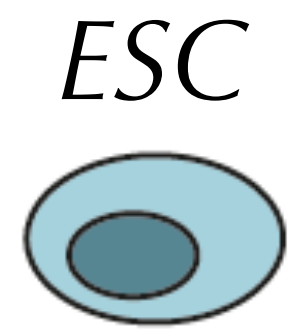


CHROMATIC
score



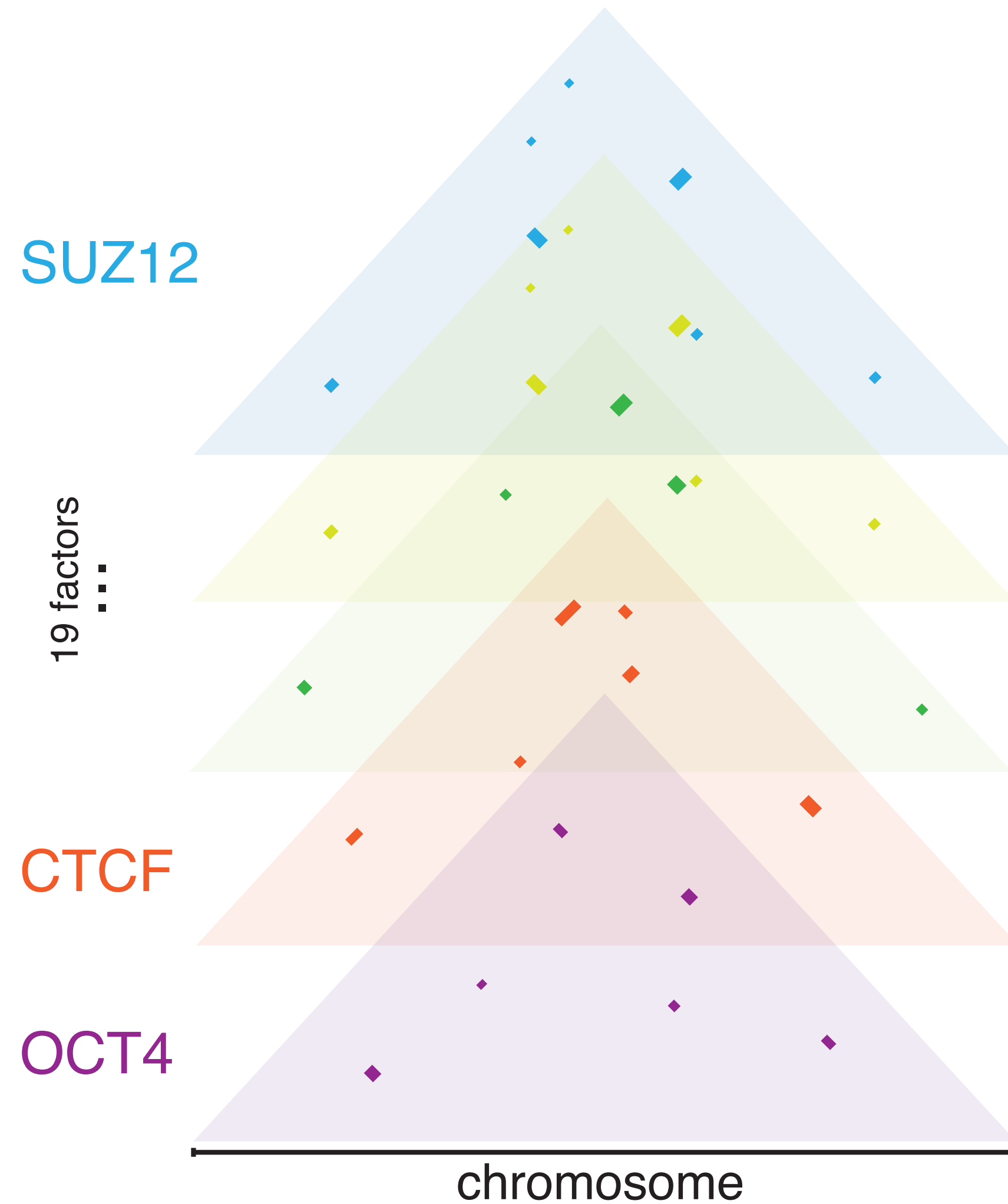
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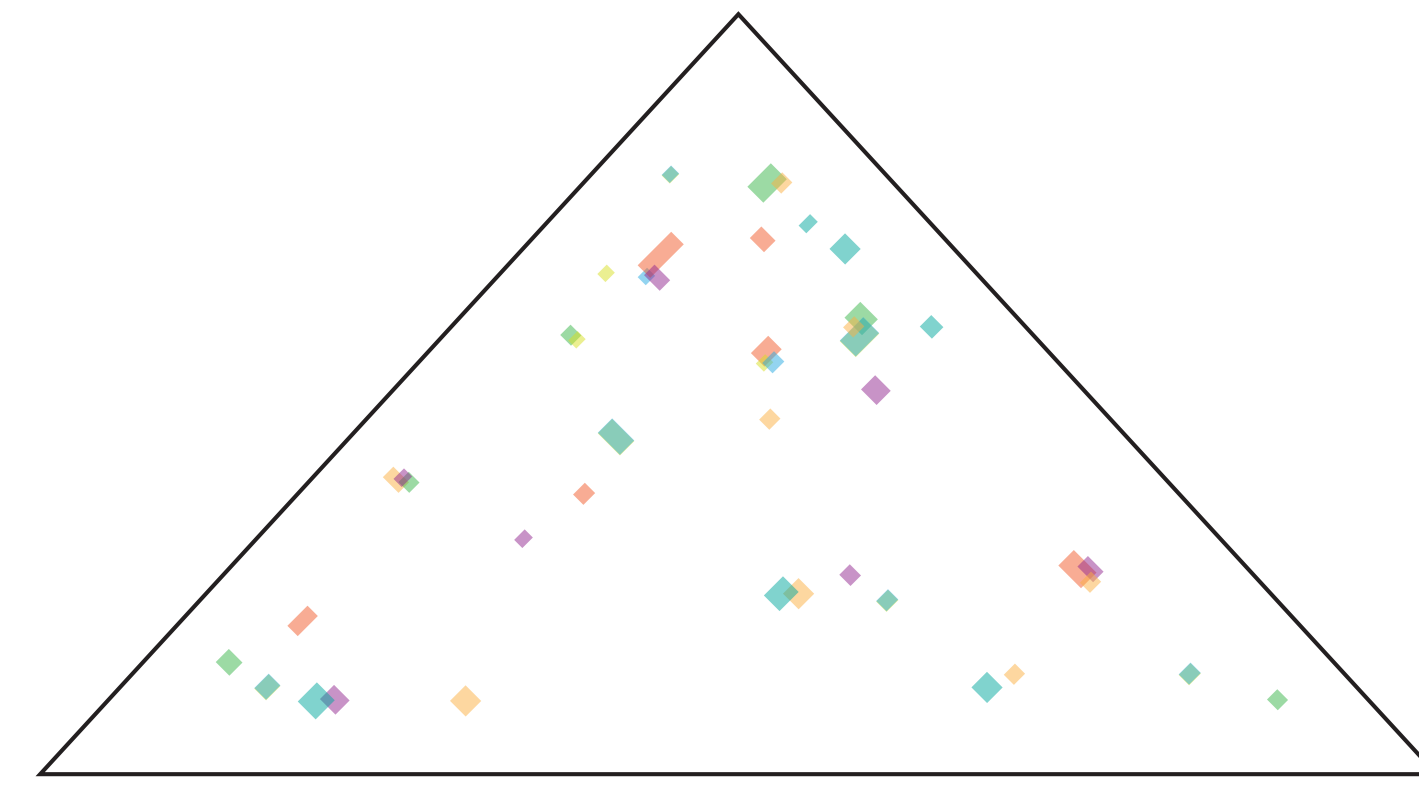


Measure the 3D co-localization of factors

CHROMATIC interactions



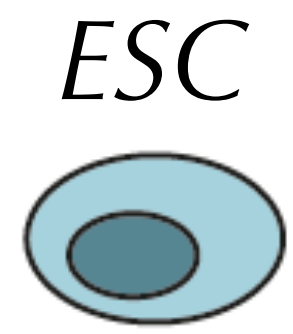
Overlap (19 factors)



Latent Semantic Analysis

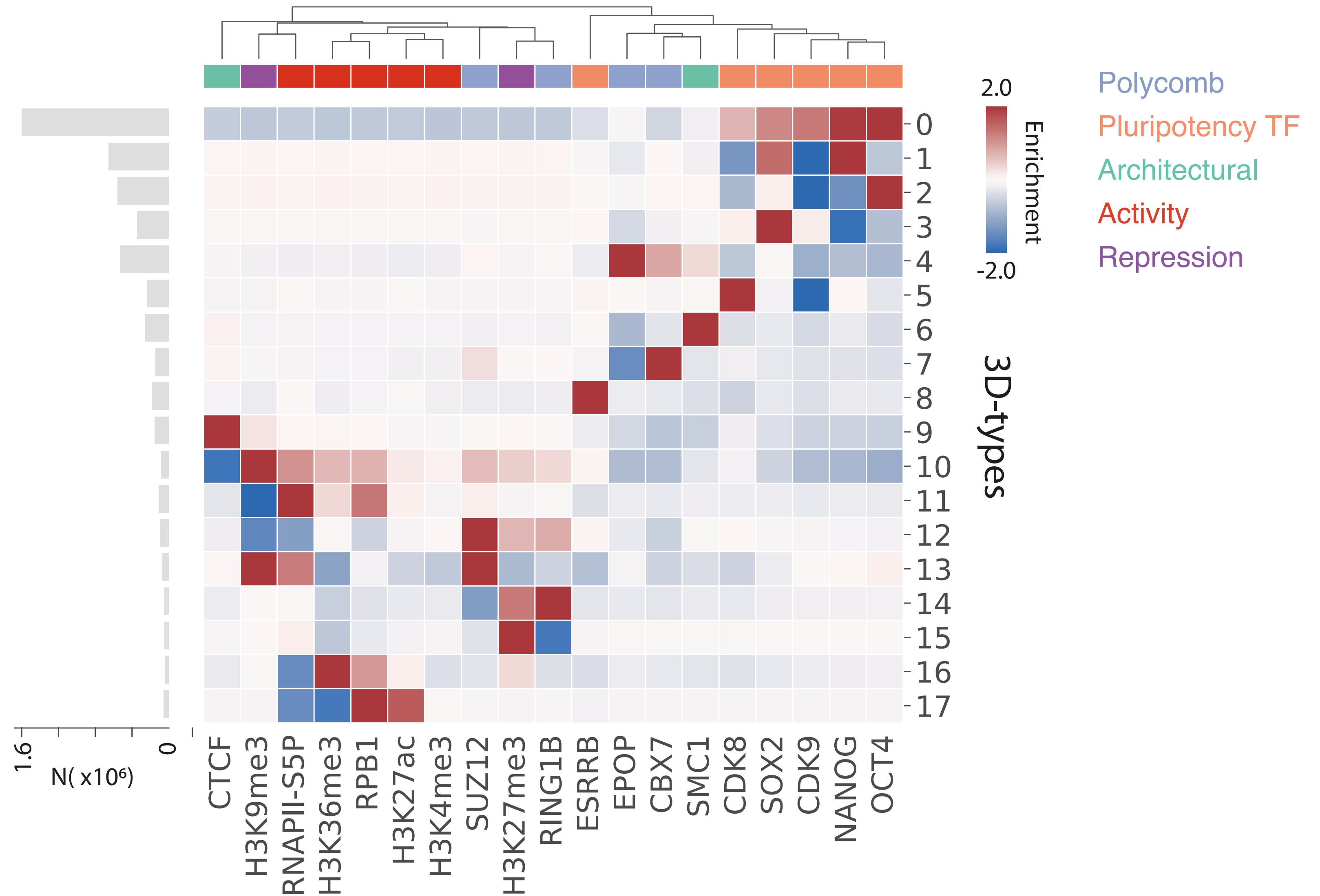
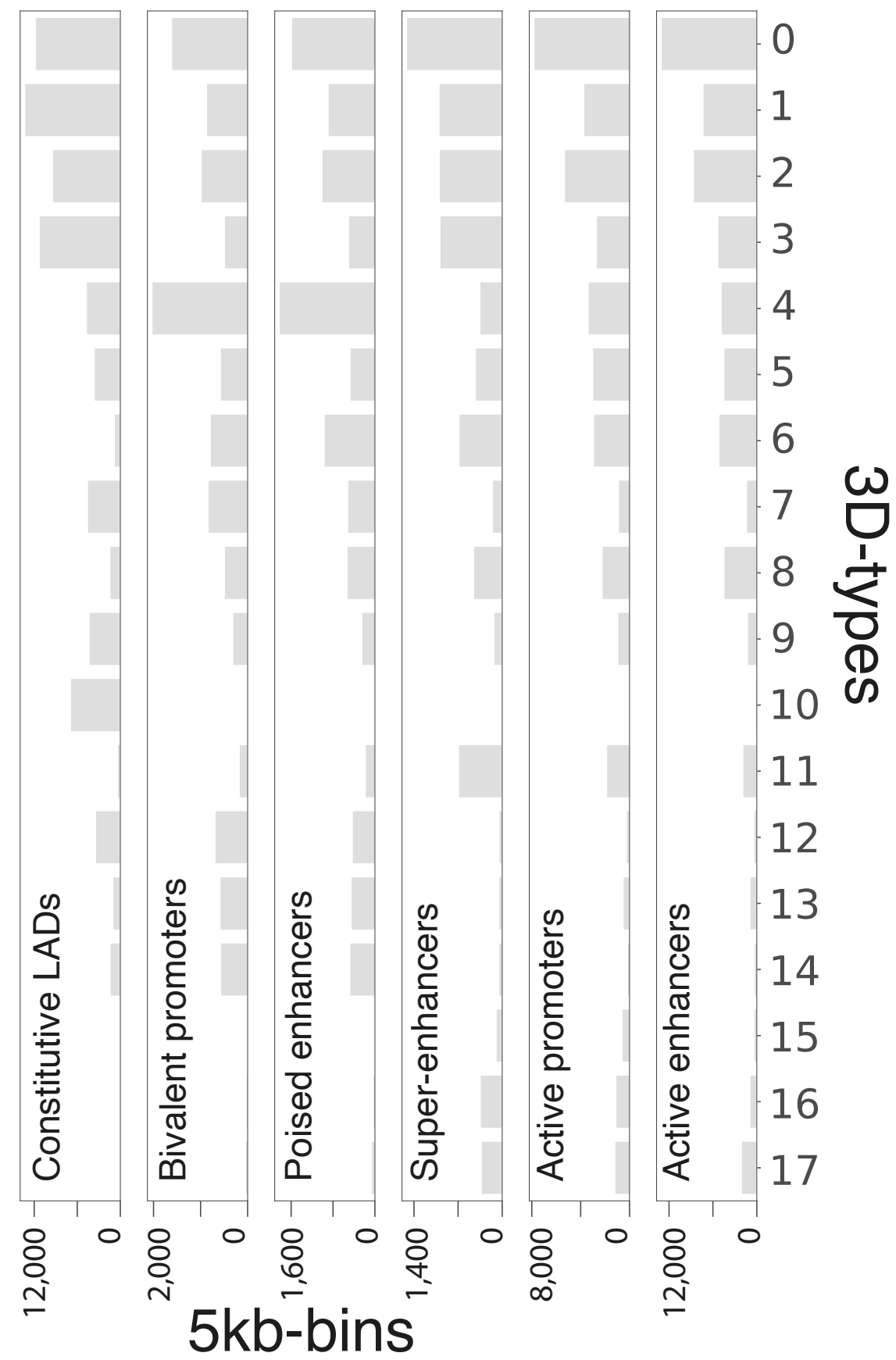
Documents

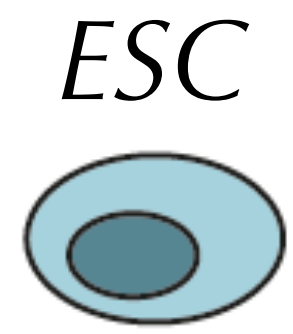
Doc1:	CBX7	NANOG	
Doc2:	OCT4	CDK8	H3K27ac
Doc3:	RING1B		
Doc4:	H3K36me3	RNAPolIII-S5P	
...			
...			



Types of 3D interactions with LSA in ESC

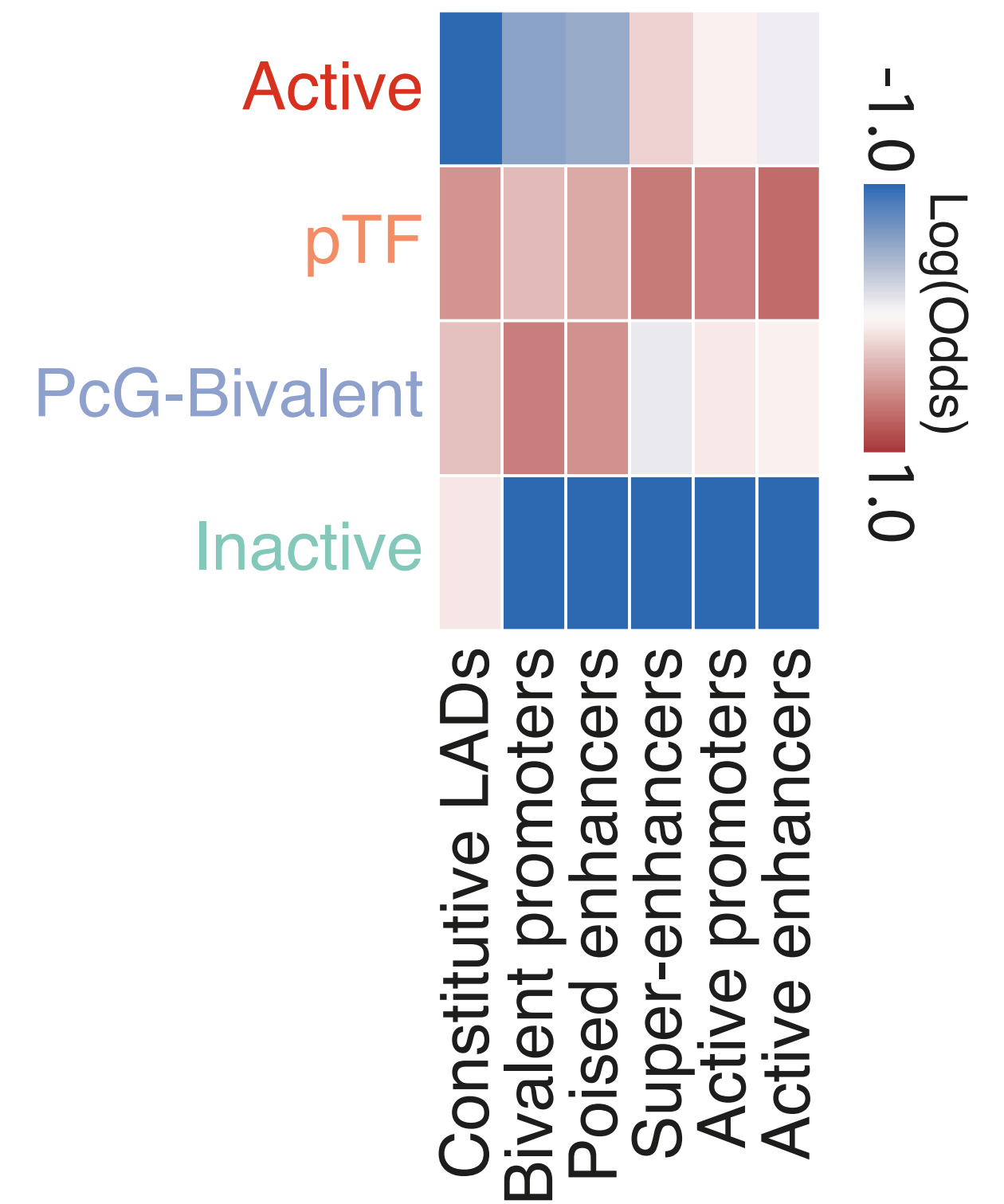
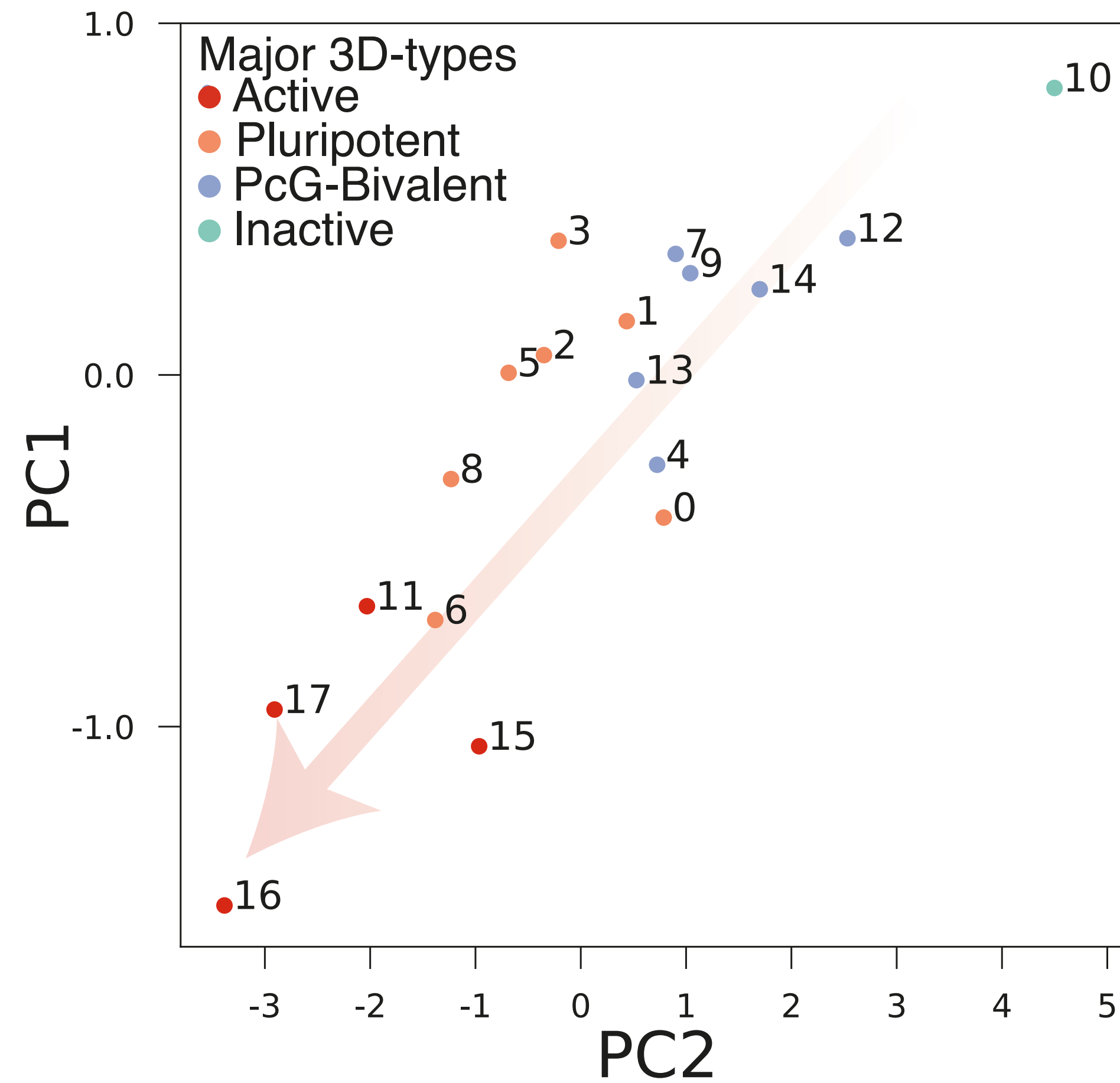
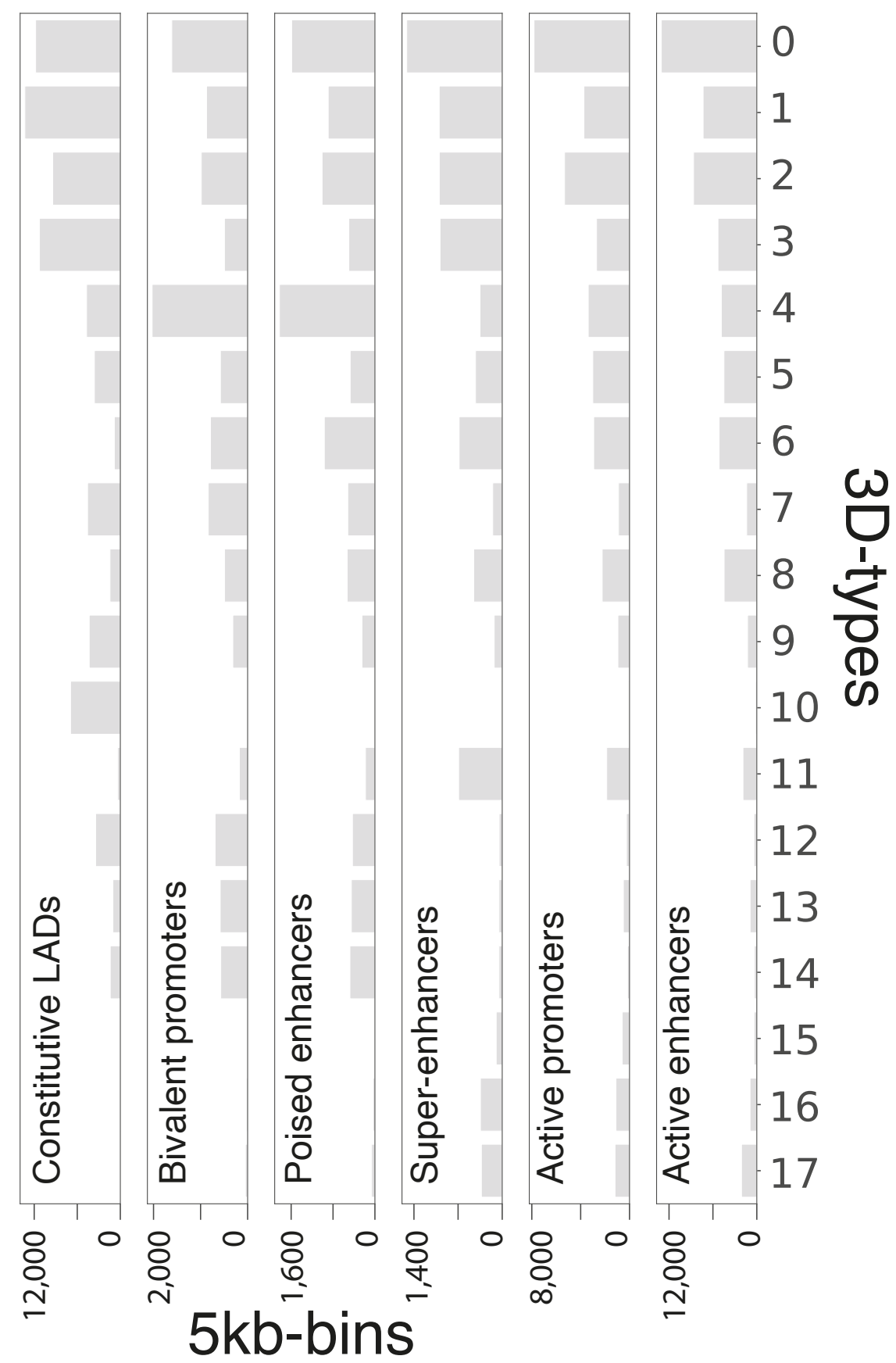
Annotated using ChIP-Seq and literature

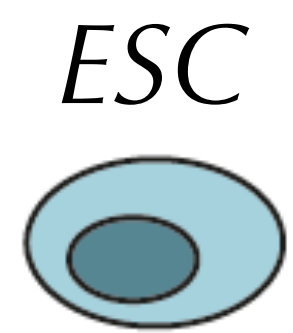




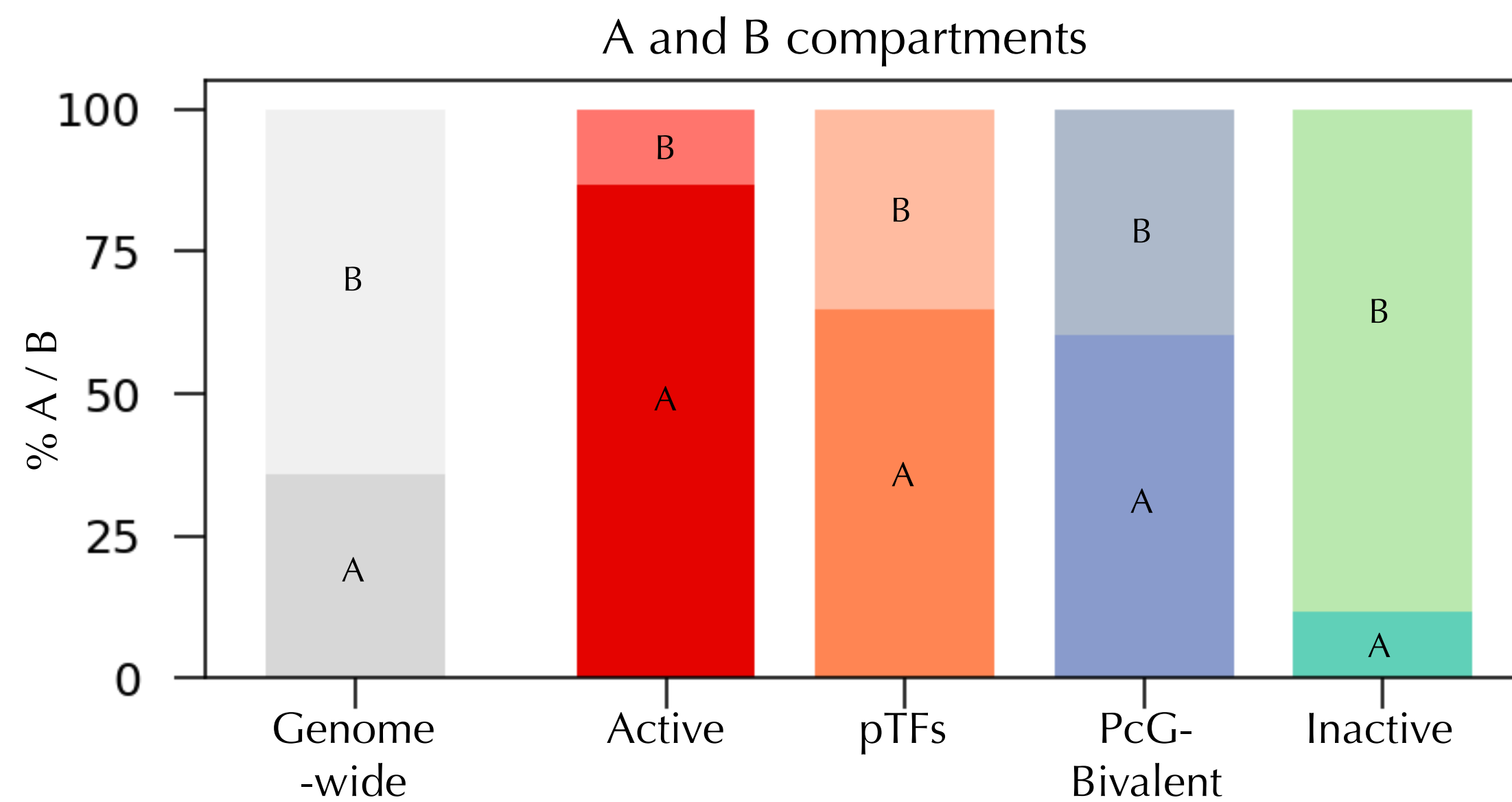
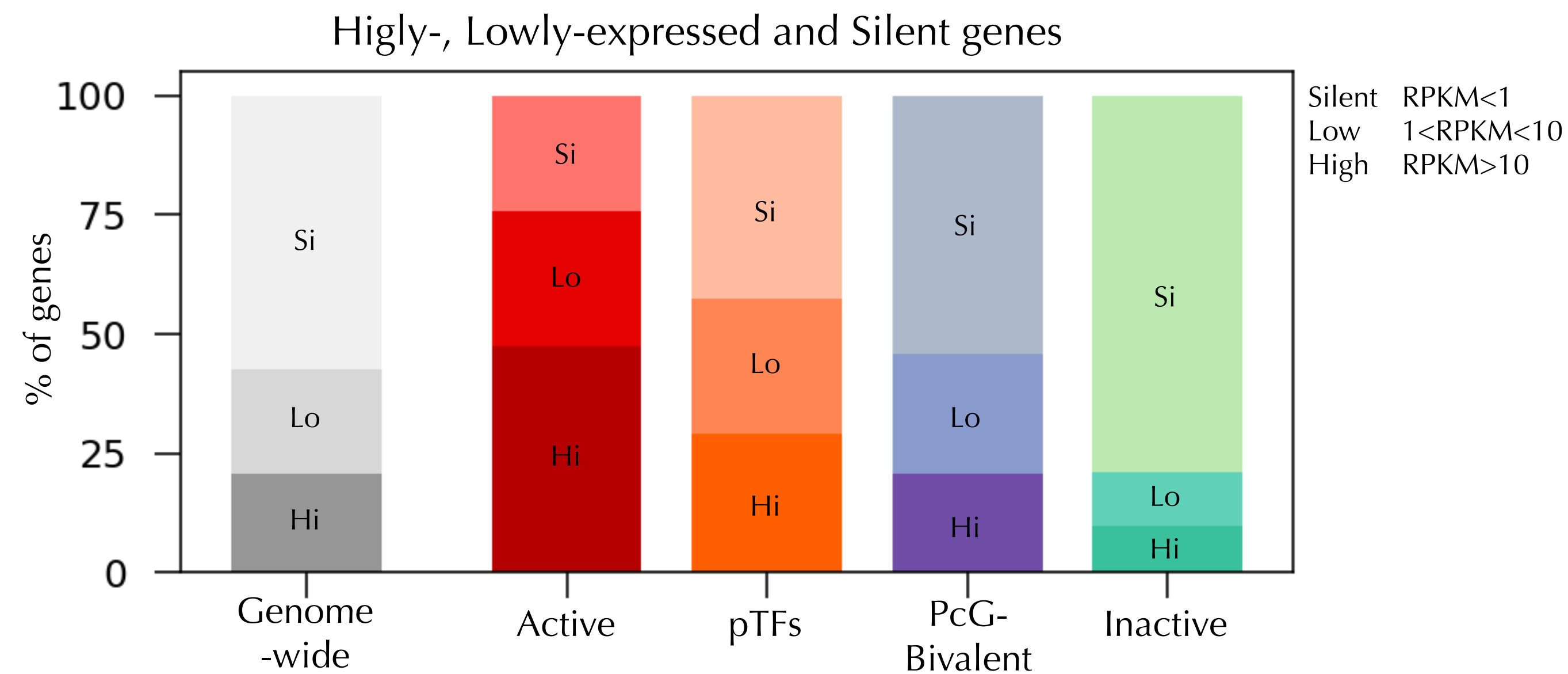
Types of 3D interactions with LSA in ESC

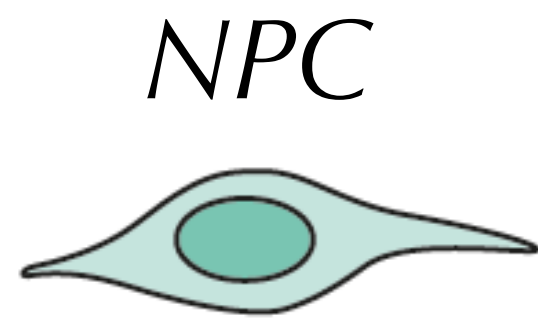
Annotated using ChIP-Seq and literature



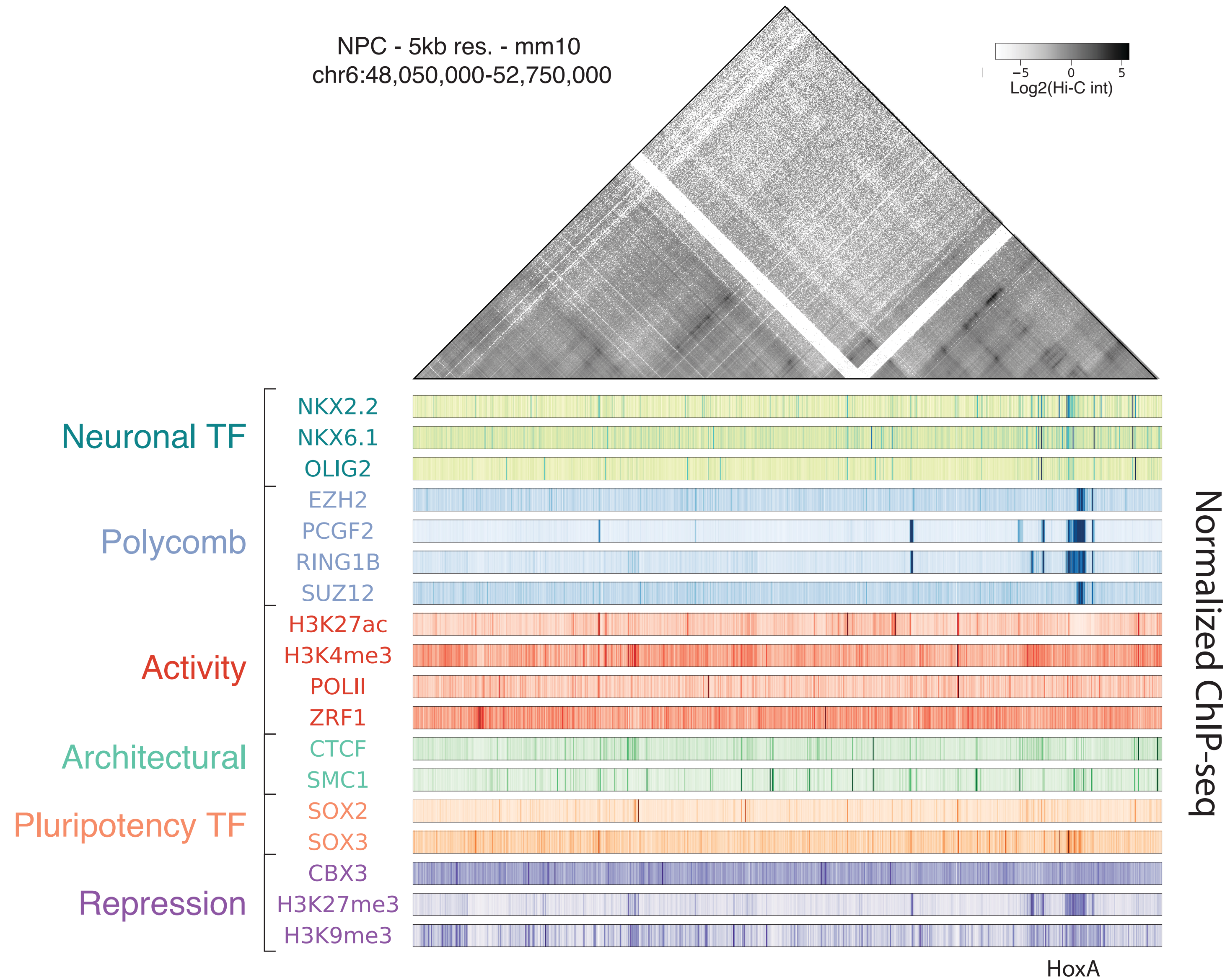


4 major types of 3D interactions in ESC





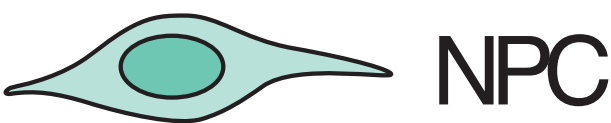
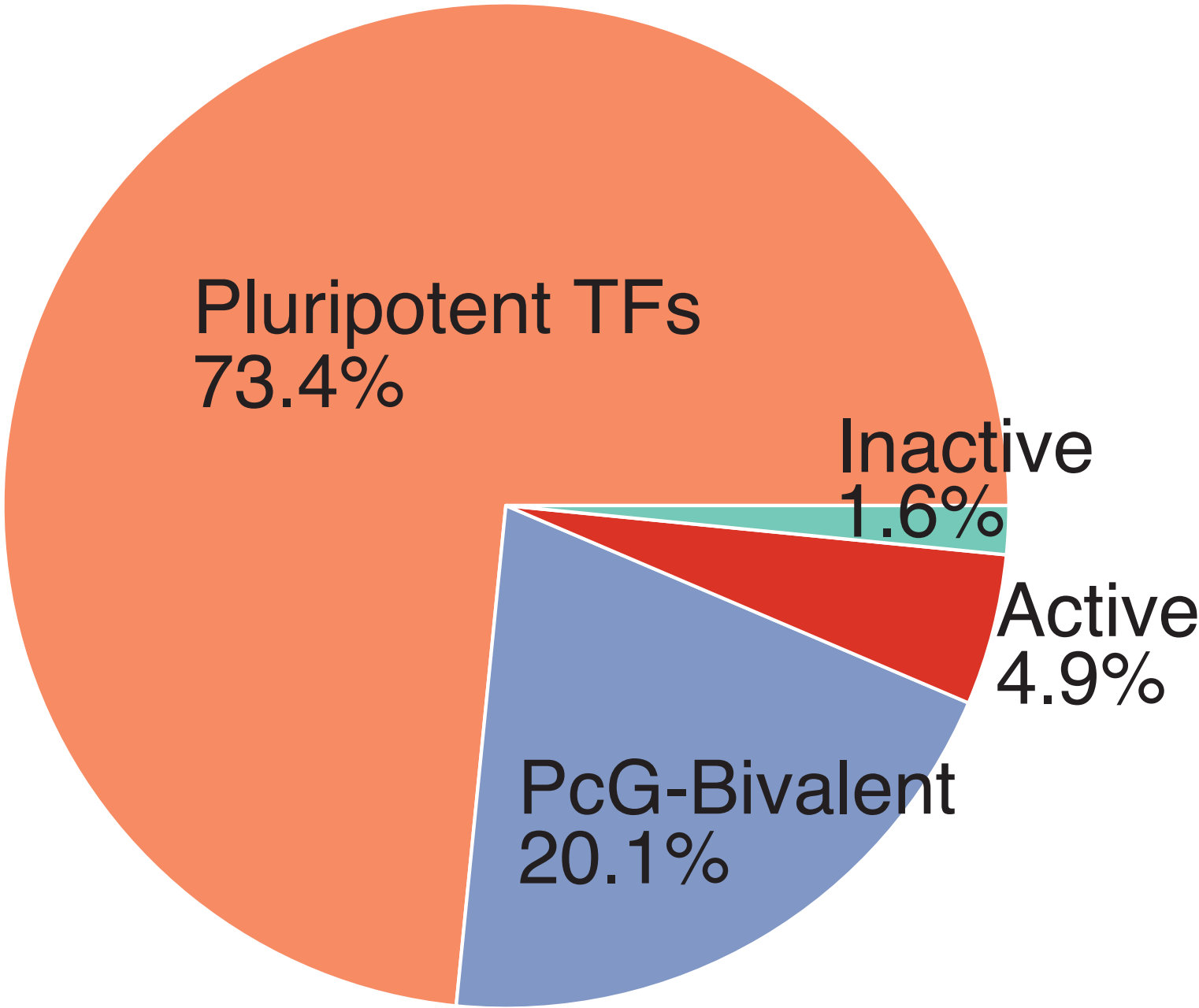
HoxA cluster (example in NPC)



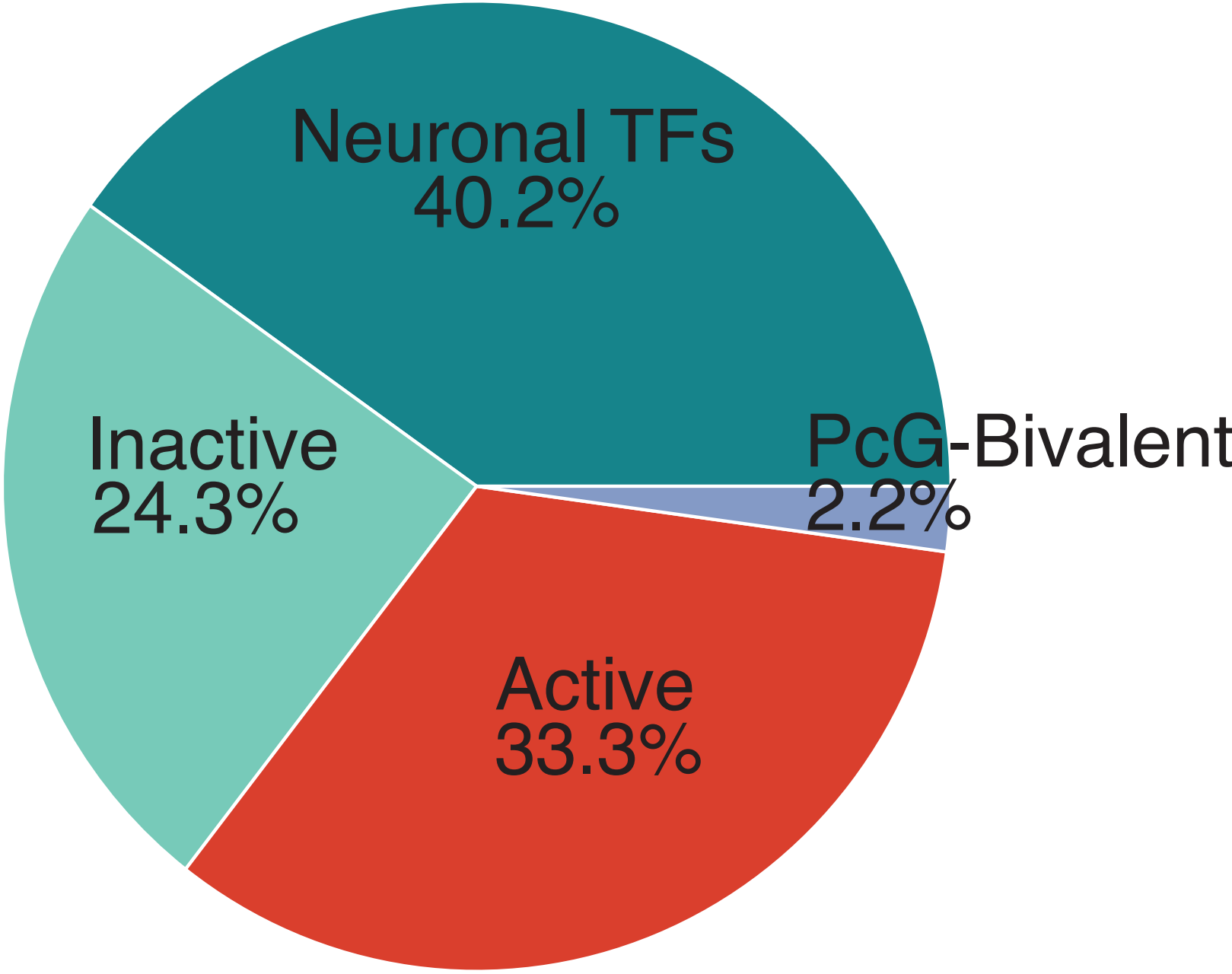
Global 3D interactions rewiring during mouse development



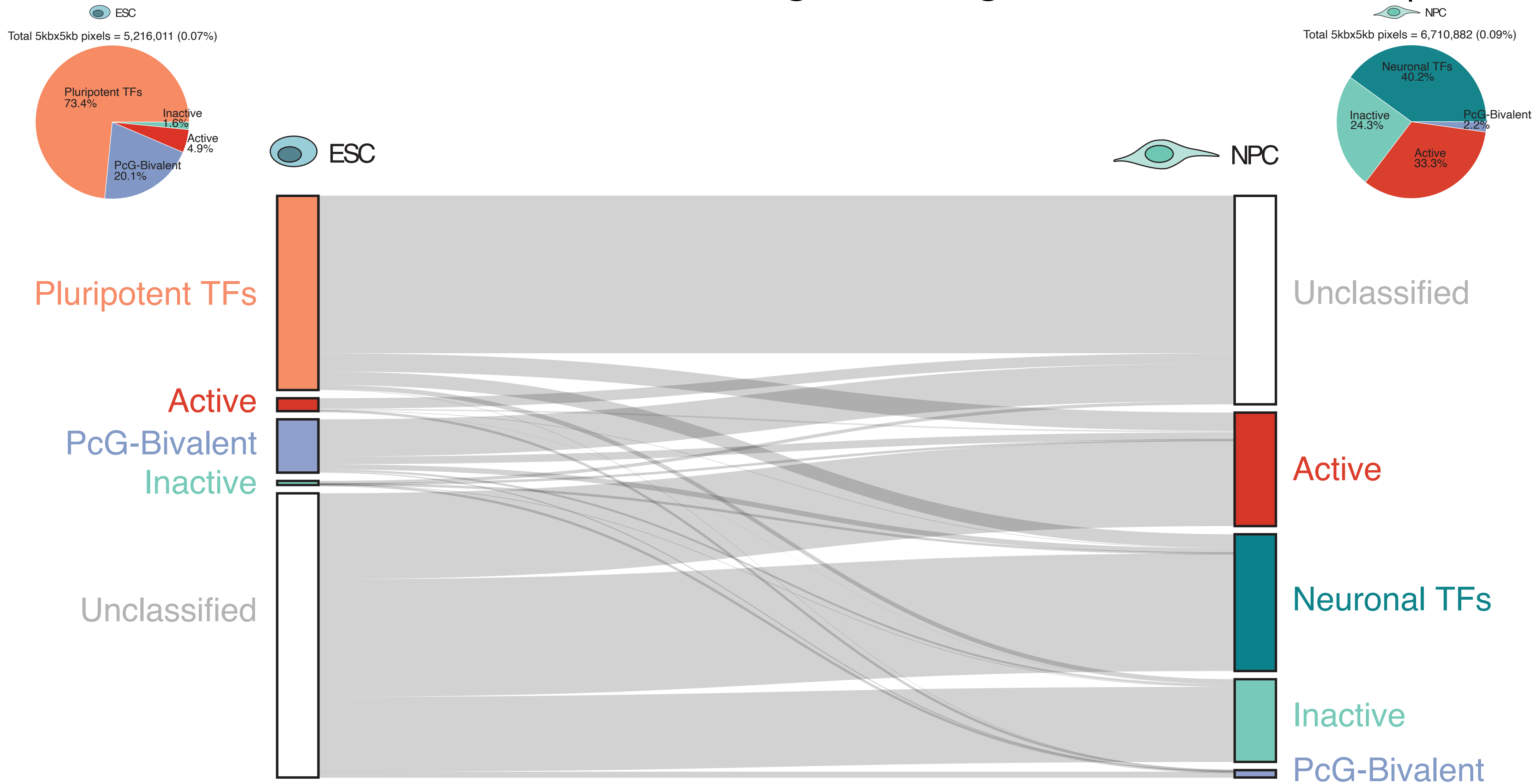
Total 5kbx5kb pixels = 5,216,011 (0.07%)



Total 5kbx5kb pixels = 6,710,882 (0.09%)



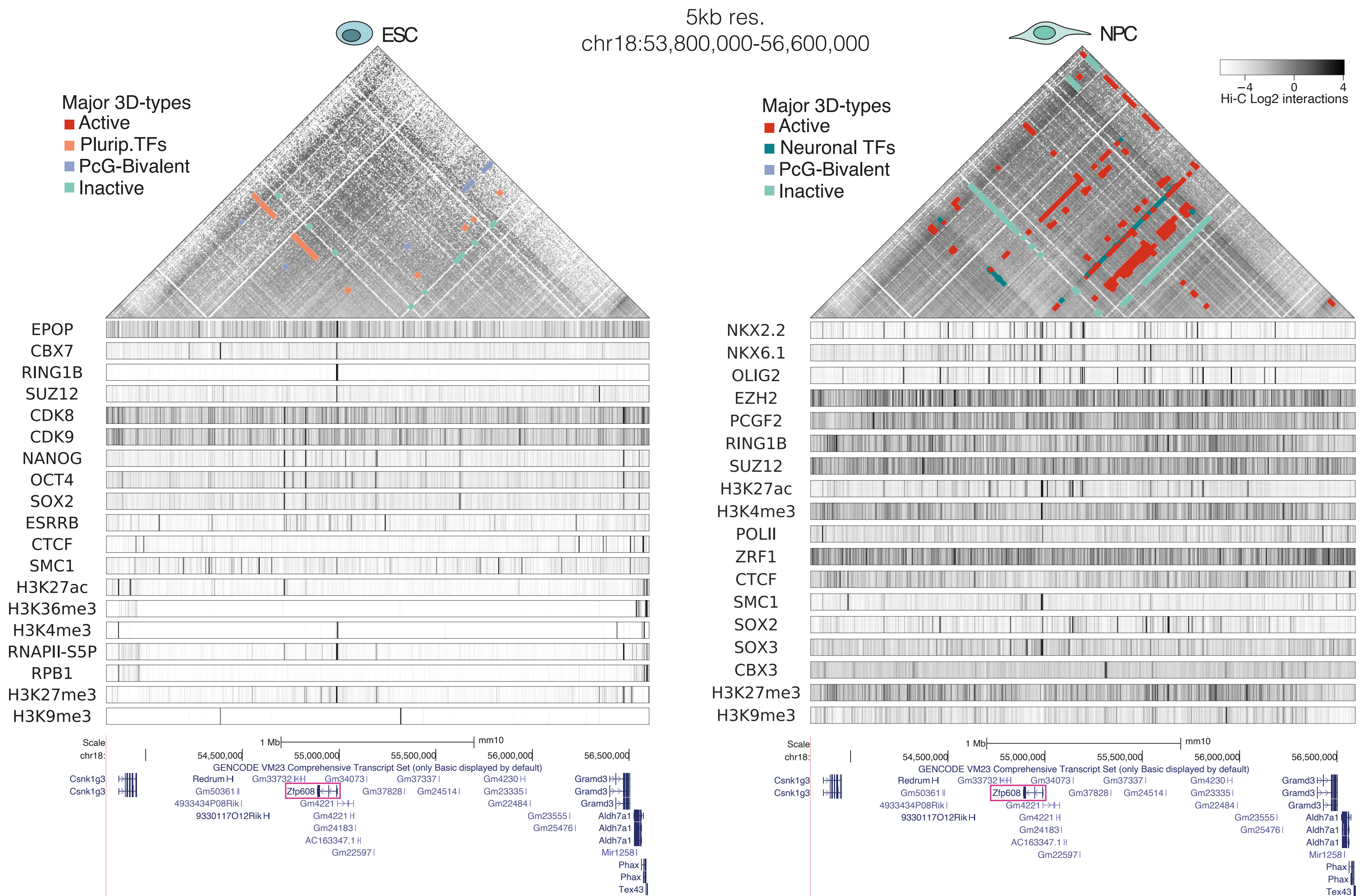
Global 3D interactions rewiring during mouse development



Global 3D interactions rewiring during mouse development



3D interactions rewiring at Zfp608 locus during mouse neural development

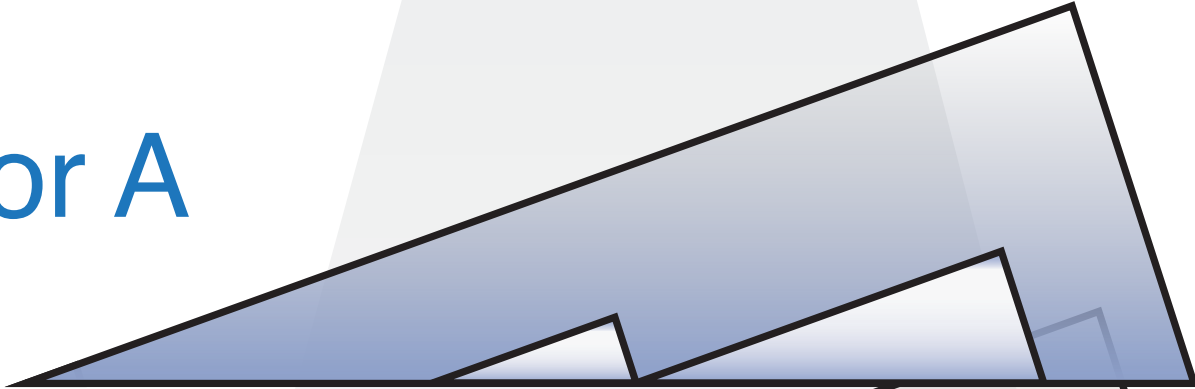


Take home message...

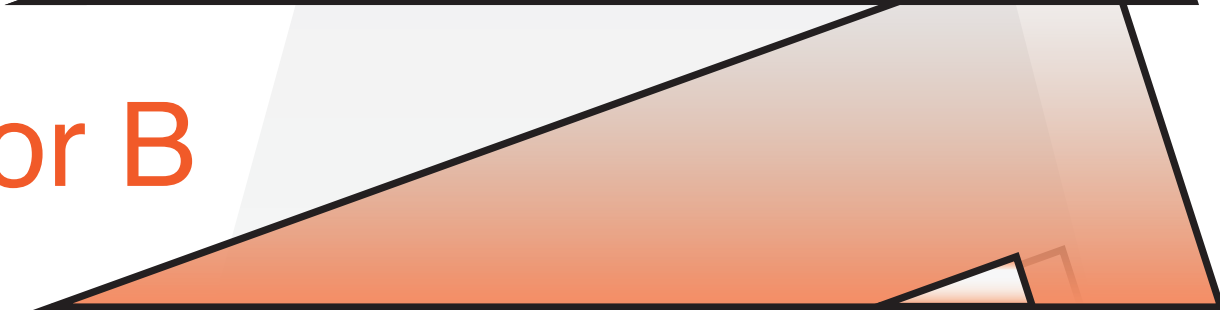
Hi-C



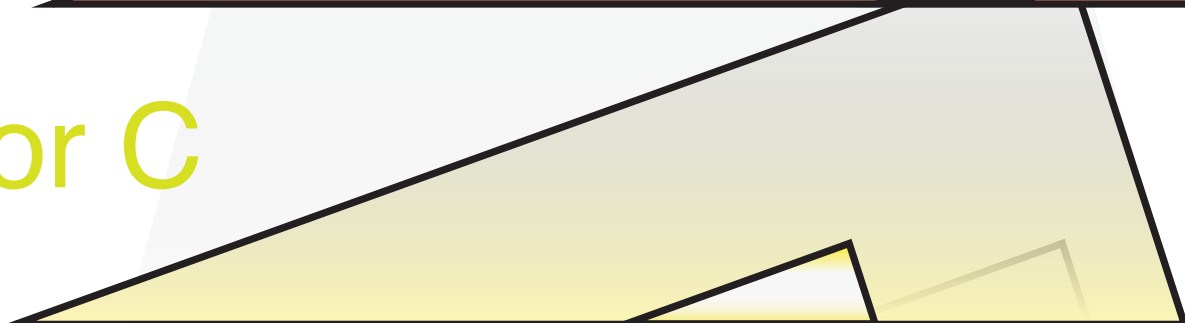
Factor A



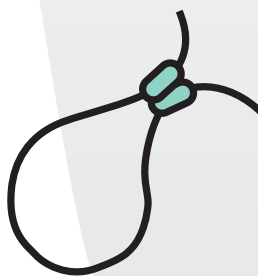
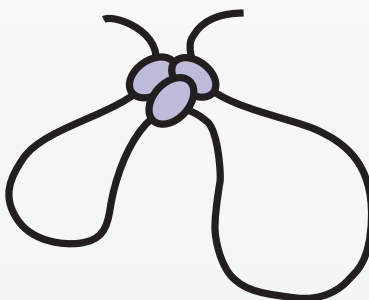
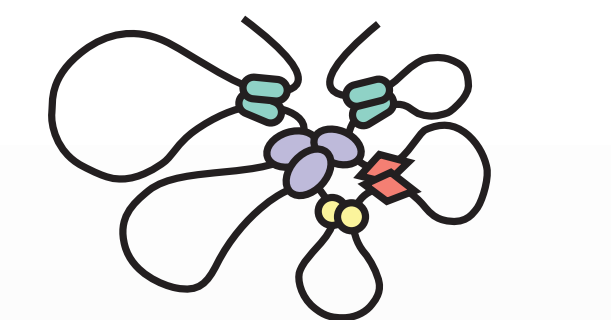
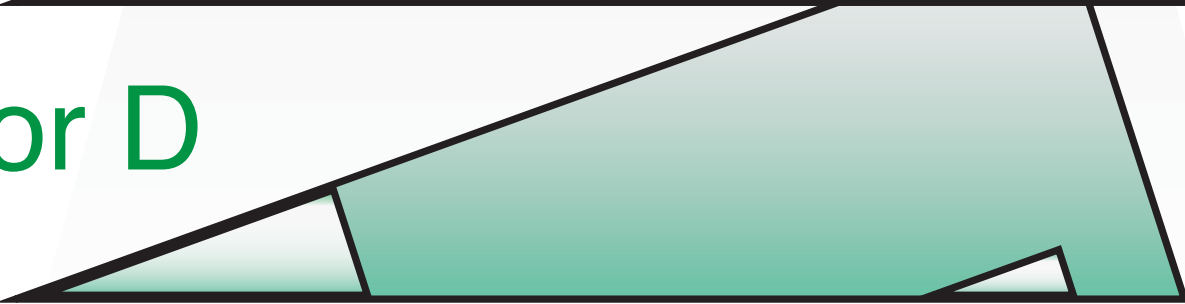
Factor B



Factor C



Factor D



<http://marciuslab.org>
<http://3DGenomes.org>

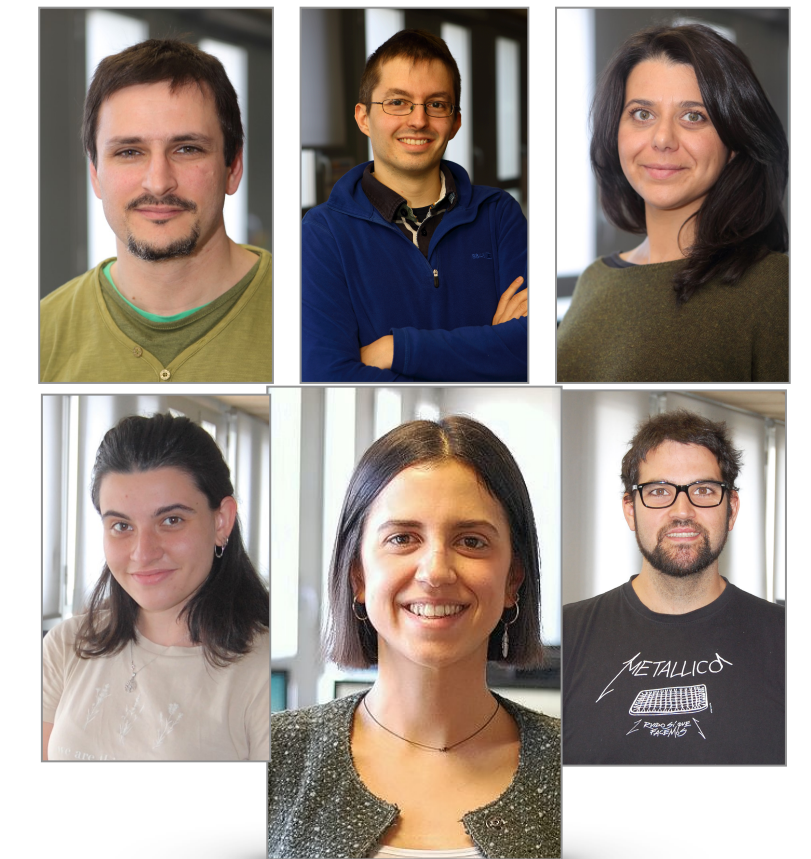
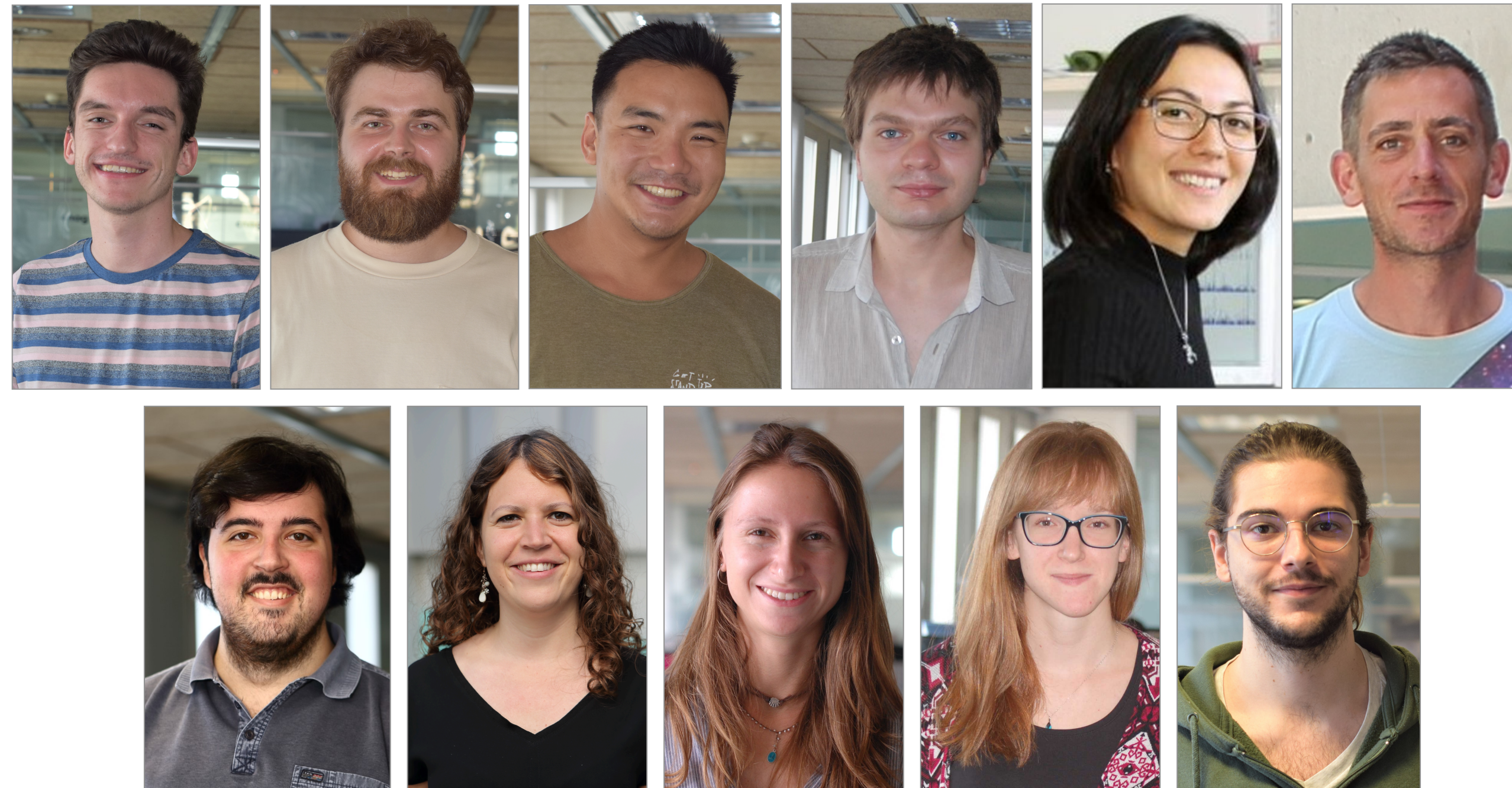
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.: Conflict of Interest Statement :.

Marc A. Marti-Renom serves as a consultant to Acuity Spatial Genomics, Inc., and receives compensation for these services.