

CHROMATIC reveals chromatinassociated factors contributing to genome topology

Marc A. Marti-Renom CNAG-CRG · ICREA

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



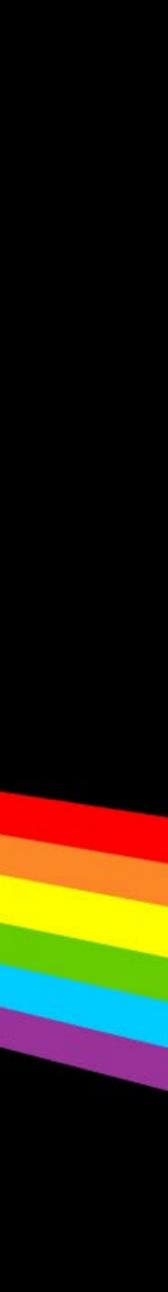




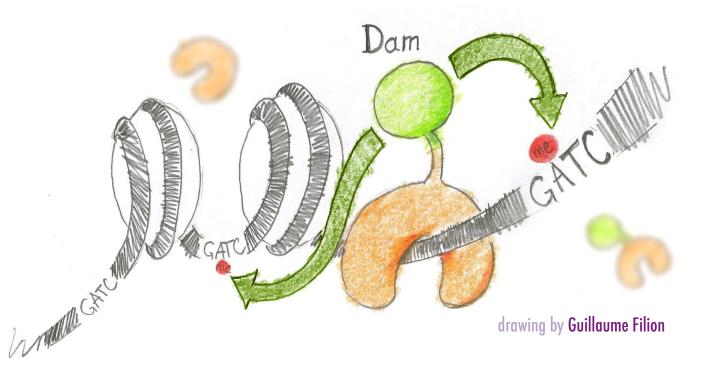
epigenome

gene expression

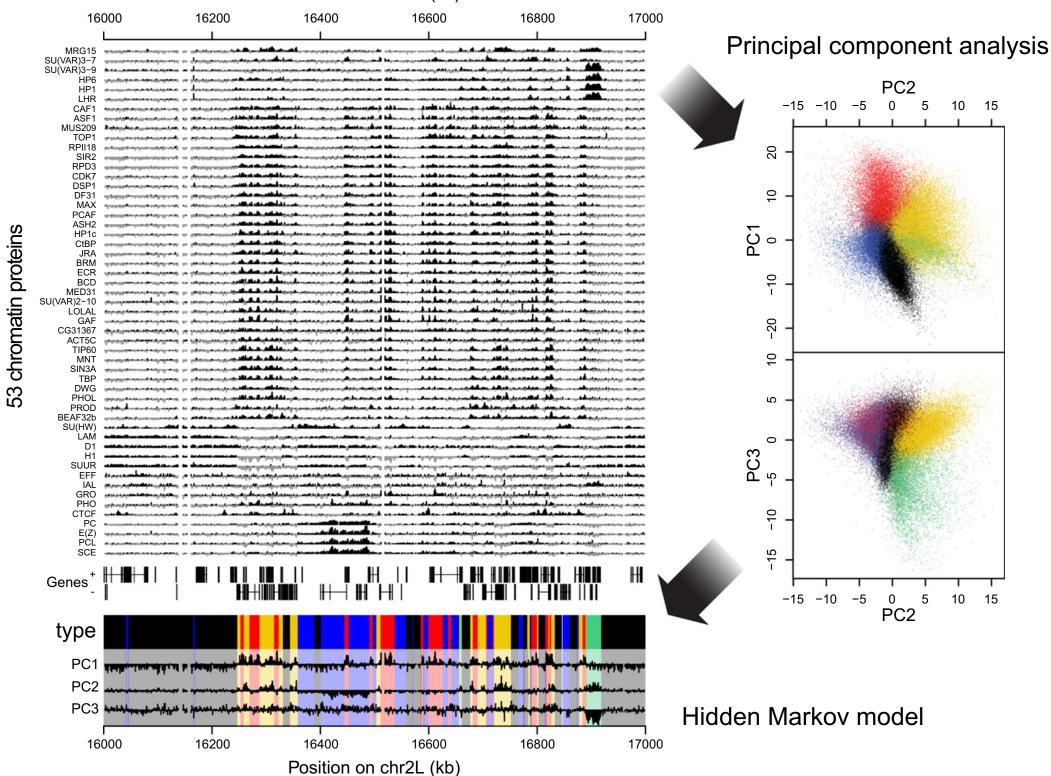


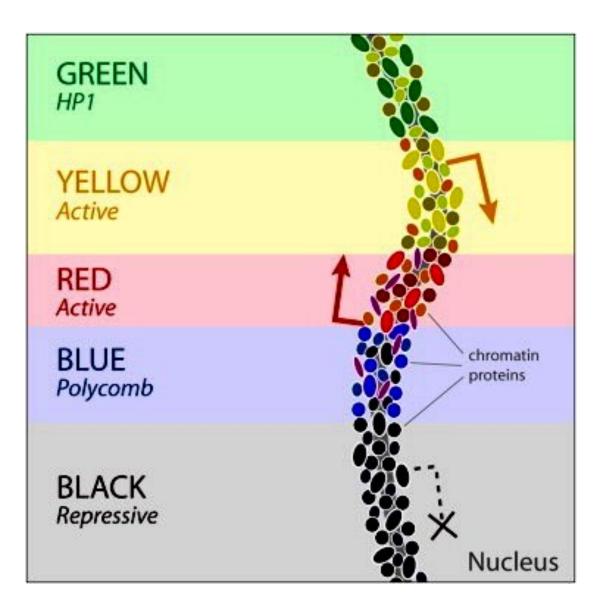


Fly Chromatin **COLORs** Filion et al. (2010). Cell, 143(2), 212–224.



Position on chr2L (kb)

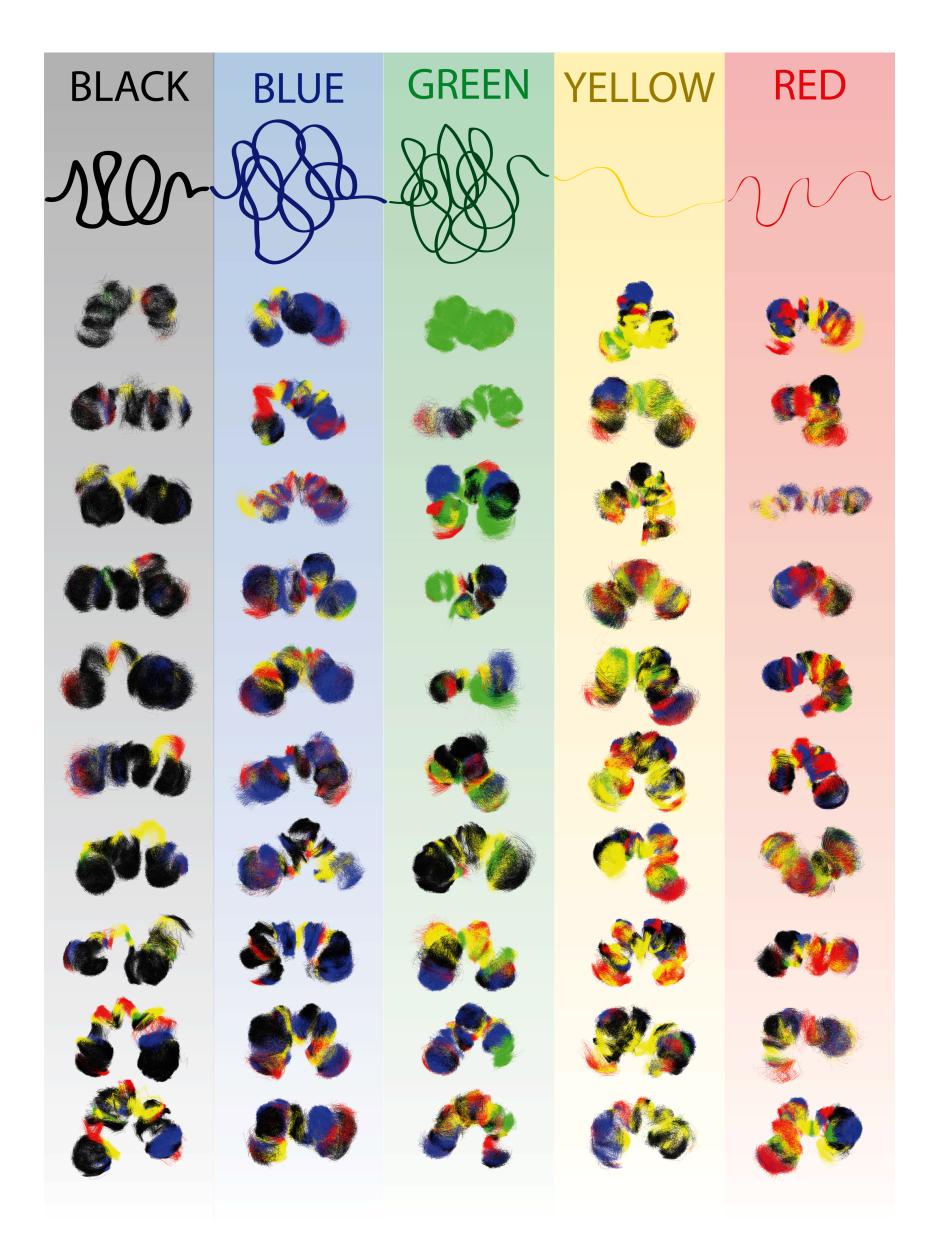




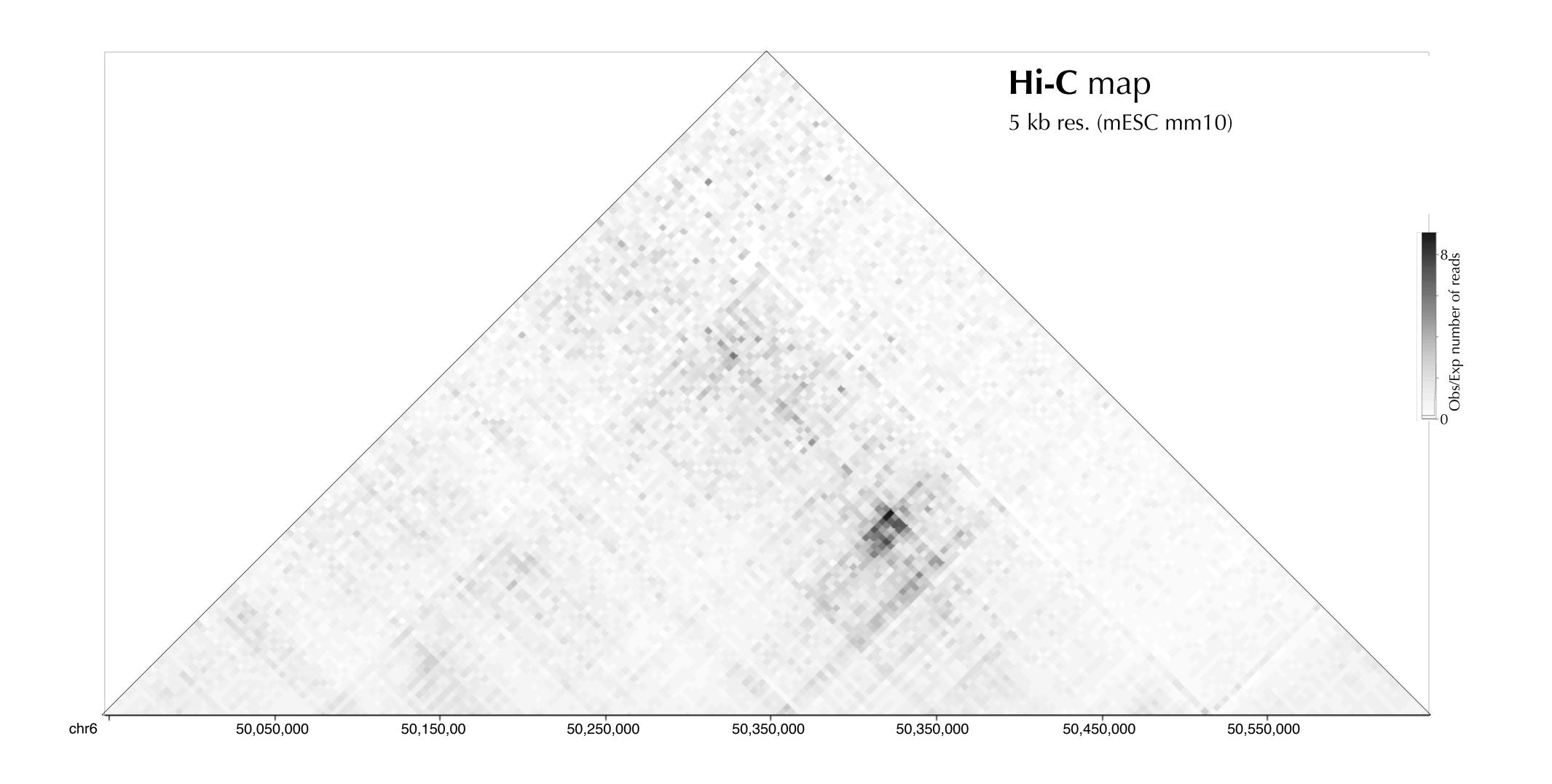
Who "holds" the genome structure? Serra et al. PLoS Comput Biol (2017) 13(7): e1005665

Position on chr2L (kb)

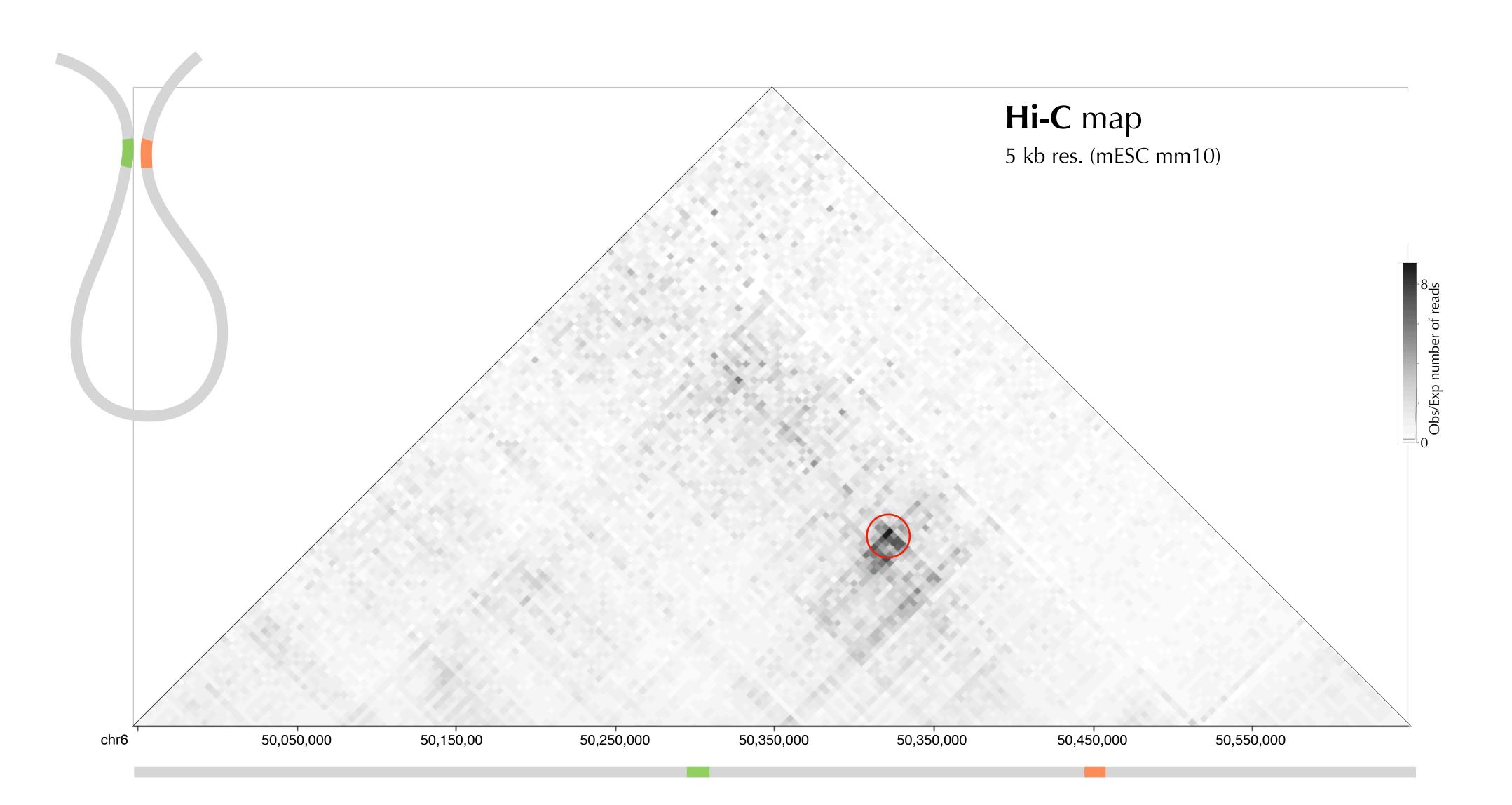
	16	000	16200	16400	16600	16800	1700
53 chromatin proteins	MRG15 SU(VAR)3-7 SU(VAR)3-9 HP6 HP1 LHR CAF1 ASF1 MUS209 TOP1 RPII18 SIR2 RPD3 CDK7 DSP1 DF31 MAX PCAF ASH2 HP1c CtBP JRA BRM ECR BCD MED31 SU(VAR)2-10 LOLAL GAF	3-7 3-9 IP6 IP1 HR AF1 SF1 209 P1 I18 R2 D3 ØK7 SP1 -31 AX AF H2 P16 BP RA RA RA RA RA CR CD 031 -10 AL					
	` LÓLAL	and a subsequence of the subsequ	a server and the serv	eren anter e e can discorre e dista est anter e e can distance e dista est anter e e can distance di tita est anter e e can distance di tita	anna - a dan dan gara ang dan sa	and a second sec	1,1,2,1,1,2,2,2,2,4,5 1,1,2,2,1,2,1,2,4,5 1,1,2,2,1,2,1,2,1,5 1,1,2,2,1,2,1,2,1,5 1,1,2,2,1,2,1,2,1,5 1,1,2,2,1,2,1,2,1,2,1,5 1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1
	ACT5C TIP60 MNT SIN3A TBP			مالها المحمود معطى معروب مربعاً مع مالها أمريك ومحمد في معروب محمد ماري مالها أمريك ومحمد في معروب محمد ماري		مر المعرب بي من	nynyy athatayn: Aynyy athatayn: Aynyy athatayyn
	DWG PHOL PROD BEAF32b SU(HW)	undysensessessessesses y spectral topdate	·	and a second secon	and a second s The second se The second se		anan ananan Manan ananan Manan Ananan
	LAM D1 H1 SUUR EFF						
	IAL GRO PHO CTCF PC E(Z)	garen angelen a angelen angelen angelen angelen angelen angelen angelen angelen	a server provide a server and a server a ser	an andre beretar beretar andre andre andre andre beretar beret	1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 1999 - 19		na na antonia (na na na antonia (na
	PCL SCE		 A construction of the second seco	and the second s			any destant

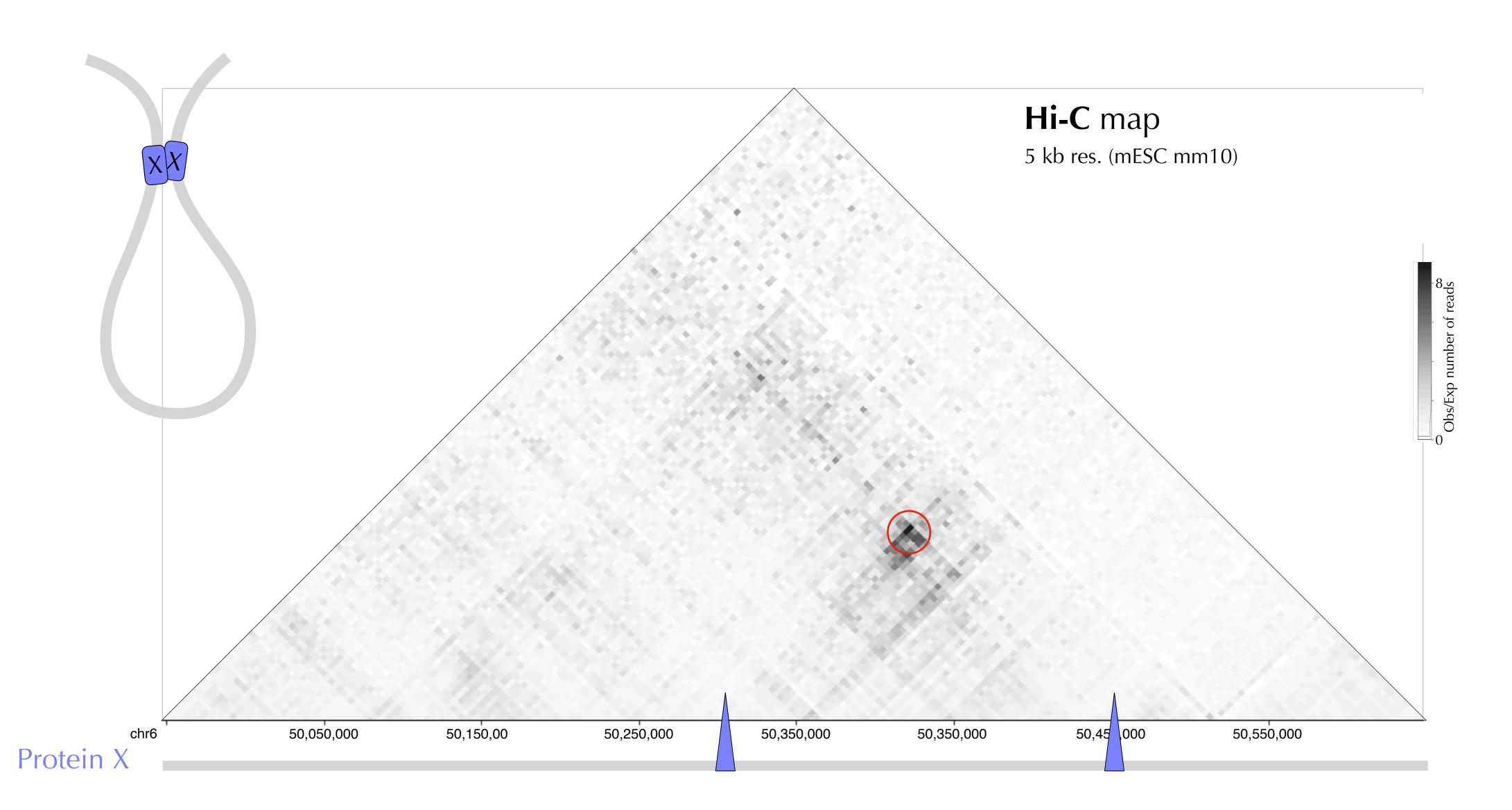


High-throughput Chromosome Conformation Capture (Hi-C)



Chromatin interaction on a Hi-C map

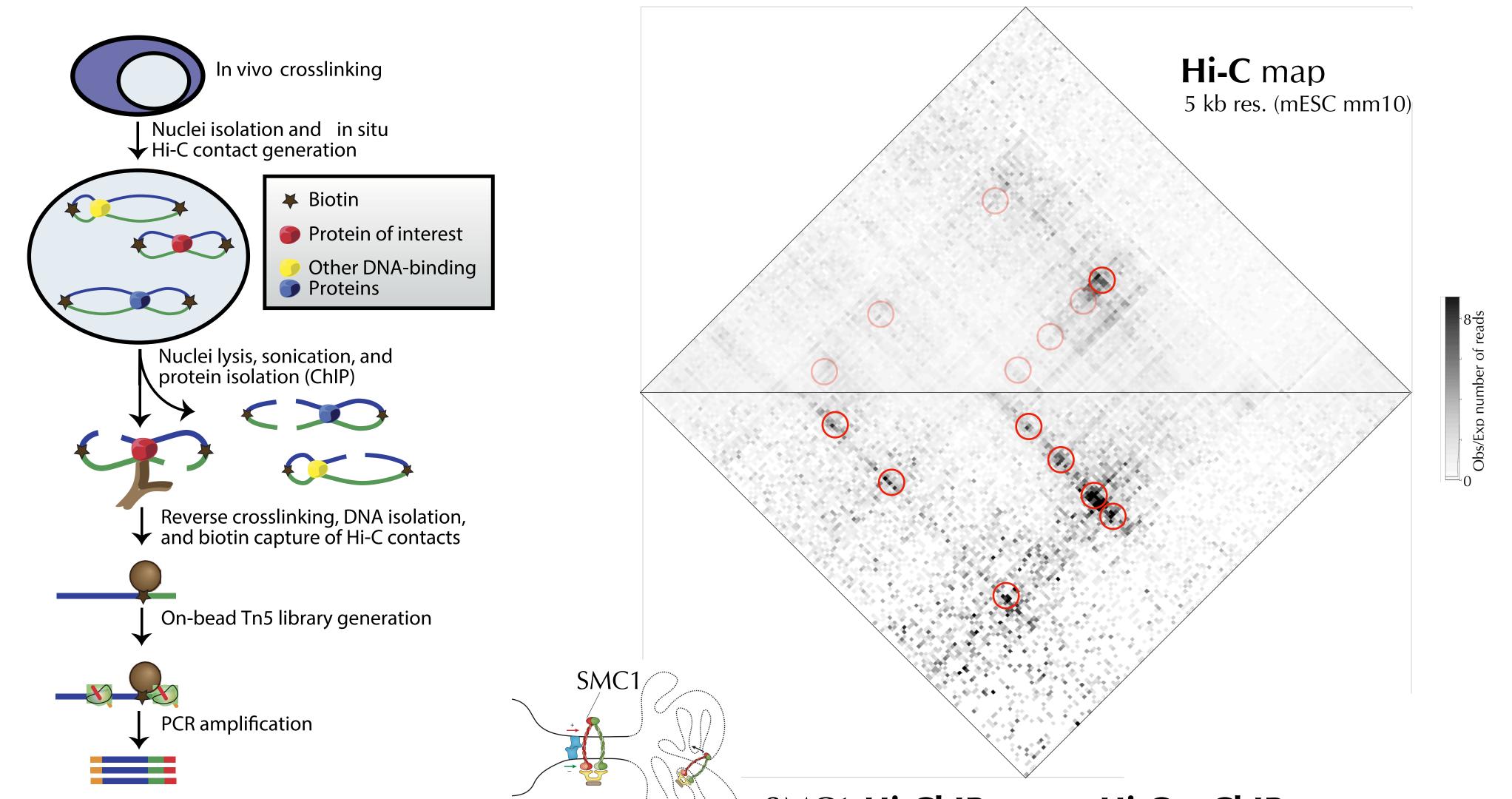




Chromatin interaction "mediated" by a protein

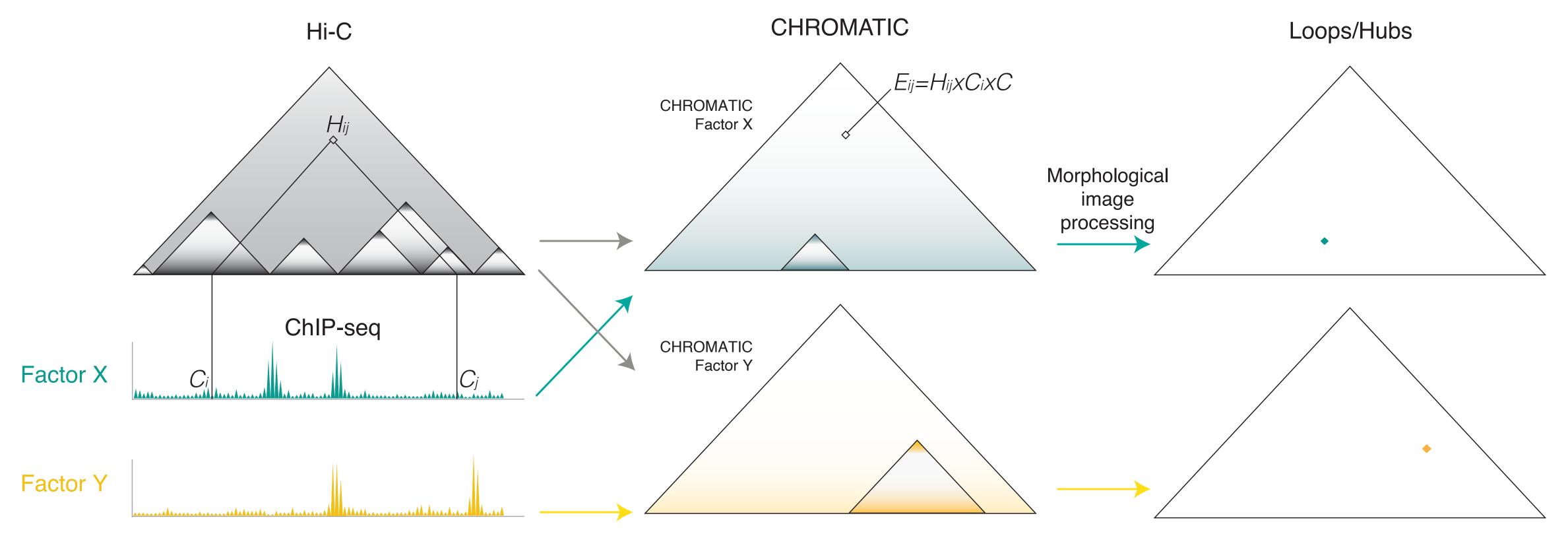
Hi-ChIP: capturing specific protein-mediated interactions

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



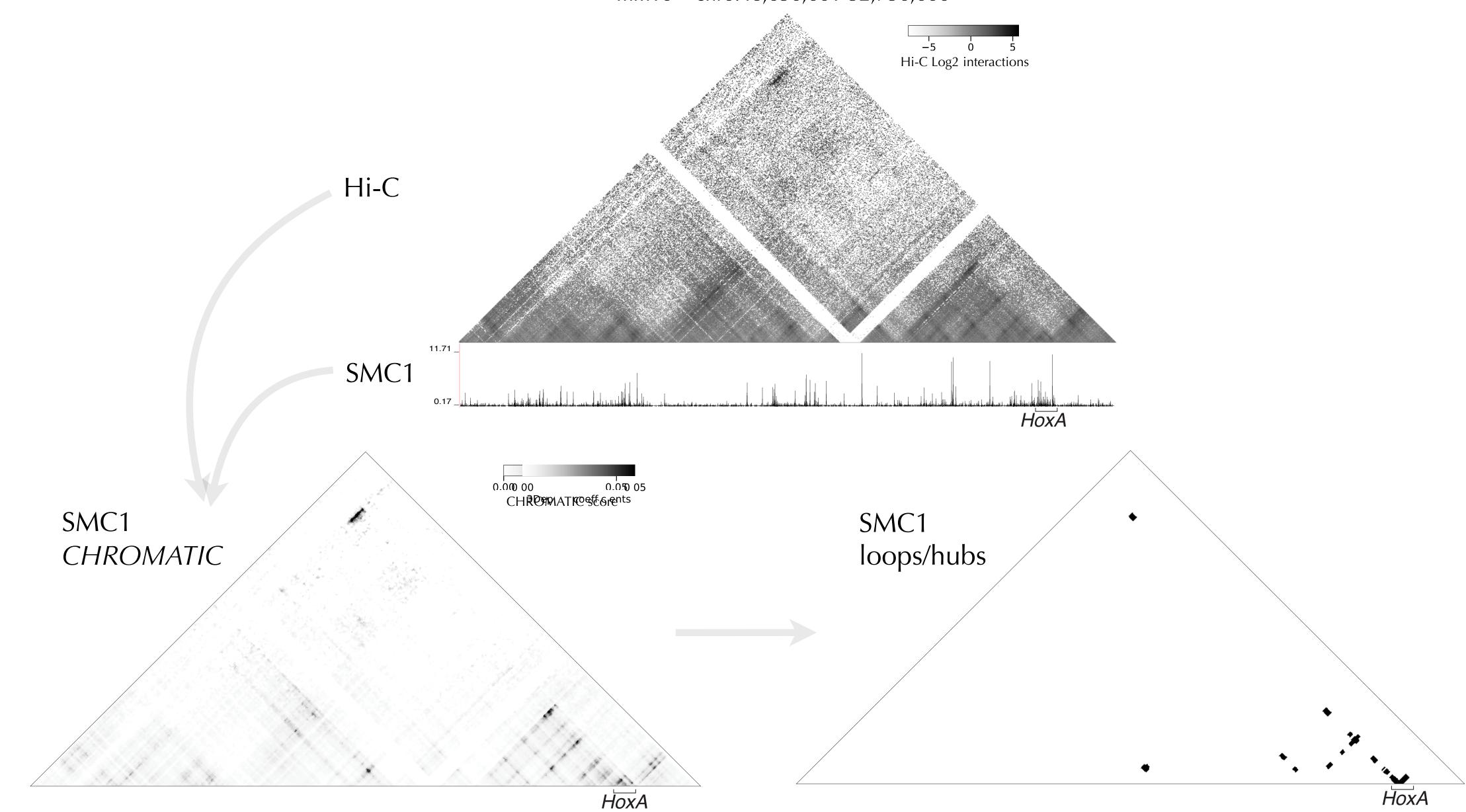
SMC1 Hi-ChIP map = Hi-C + ChIP

5 kb res. (mESC mm10)



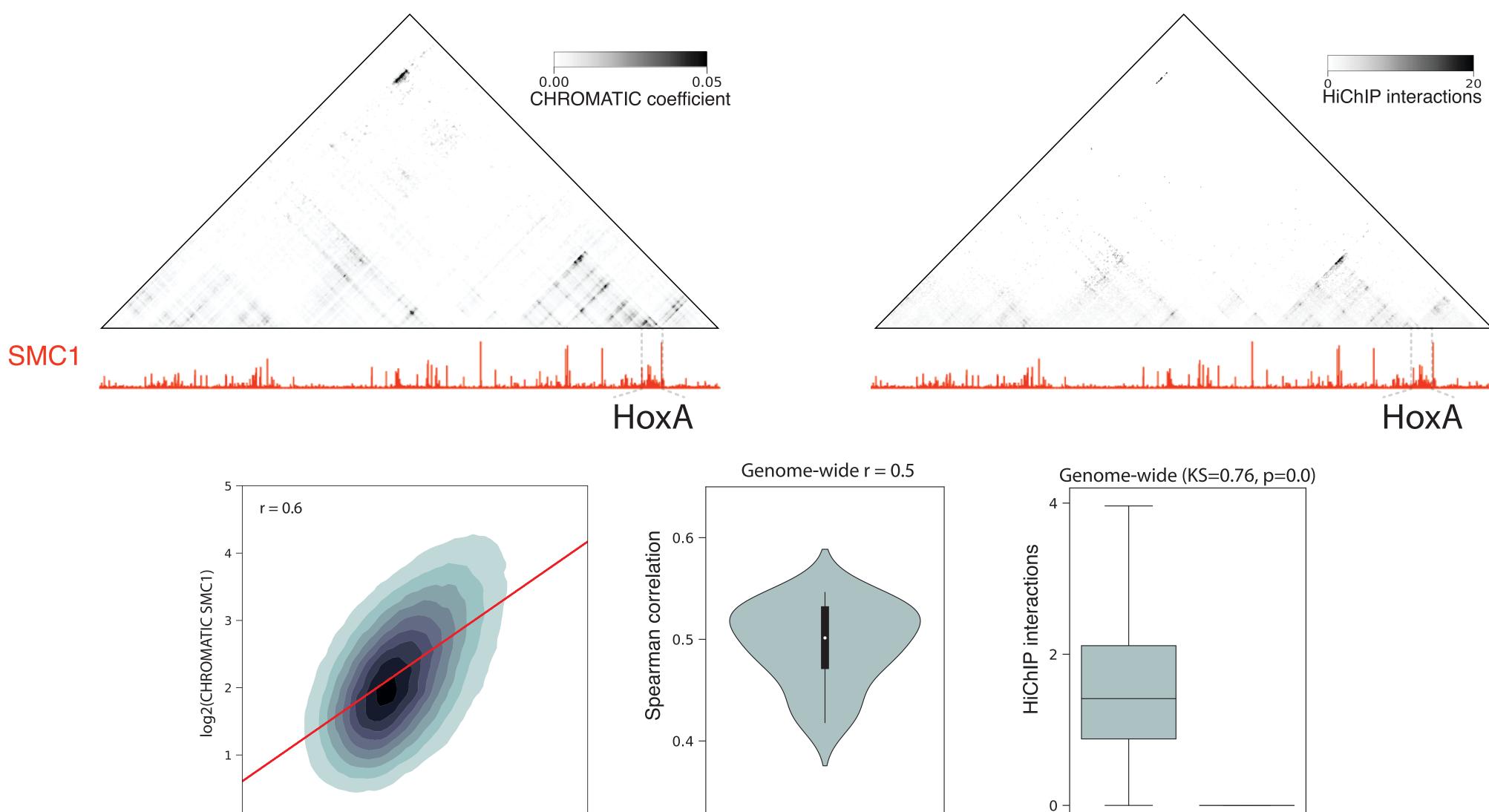
CHROMATIC

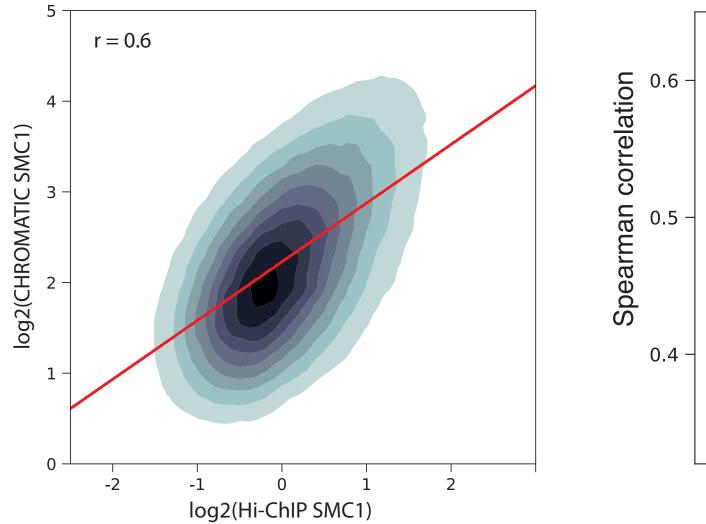




CHROMATIC example

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





Validation with HiChIP as benchmark

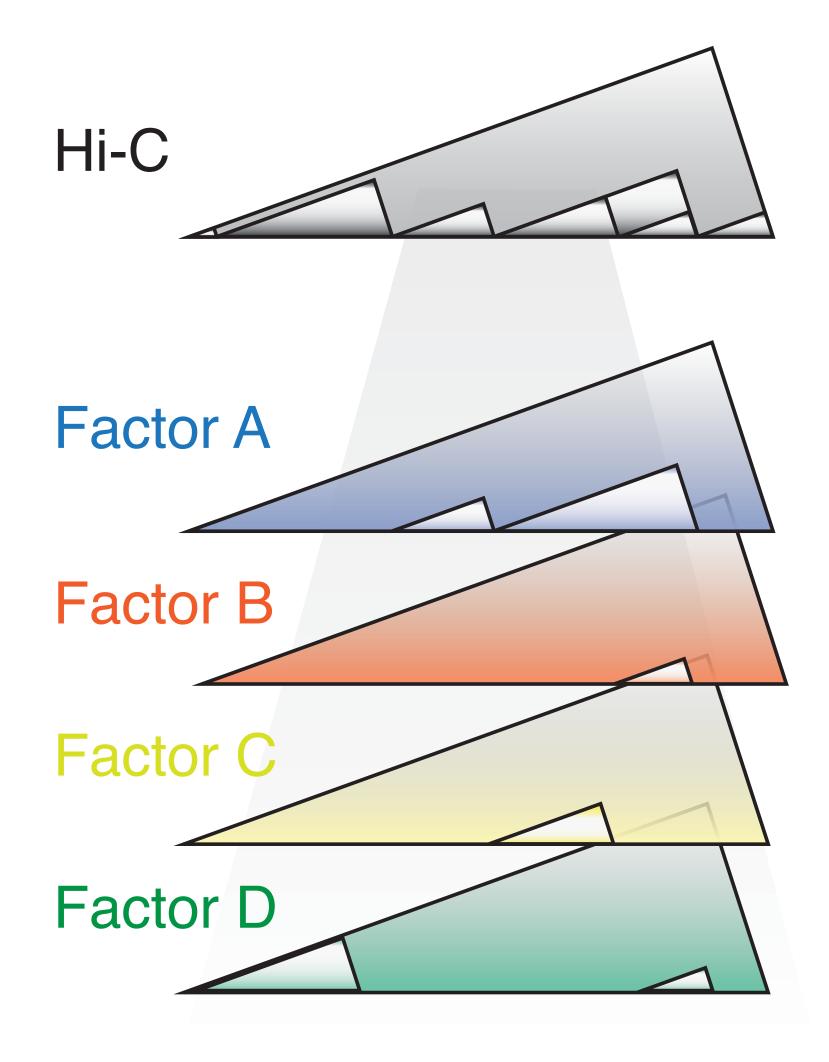
mm10 - mESC - 5kb - chr6:48,050,001-52,750,006

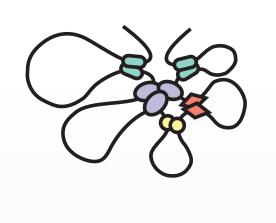
Per chromosome

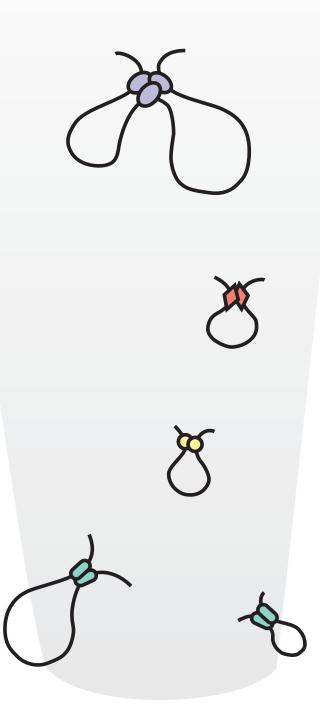
Loops/Hubs

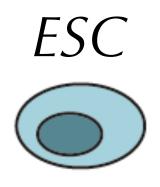
Rest

The role of chromatin factors in genome topology

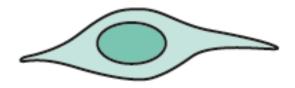


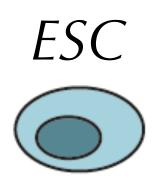


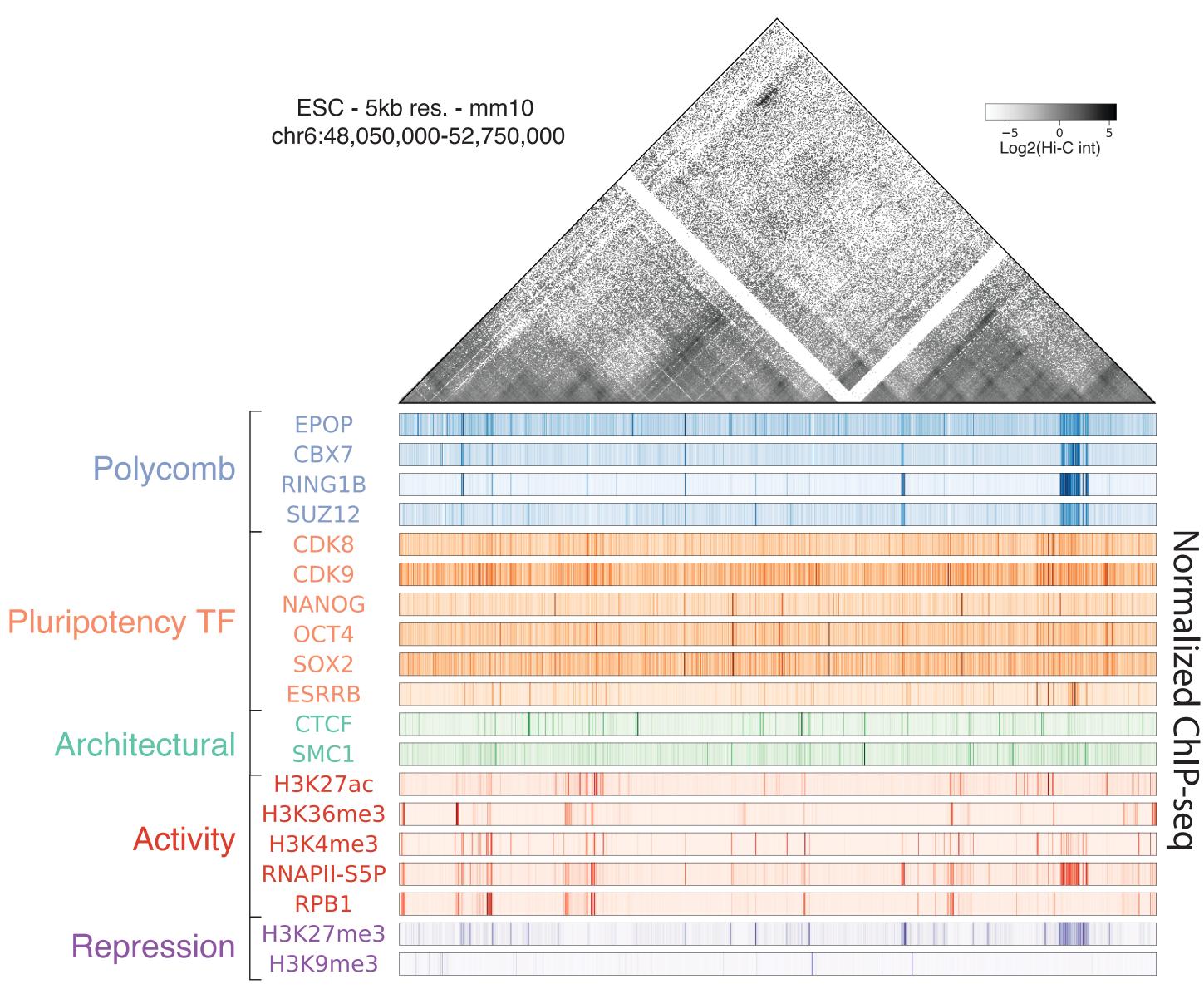








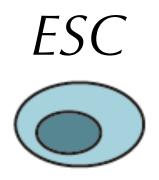


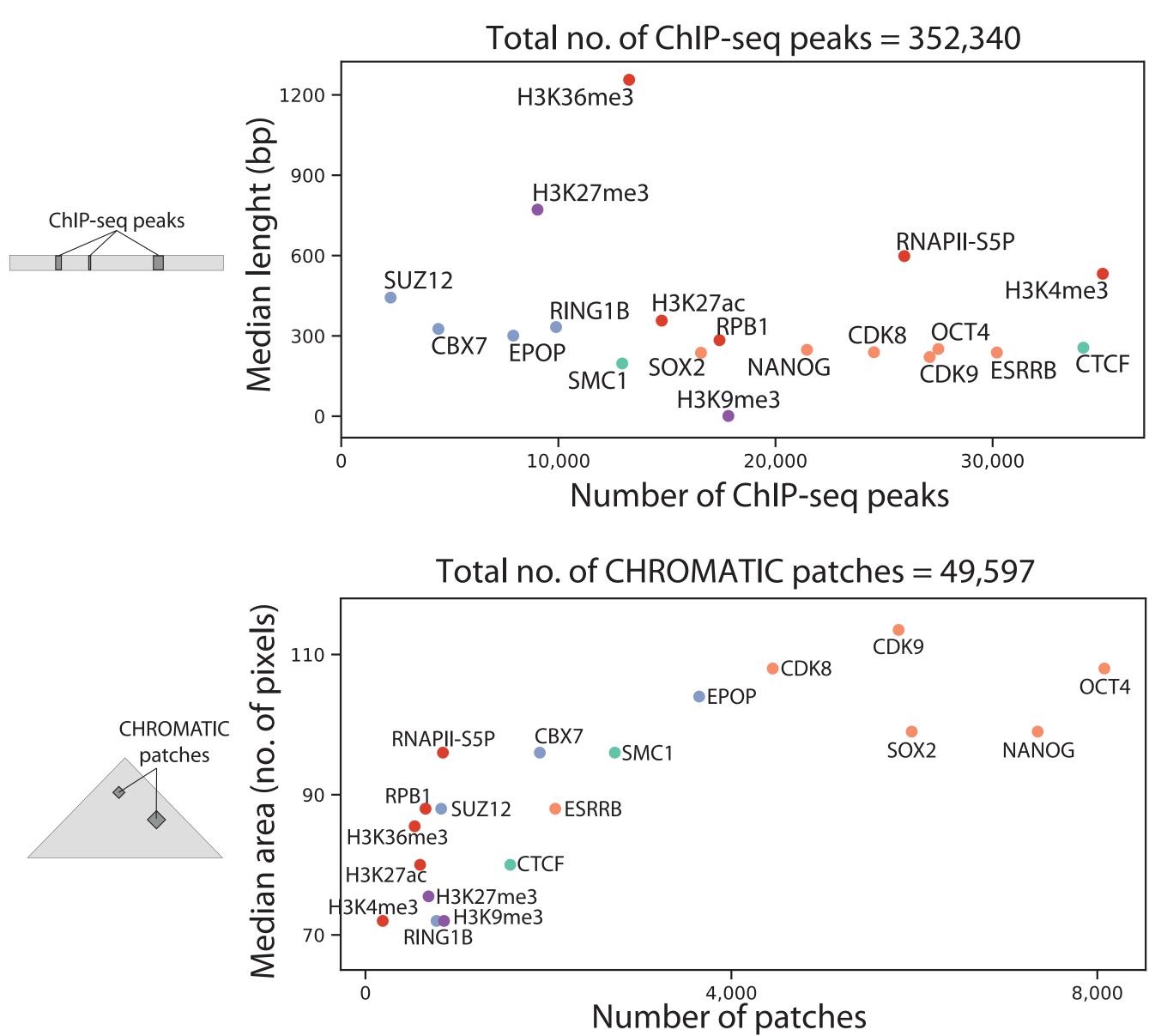


HoxA cluster (example in ESC)

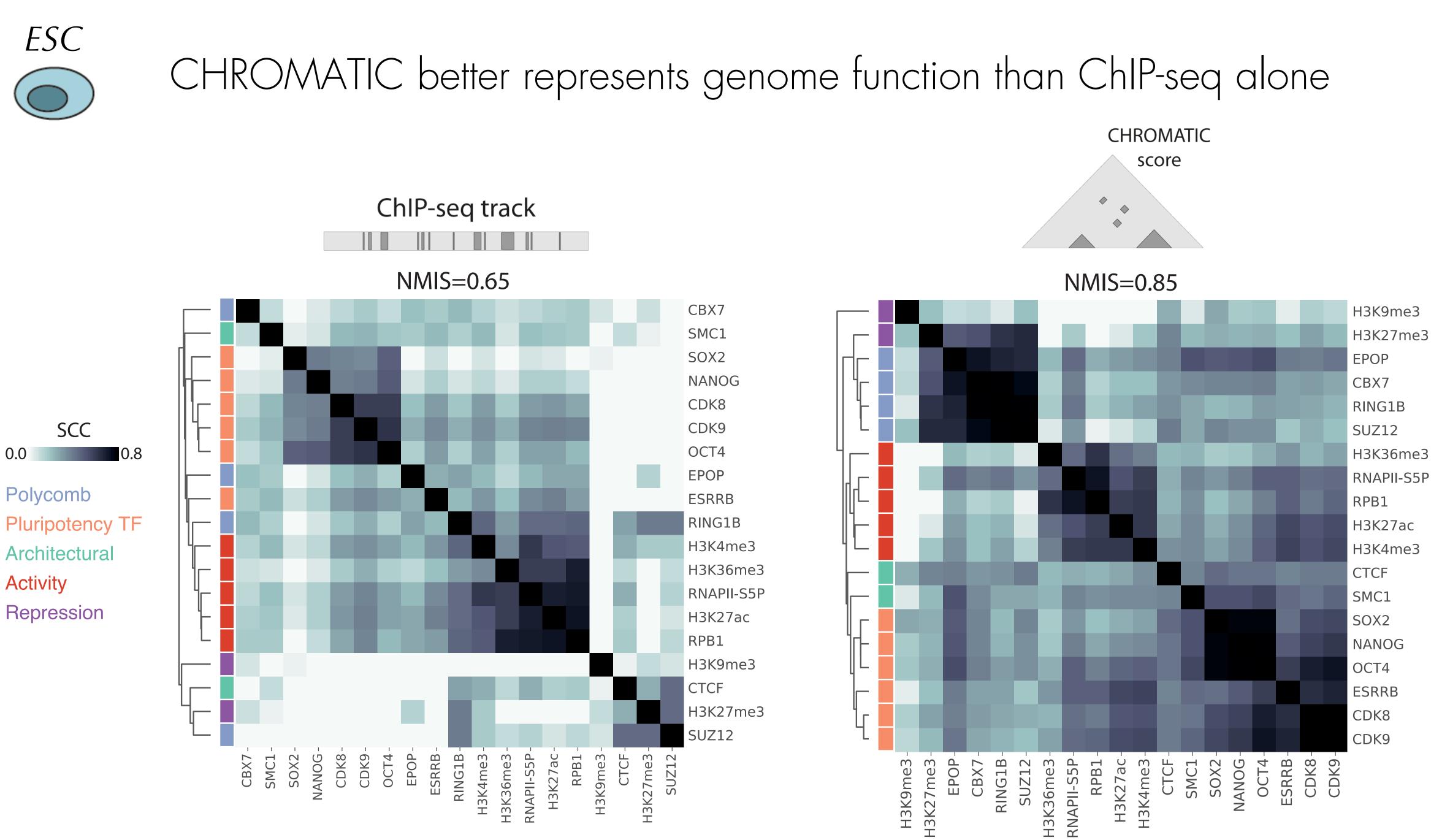
HoxA

3D interactions are mostly associated with pluripotent TFs

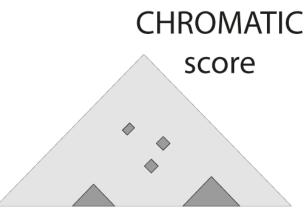


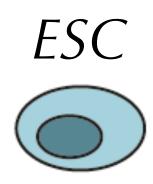


Polycomb **Pluripotency TF** Architectural Activity Repression



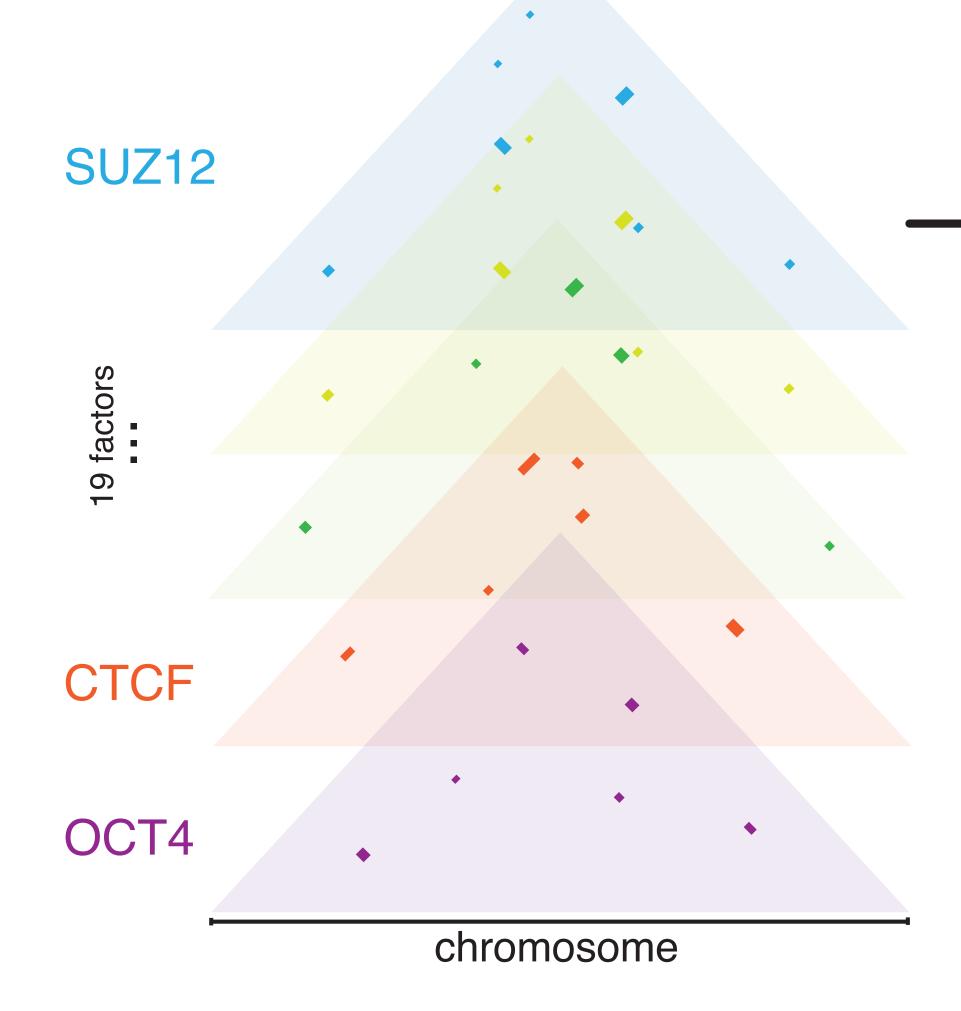




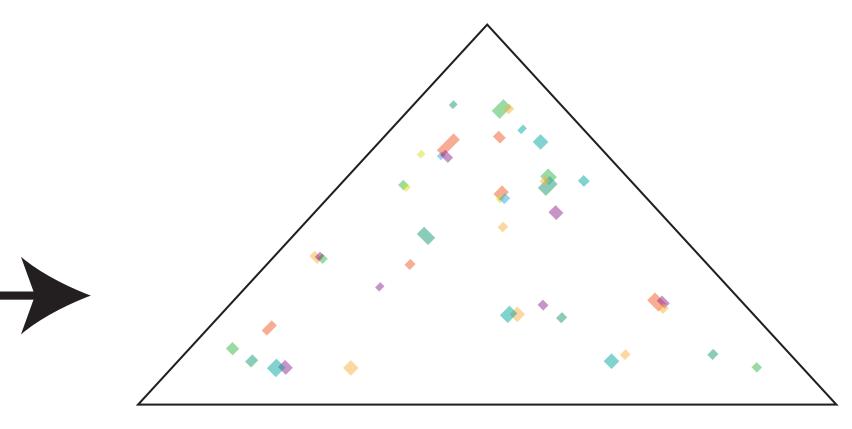


Measure the 3D co-localization of factors

CHROMATIC interactions



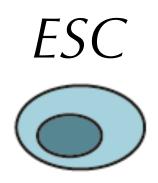
Overlap (19 factors)



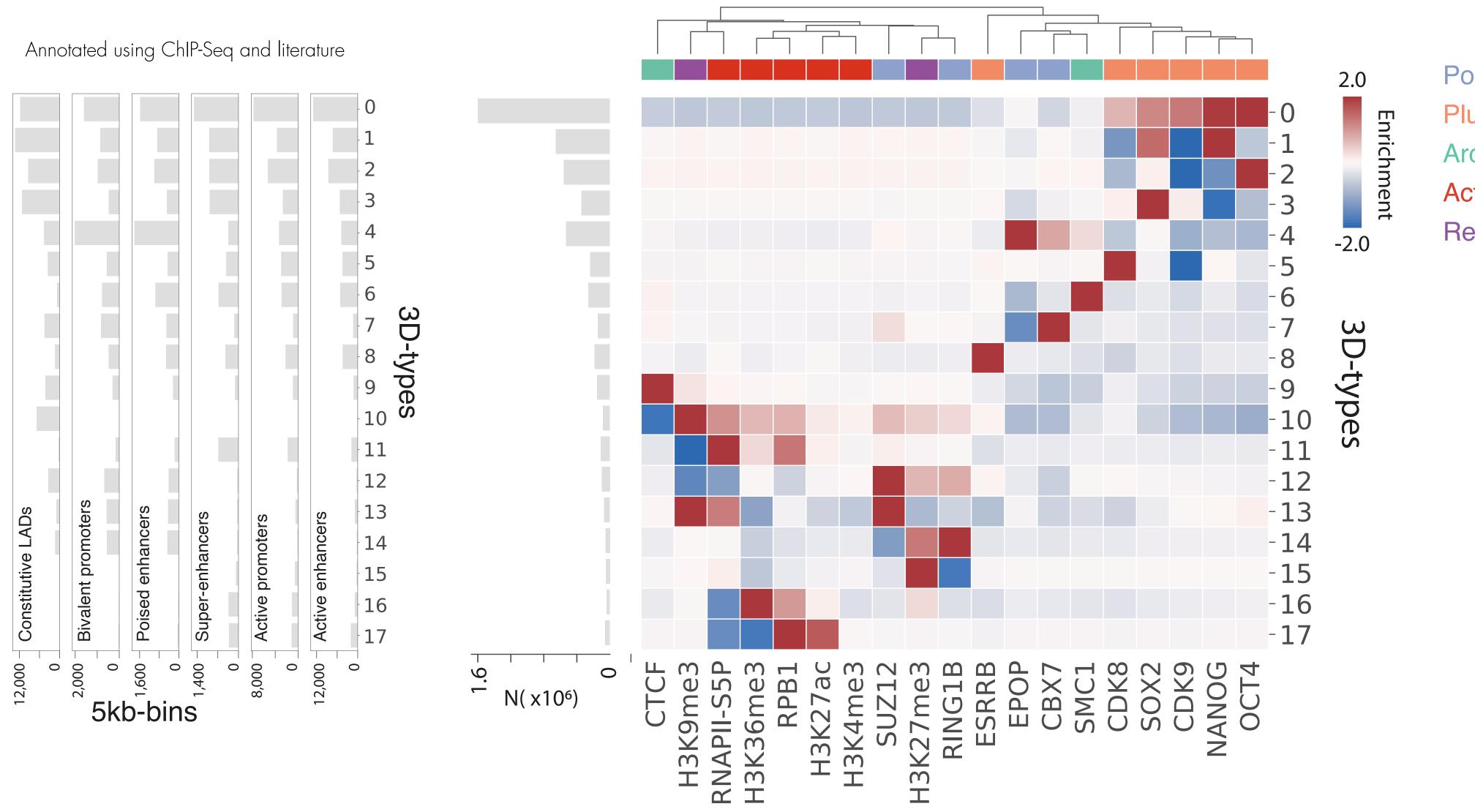


Latent Semantic Analysis

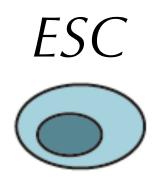
- - -



Types of 3D interactions with LSA in ESC

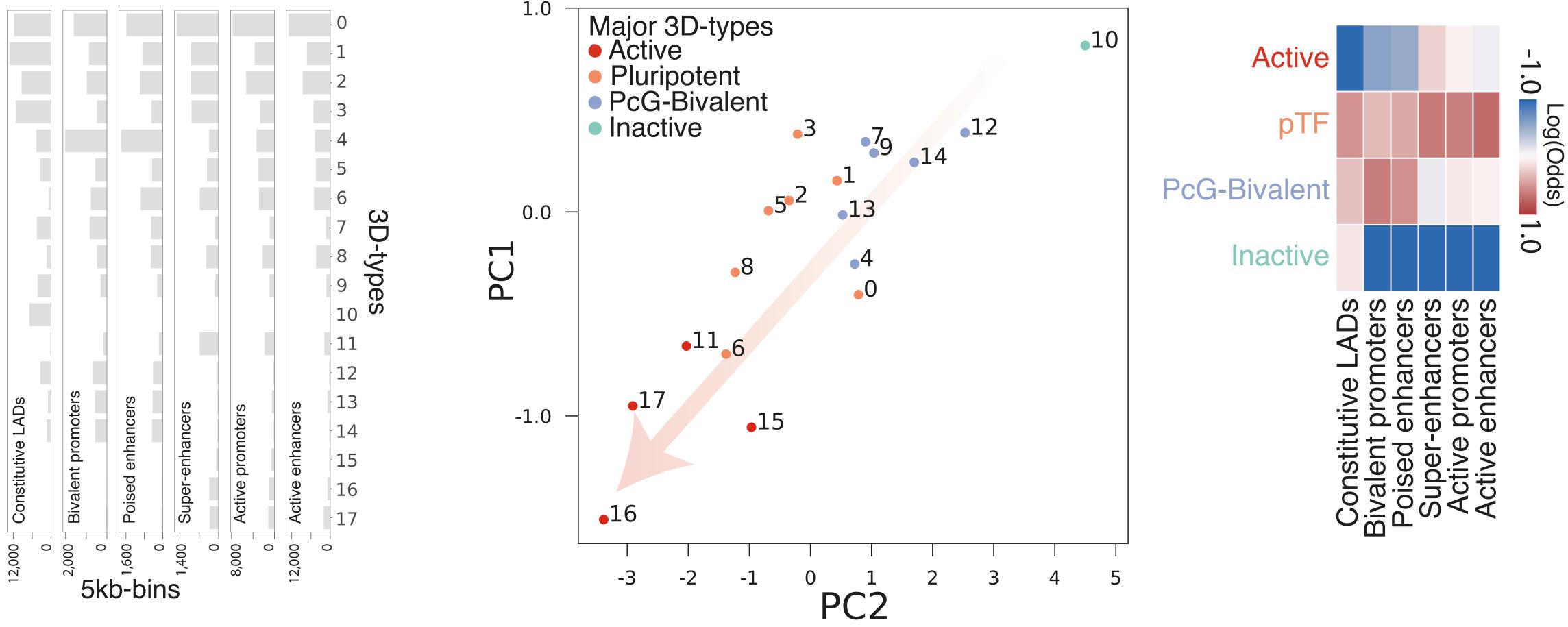


Polycomb Pluripotency TF Architectural Activity Repression

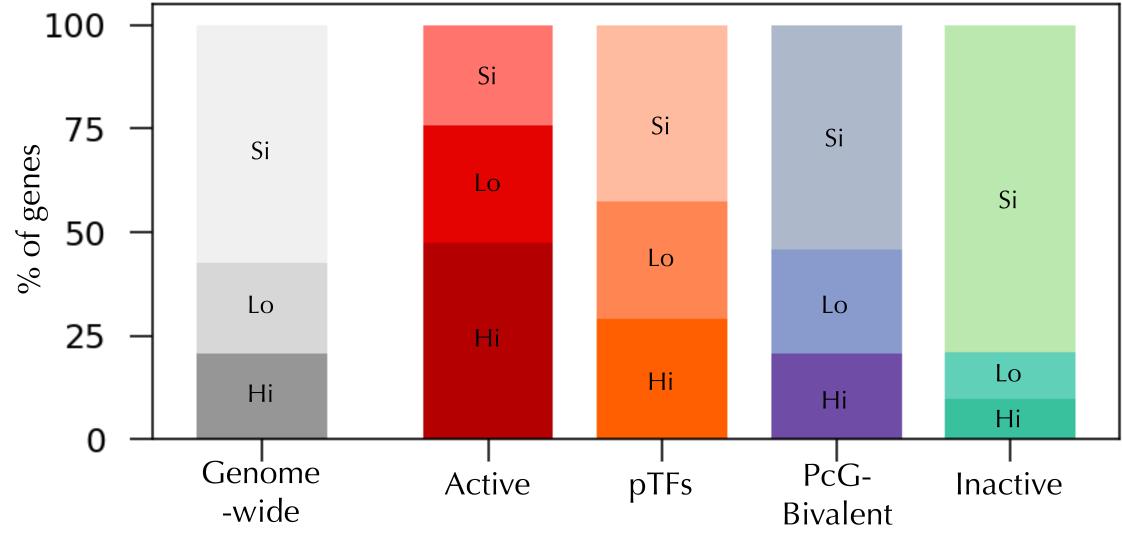


Types of 3D interactions with LSA in ESC

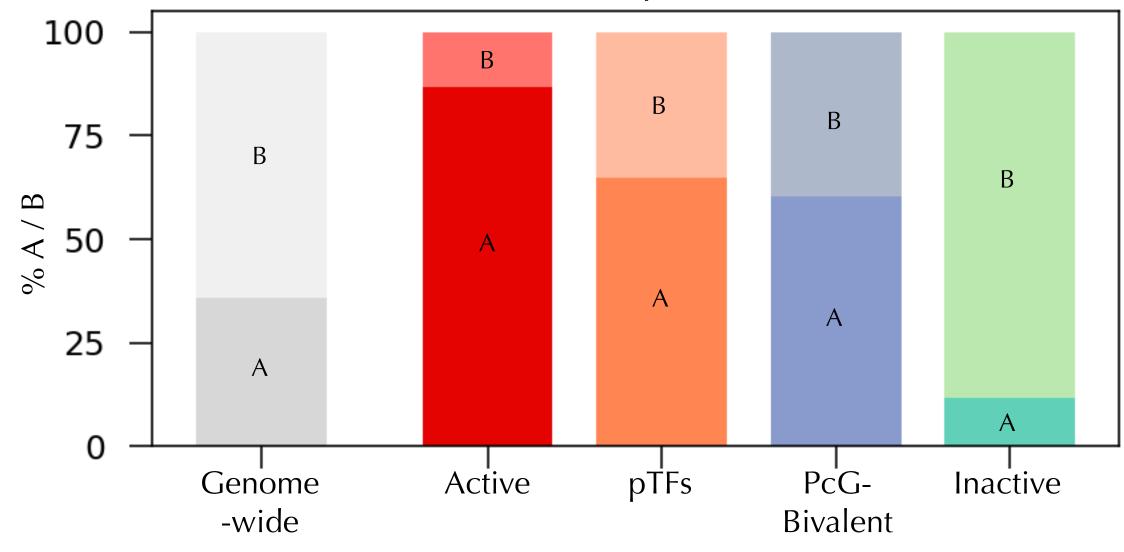
Annotated using ChIP-Seq and literature

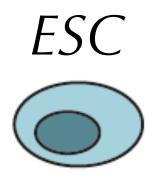


4 major types of 3D interactions in ESC





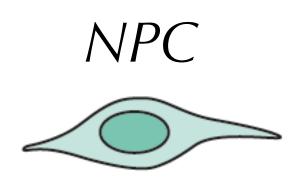


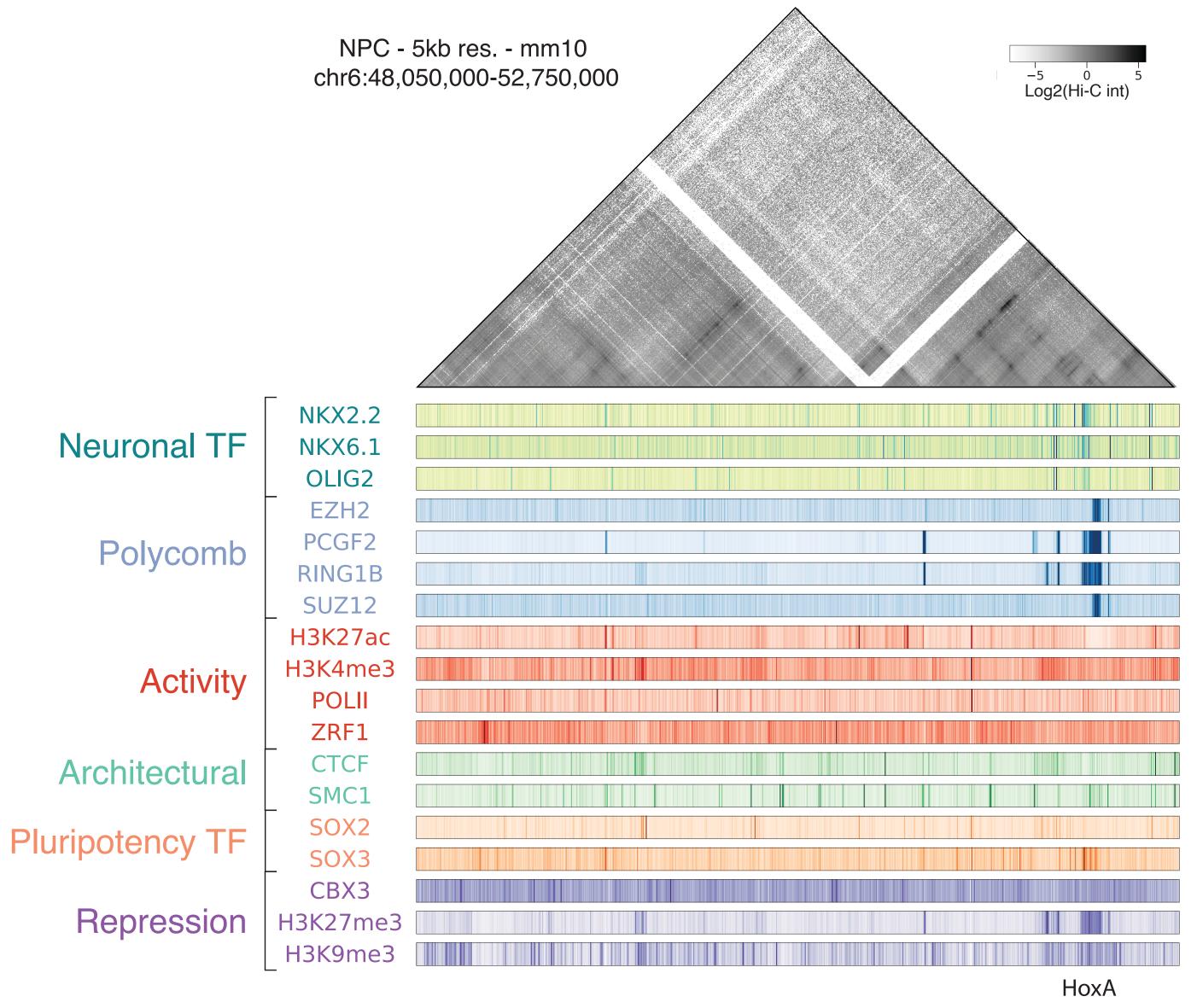


Higly-, Lowly-expressed and Silent genes

Silent RPKM<1 1<RPKM<10 Low High RPKM>10

A and B compartments





HoxA cluster (example in NPC)

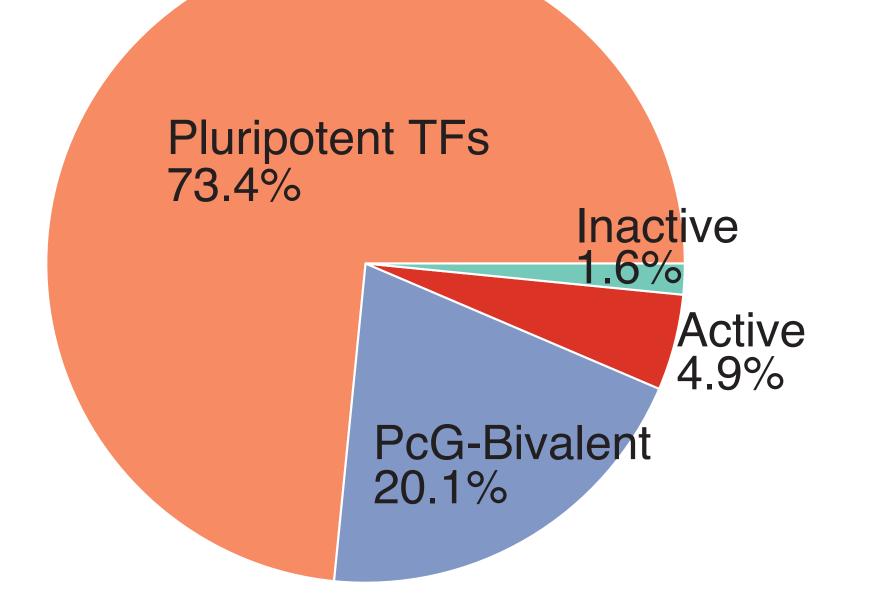
Normalized

ChIP-seq

Global 3D interactions rewiring during mouse development

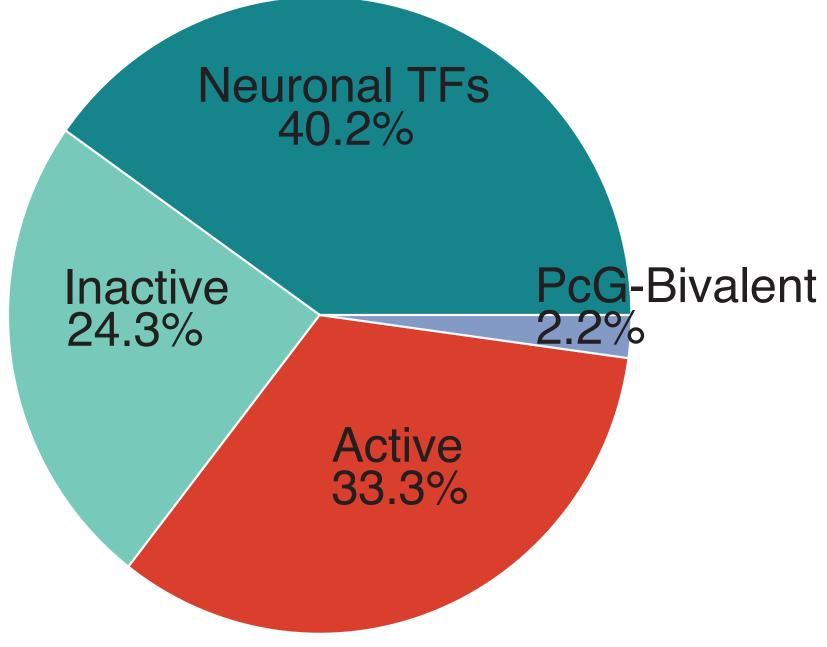


Total 5kbx5kb pixels = 5,216,011 (0.07%)

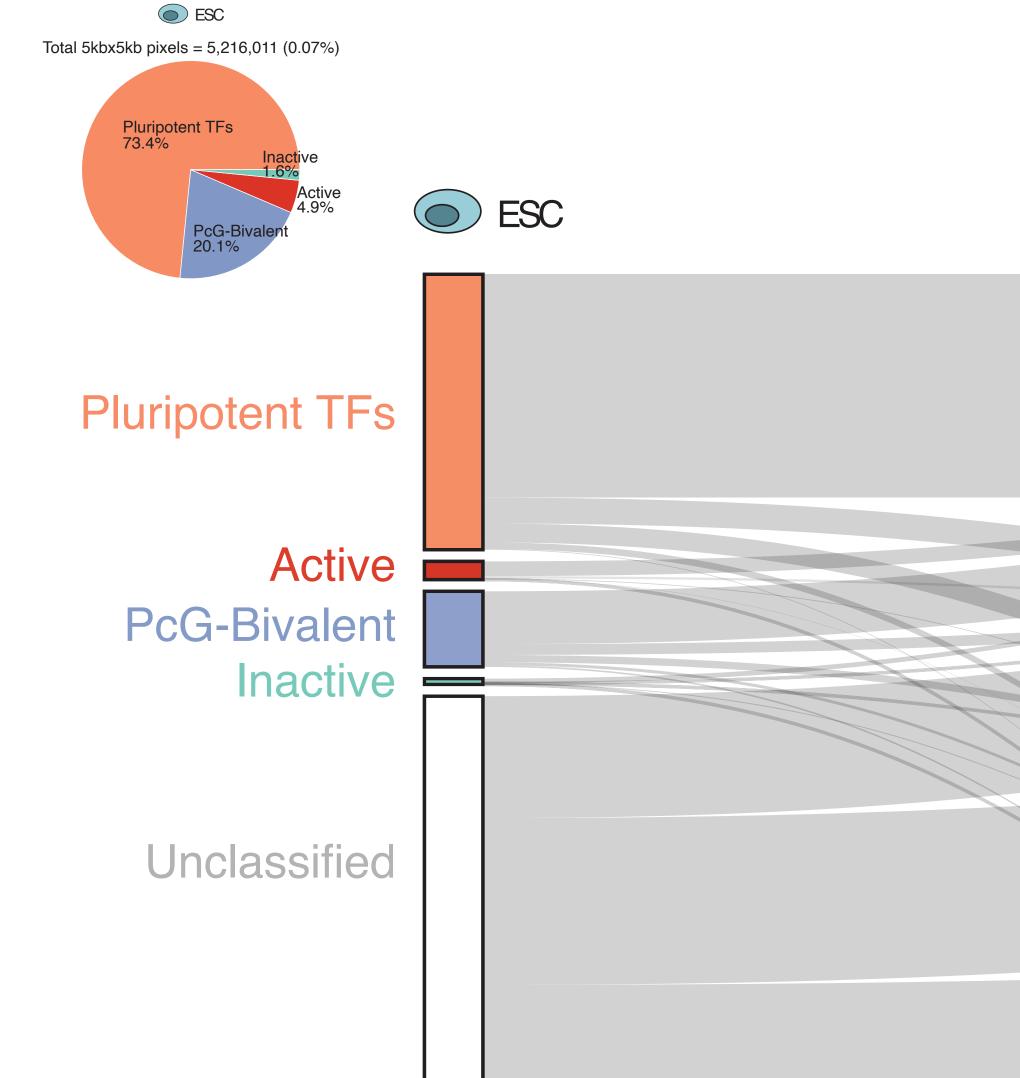




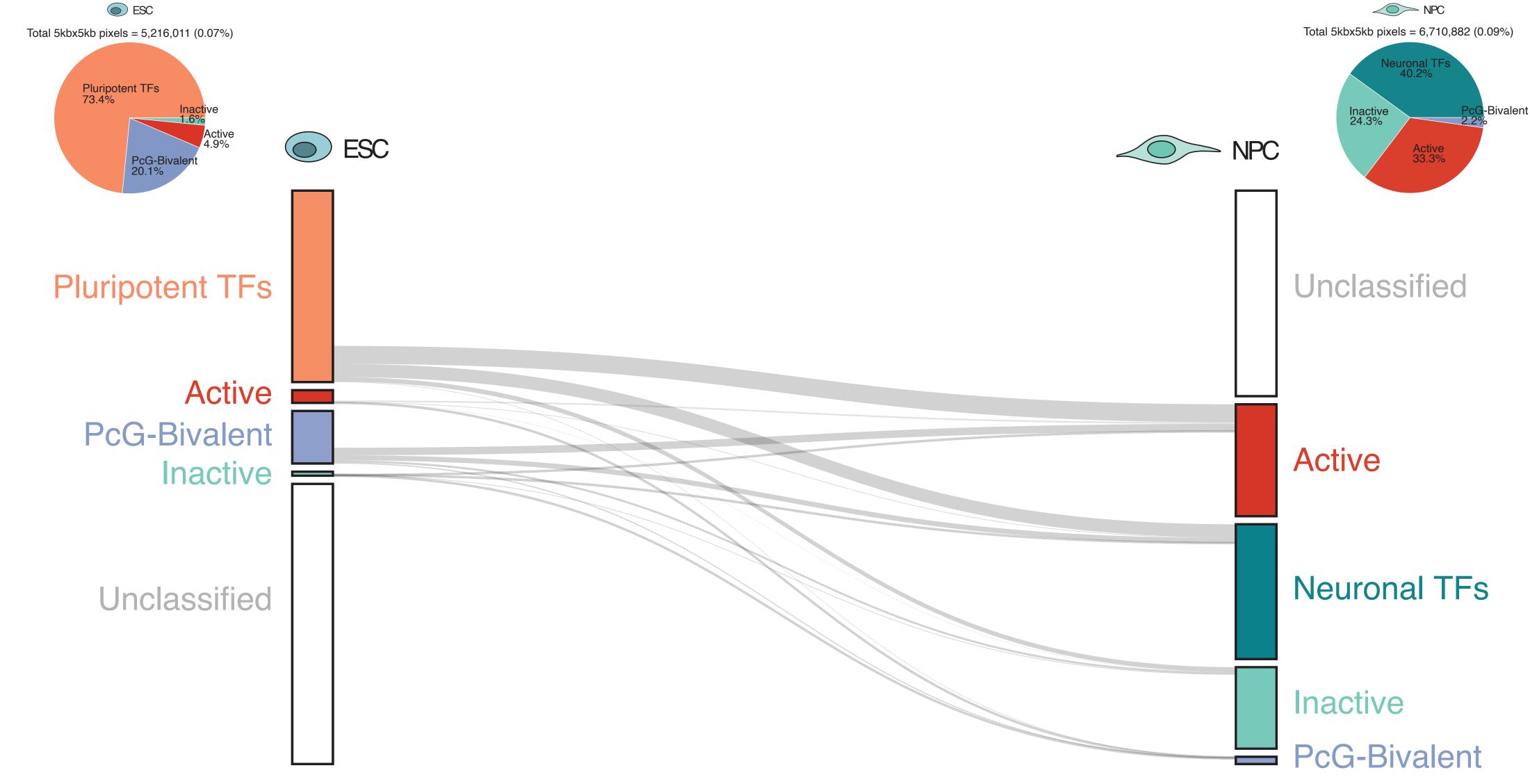
Total 5kbx5kb pixels = 6,710,882 (0.09%)



Global 3D interactions rewiring during mouse development (ESC Total 5kbx5kb pixels = 6,710,882 (0.09%) Total 5kbx5kb pixels = 5,216,011 (0.07%) leuronal Tl 40.2% Pluripotent TFs 73.4% Inactive 24.3% Bivalent Active ESC NPC Active 33.3% PcG-Biva 20.1% **Pluripotent TFs** Unclassified Active **PcG-Bivalent** Active Inactive Neuronal TFs Unclassified Inactive **PcG-Bivalent**

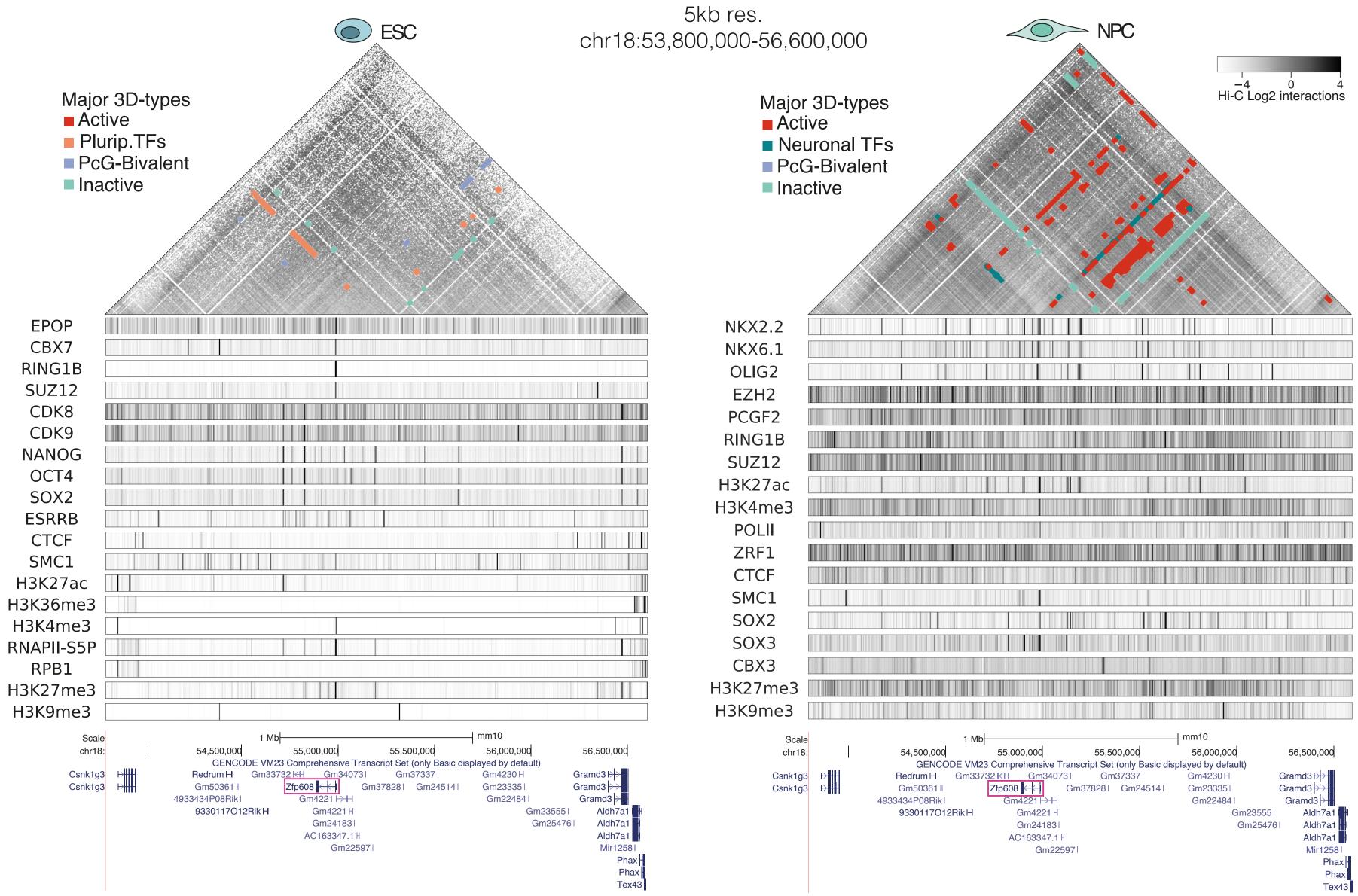


Global 3D interactions rewiring during mouse development

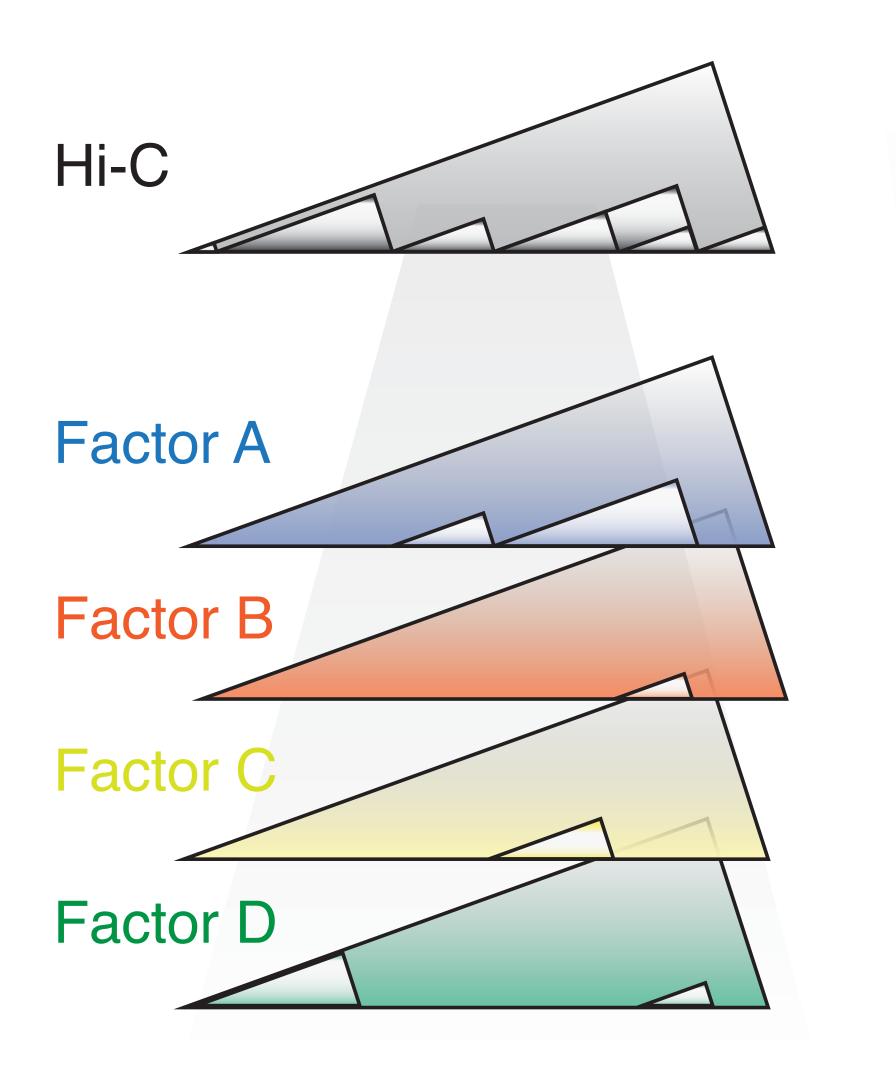


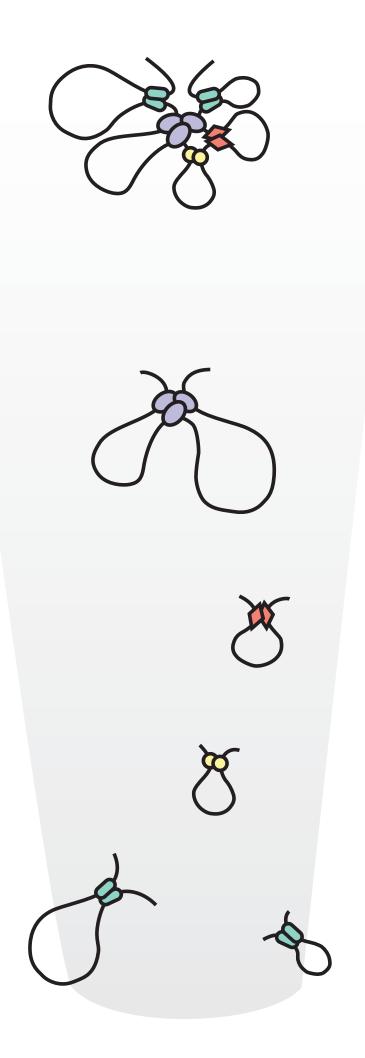
t

3D interactions rewiring at Zfp608 locus during mouse neural development



Take home message...

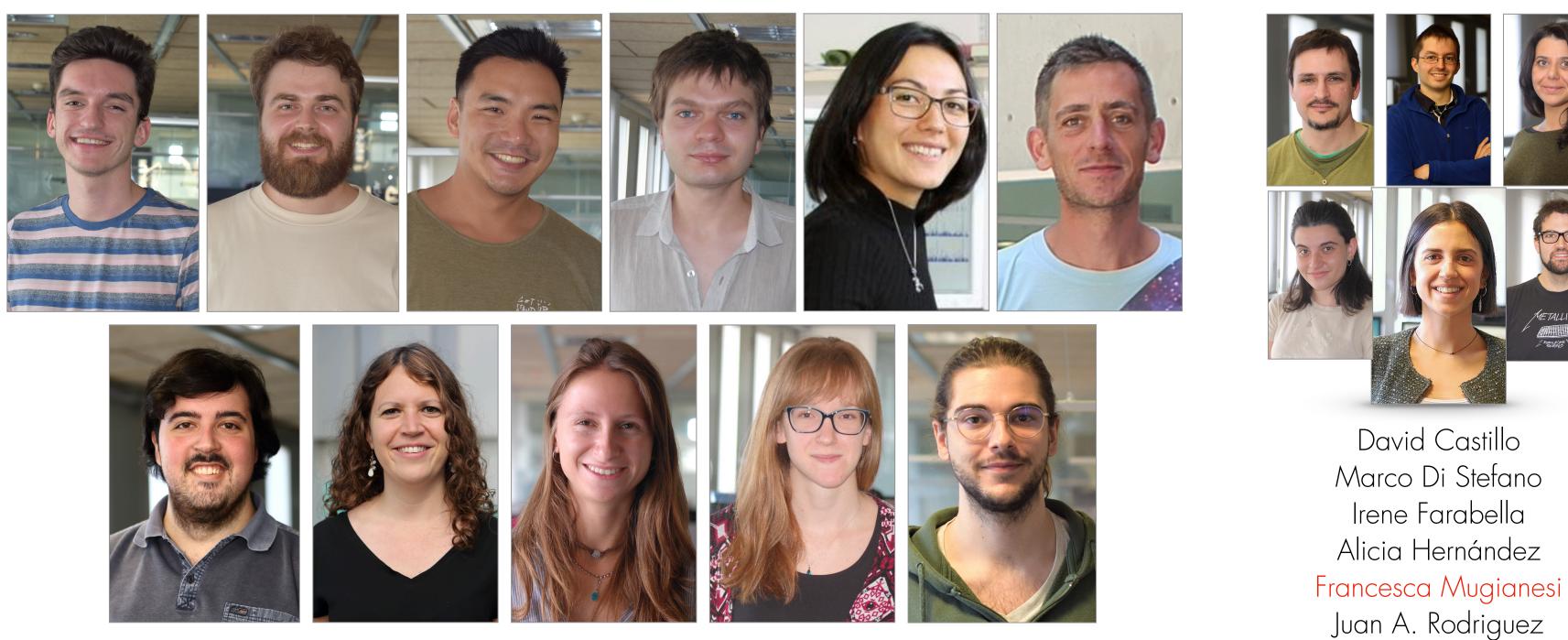




http://marciuslab.org http://3DGenomes.org



Alexander Barclay Nikolai Bykov Constantin Diekmann Ronan Duchesne lana Kim François Le Dily lago Maceda Maria Marti-Marimon Meritxell Novillo Aleksandra Sparavier Leo Zuber





In collaboration with the Di Croce Lab @CRG









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





.: Our current sponsors :.





National Human Genome Research Institute







