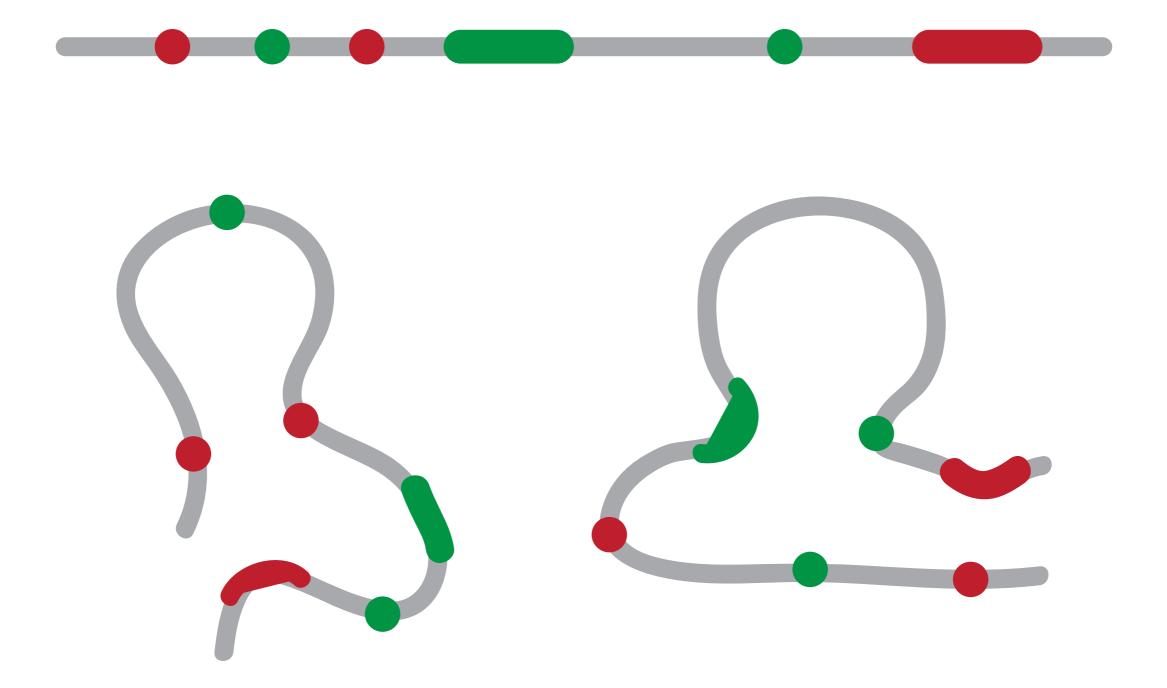
3DGENOMICS

Marc A. Marti-Renom Structural Genomics Group (ICREA, CNAG-CRG)

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







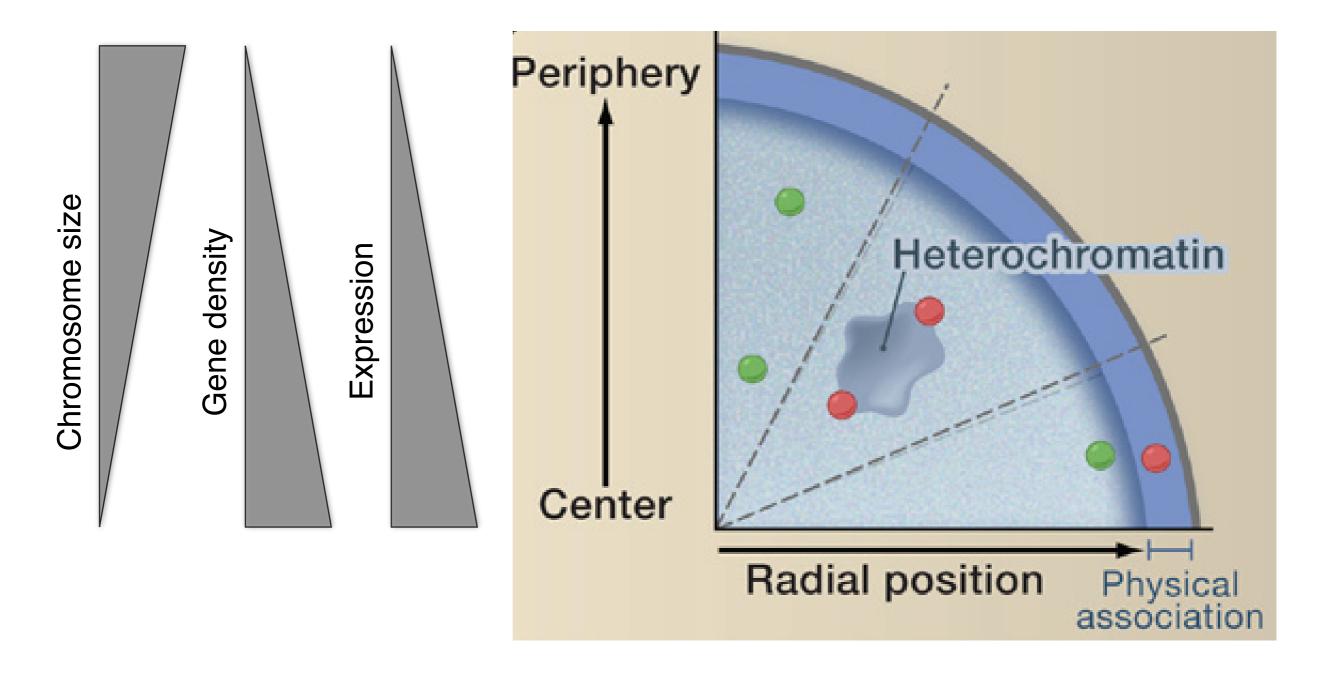
Resolution Gap

Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)

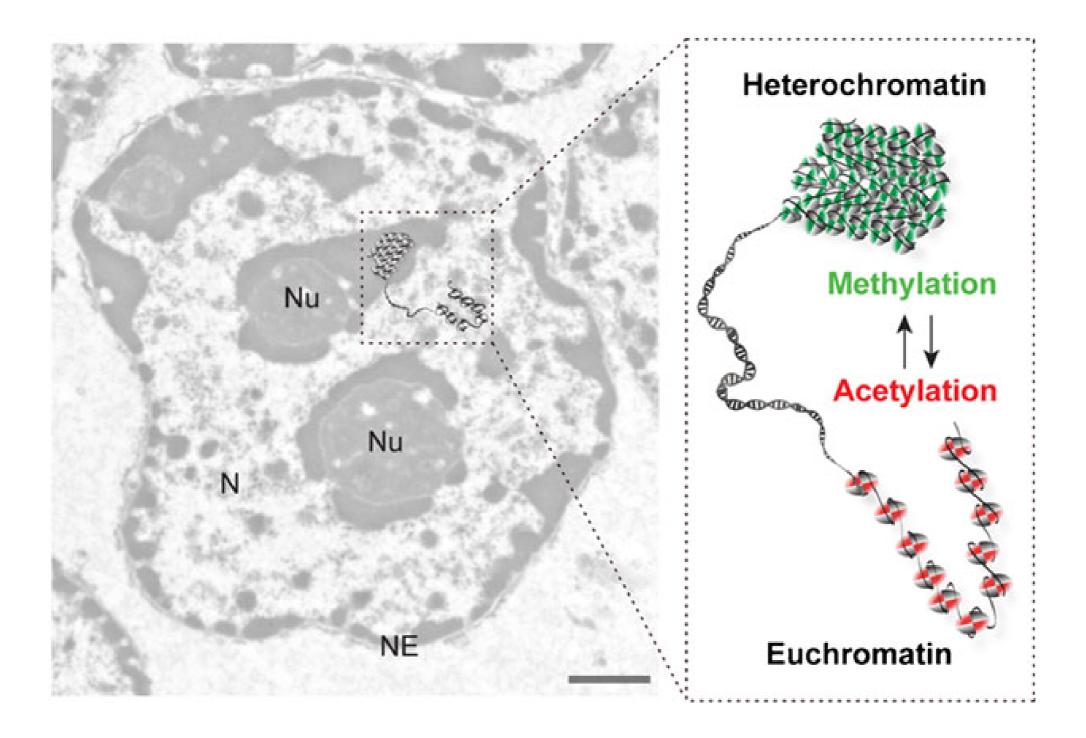
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10 ⁻³			10 ⁻²				10 ⁻¹		μ

Level I: Radial genome organization

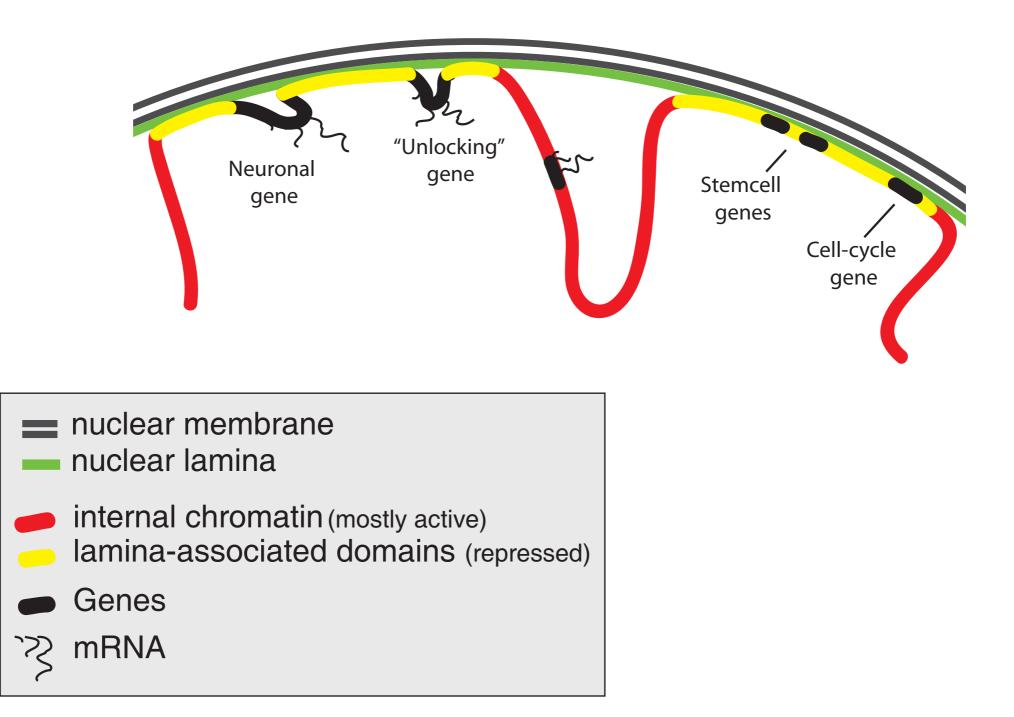
Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



Level II: Euchromatin vs heterochromatin

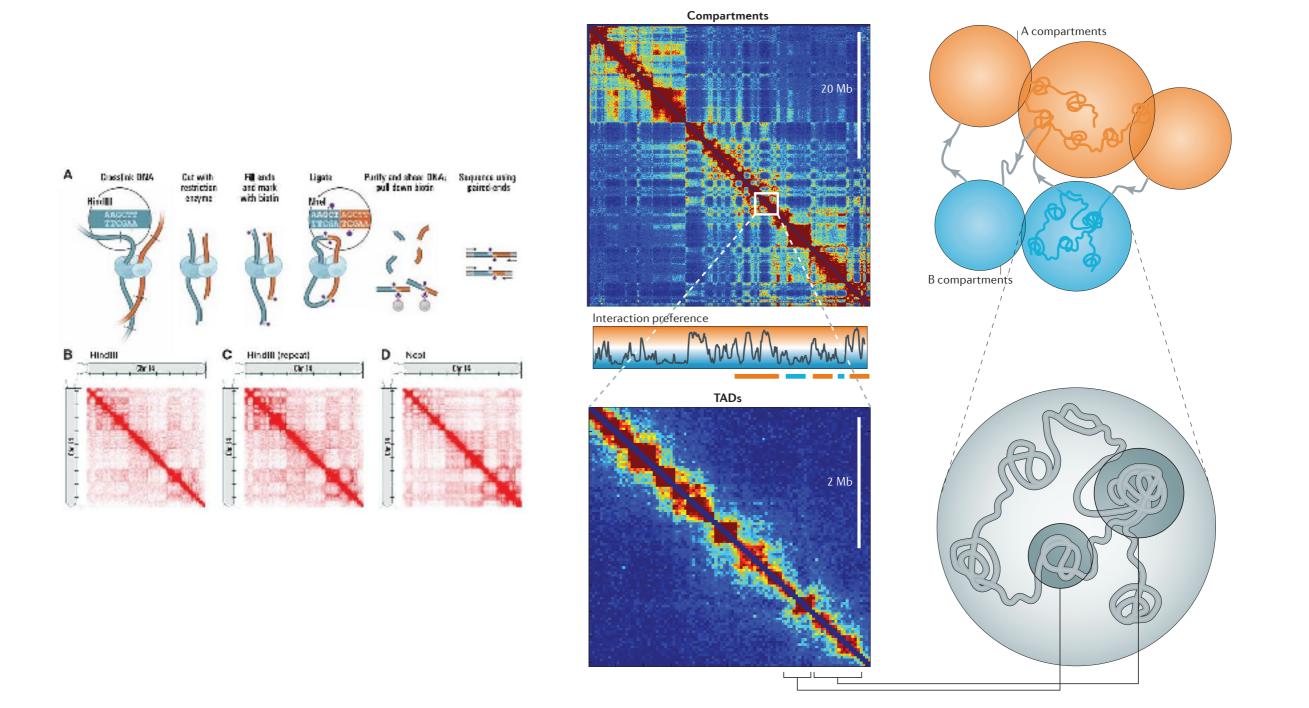


Level III: Lamina-genome interactions



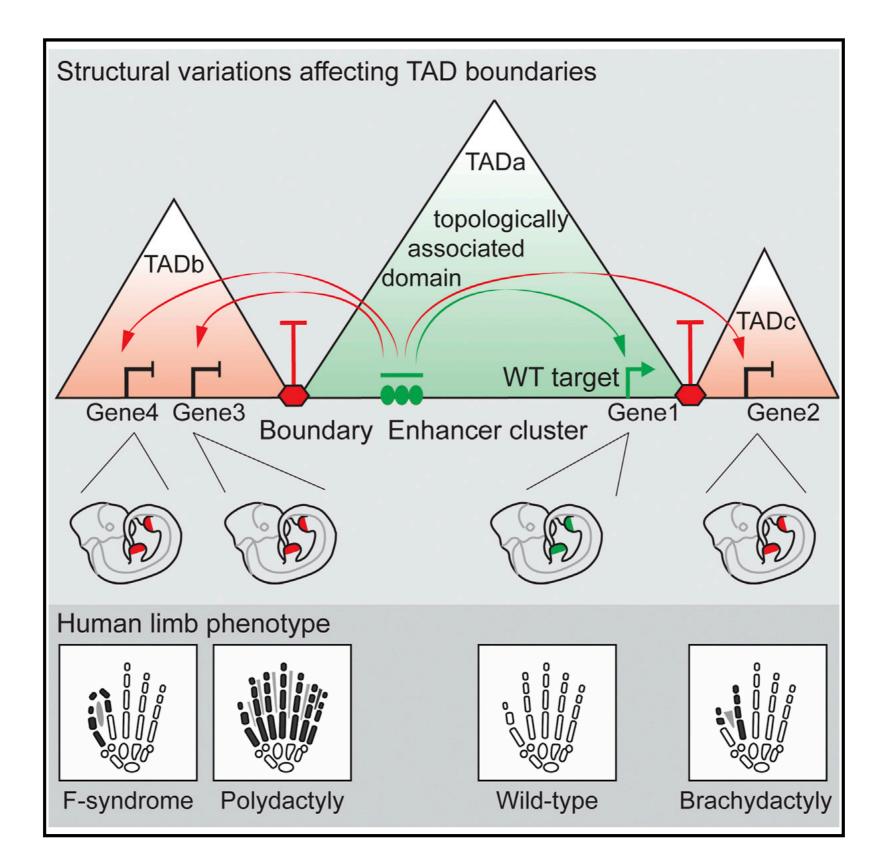
Level IV: Higher-order organization

Dekker, J., Marti-Renom, M. A. & Mirny, L. A. Nat Rev Genet 14, 390–403 (2013).



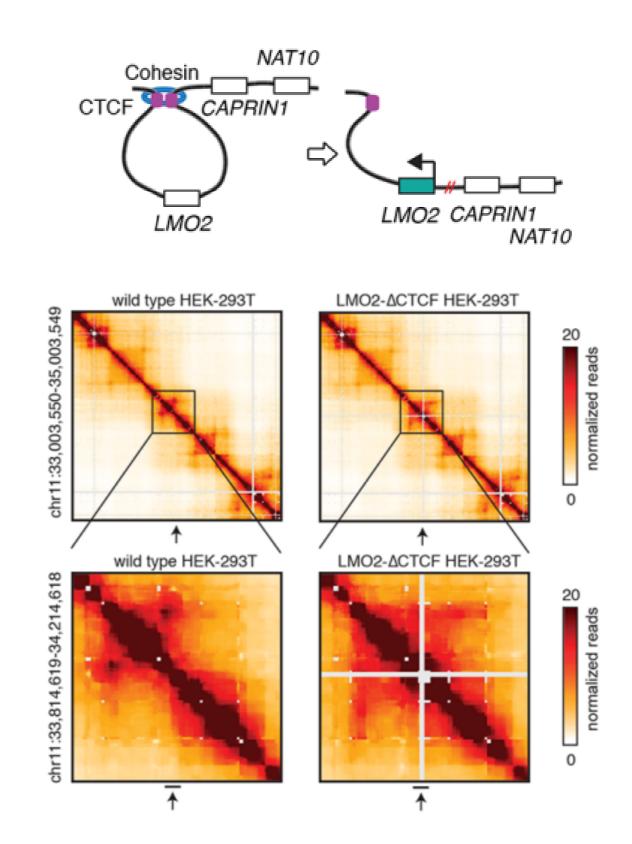
TADs are functional units

Lupiáñez, et al. (2015). Cell, 1–15.

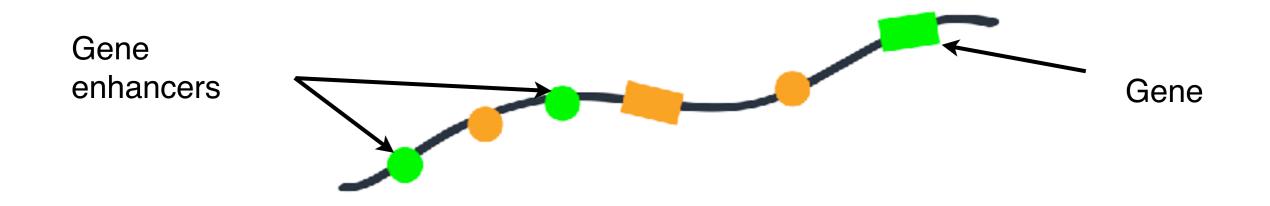


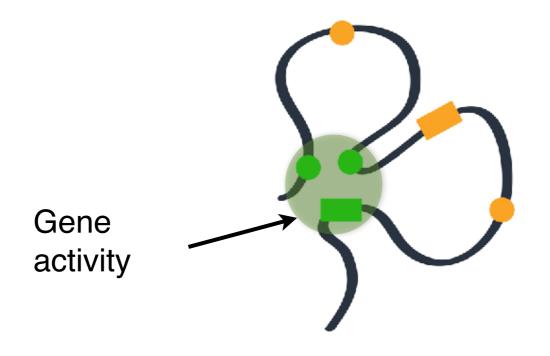
TADs are functional units

Hnisz, D., et al. (2016). Science, on line



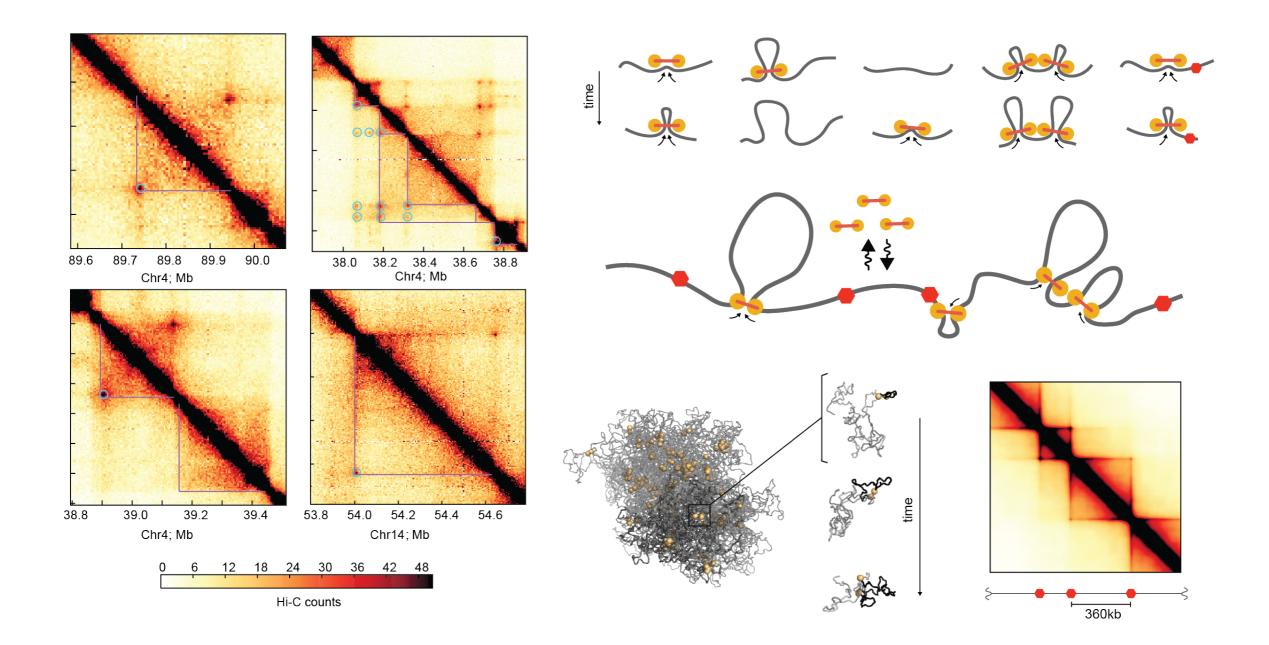
Level V: Chromatin loops



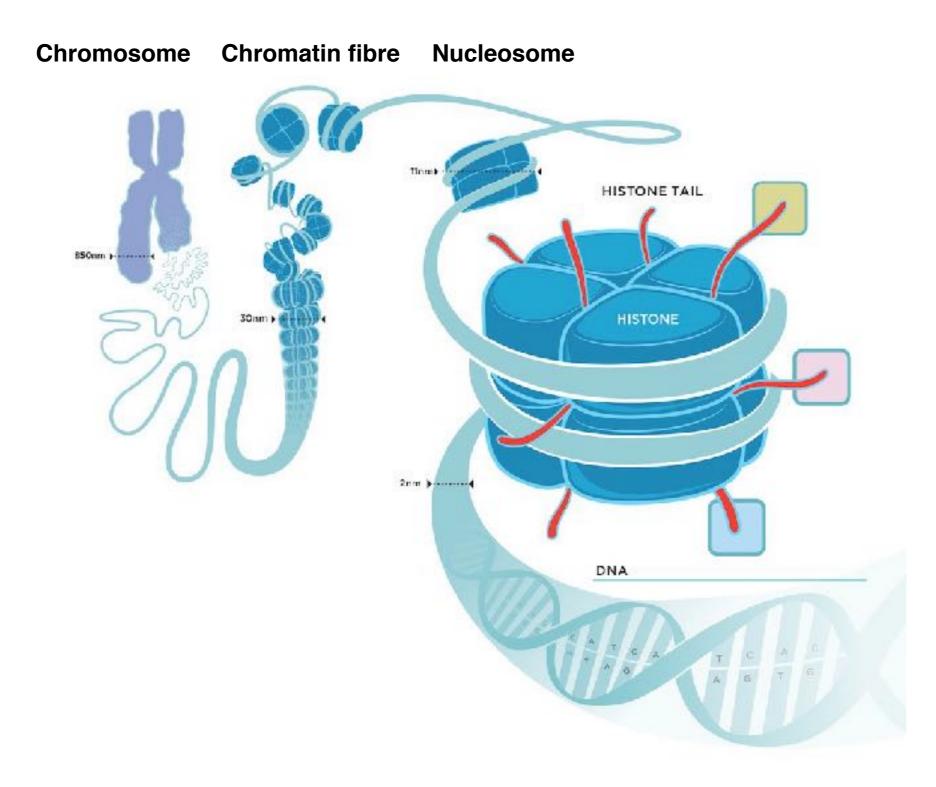


Level V: Loop-extrusion as a driving force

Fudenberg, G., Imakaev, M., Lu, C., Goloborodko, A., Abdennur, N., & Mirny, L. A. (2015). Formation of Chromosomal Domains by Loop Extrusion. bioRxiv.

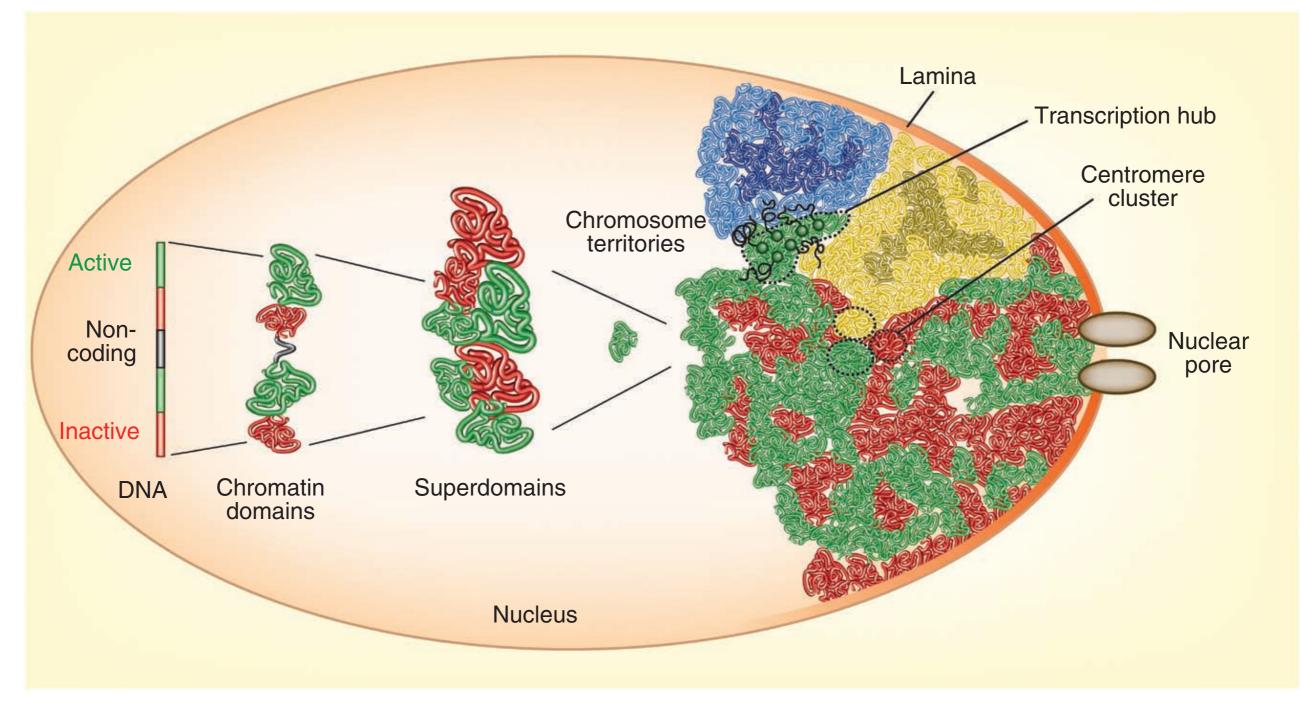


Level VI: Nucleosome

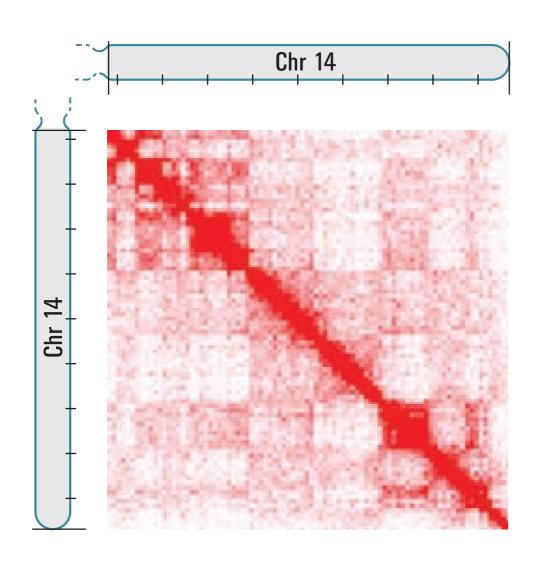


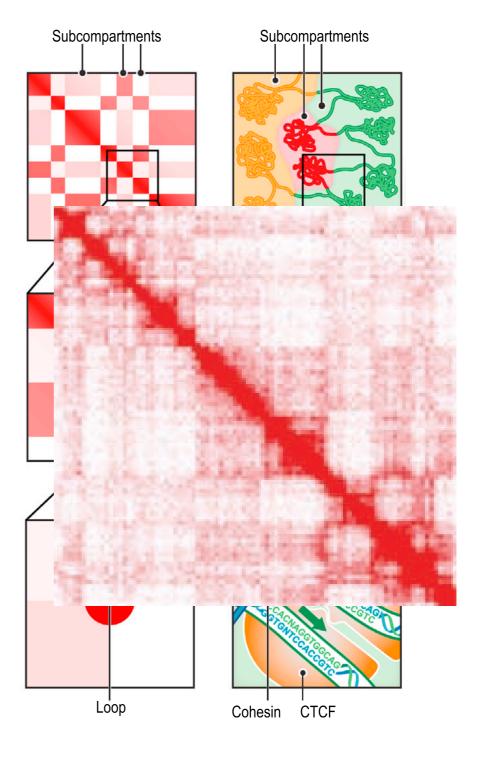
Complex genome organization

Cavalli, G. & Misteli, T. Functional implications of genome topology. Nat Struct Mol Biol 20, 290–299 (2013).



- Chical genome organisation





Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293. Rao, S. S. P., et al. (2014). Cell, 1–29.

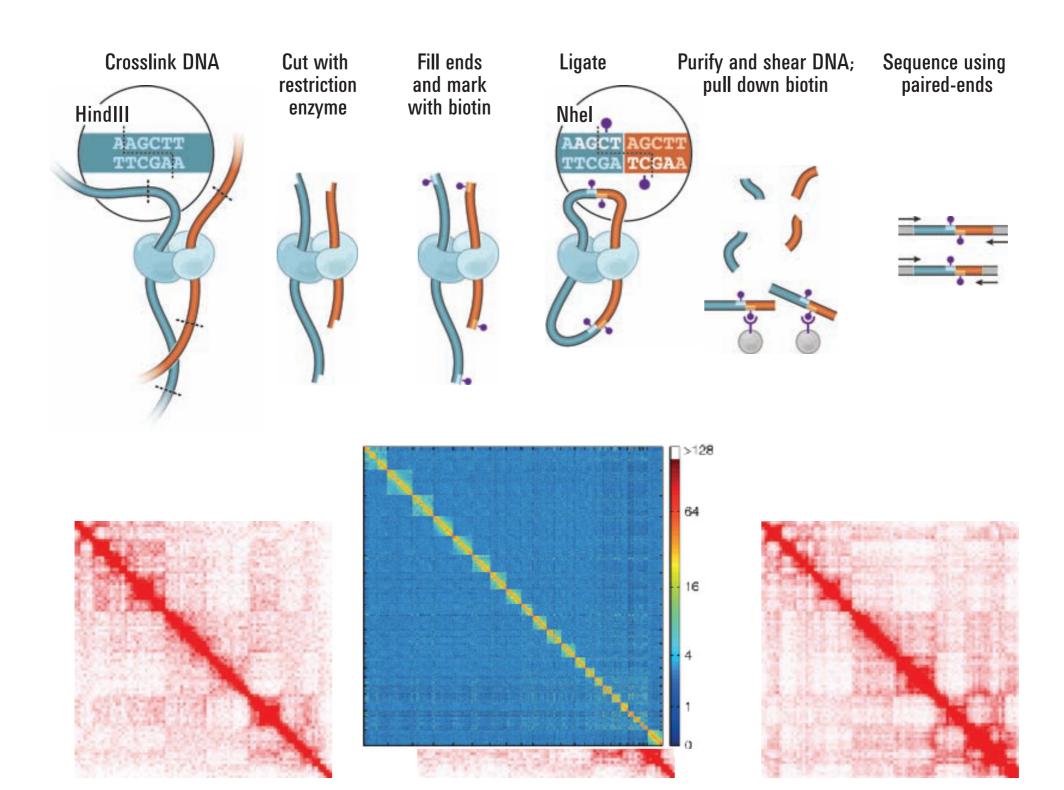
Resolution Gap

Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)

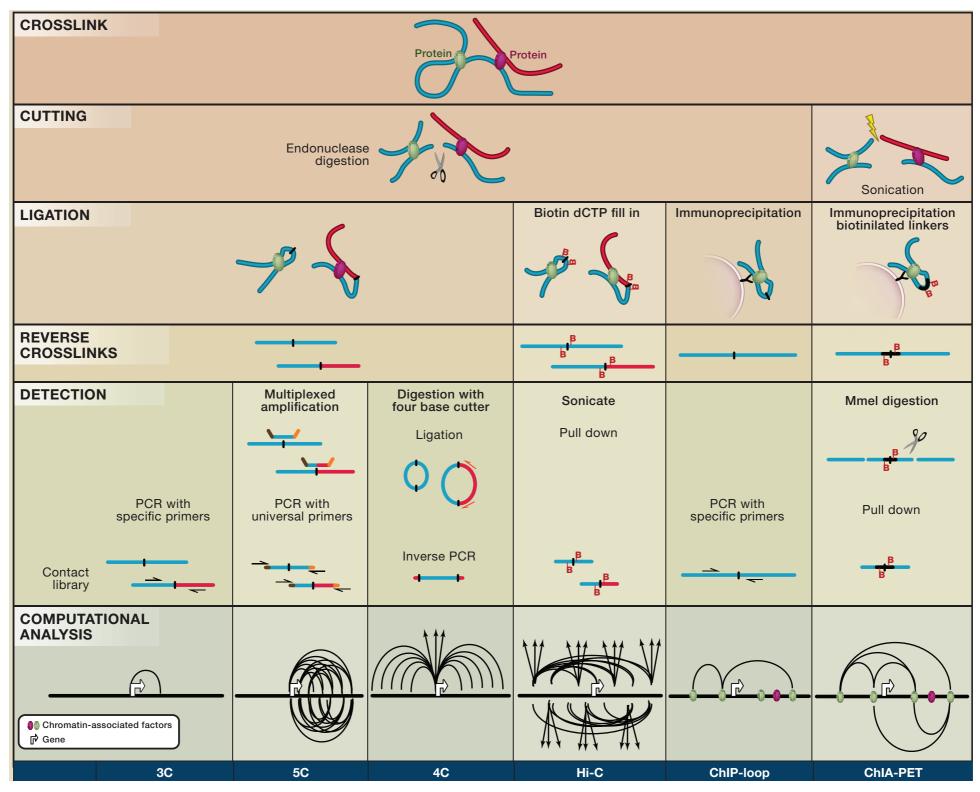
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								DNA length	
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10 ⁻¹⁰	10 ⁻⁸	10 ⁻⁶	10 ⁻⁴	10 ⁻²		10 ⁰	10 ²	10 ³	S
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Chromosome Conformation Capture

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.

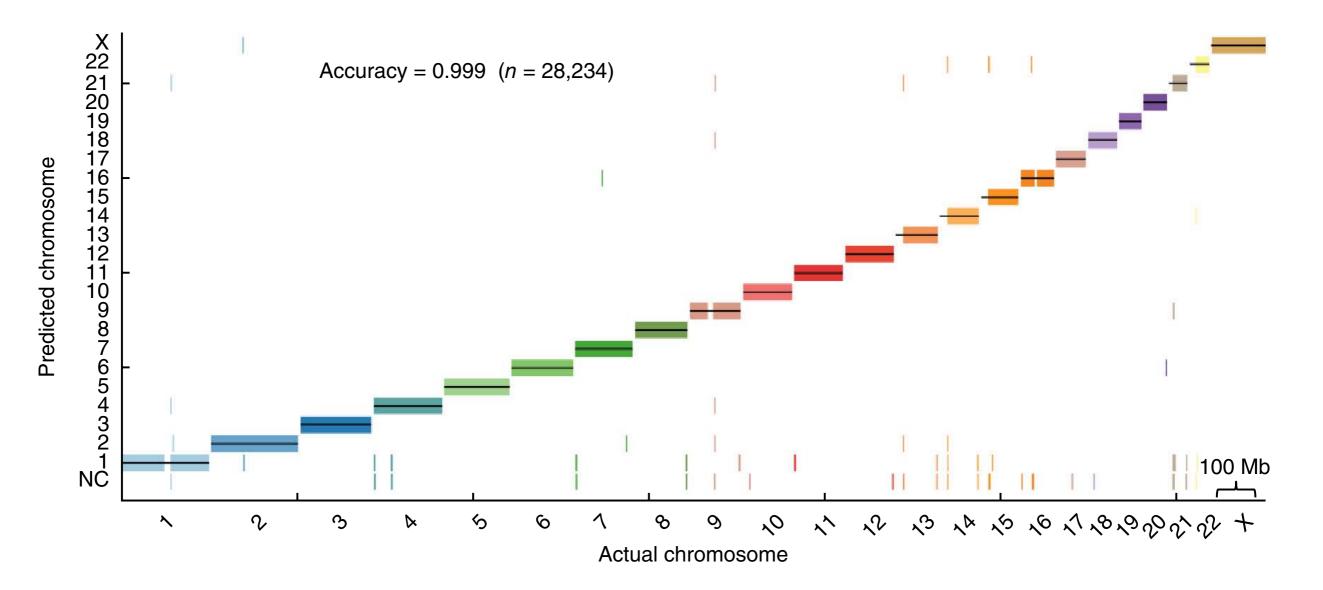


Chromosome Conformation Capture



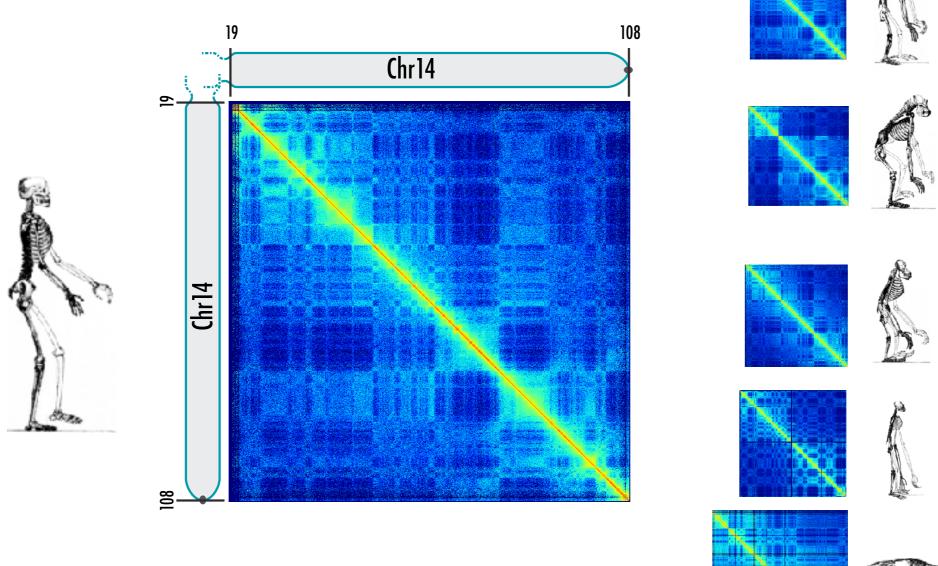
Hakim, O., & Misteli, T. (2012). SnapShot: Chromosome Confirmation Capture. Cell, 148(5), 1068–1068.e2.

srmation Capture _____assembly



Kaplan, N., & Dekker, J. (2013). High-throughput genome scaffolding from in vivo DNA interaction frequency. Nature

Great apes lymphoblast maps Chromosome 14

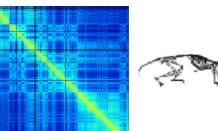


Chimpanzee

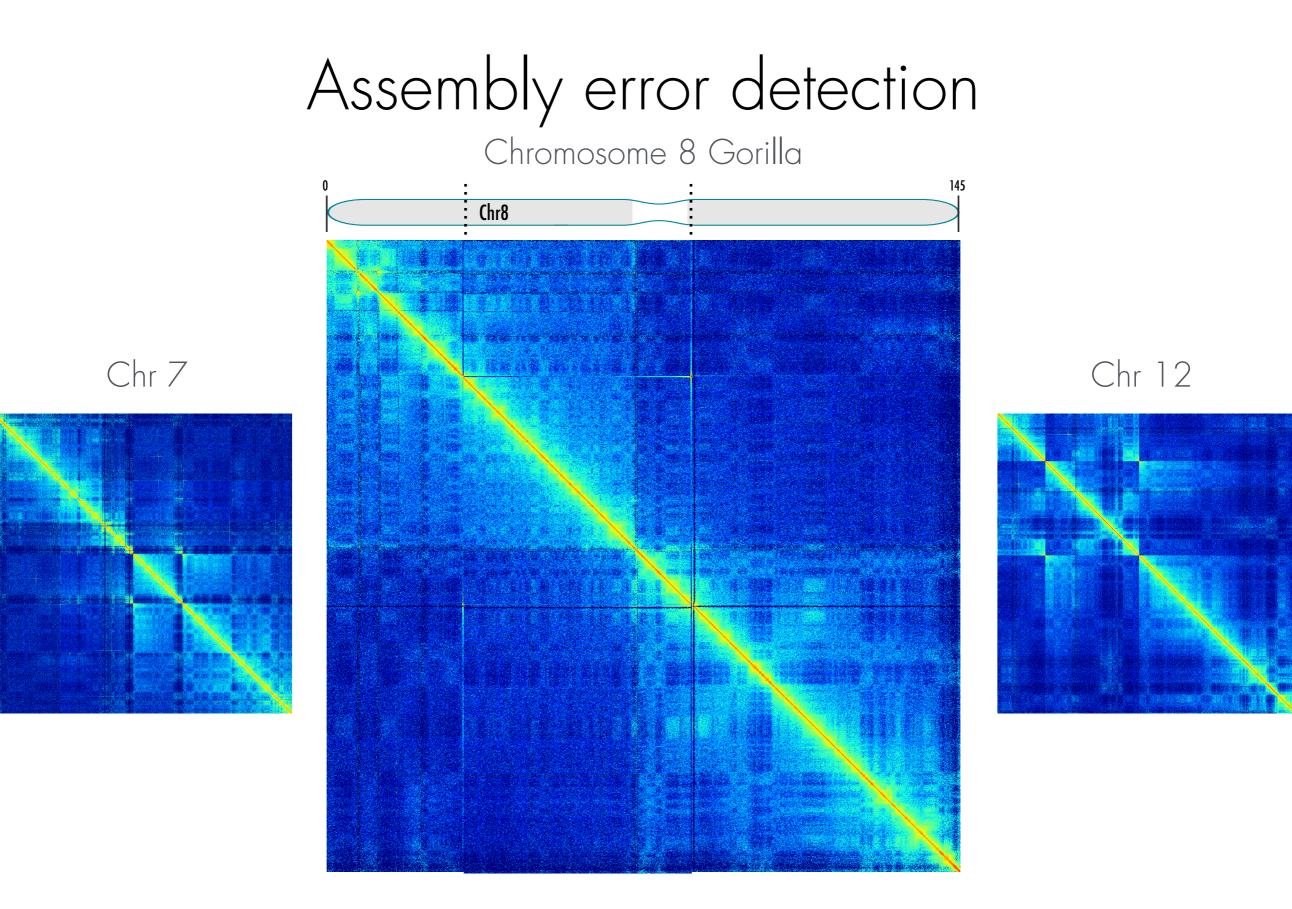
Gorilla

Orangutan

Gibbon

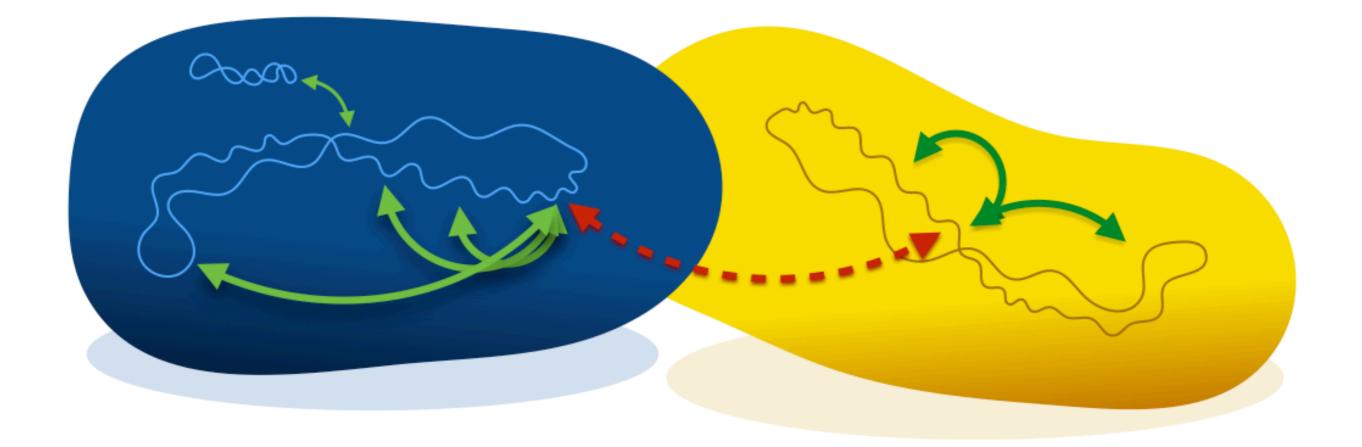


Mouse



GGO8 has an inversion of the region corresponding to HSA8:30.0-86.9Mb Aylwyn Scally (Department of Genetics, University of Cambridge)

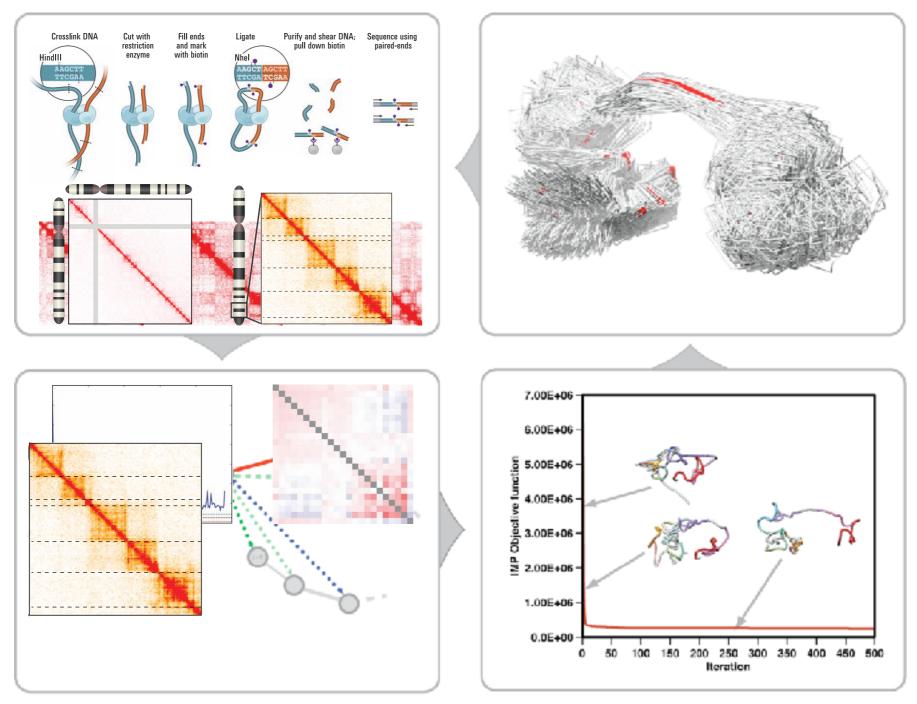
Chromosome Conformation Capture for meta genomics



Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Michelmore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/ peerj.preprints.260v1

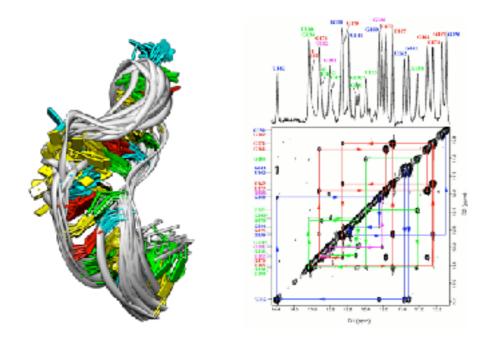
Hybrid Method Baù, D. & Marti-Renom, M. A. Methods 58, 300–306 (2012).

Experiments

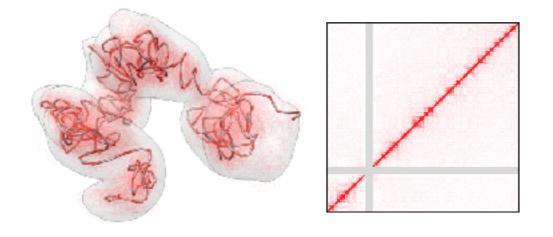


Computation

Structure determination using Hi-C data



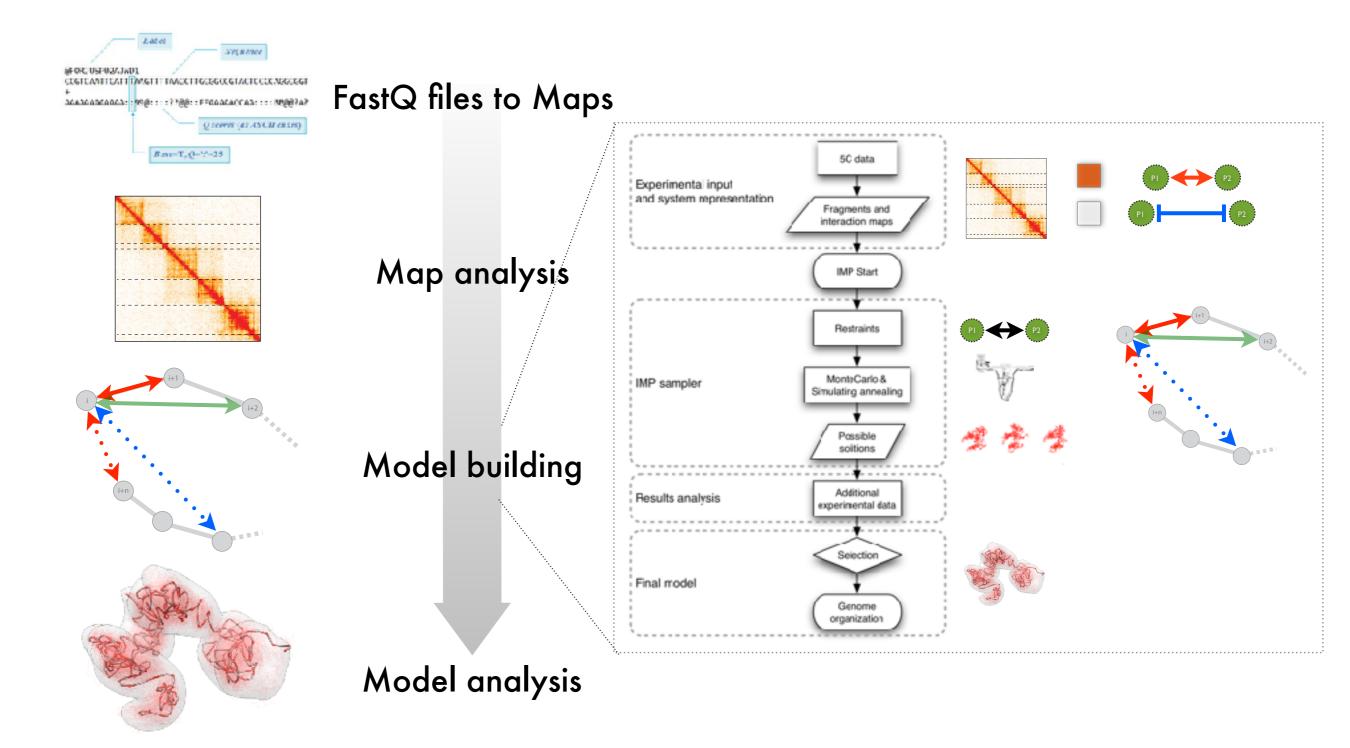
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data

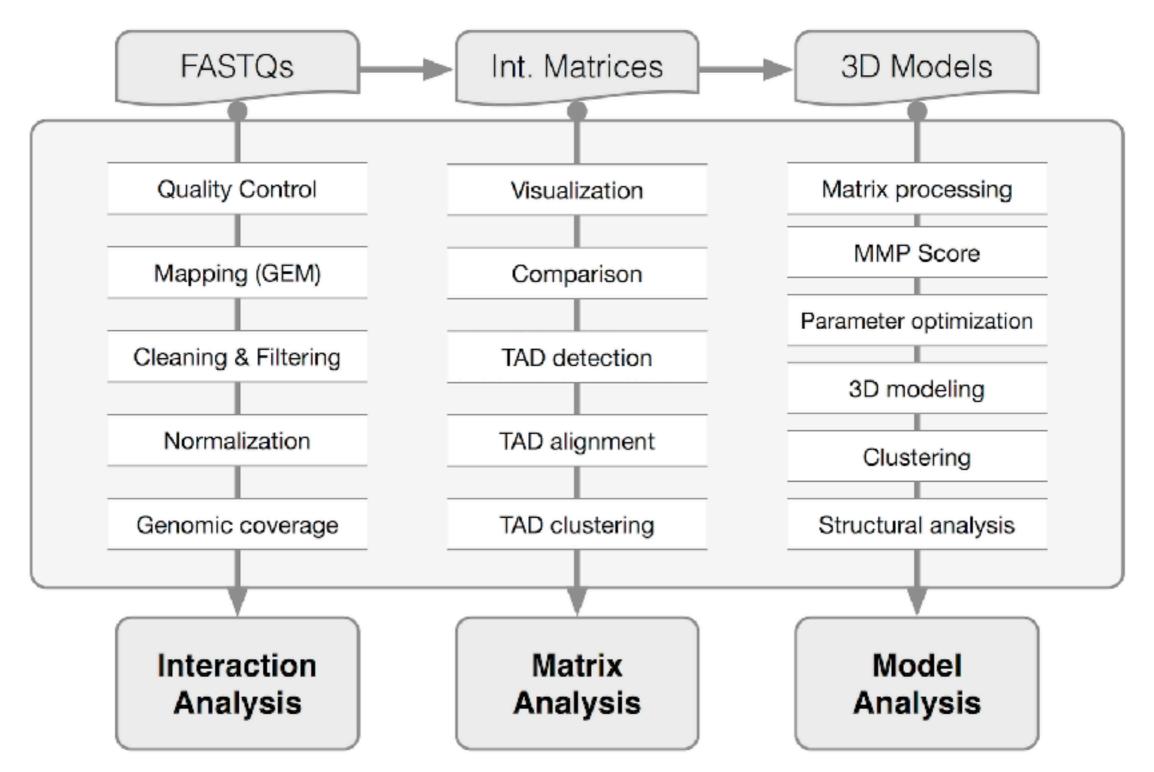


http://3DGenomes.org



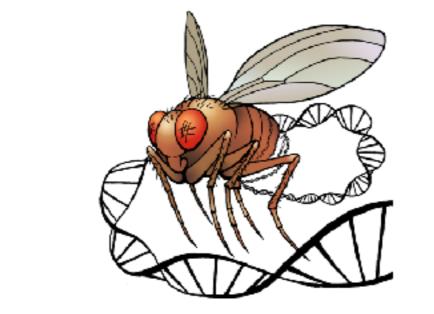


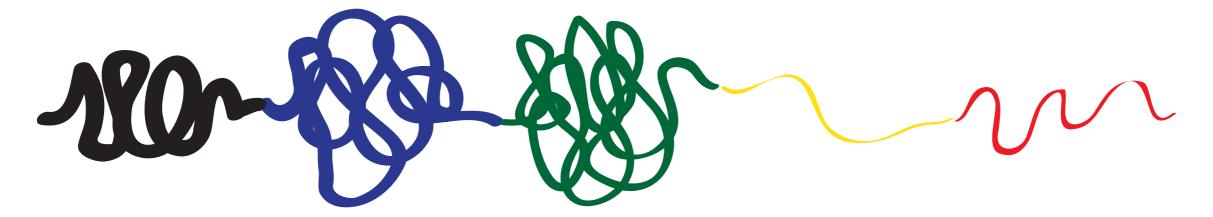
Serra, Baù, et al. (2017). PLOS CompBio



Structuring the **COLORs** of chromatin

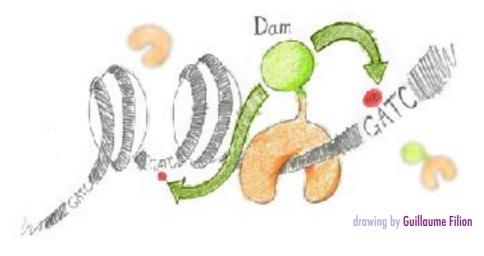
Serra, Baù et al. (2017) PLOS CompBio.





Fly Chromatin **COLORs**

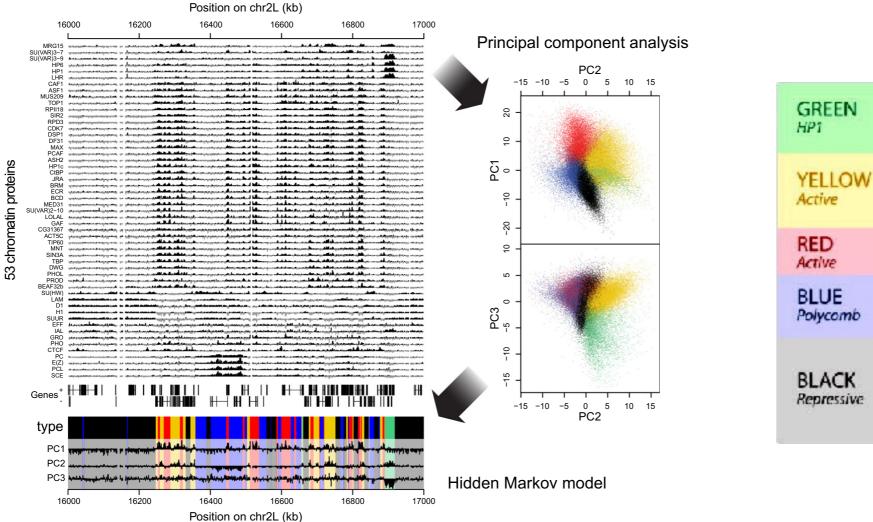
Filion et al. (2010). Cell, 143(2), 212–224.



chromatin

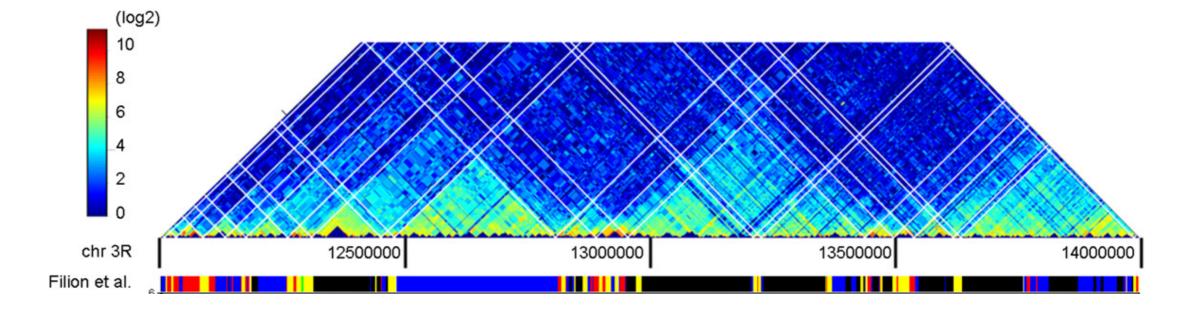
Nucleus

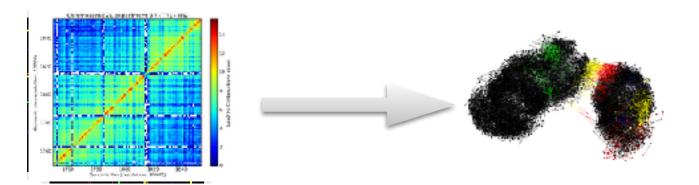
proteins



Fly Chromatin **COLORs**

Hou et al. (2012). Molecular Cell, 48(3), 471–484.

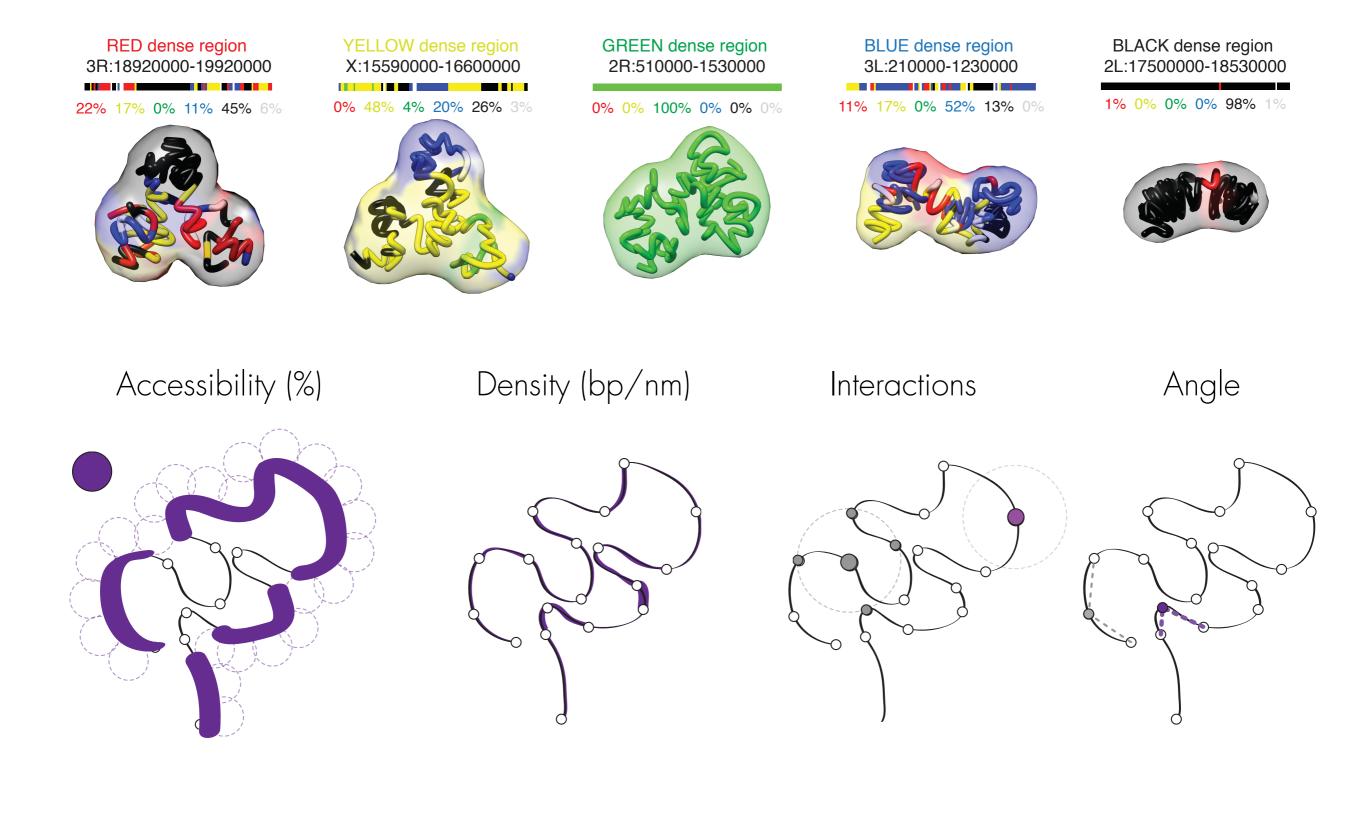




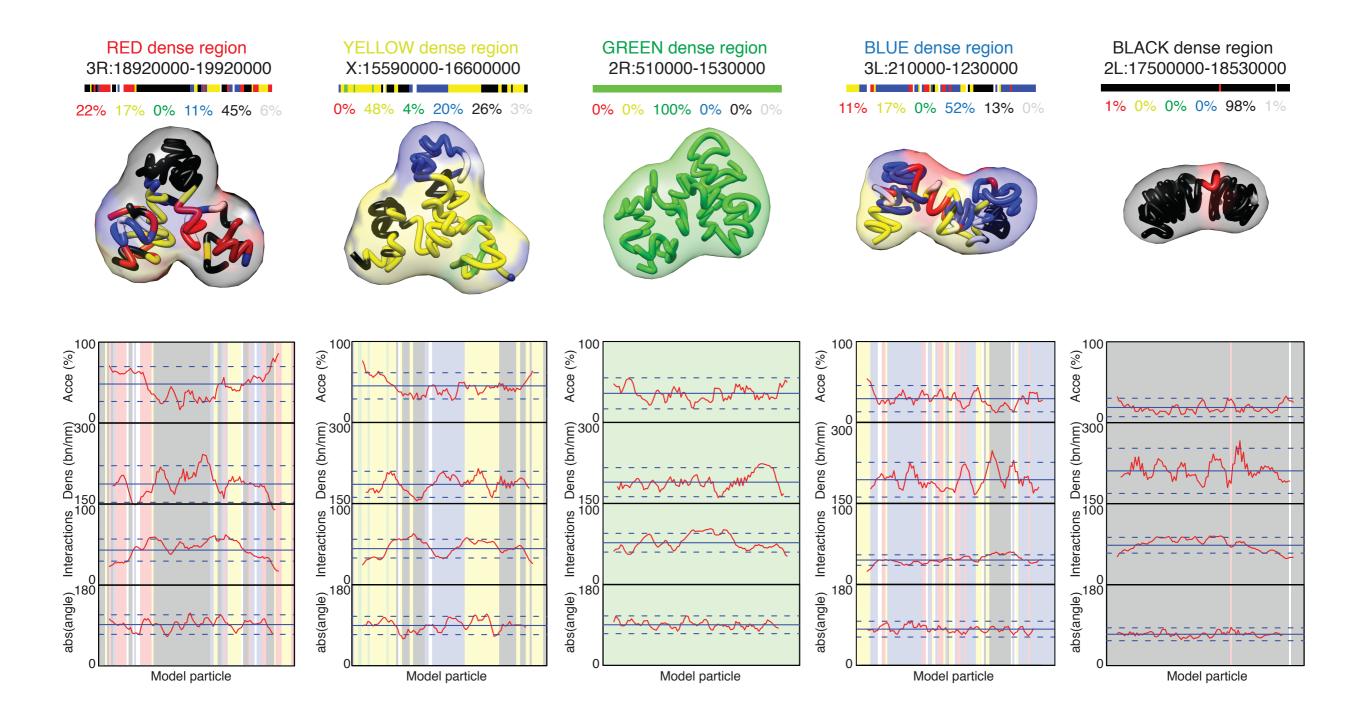
~200 regions of ~5Mb each 2Kb resolution

Structural properties

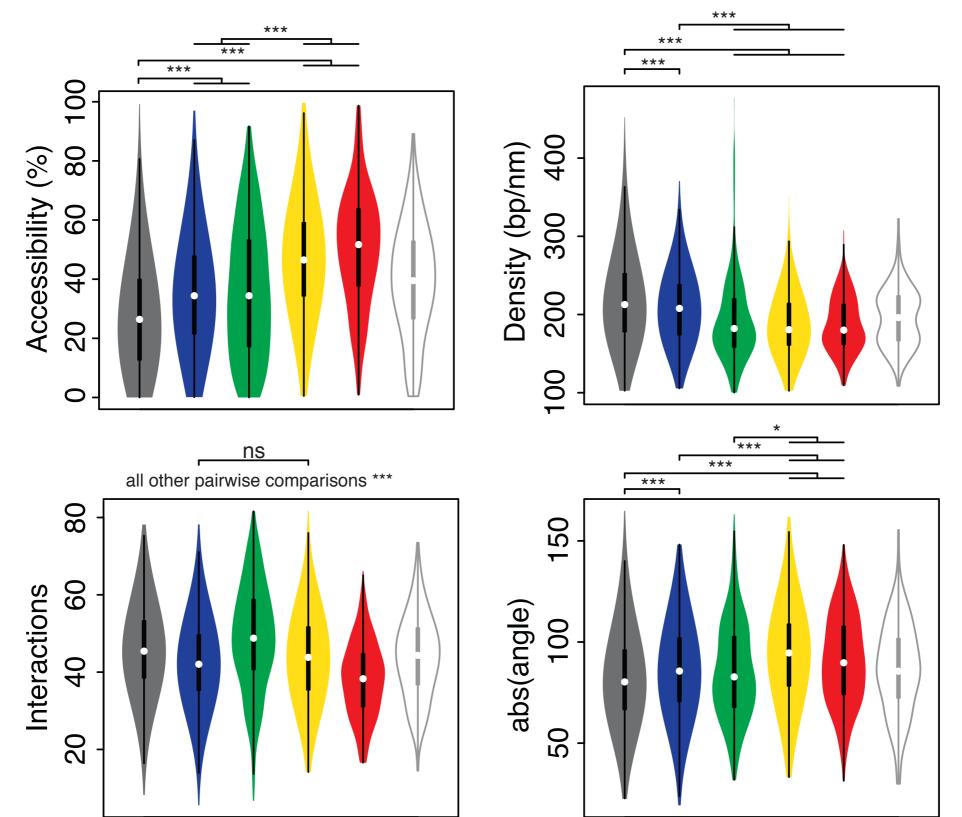
50 1Mb regions. 10 enriched for each color.



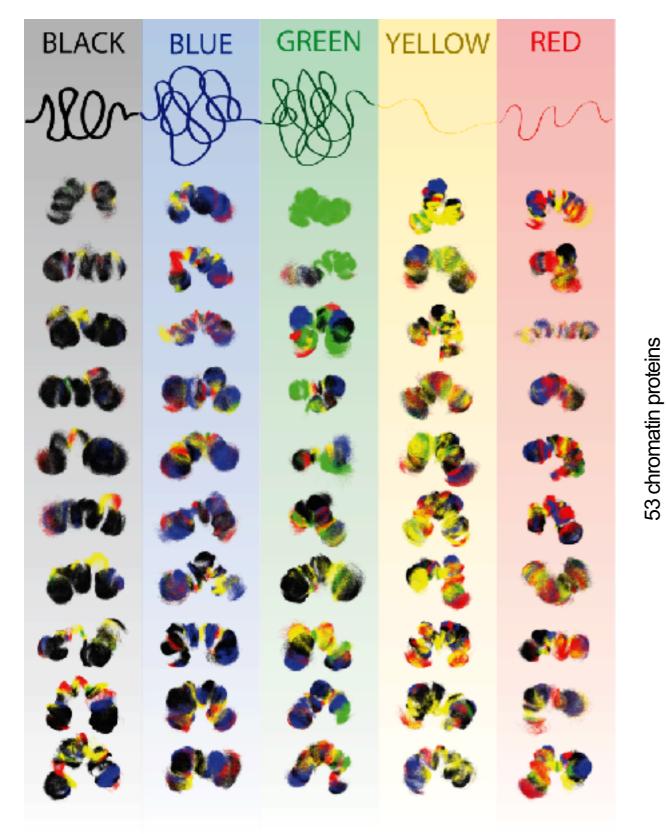
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Structural **COLORs**



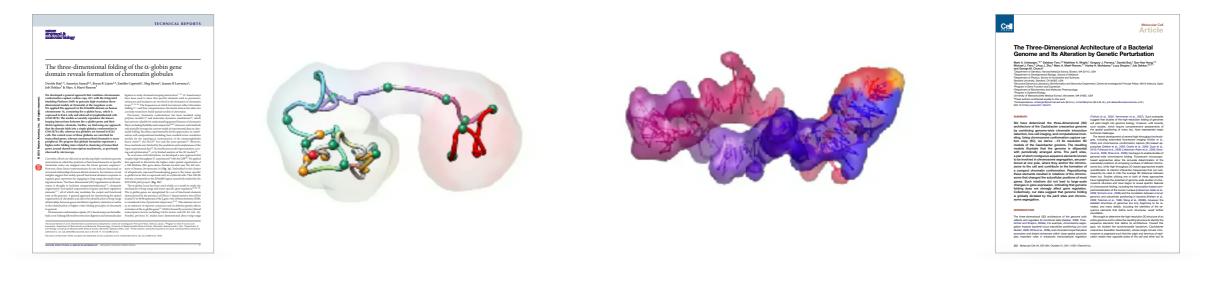
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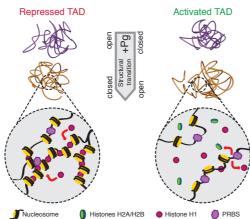
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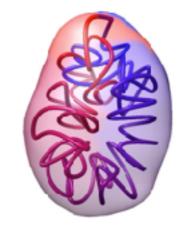
Baù, D. et al. Nat Struct Mol Biol (2011) Umbarger, M. A. et al. Mol Cell (2011) Le Dily, F. et al. Genes & Dev (2014) Trussart et al. Nature Comm. (2017)







Histones H2A/H2B Histone H1







David Castillo Yasmina Cuartero Irene Farabella Silvia Galan Mike Goodstadt Julen Mendieta Francesca Mugianesi Juan Rodríguez François Serra Paula Soler Aleksandra Sparavier Marco di Stefano

http://sgt.cnag.cat/www/presentations/



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