

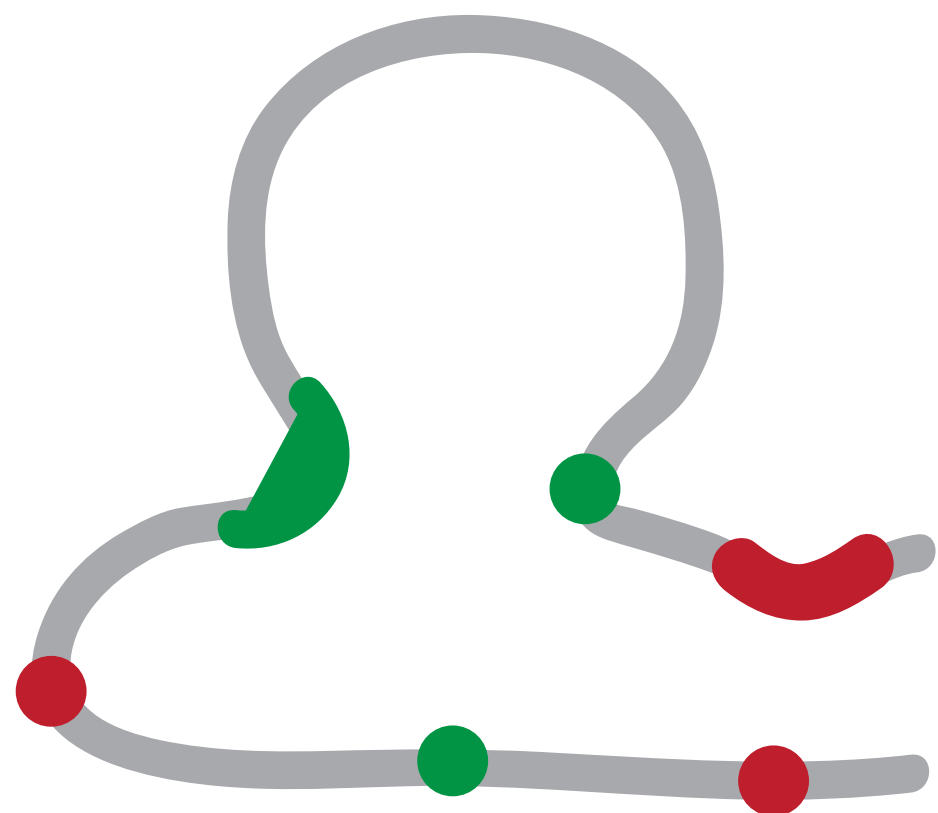
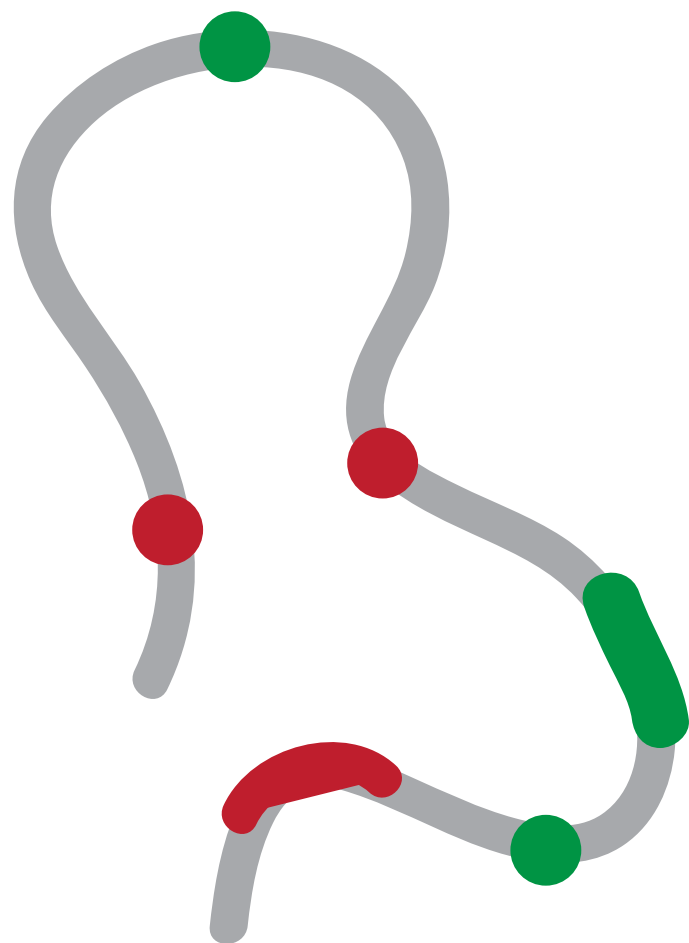
3DGENOMICS

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

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

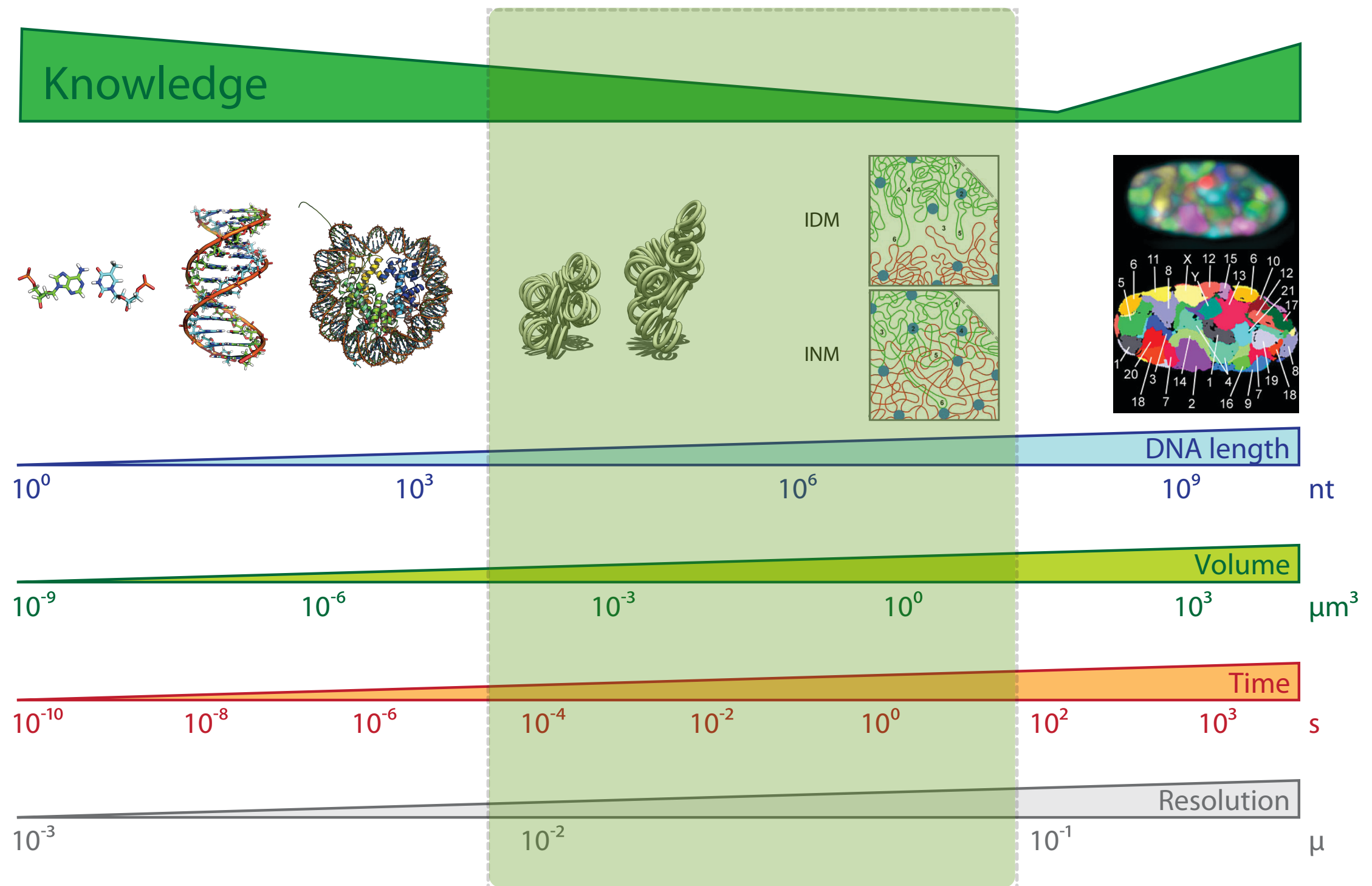
cnag **CRG**   **ICREA**





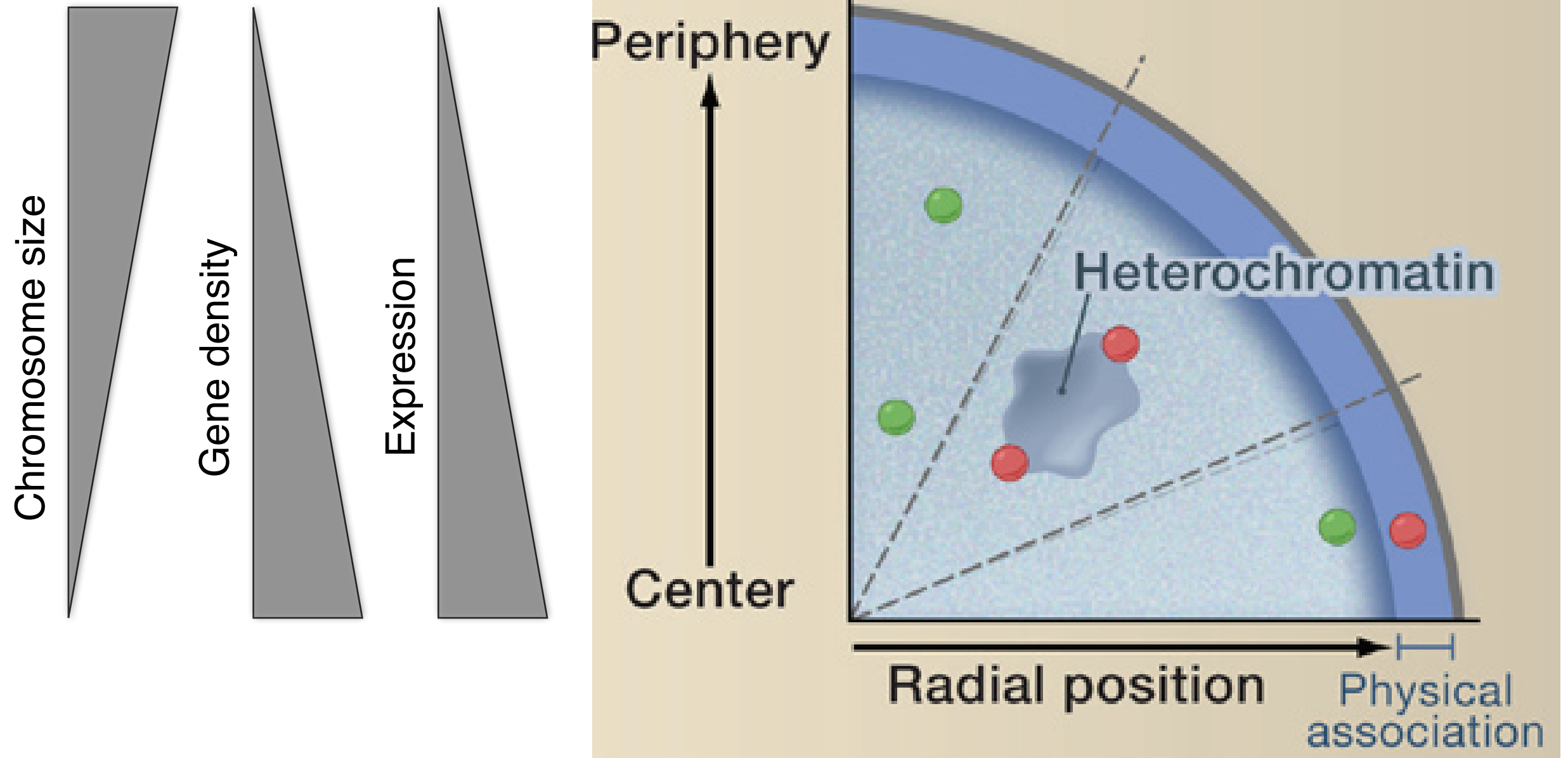
Resolution Gap

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

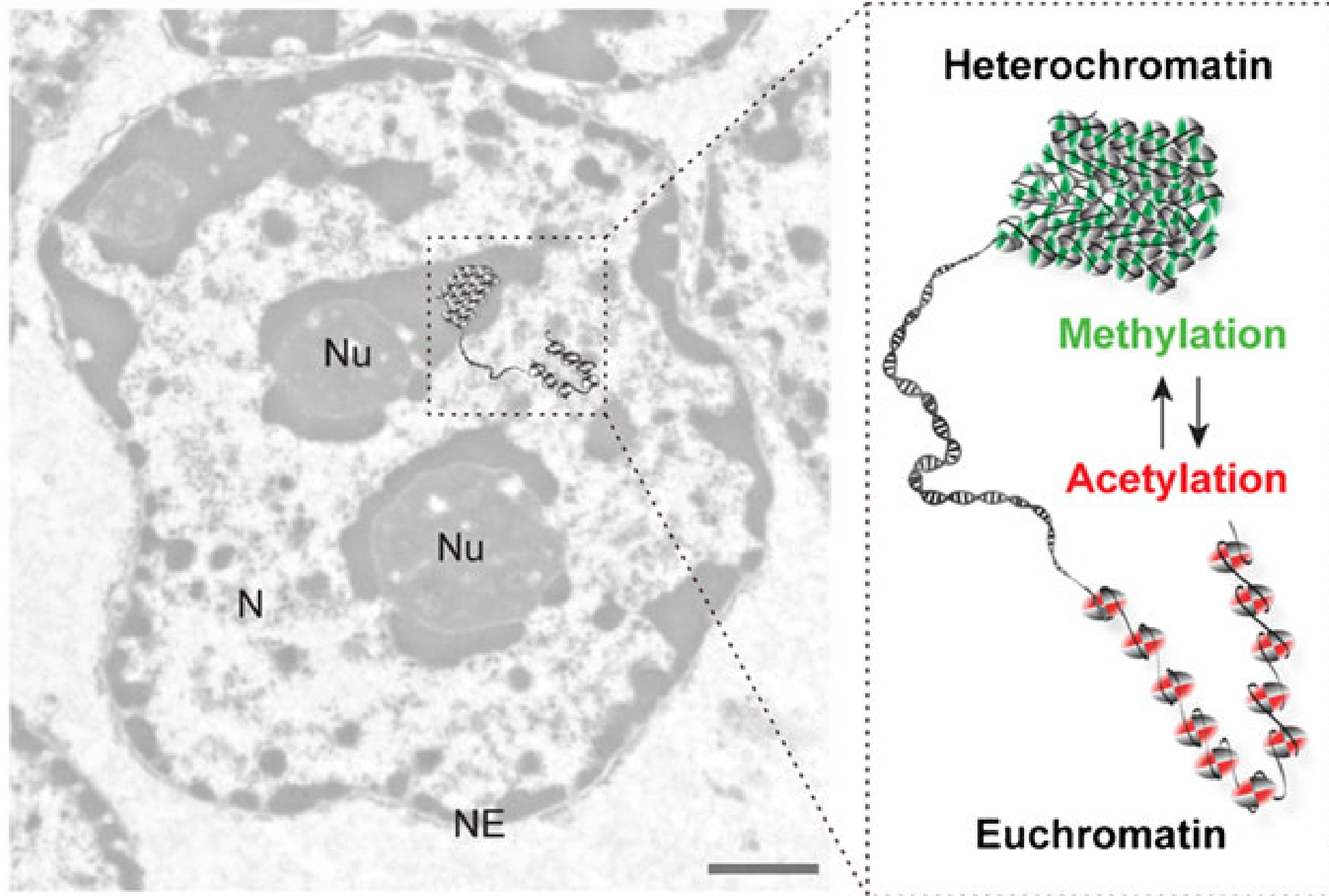


Level I: Radial genome organization

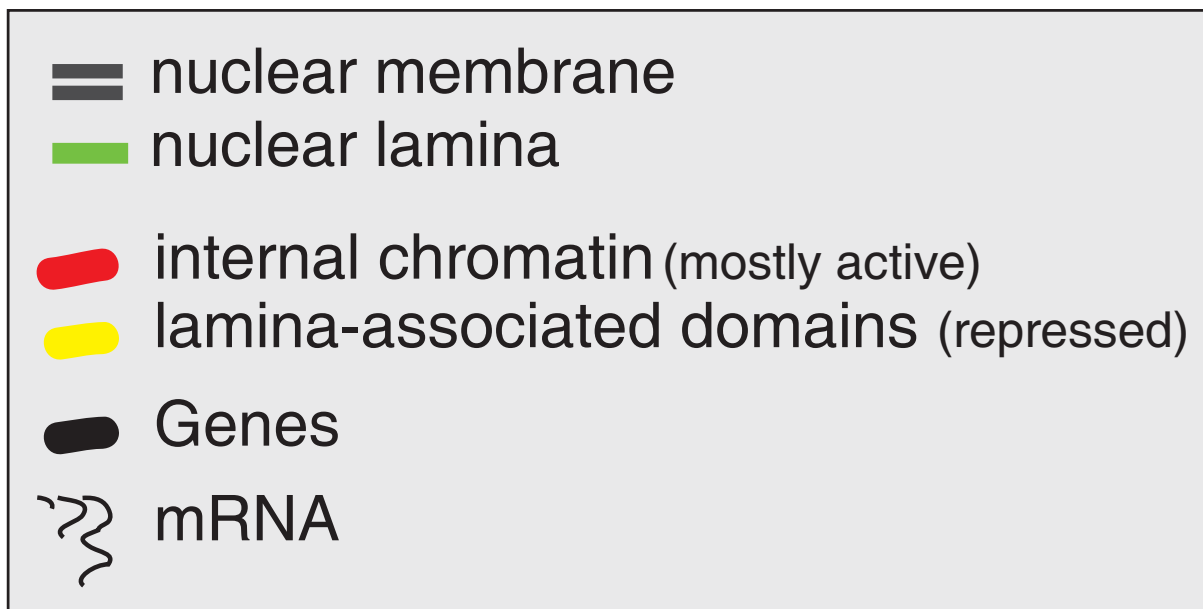
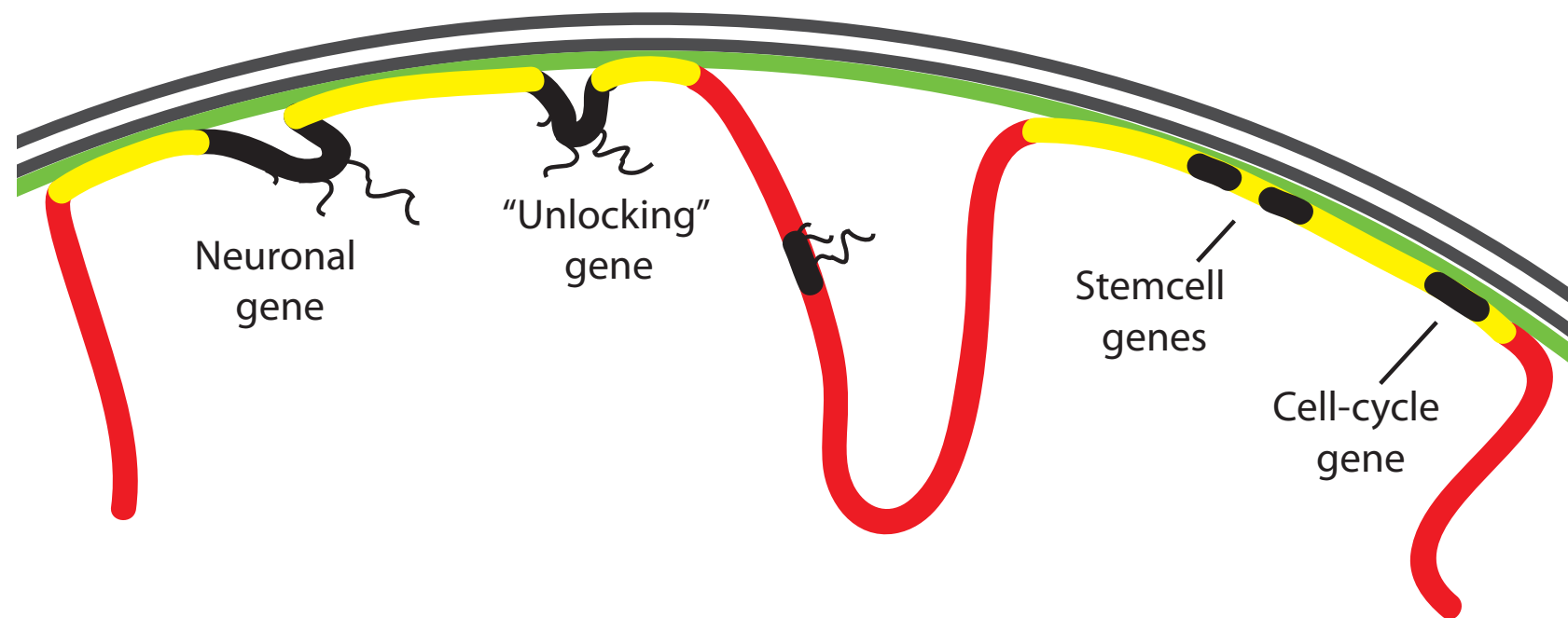
Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



Level II: Euchromatin vs heterochromatin

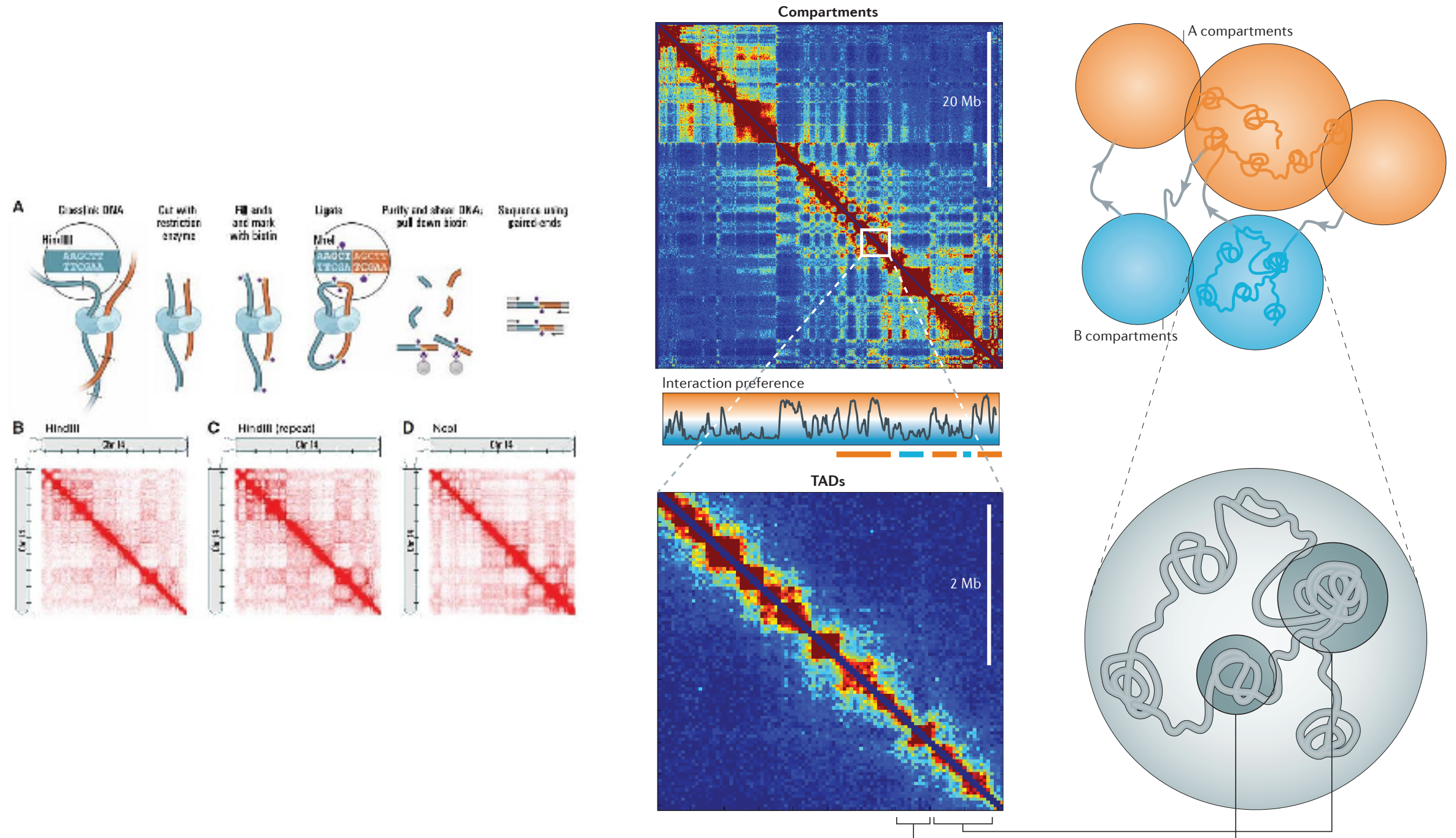


Level III: Lamina-genome interactions



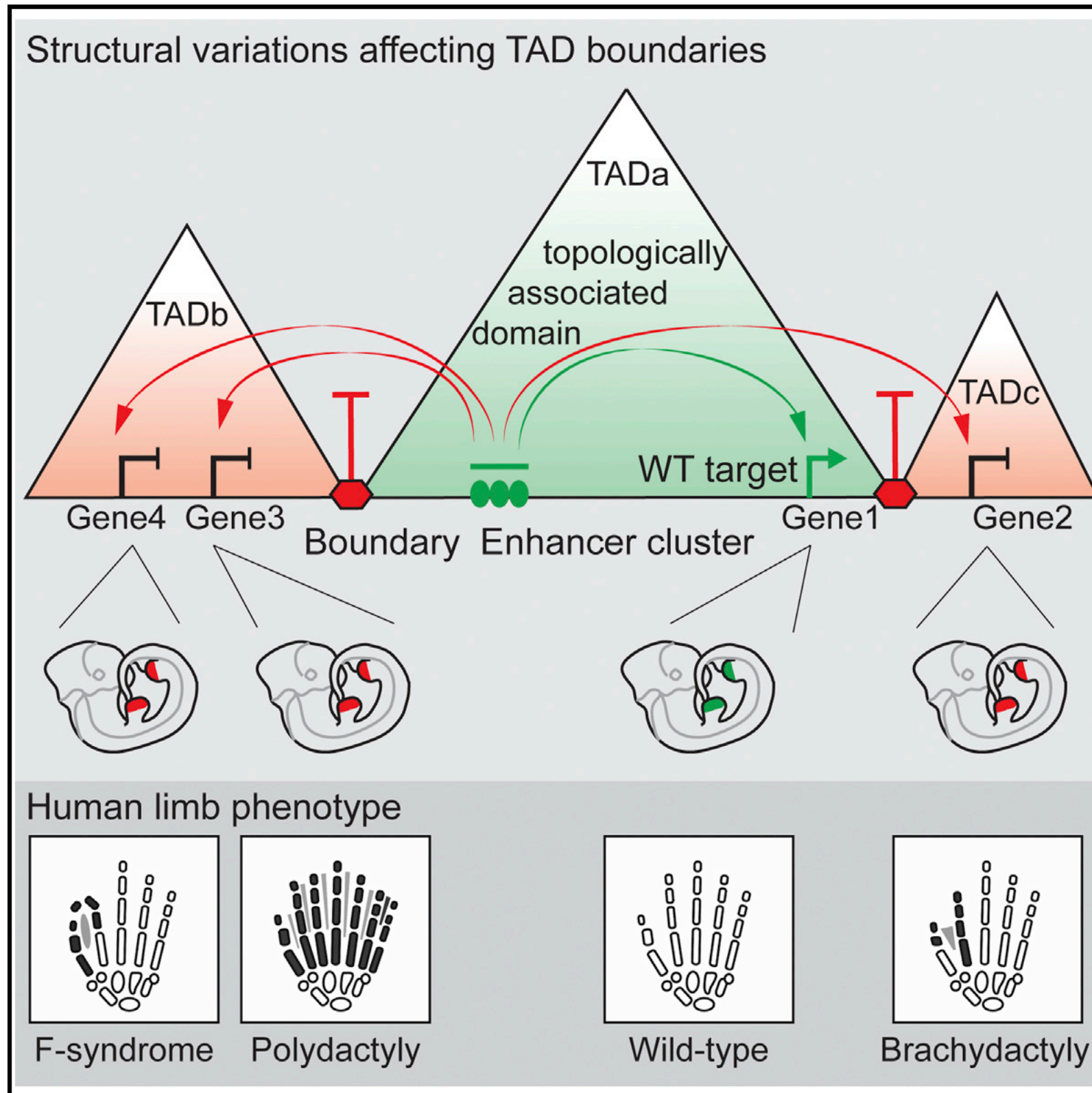
Level IV: Higher-order organization

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



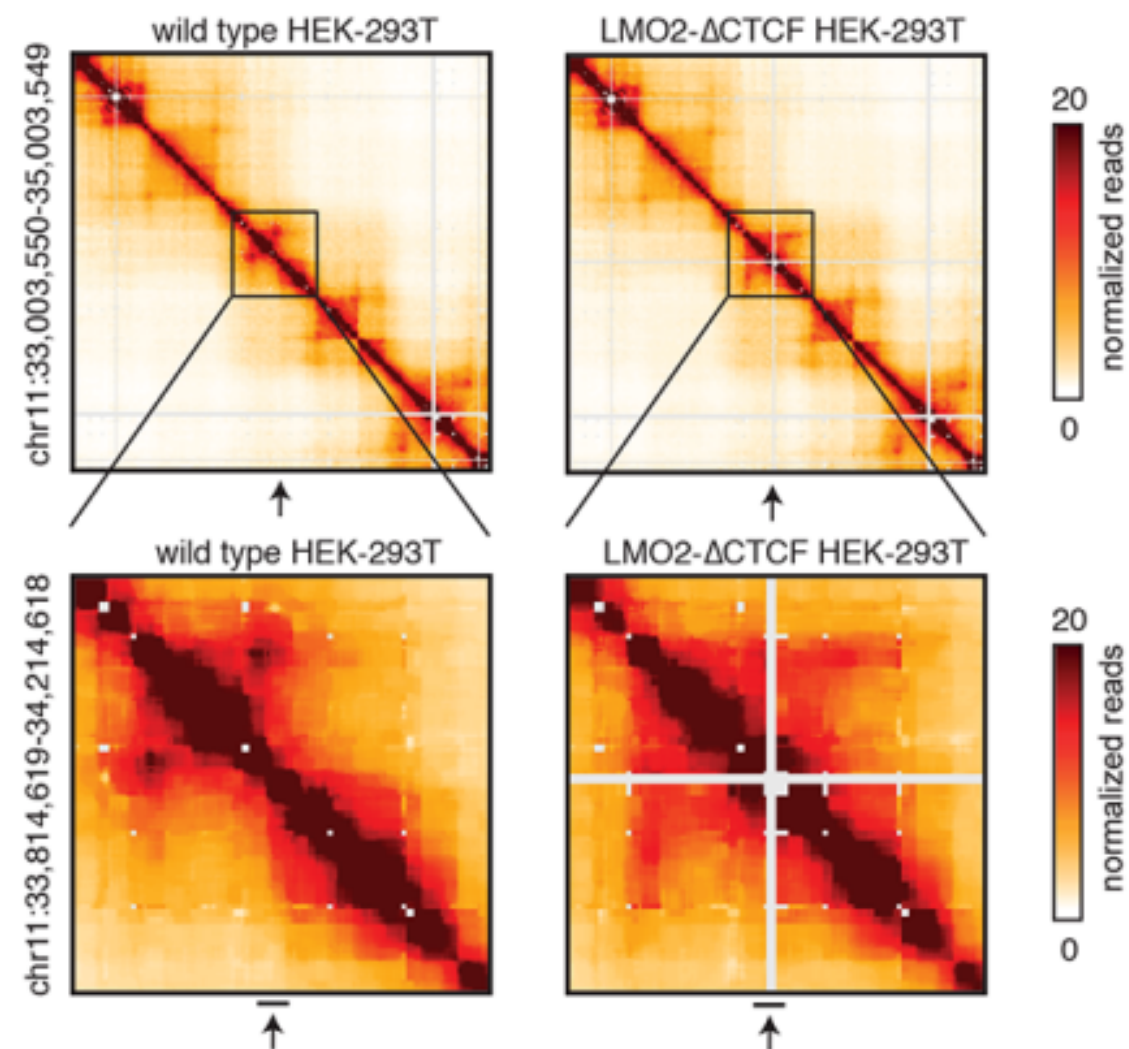
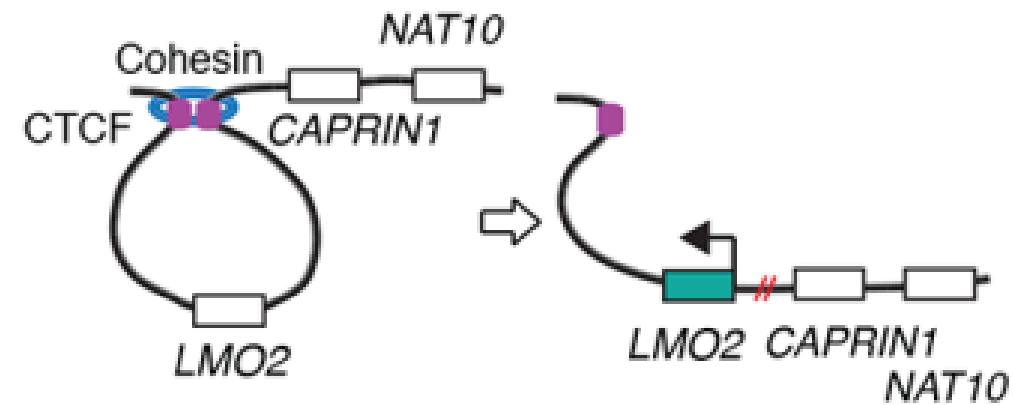
TADs are functional units

Lupiáñez, et al. (2015). Cell, 1–15.



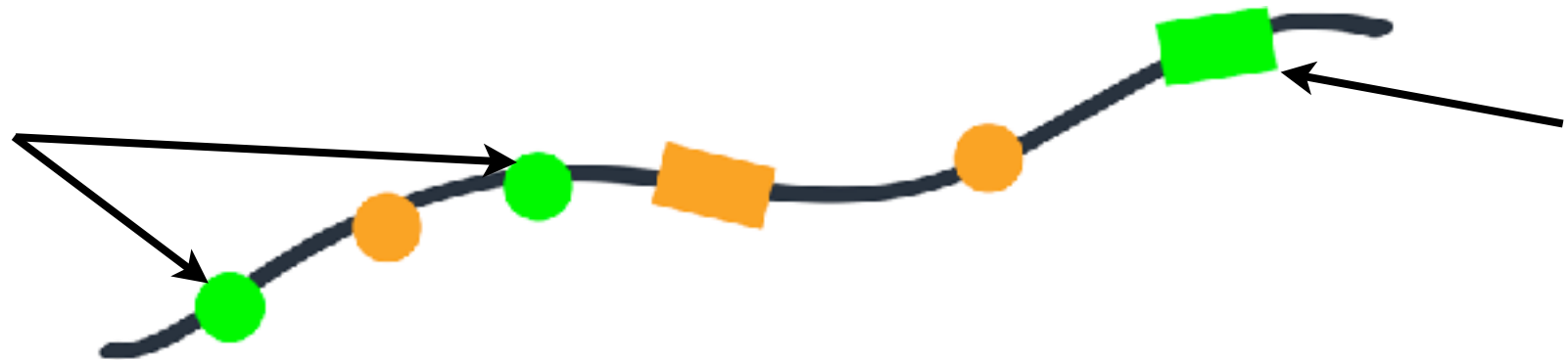
TADs are functional units

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



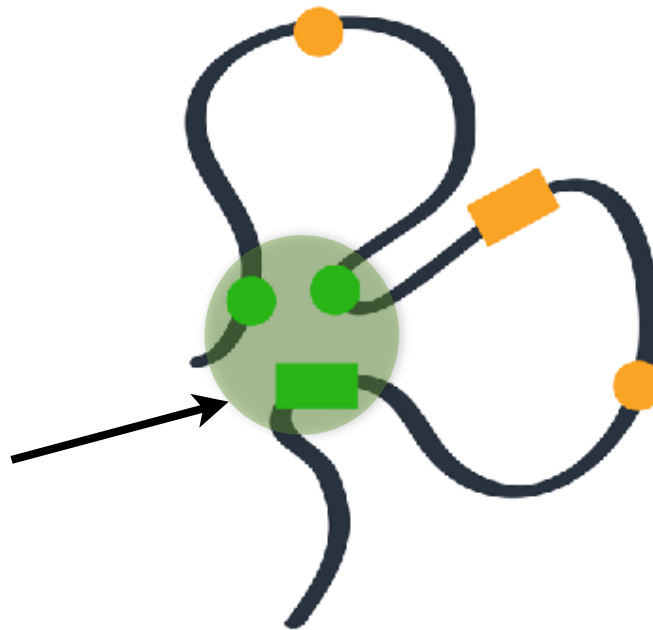
Level V: Chromatin loops

Gene
enhancers



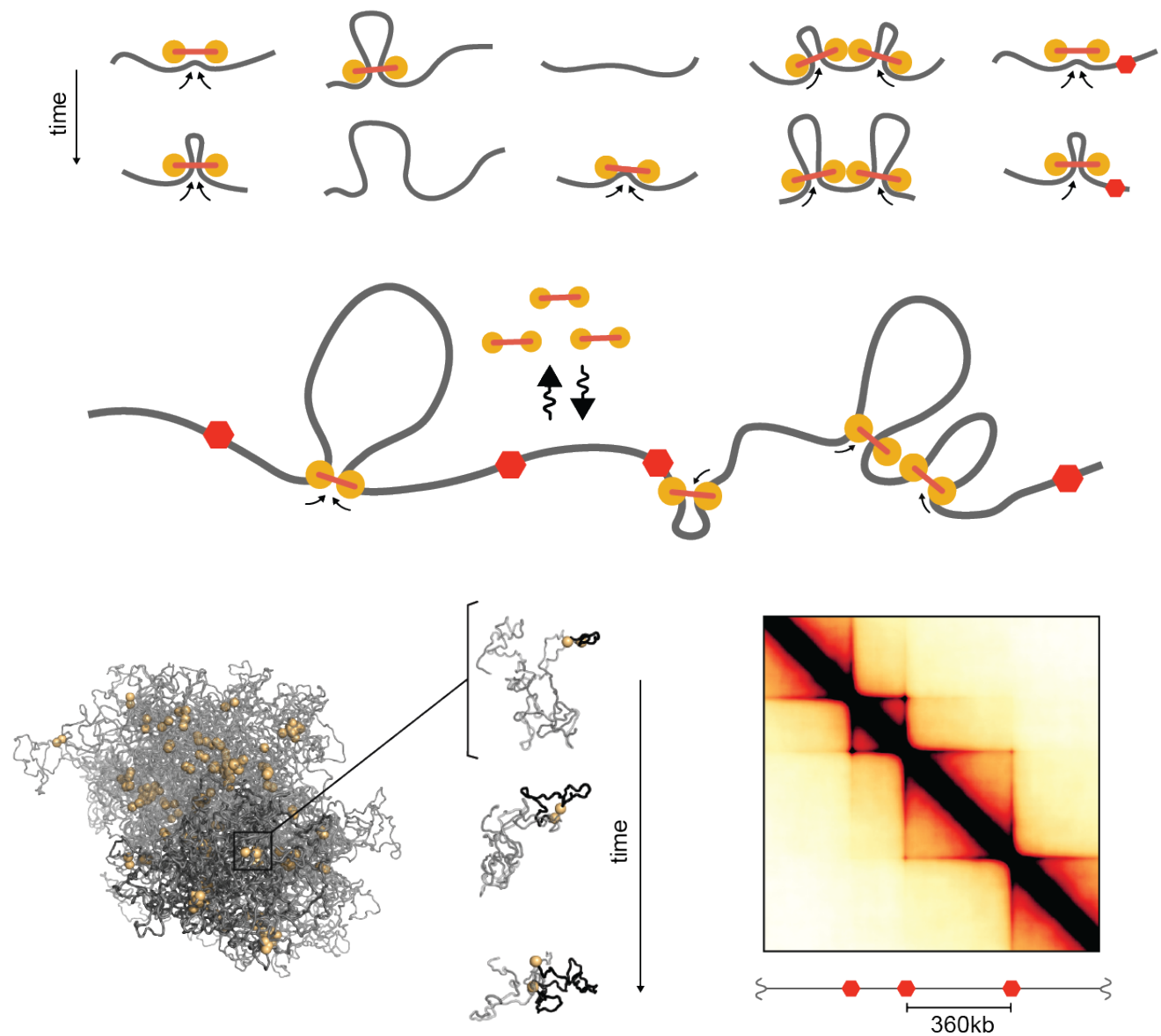
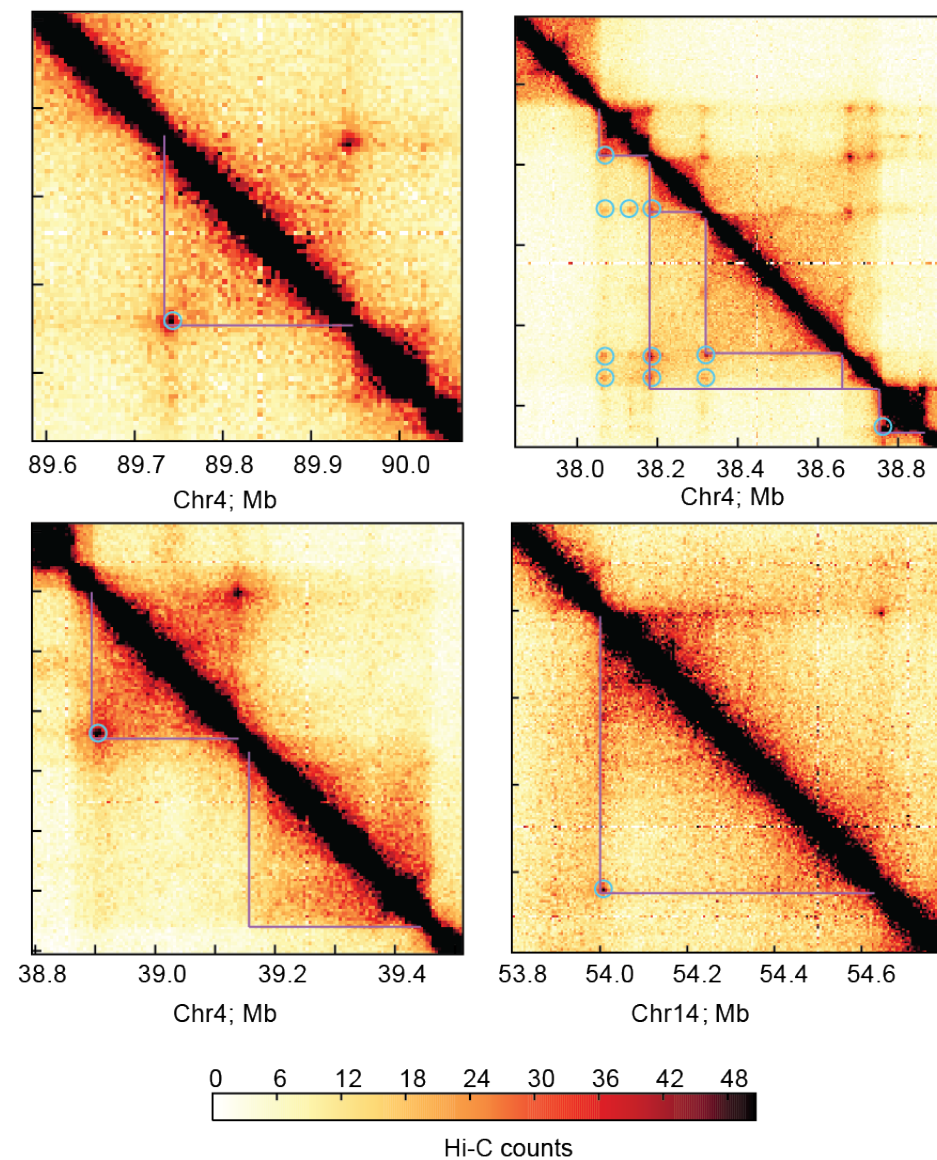
Gene

Gene
activity



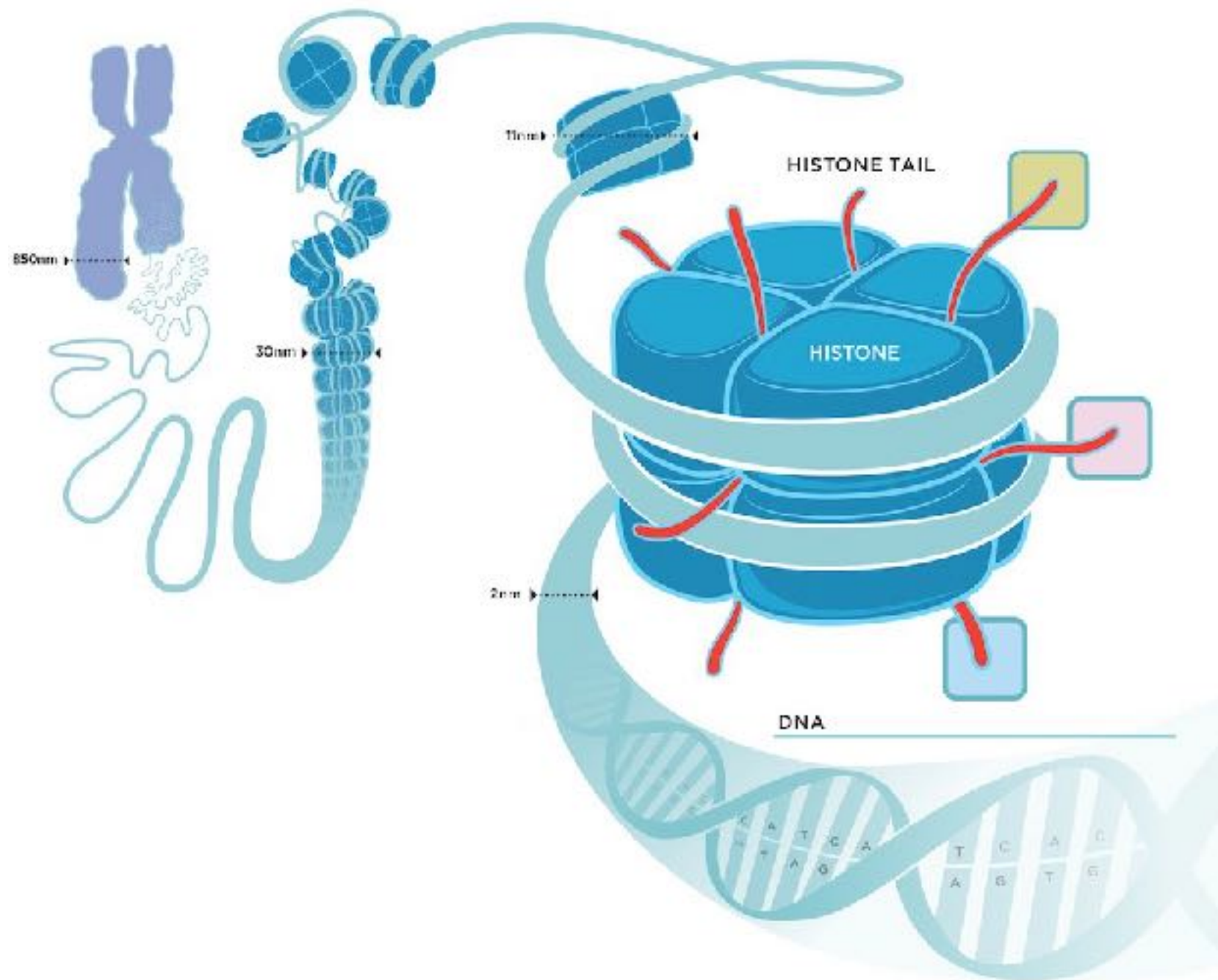
Level V: Loop-extrusion as a driving force

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



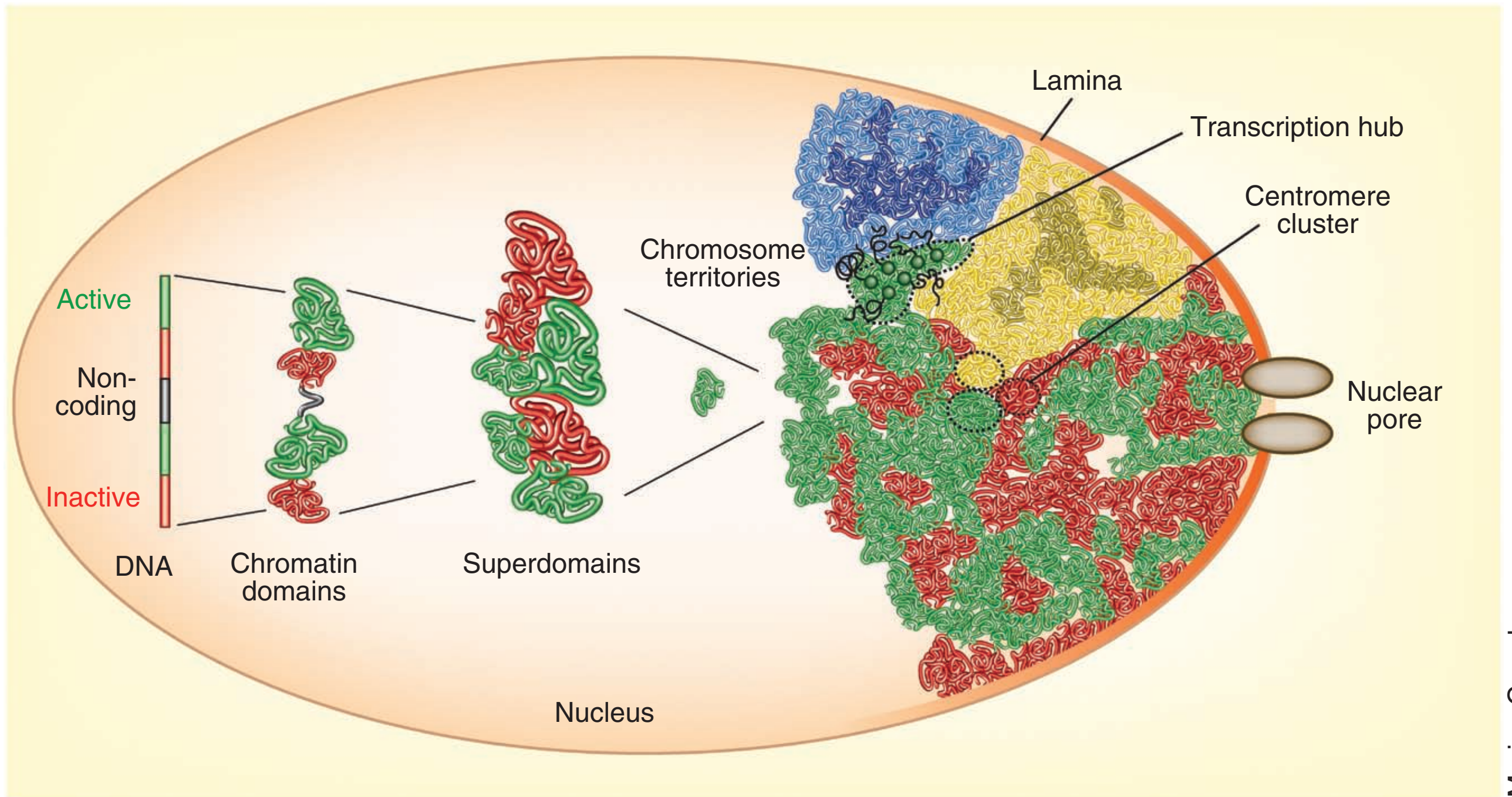
Level VI: Nucleosome

Chromosome Chromatin fibre Nucleosome

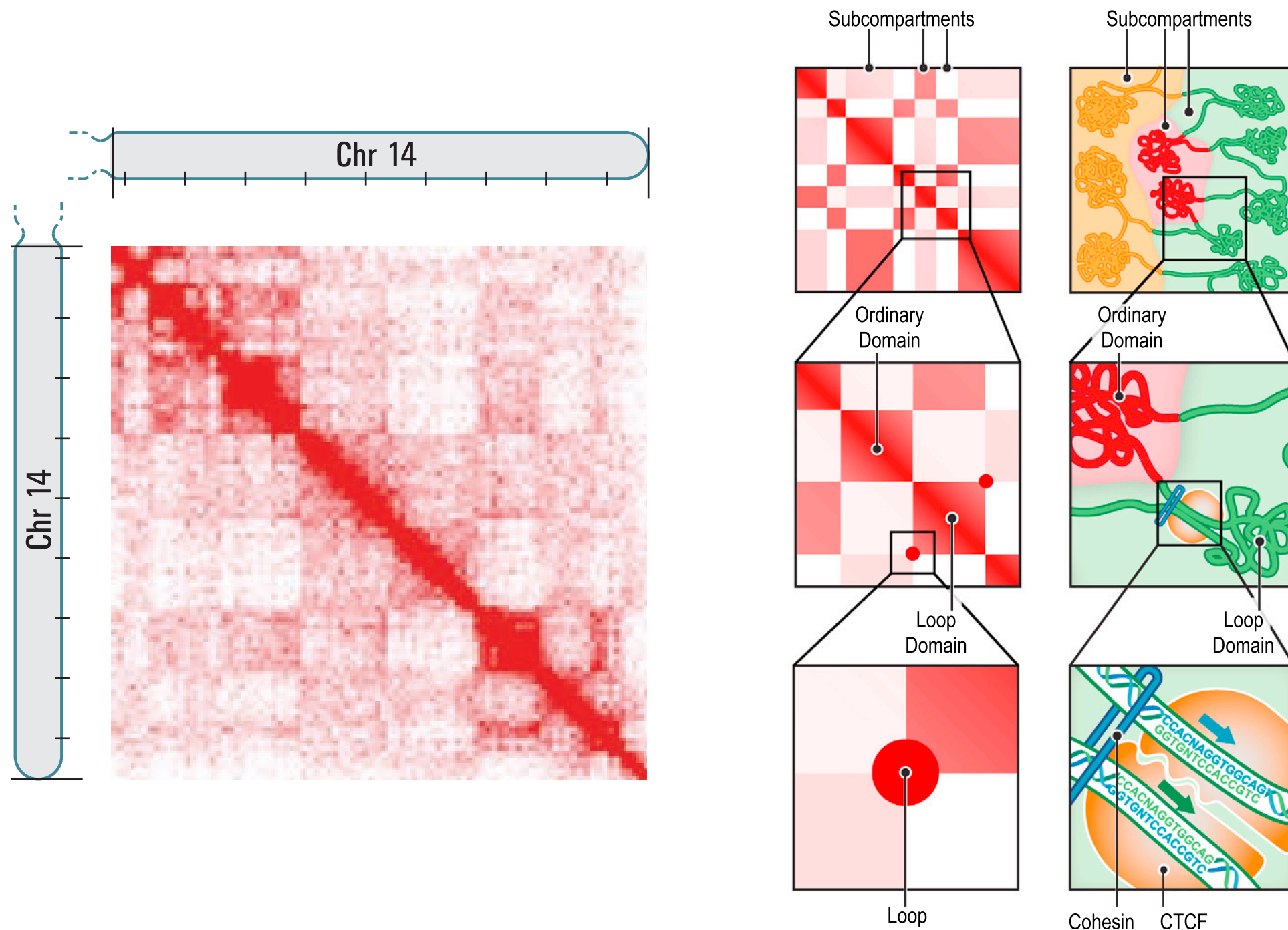


Complex genome organization

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



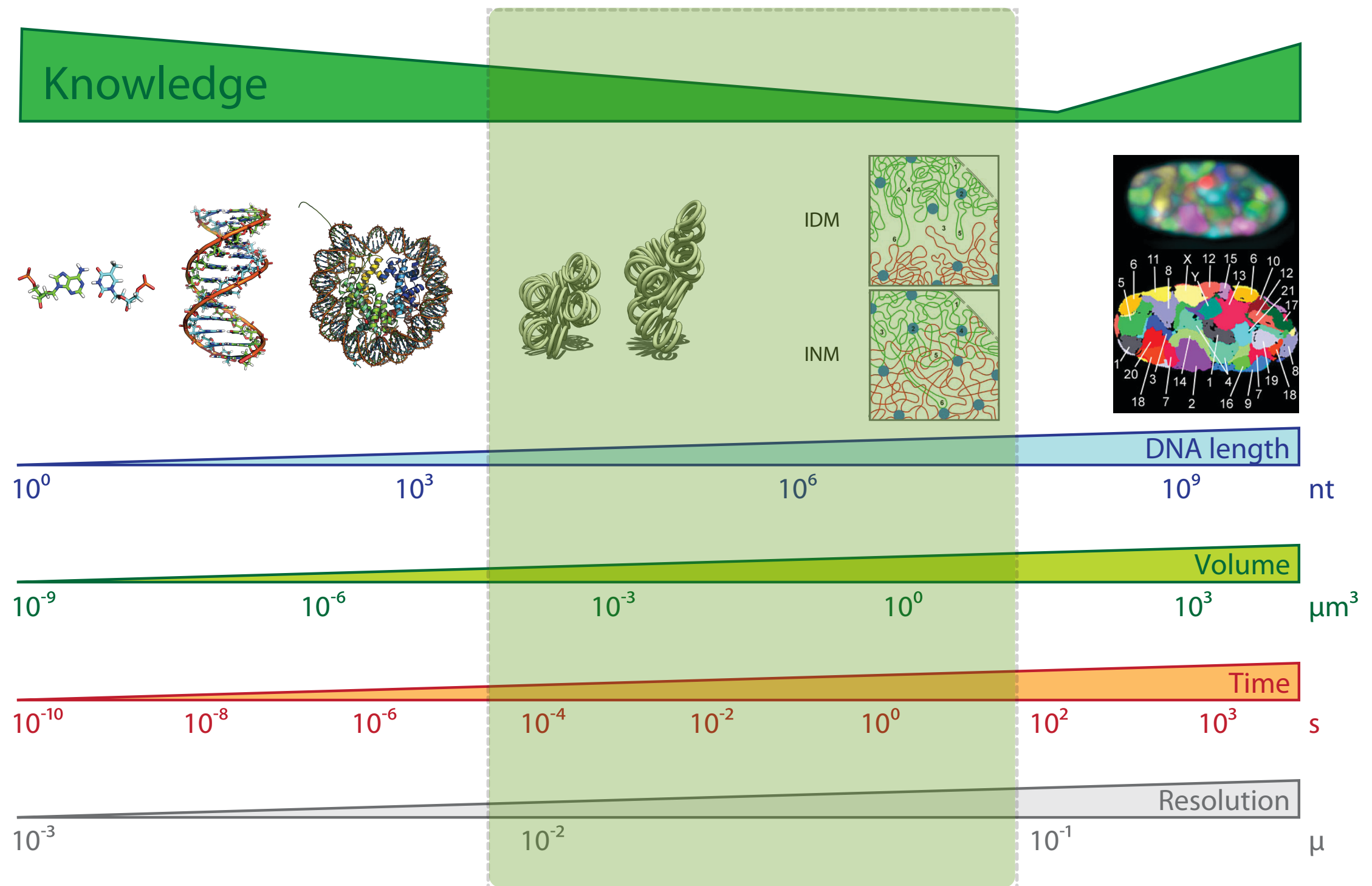
Hierarchical genome organisation



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

Resolution Gap

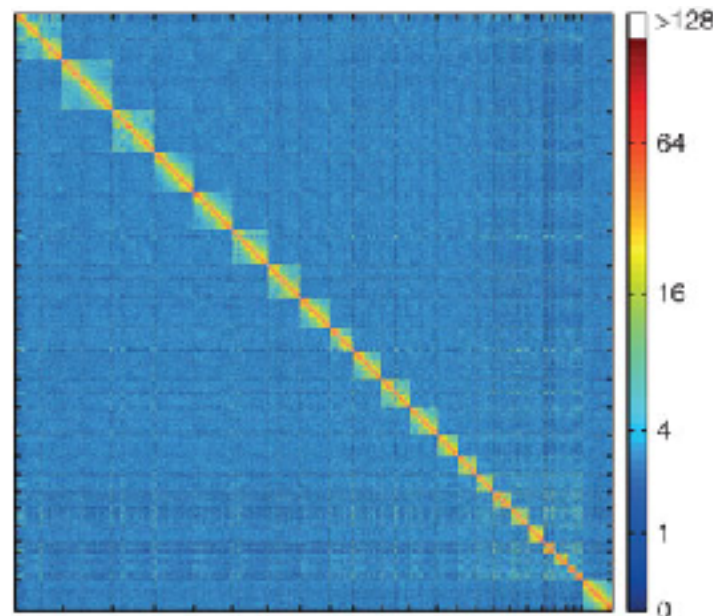
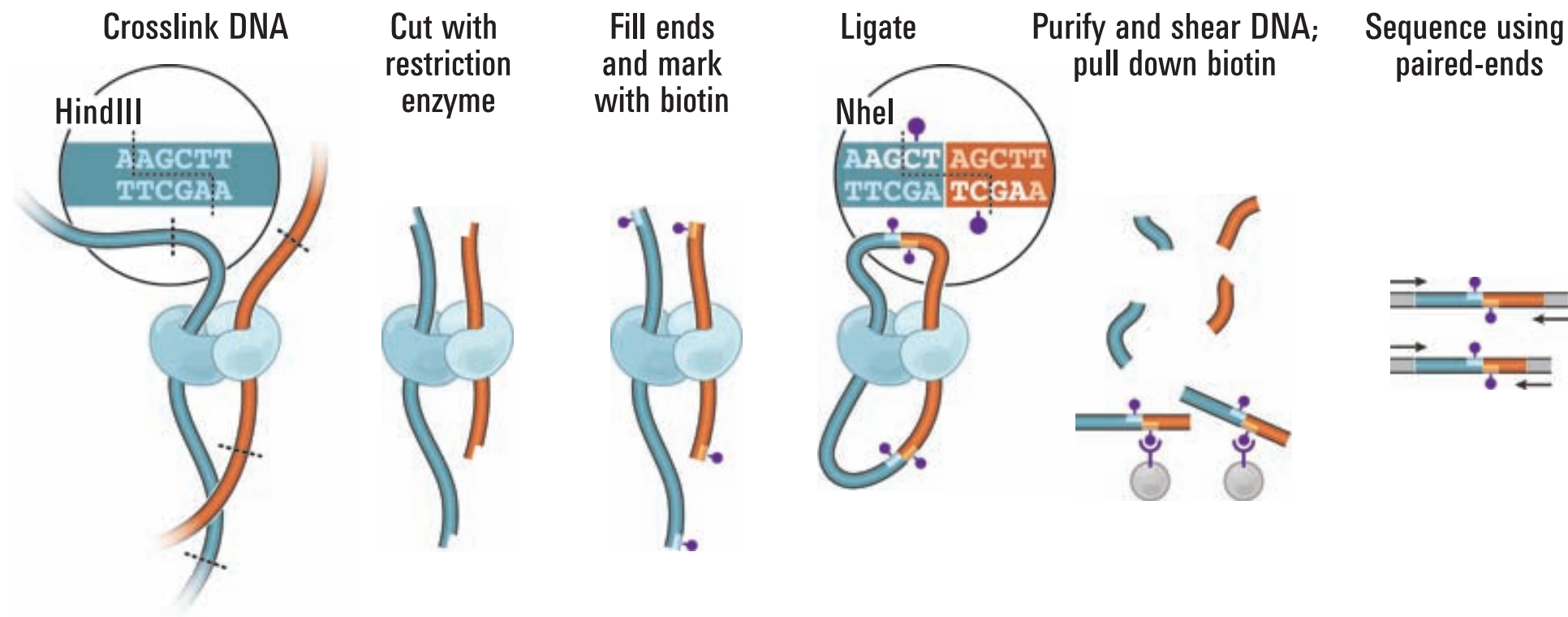
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)



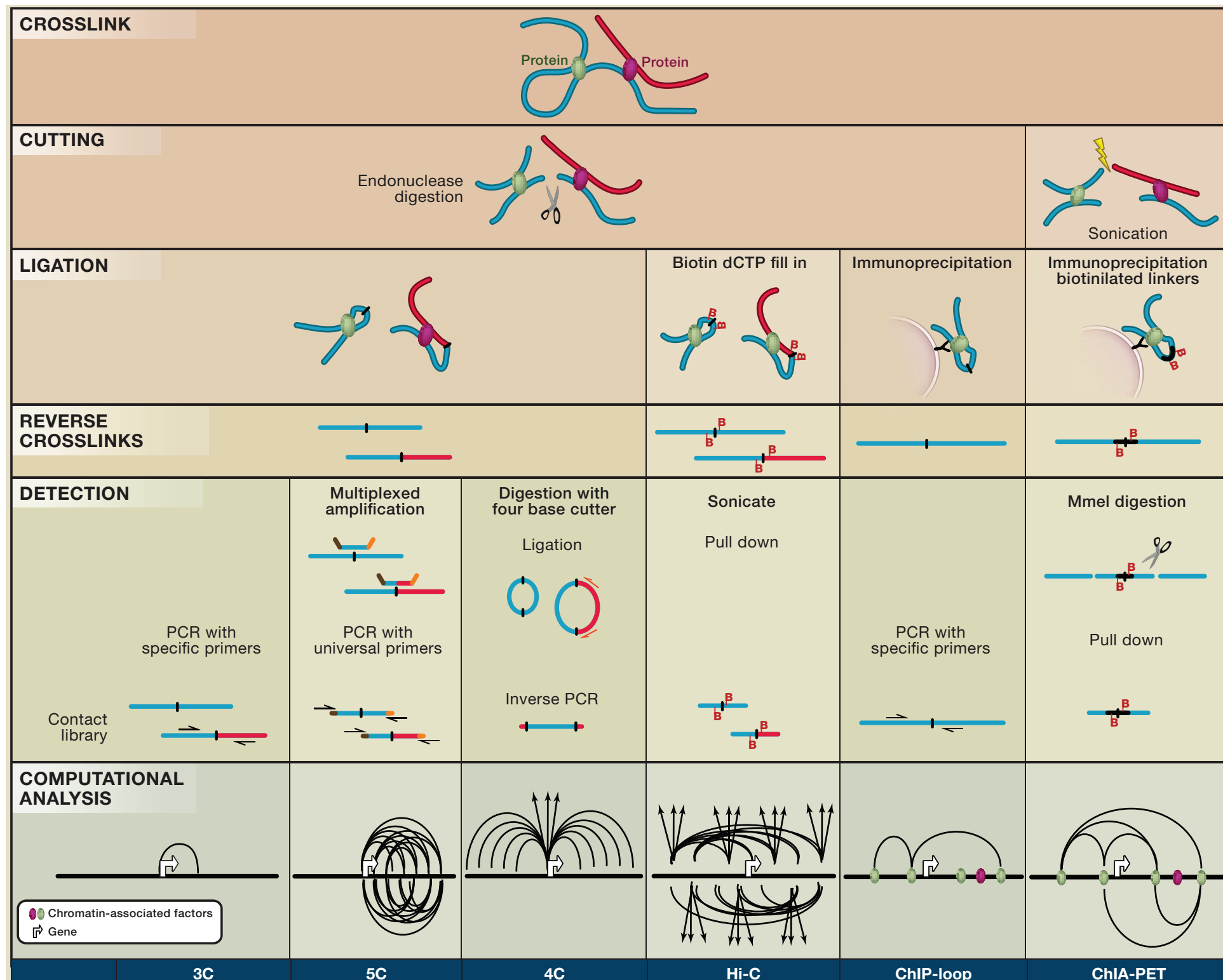
Chromosome Conformation Capture

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.

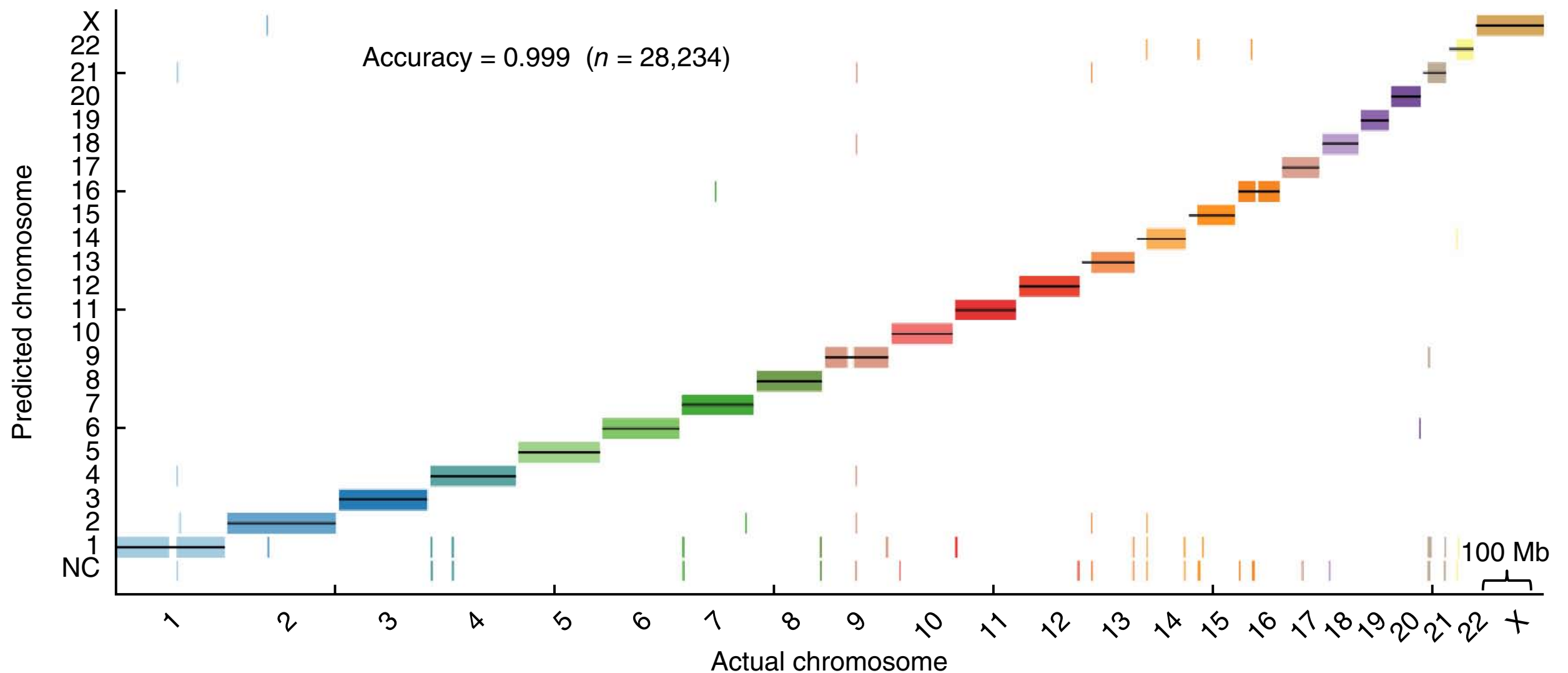


Chromosome Conformation Capture



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

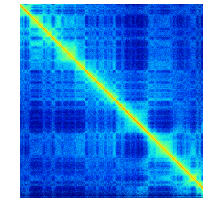
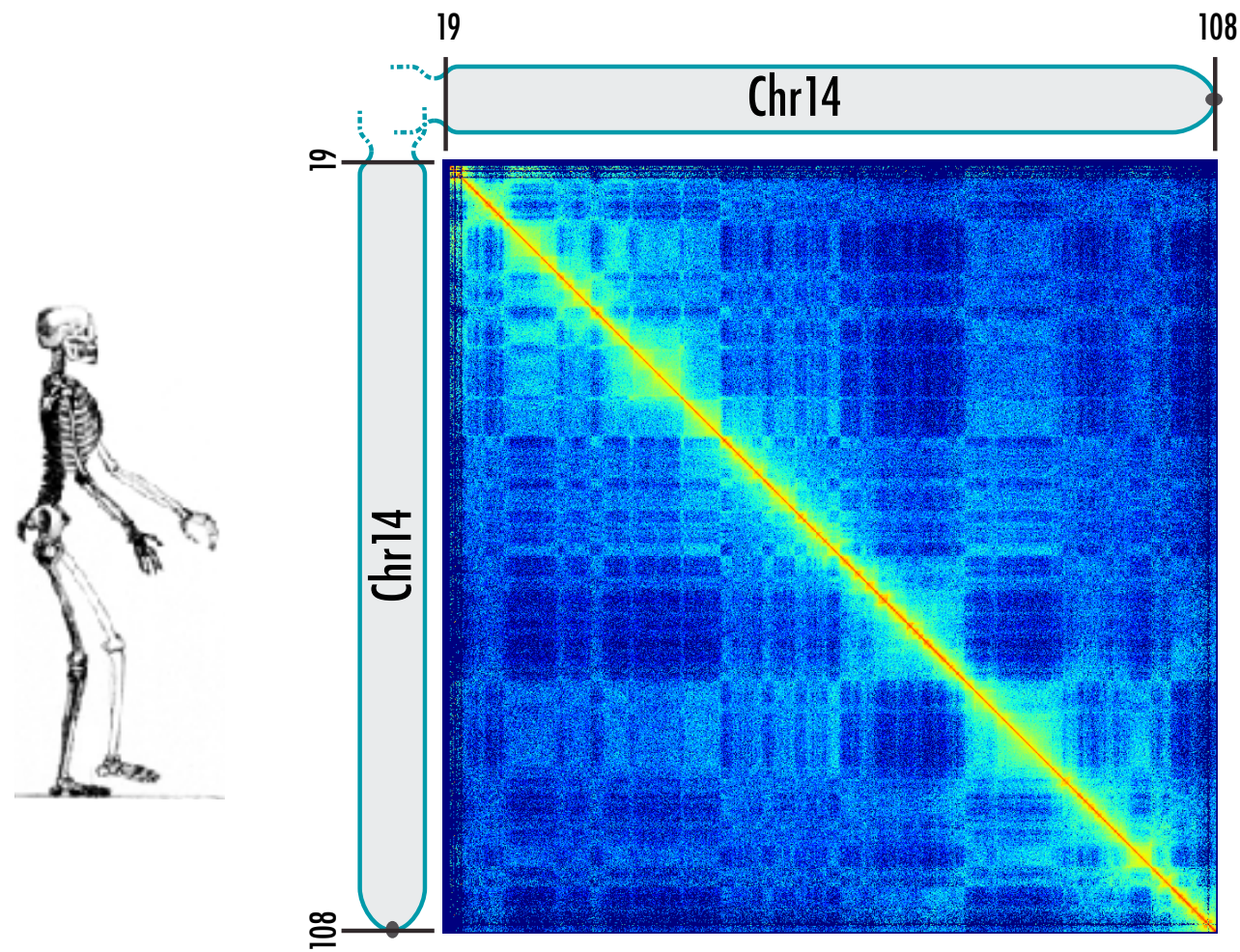
Chromosome Conformation Capture for de-novo assembly



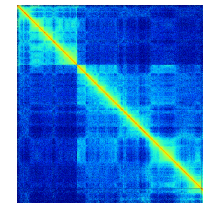
Kaplan, N., & Dekker, J. (2013). High-throughput genome scaffolding from in vivo DNA interaction frequency. *Nature Biotechnology*, 31(12), 1143–1147.

Great apes lymphoblast maps

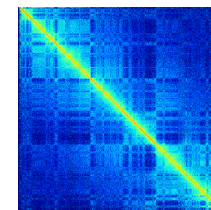
Chromosome 14



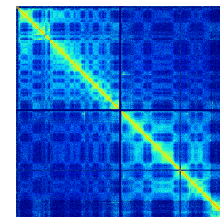
Chimpanzee



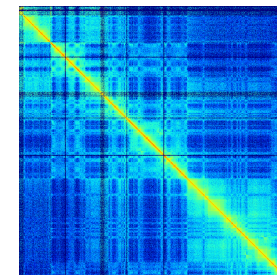
Gorilla



Orangutan



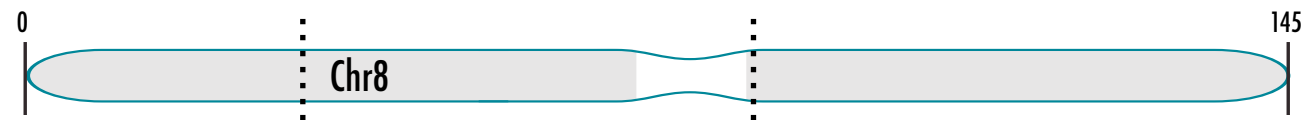
Gibbon



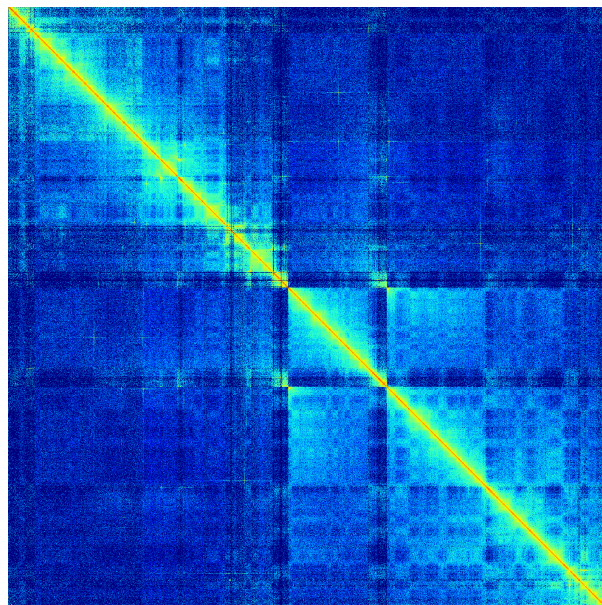
Mouse

Assembly error detection

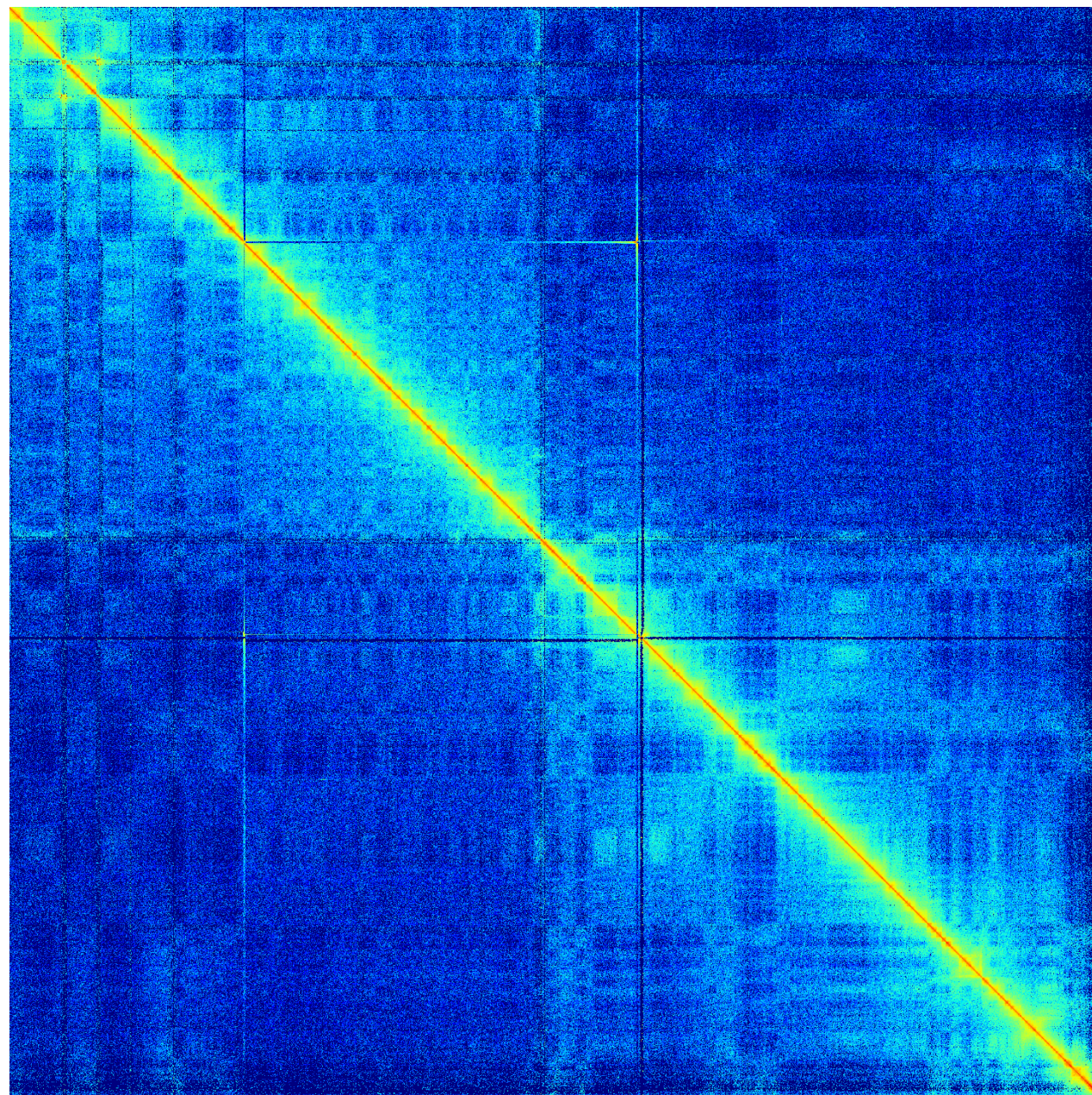
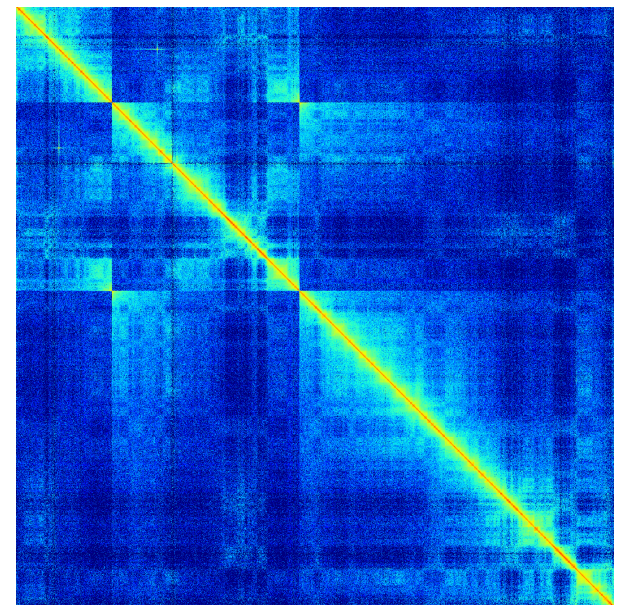
Chromosome 8 Gorilla



Chr 7

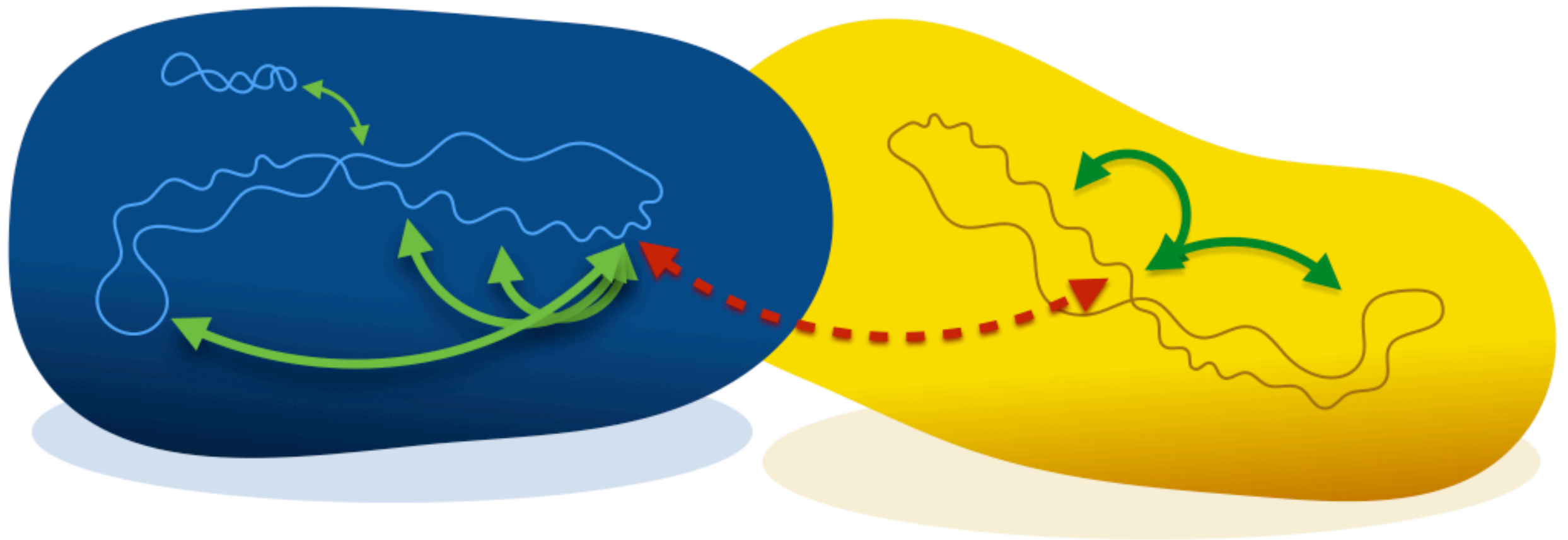


Chr 12



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

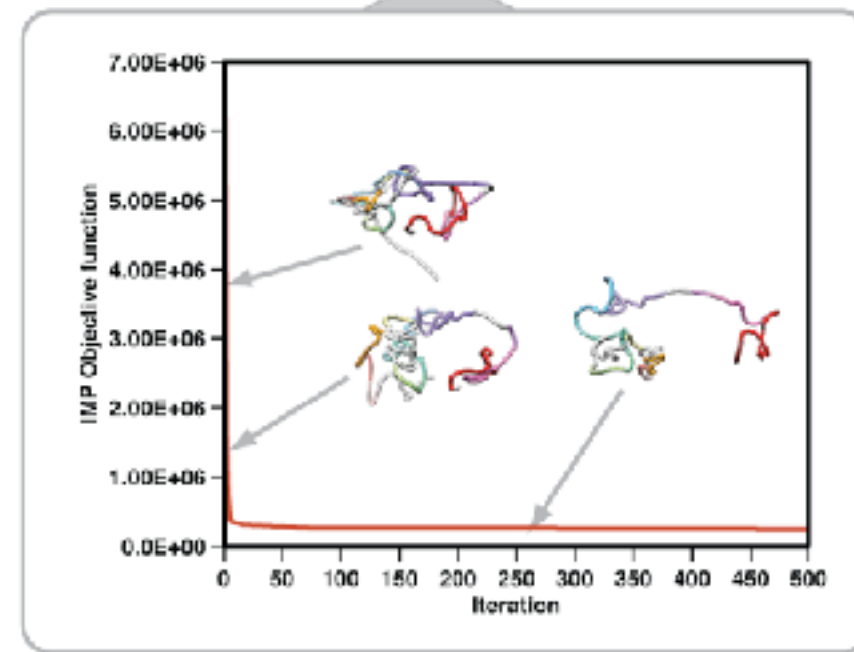
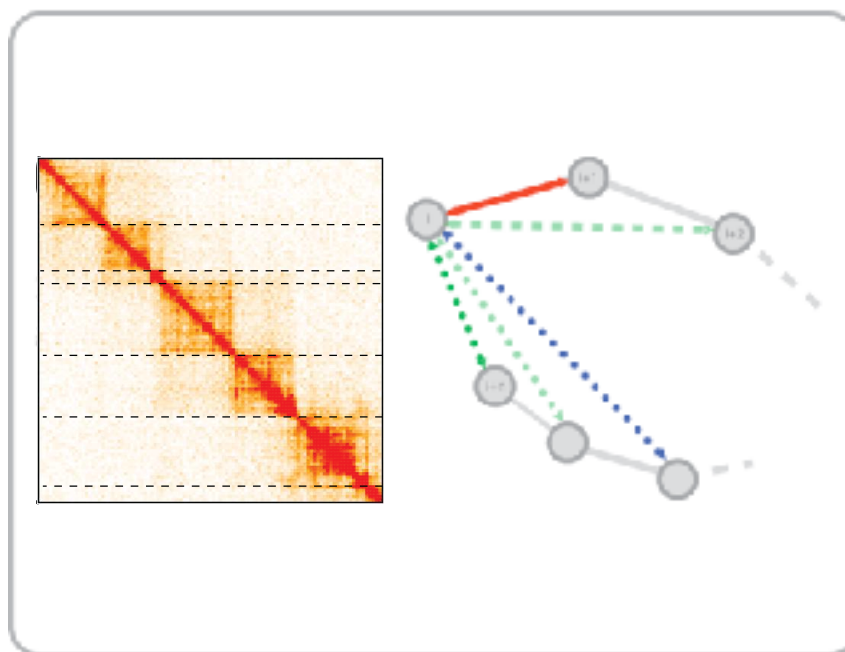
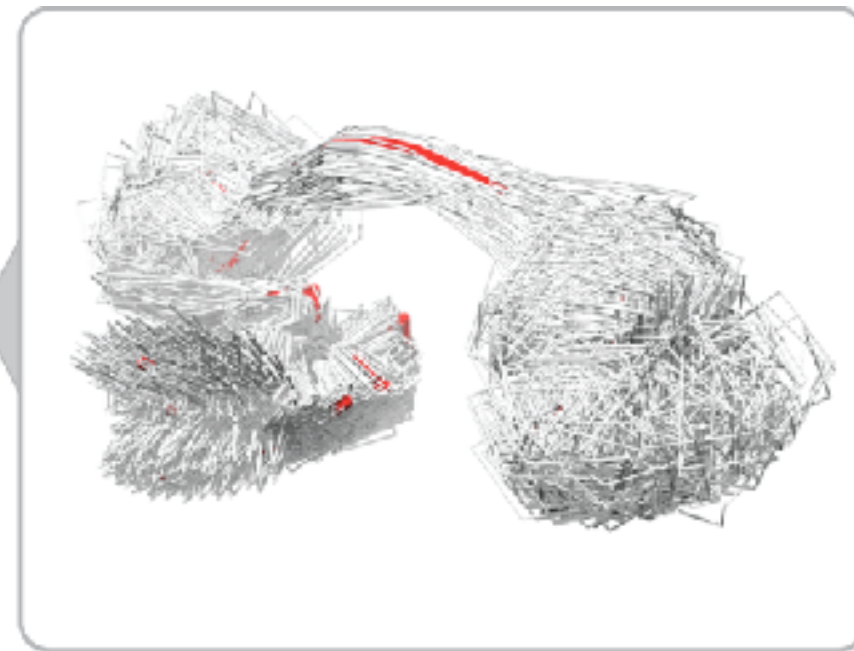
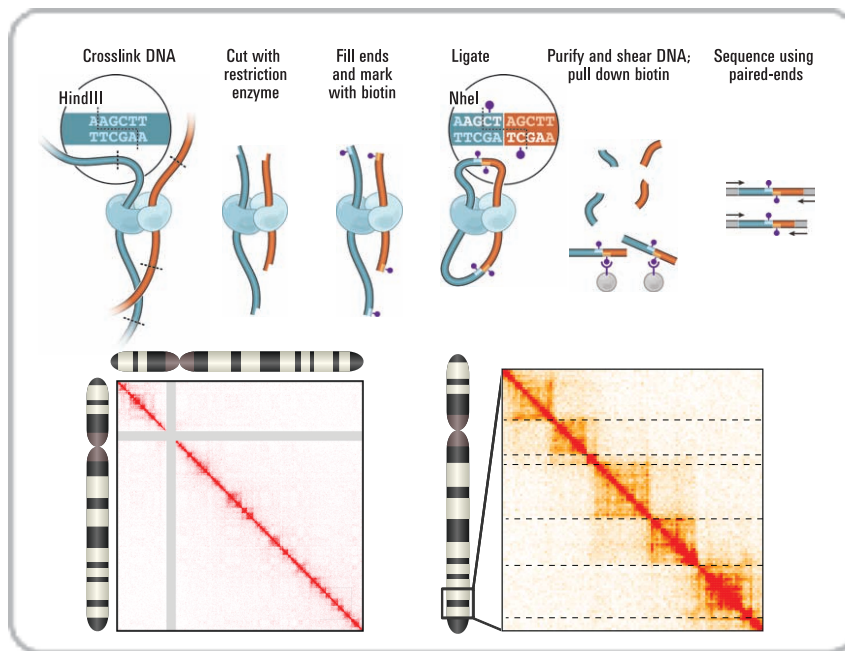


Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Micheltore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/peerj.preprints.260v1

Hybrid Method

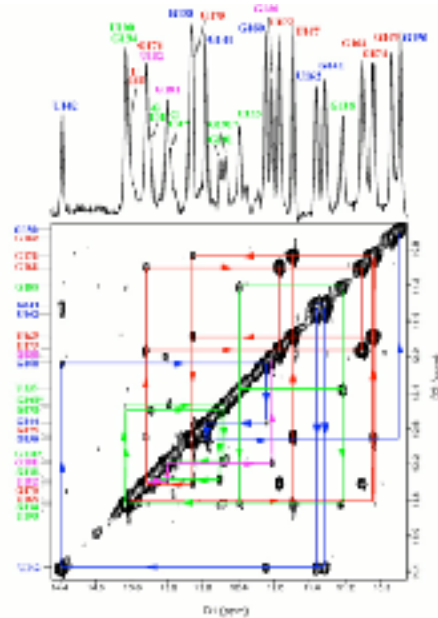
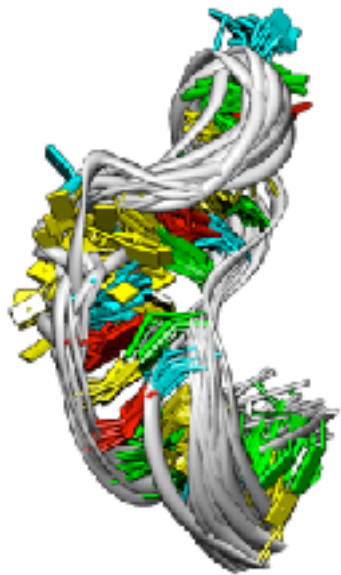
Baù, D. & Marti-Renom, M. A. *Methods* 58, 300–306 (2012).

Experiments

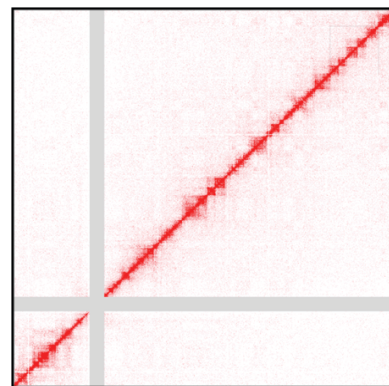
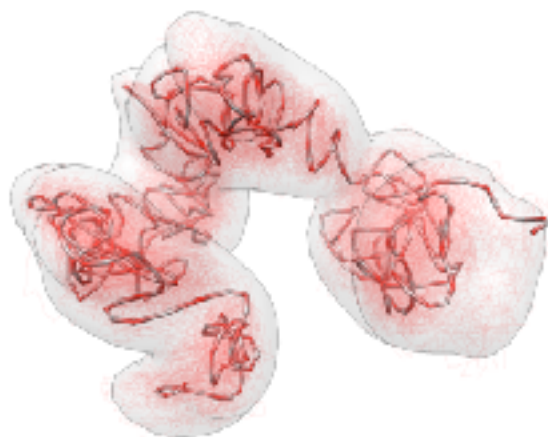


Computation

Structure determination using Hi-C data



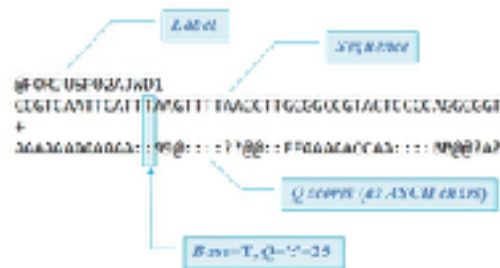
Biomolecular structure determination
2D-NOESY data



Chromosome structure determination
3C-based data



<http://3DGenomes.org>

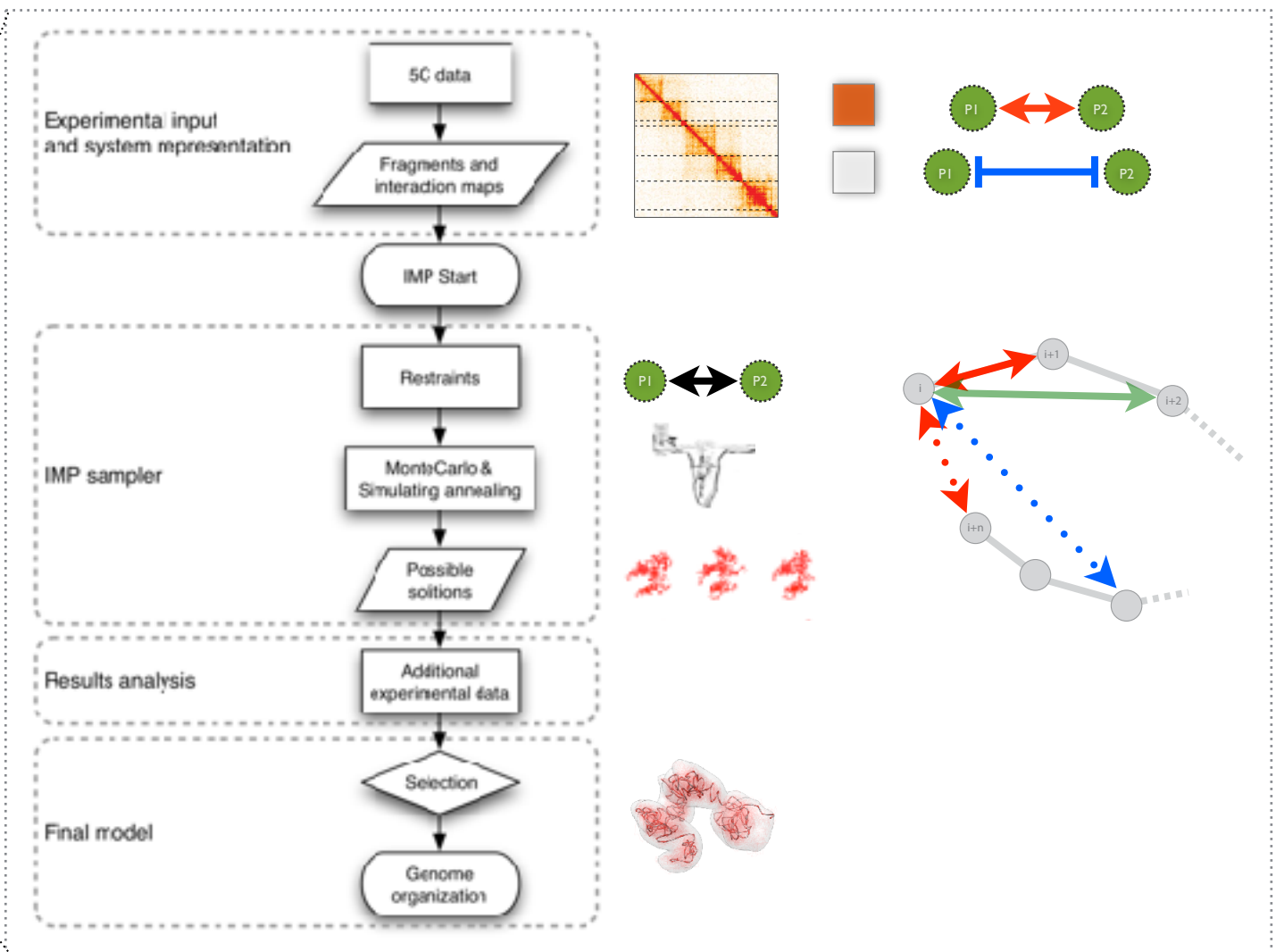


FastQ files to Maps

Map analysis

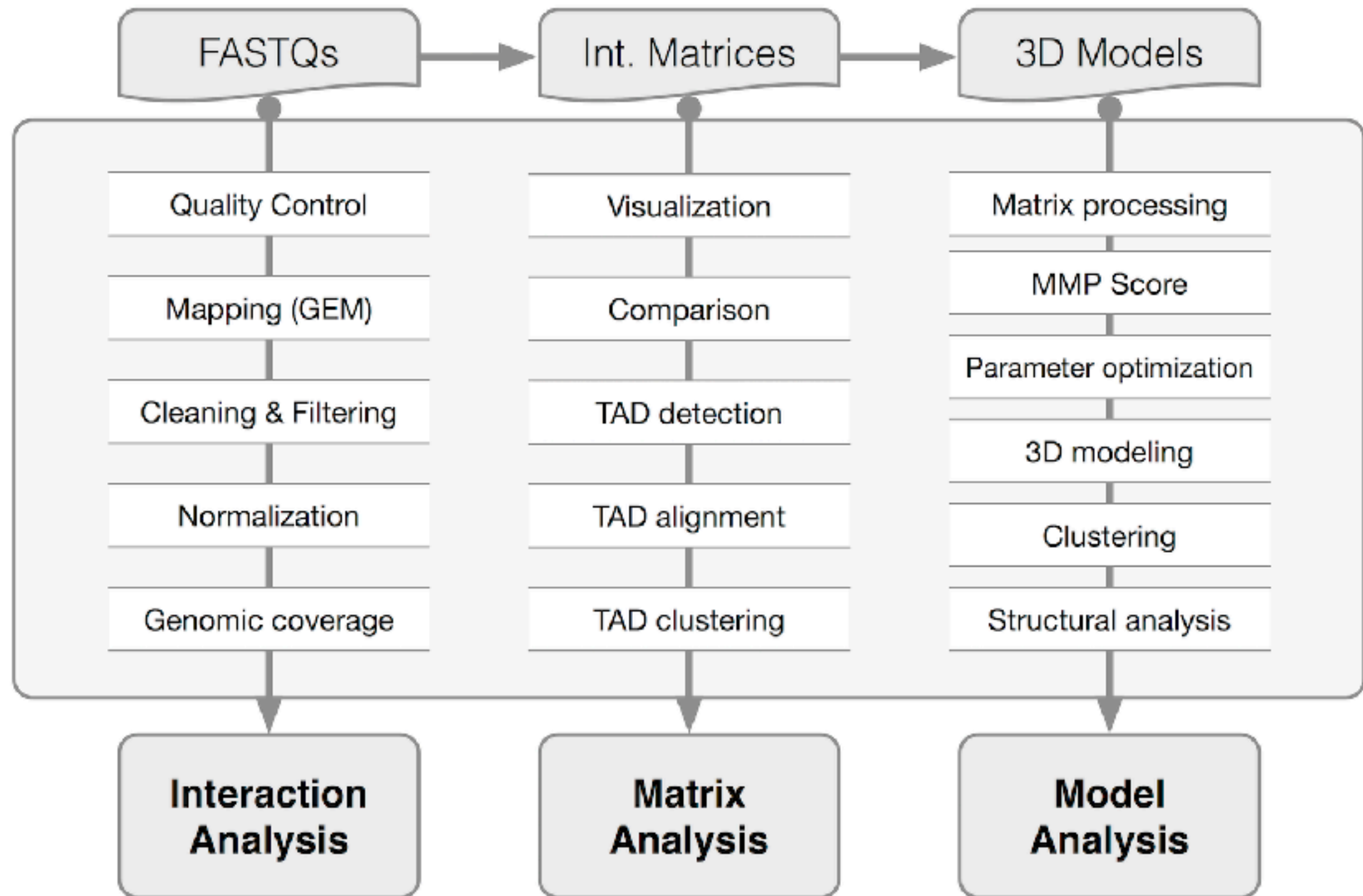
Model building

Model analysis



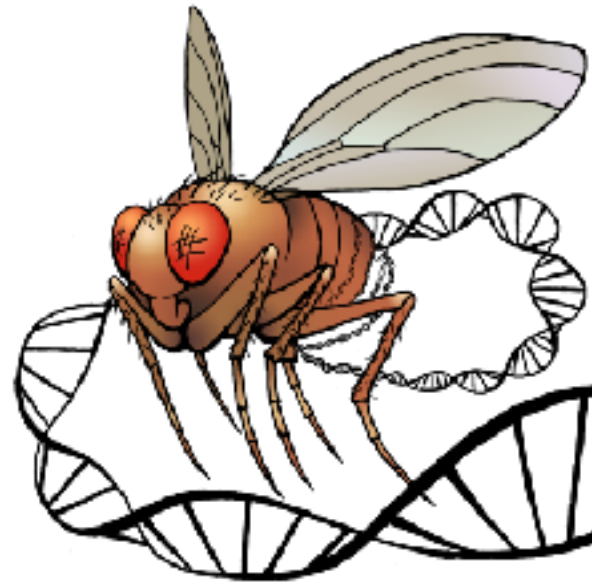


Serra, Baù, et al. (2017). PLOS CompBio



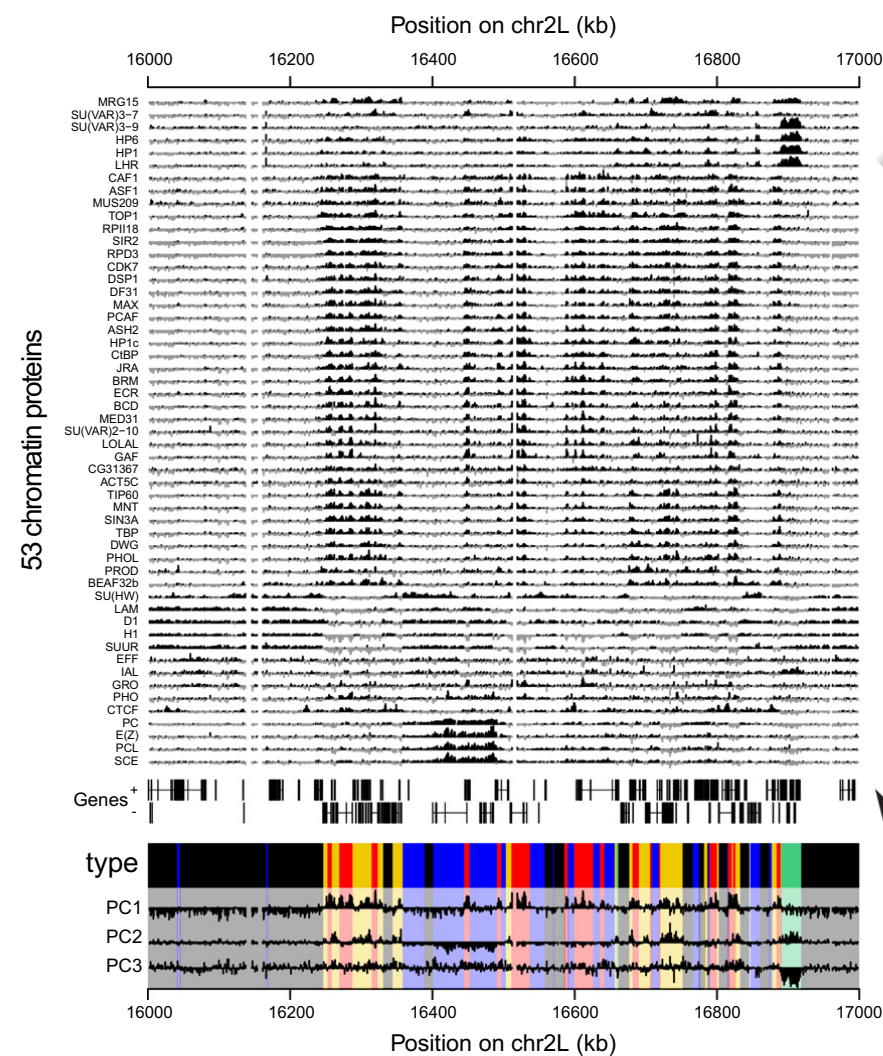
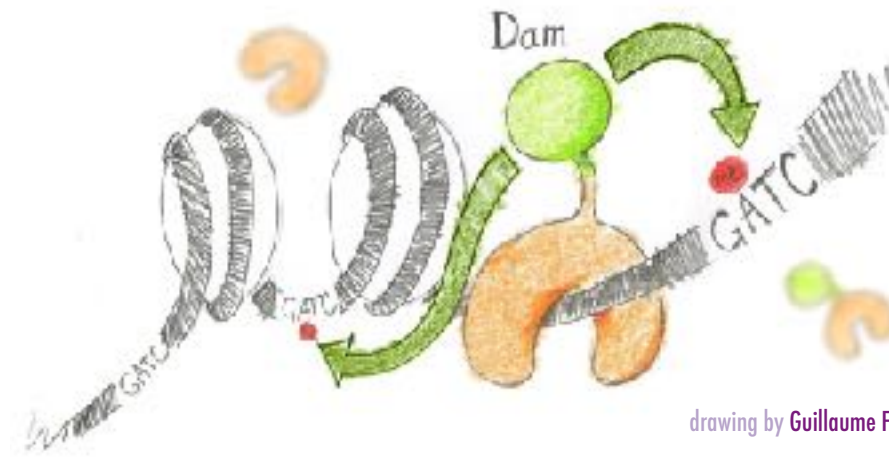
Structuring the **COLORs** of chromatin

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

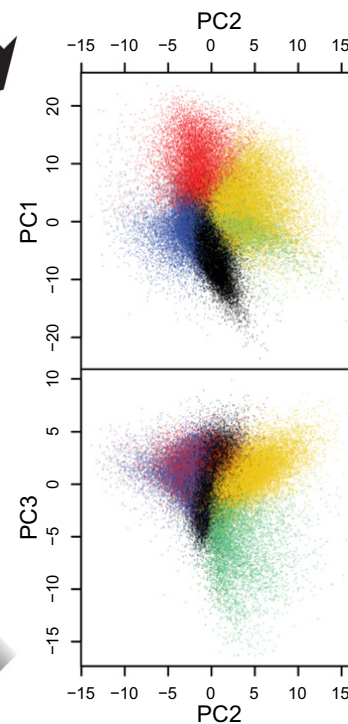


Fly Chromatin **COLORs**

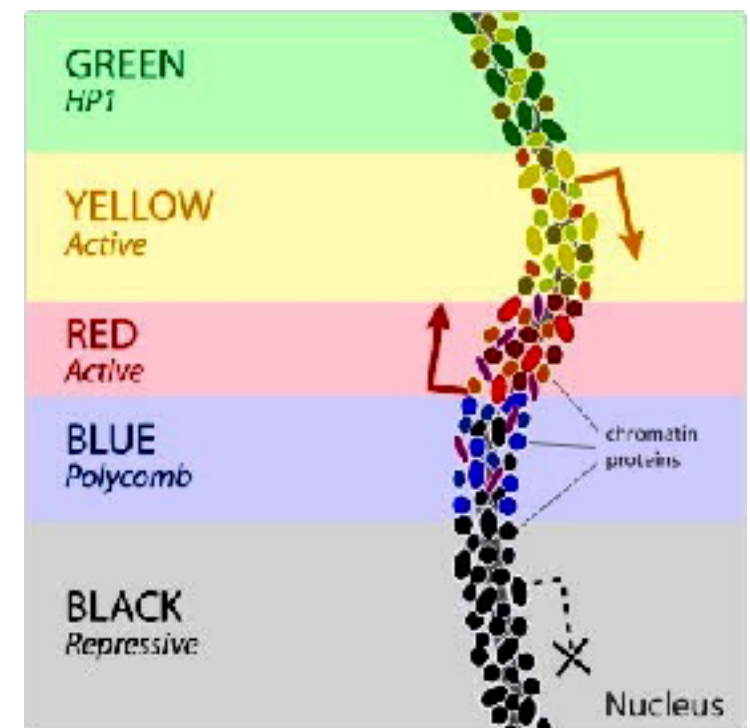
Filion et al. (2010). Cell, 143(2), 212–224.



Principal component analysis

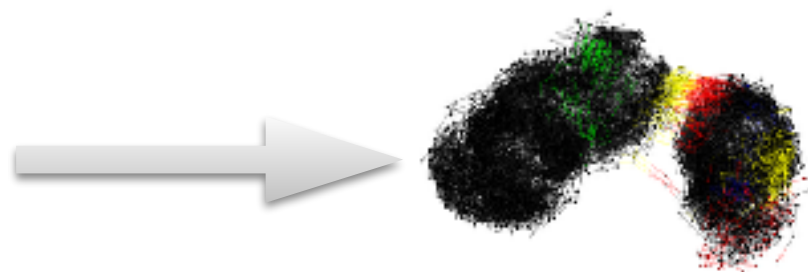
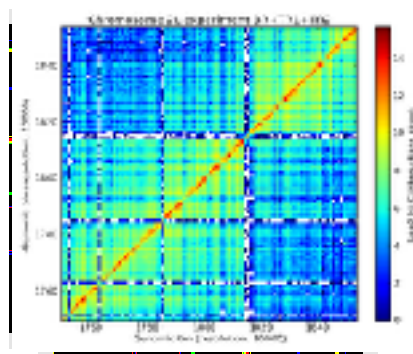
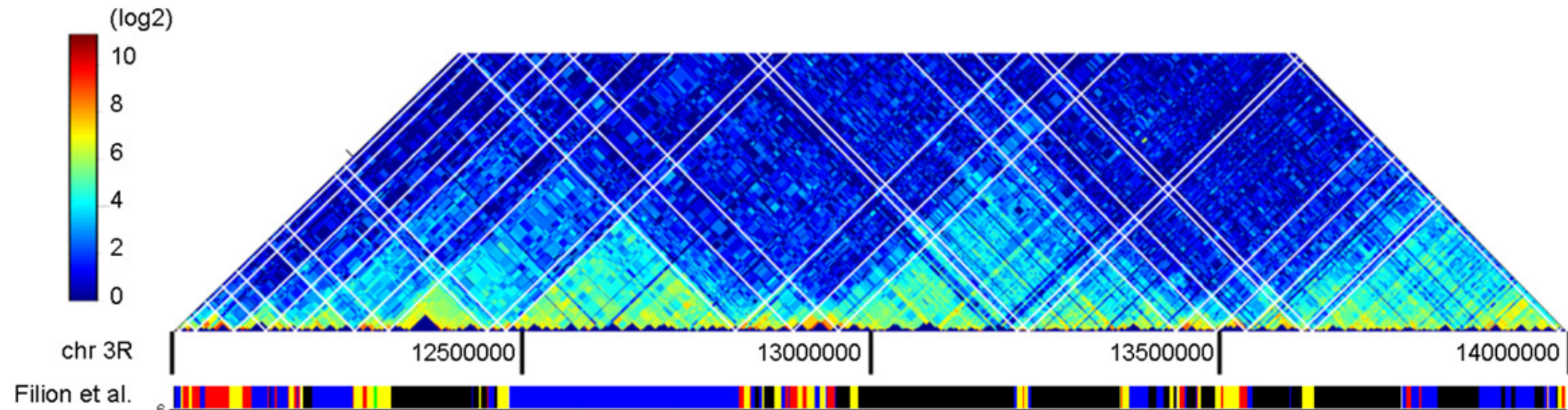


Hidden Markov model



Fly Chromatin **COLORs**

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

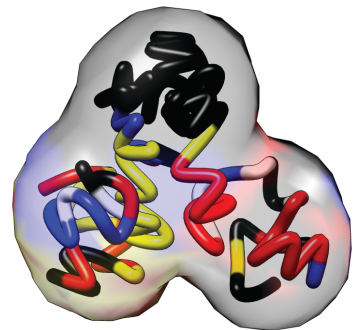


~200 regions of ~5Mb each
2Kb resolution

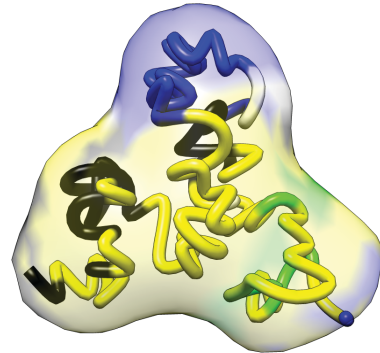
Structural properties

50 1Mb regions. 10 enriched for each color.

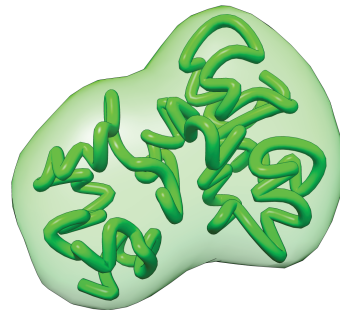
RED dense region
3R:18920000-19920000
22% 17% 0% 11% 45% 6%



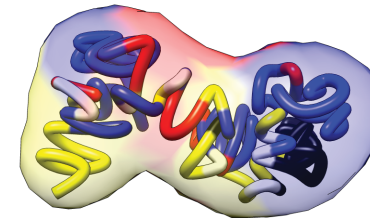
YELLOW dense region
X:15590000-16600000
0% 48% 4% 20% 26% 3%



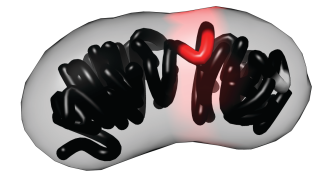
GREEN dense region
2R:510000-1530000
0% 0% 100% 0% 0% 0%



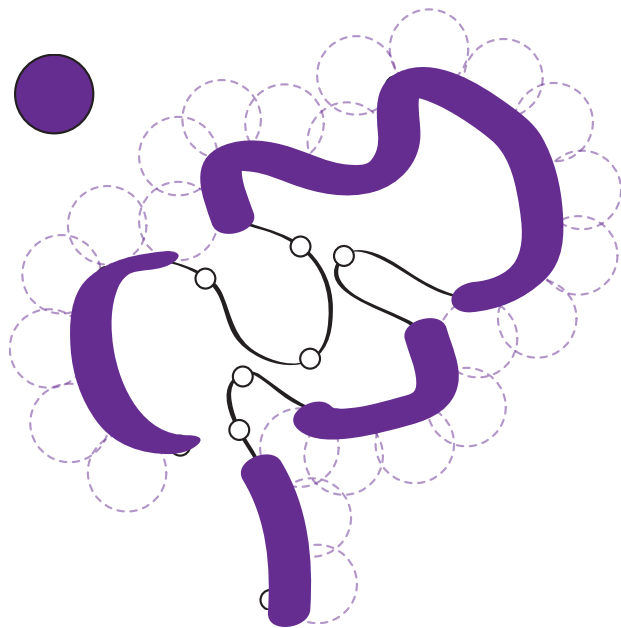
BLUE dense region
3L:210000-1230000
11% 17% 0% 52% 13% 0%



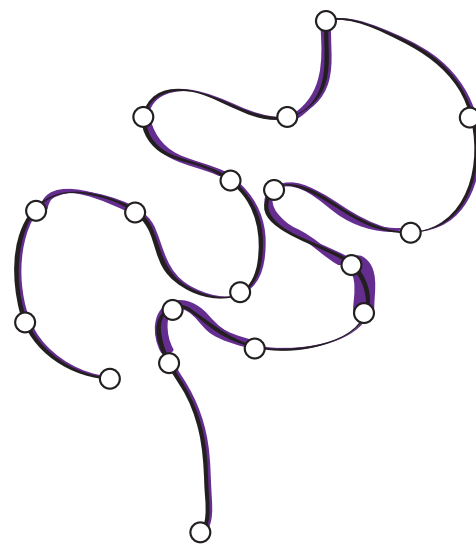
BLACK dense region
2L:17500000-18530000
1% 0% 0% 0% 98% 1%



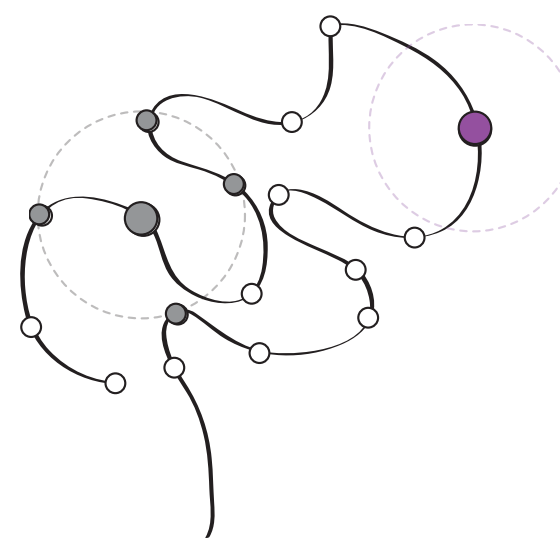
Accessibility (%)



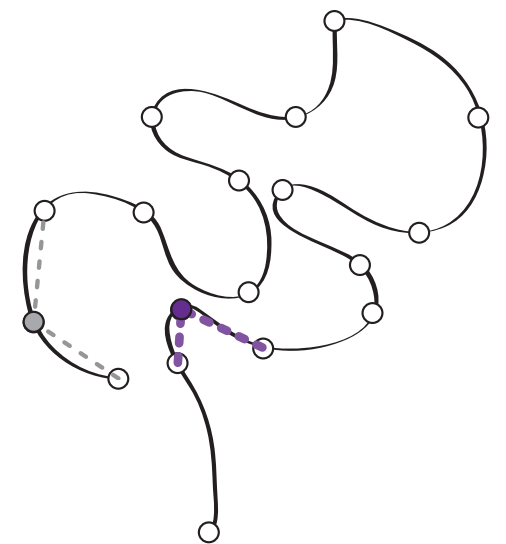
Density (bp/nm)



Interactions



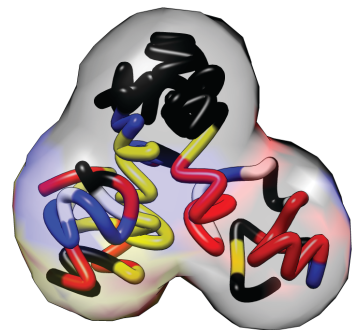
Angle



Structural **CO**LO**R**s

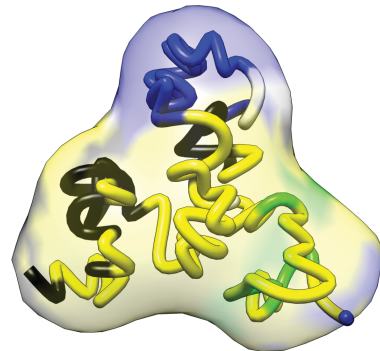
RED dense region
3R:18920000-19920000

22% 17% 0% 11% 45% 6%



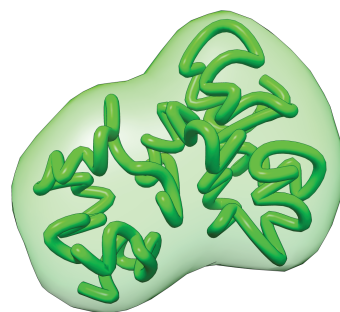
YELLOW dense region
X:15590000-16600000

0% 48% 4% 20% 26% 3%



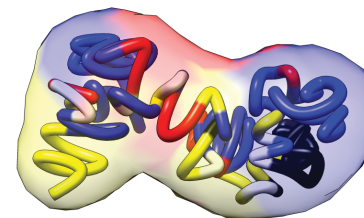
GREEN dense region
2R:510000-1530000

0% 0% 100% 0% 0% 0%



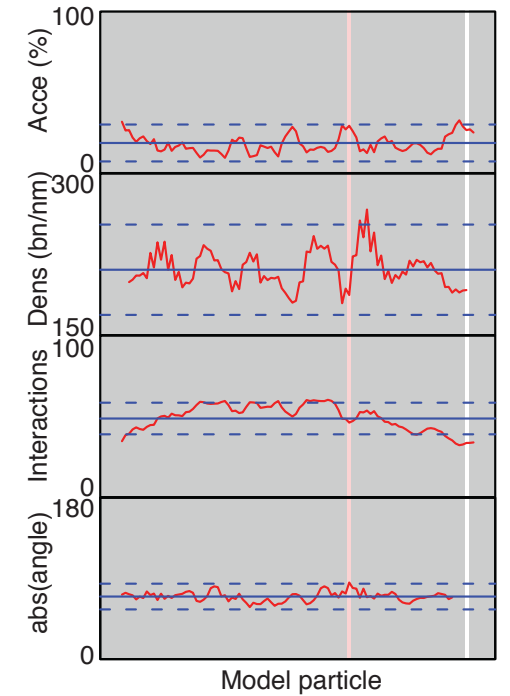
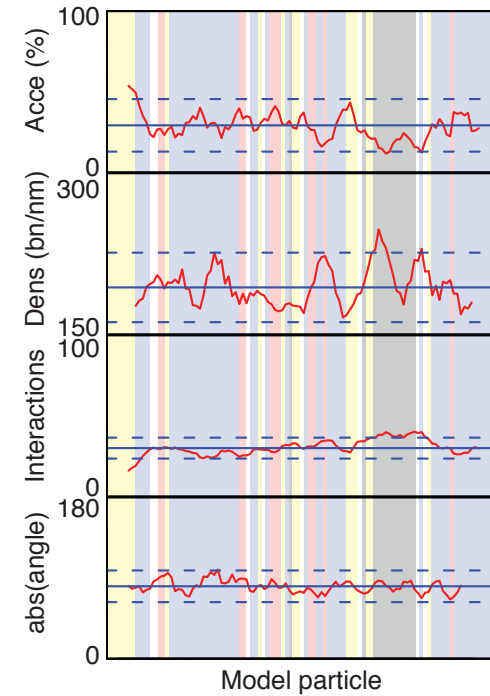
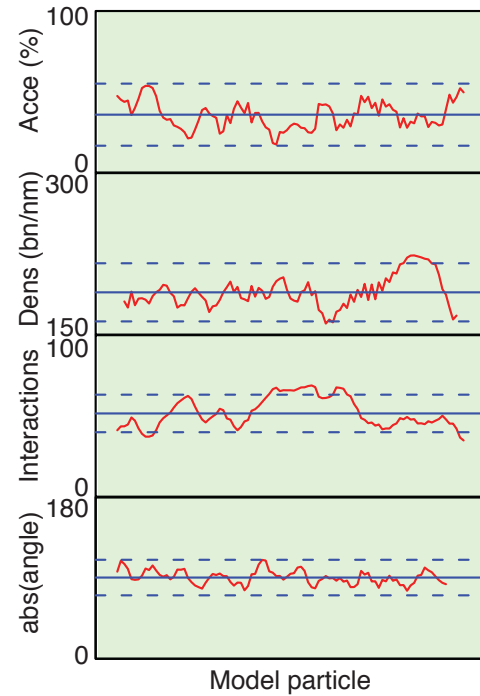
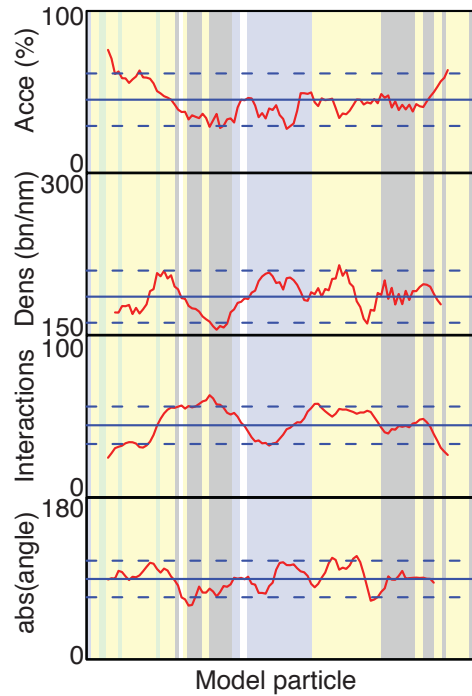
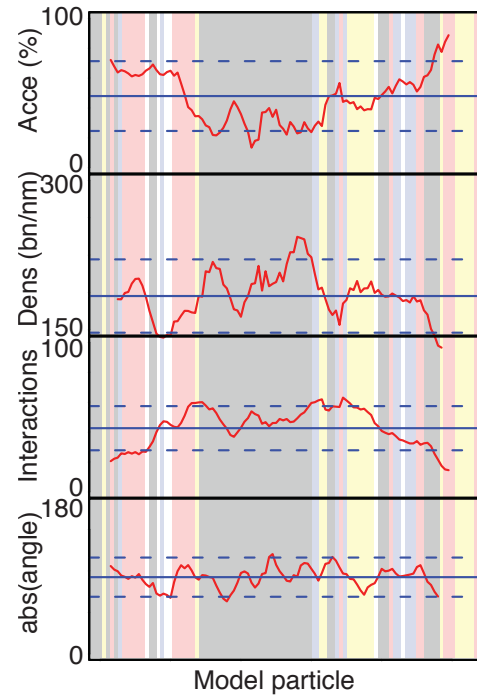
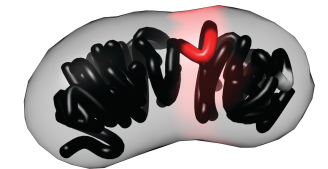
BLUE dense region
3L:210000-1230000

11% 17% 0% 52% 13% 0%

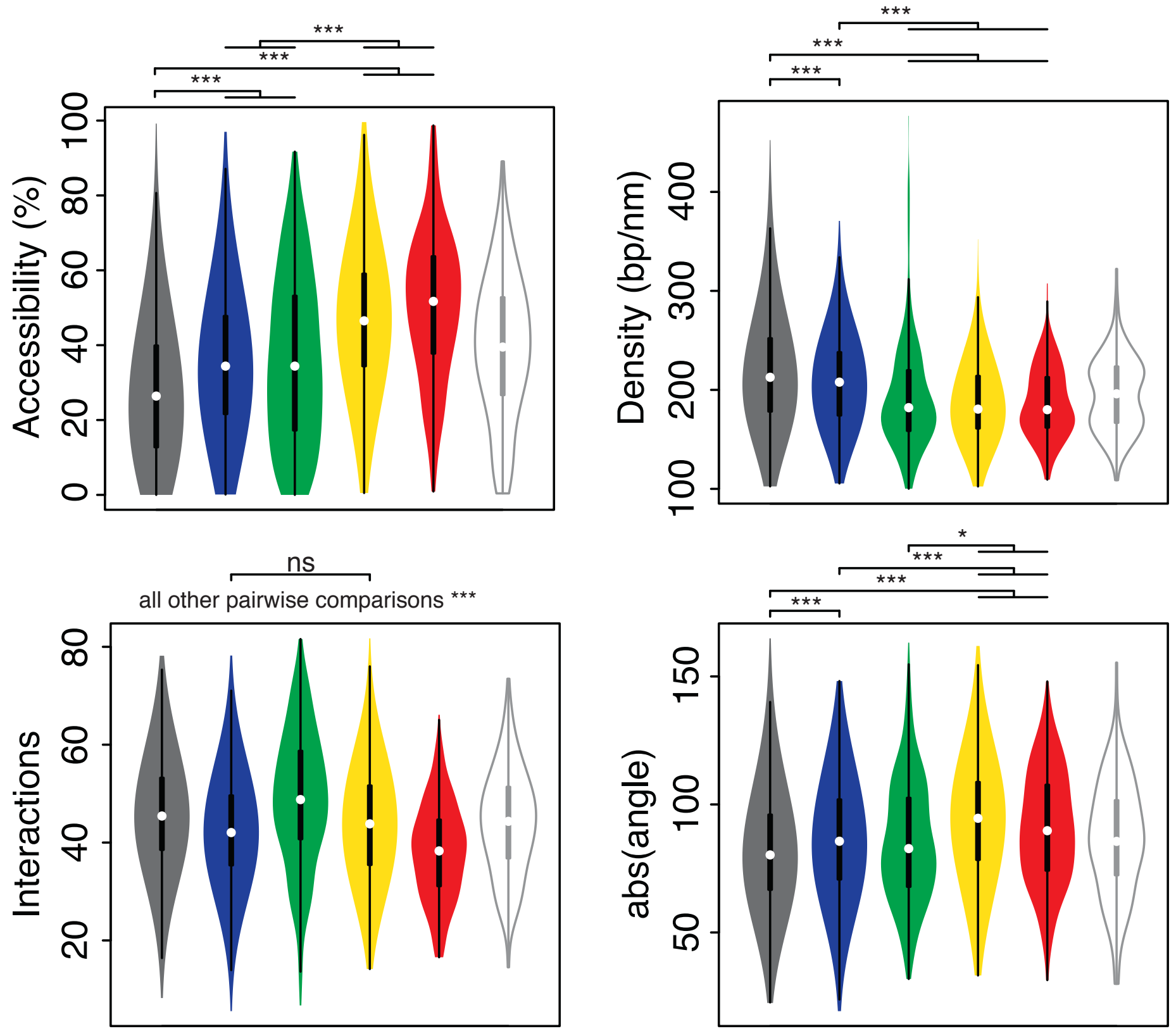


BLACK dense region
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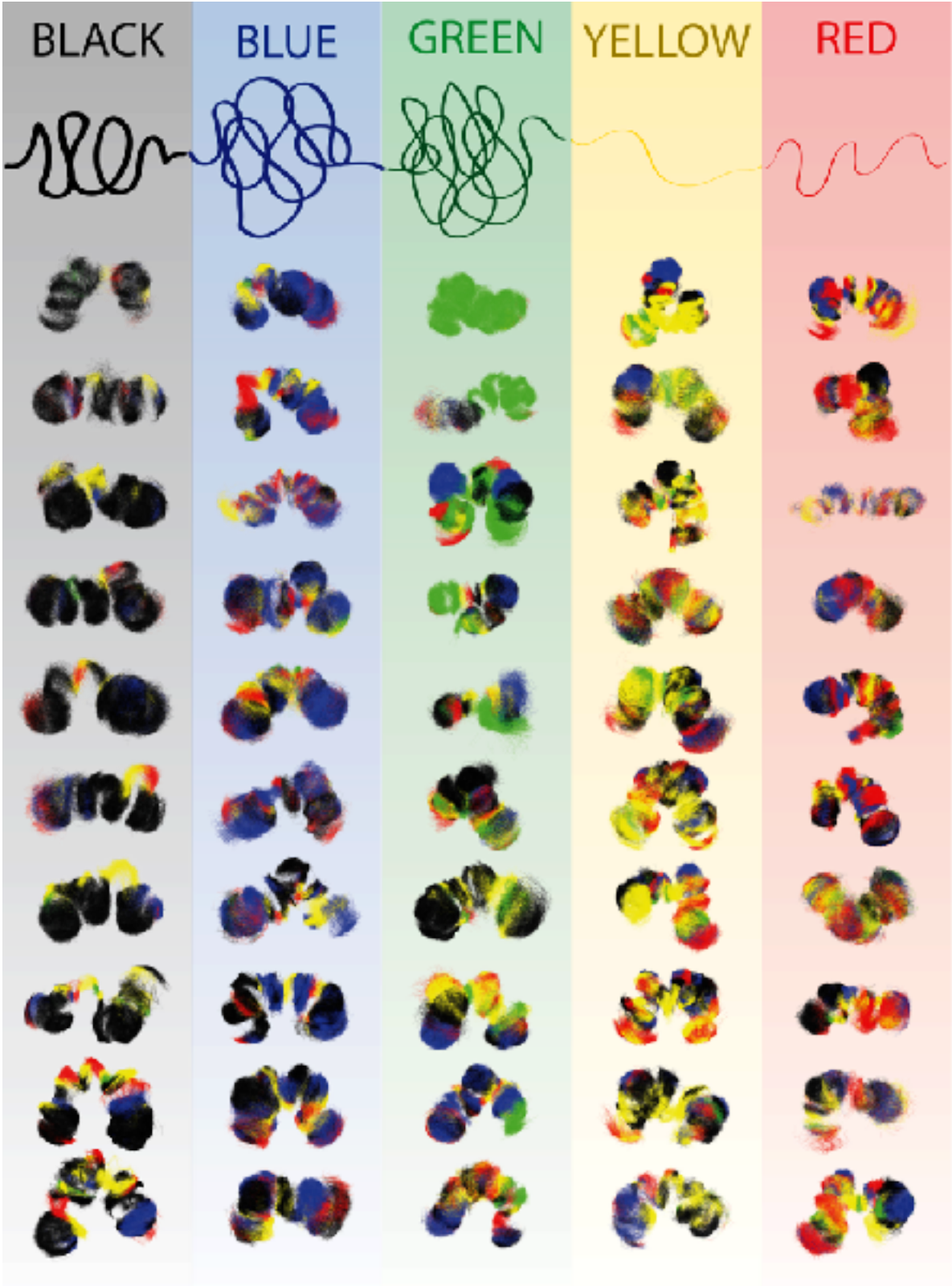
1% 0% 0% 0% 98% 1%



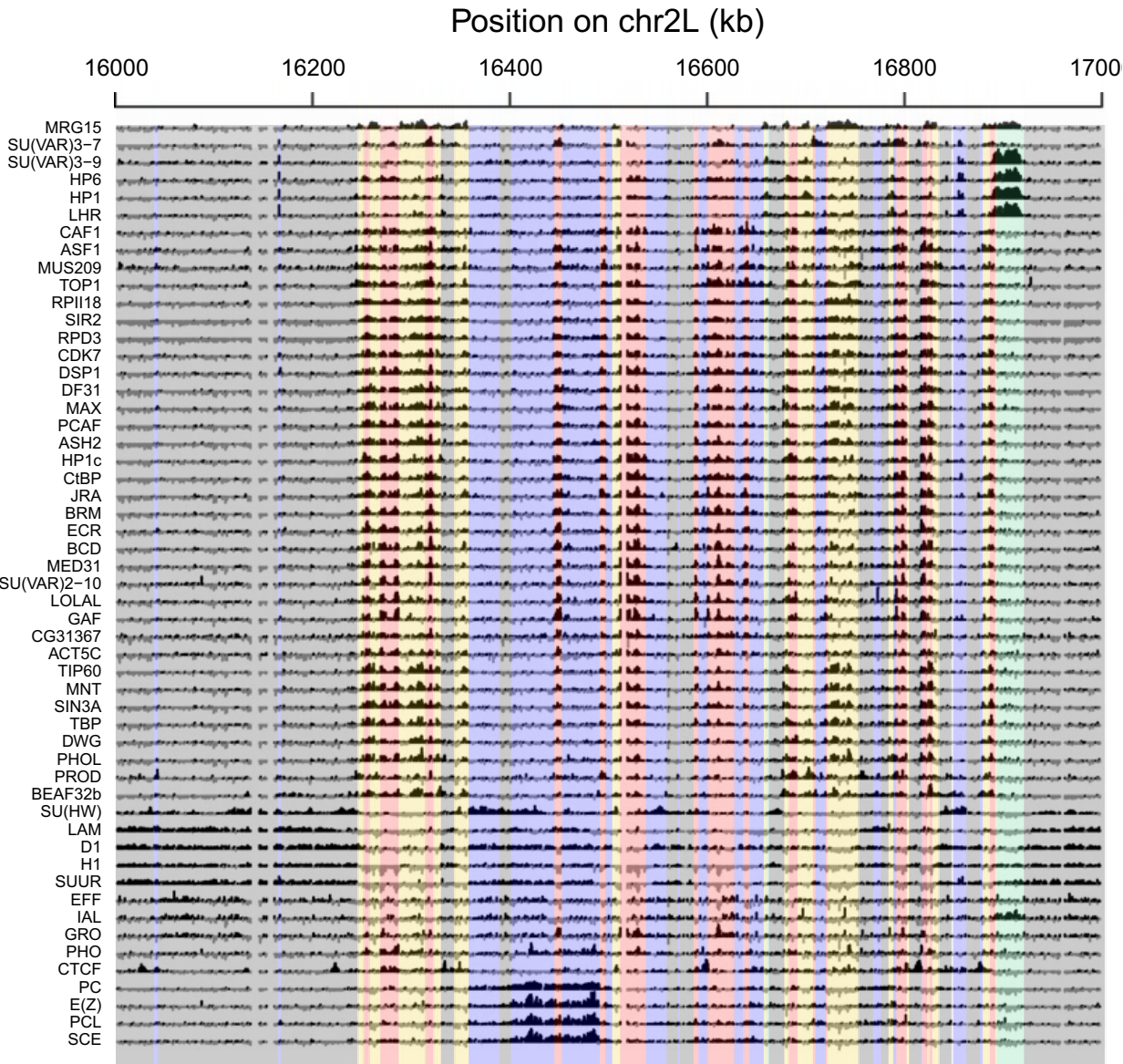
Structural **COLORs**



Structural COLOrS



53 chromatin proteins



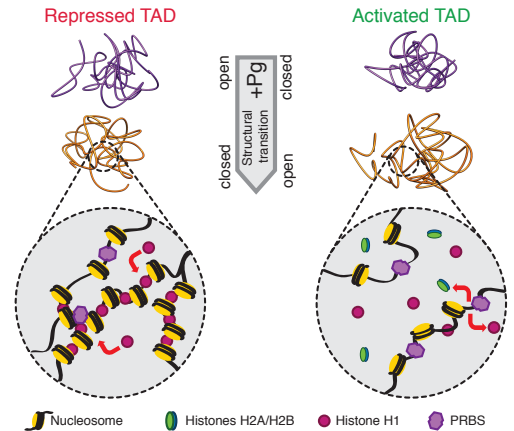
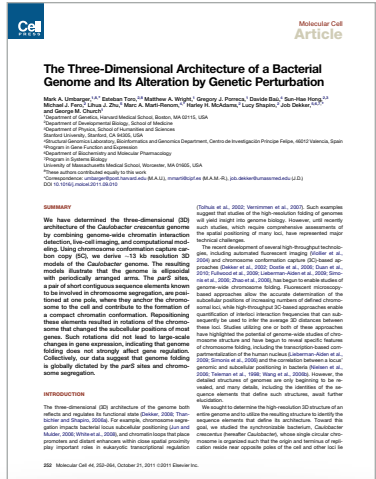
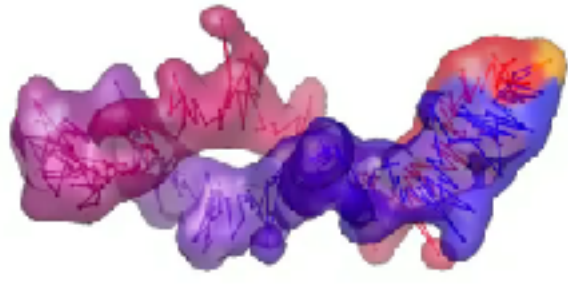
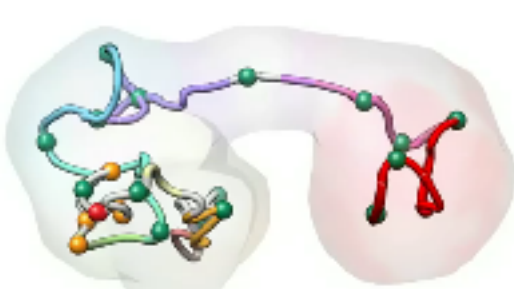
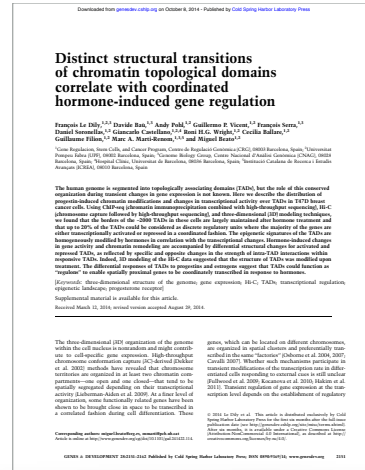
TADbit other applications...

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)





David Castillo
 Yasmina Cuartero
 Irene Farabella
 Silvia Galan
 Mike Goodstadt
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 Juan Rodríguez
 François Serra
 Paula Soler
 Aleksandra Sparavier
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<http://sgt.cnag.cat/www/presentations/>

<http://marciuslab.org>
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