

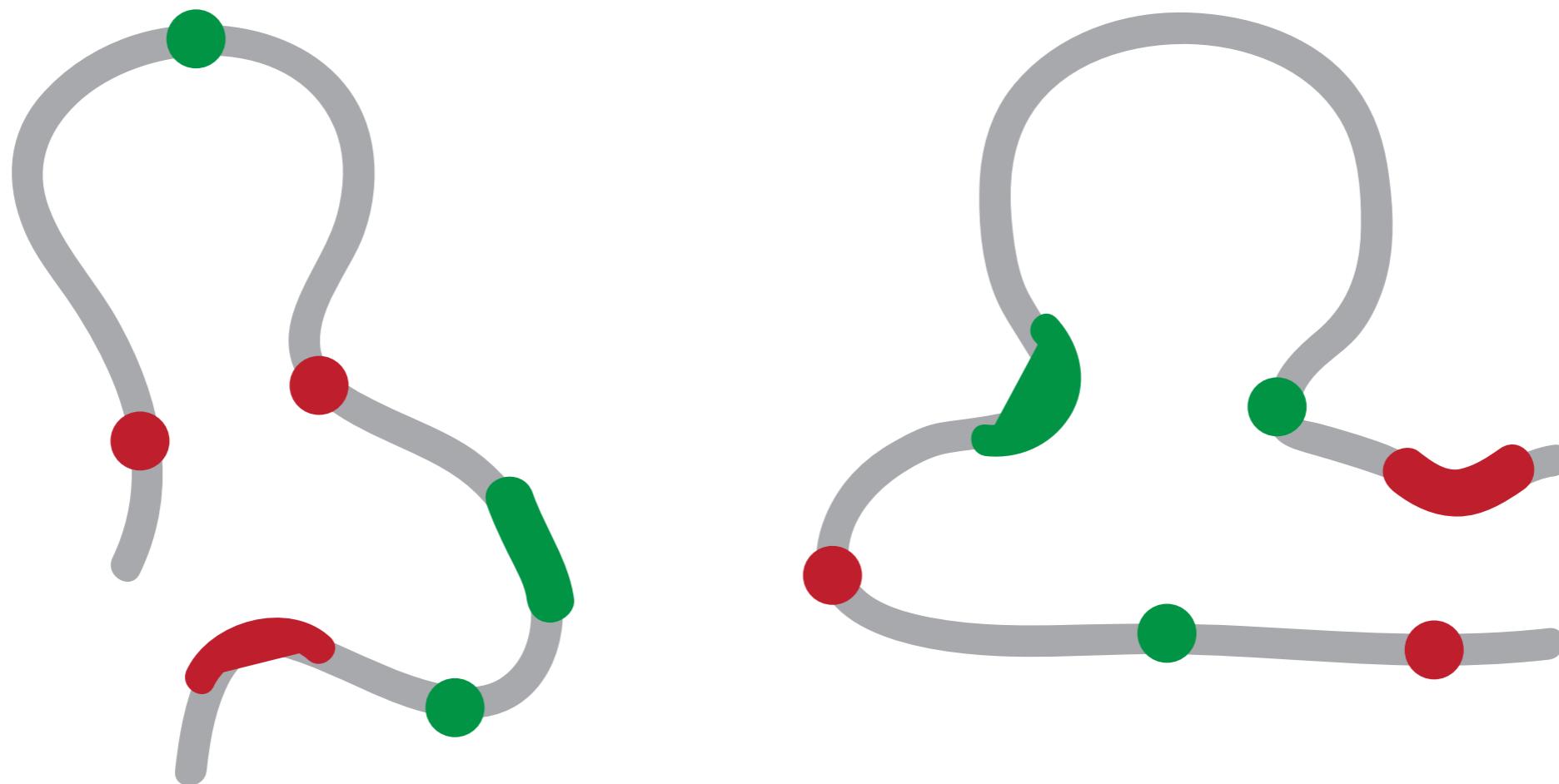
3DGENOMICS

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

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

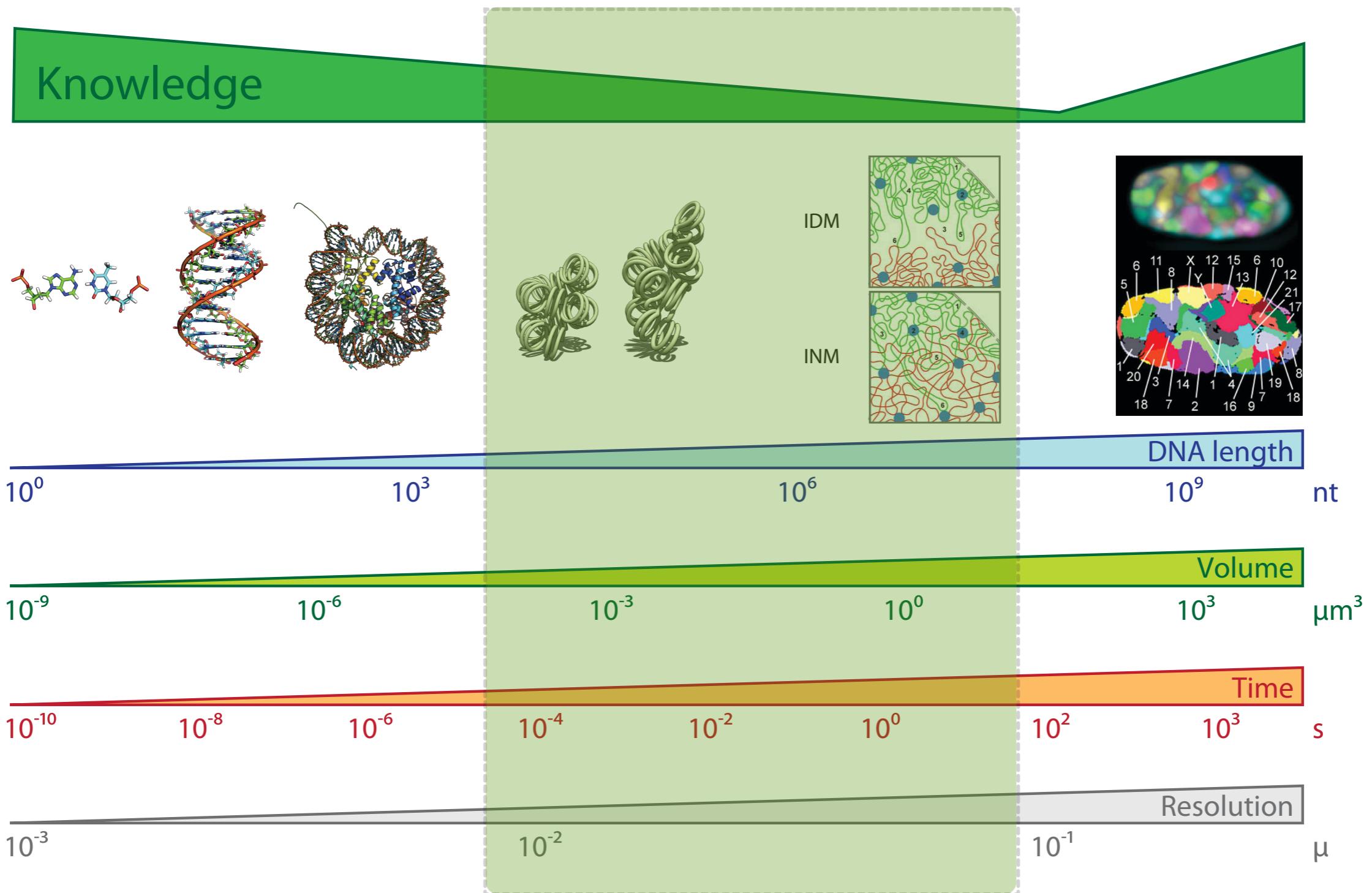
cnag CRG ICREA





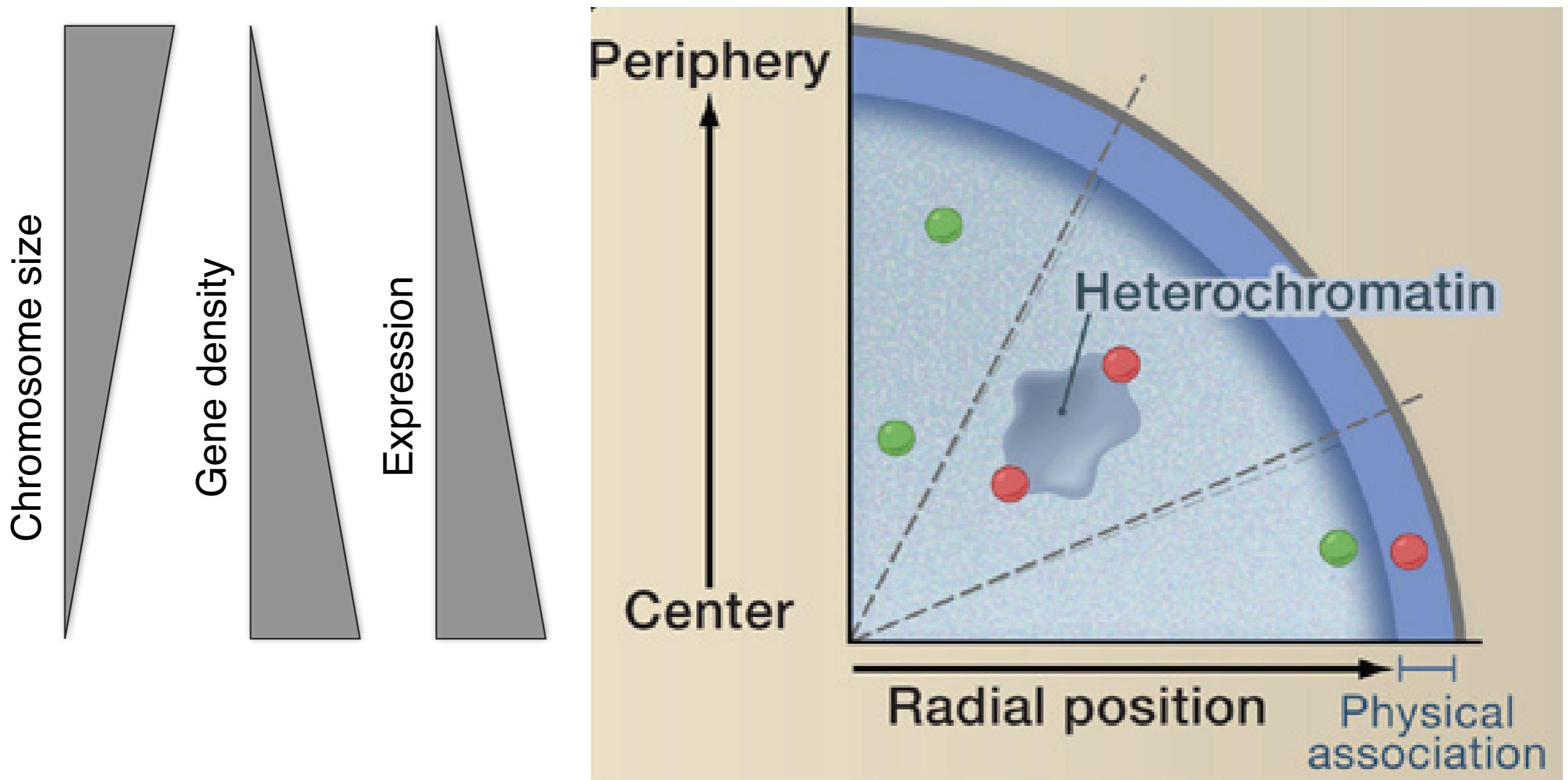
Resolution Gap

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

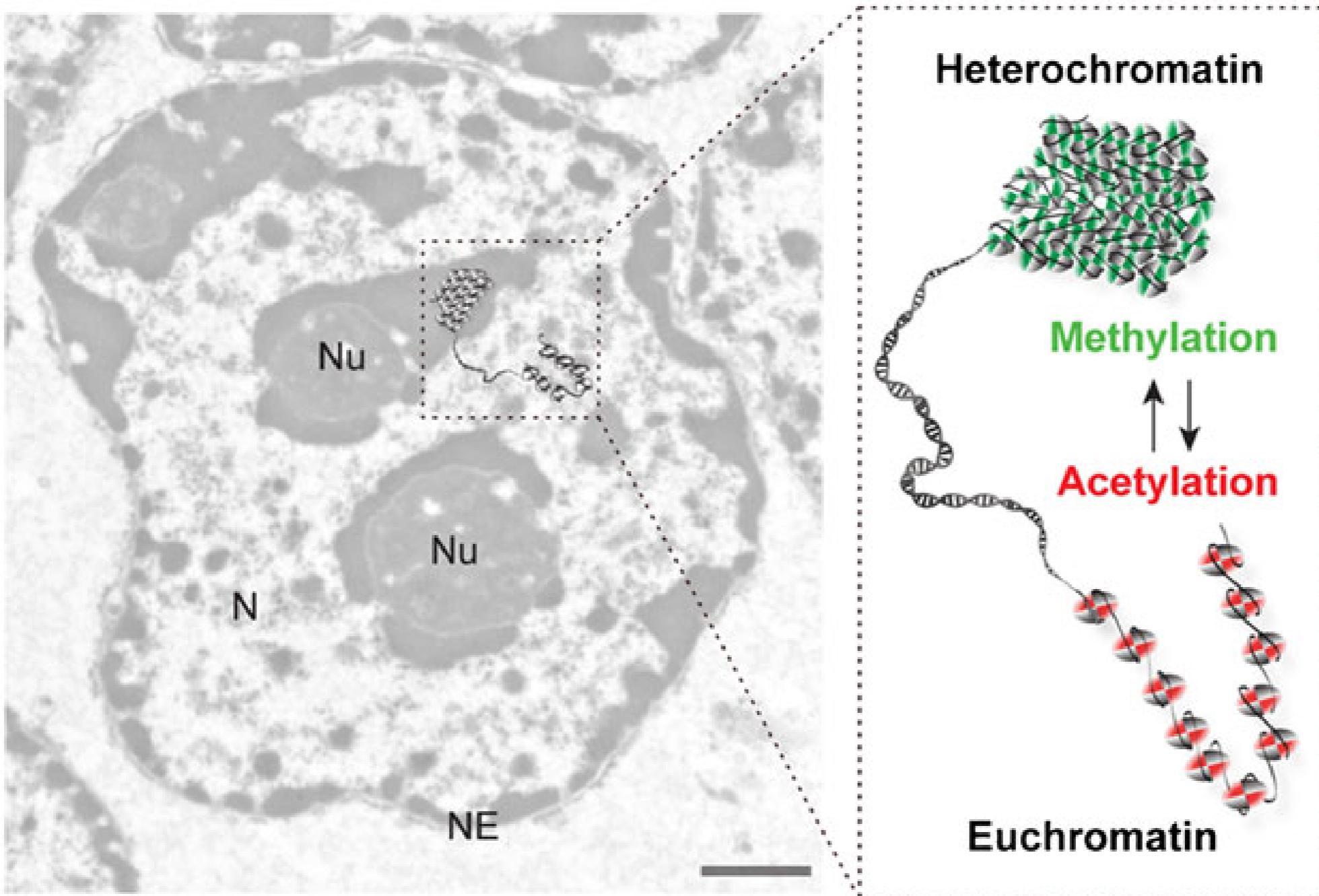


Level I: Radial genome organization

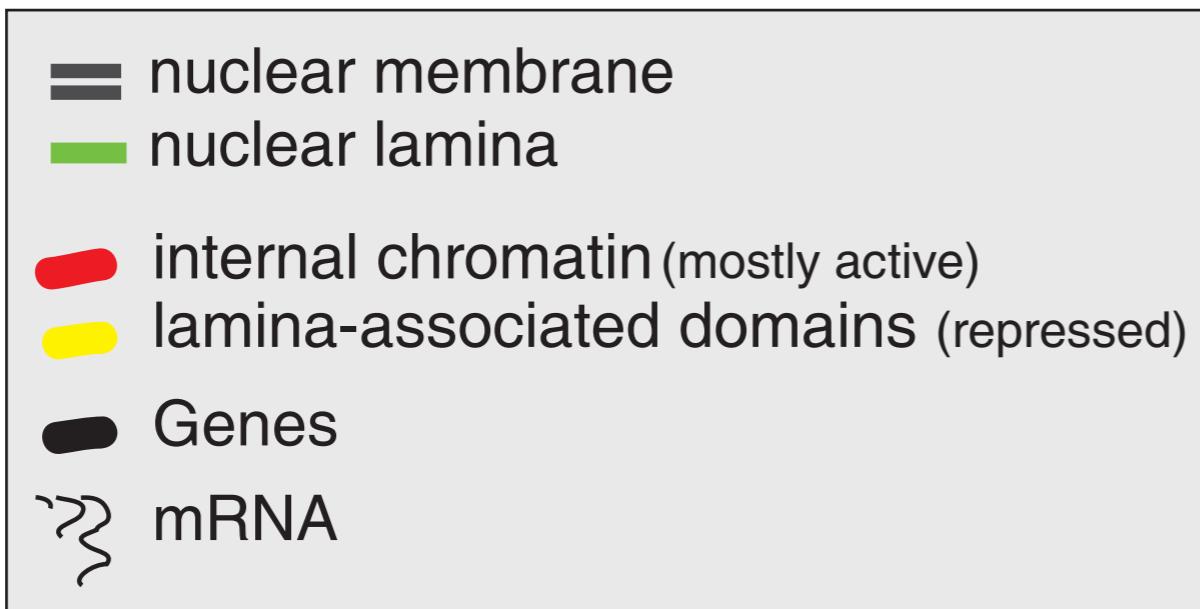
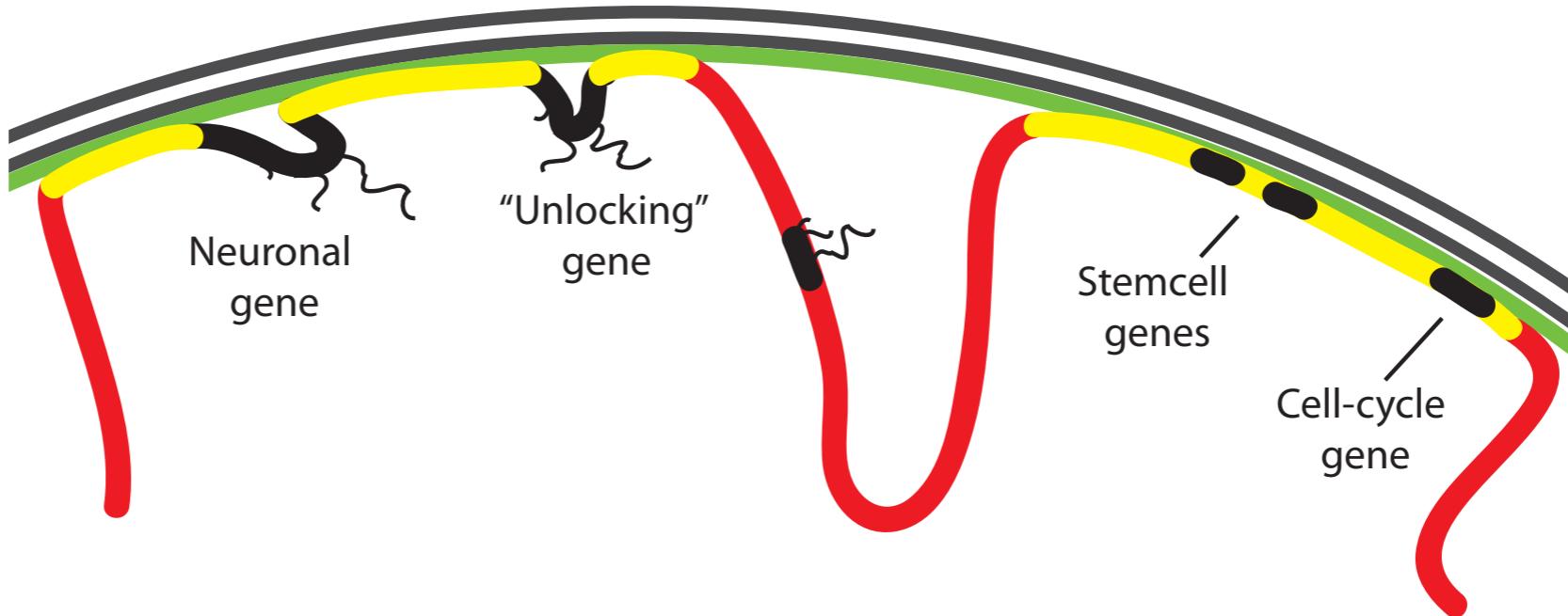
Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



Level II: Euchromatin vs heterochromatin

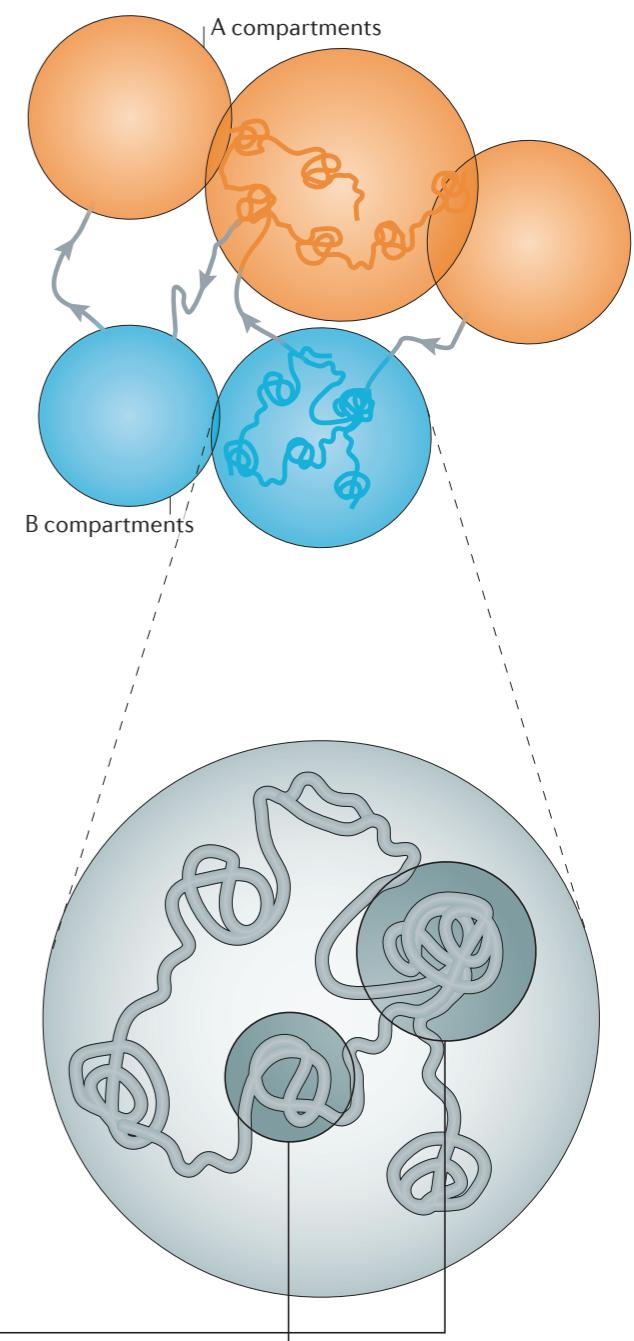
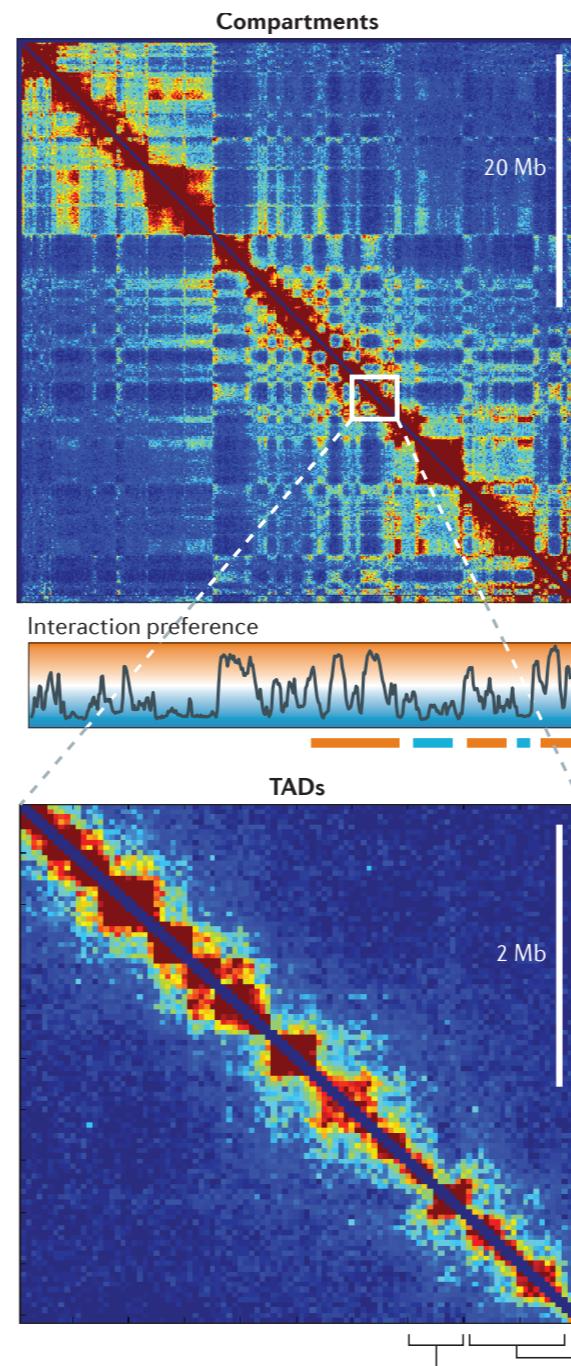
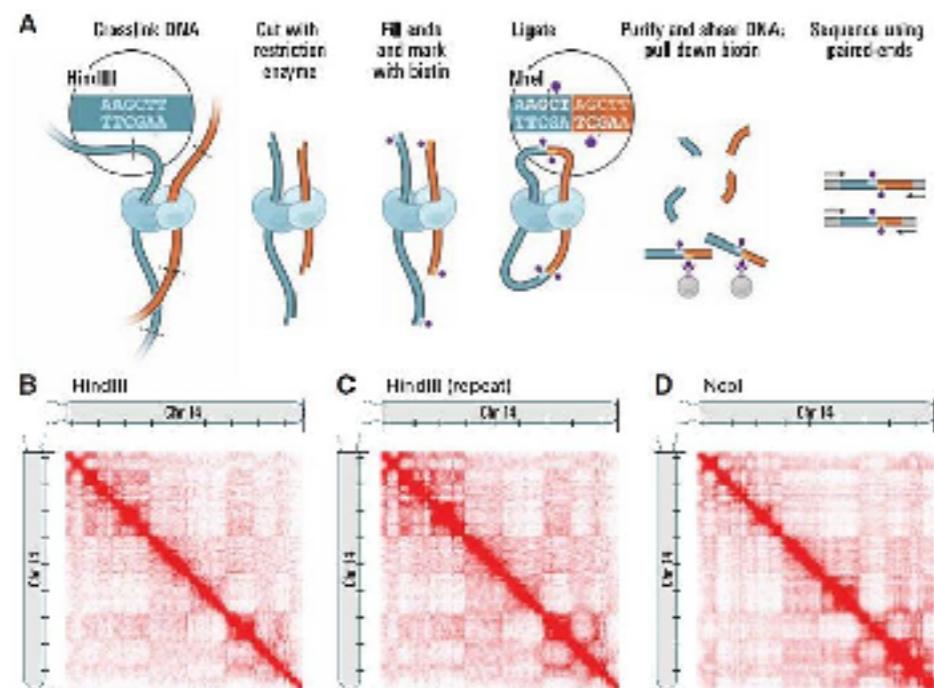


Level III: Lamina-genome interactions



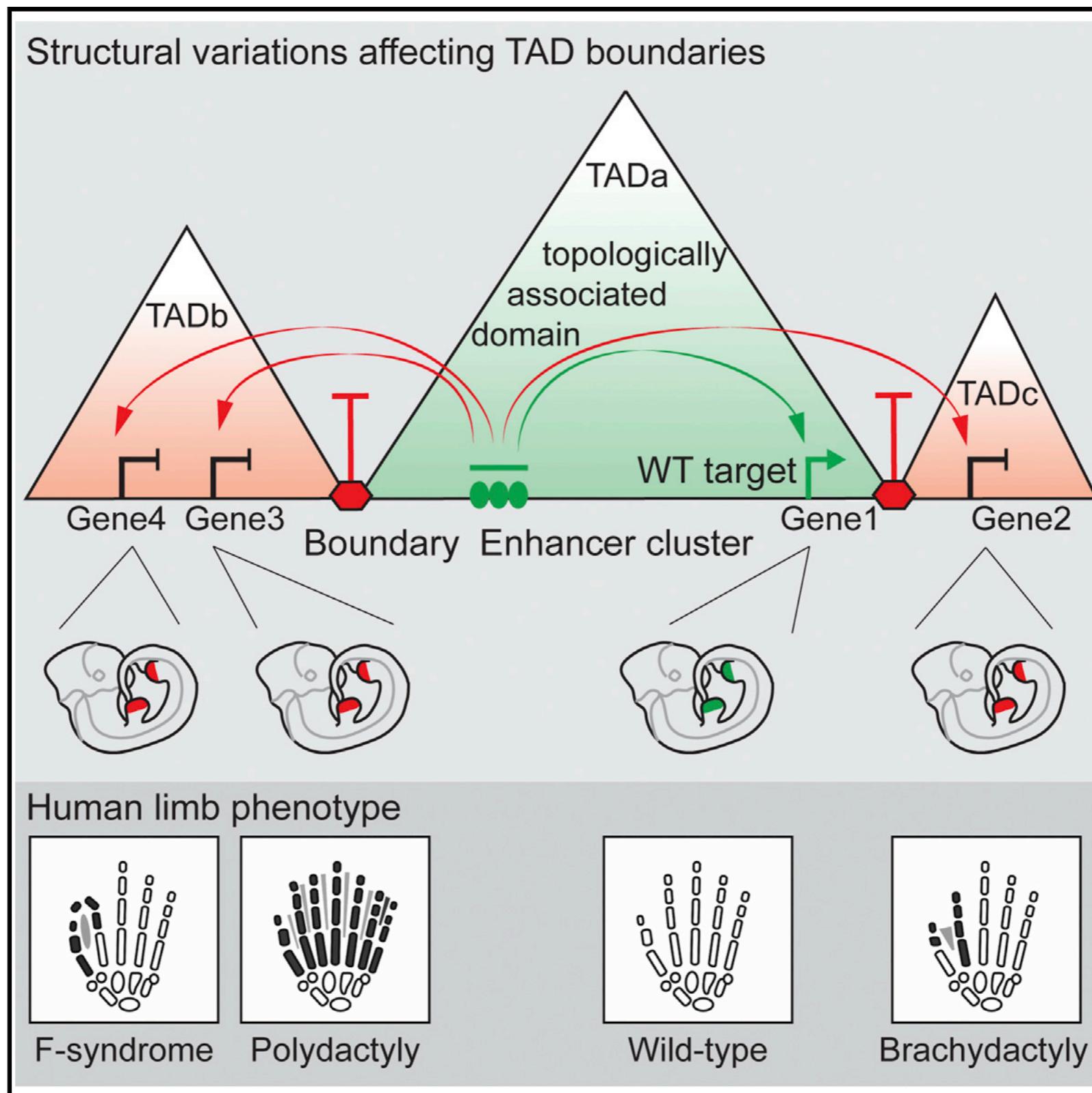
Level IV: Higher-order organization

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



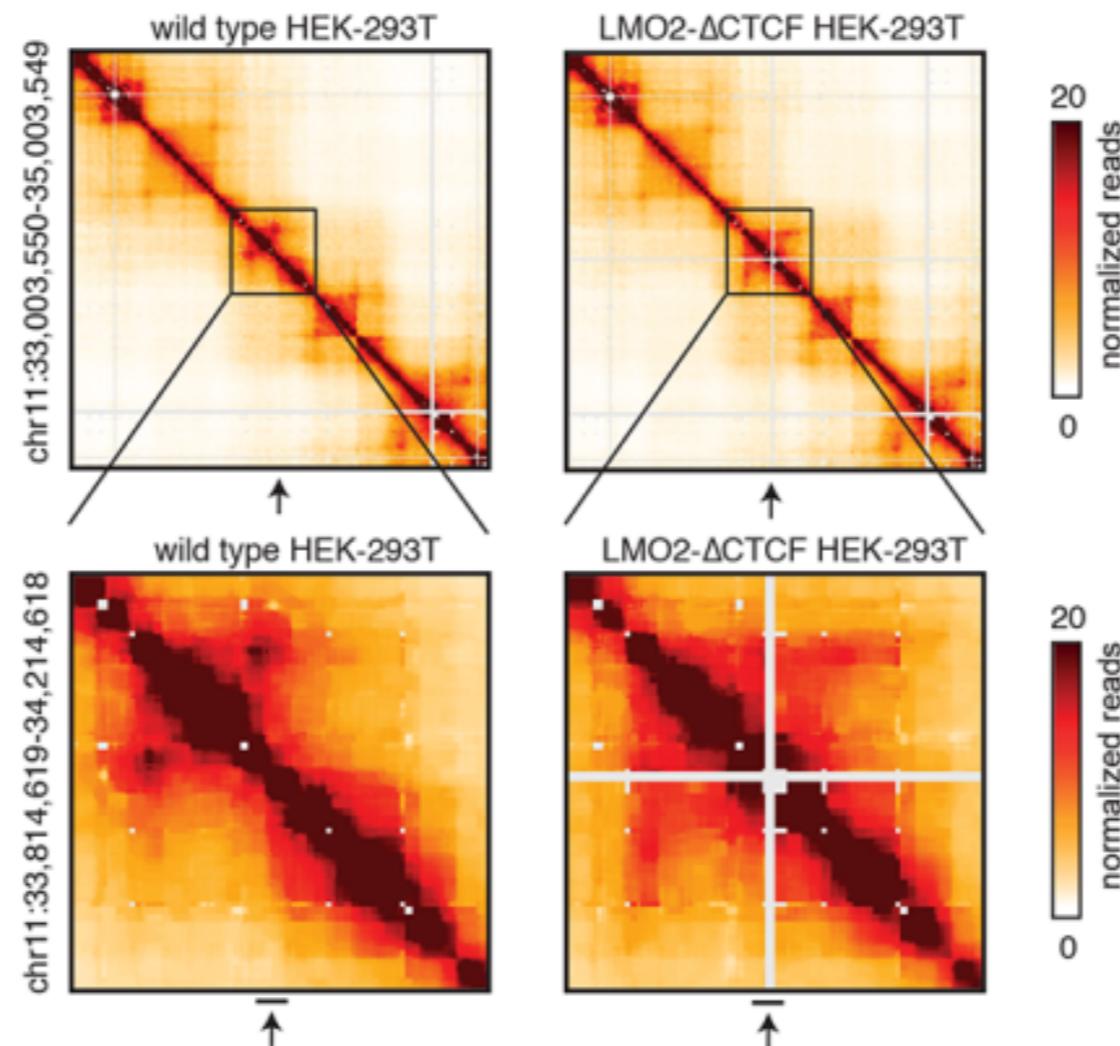
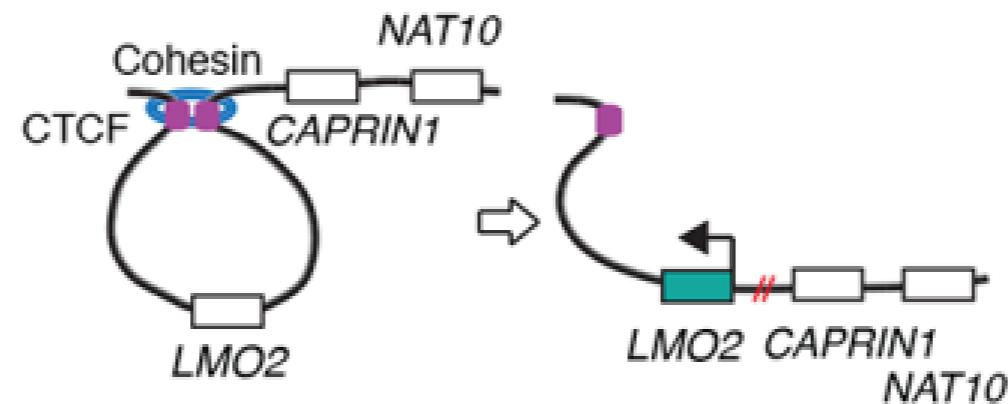
TADs are functional units

Lipiáñez, et al. (2015). Cell, 1–15.

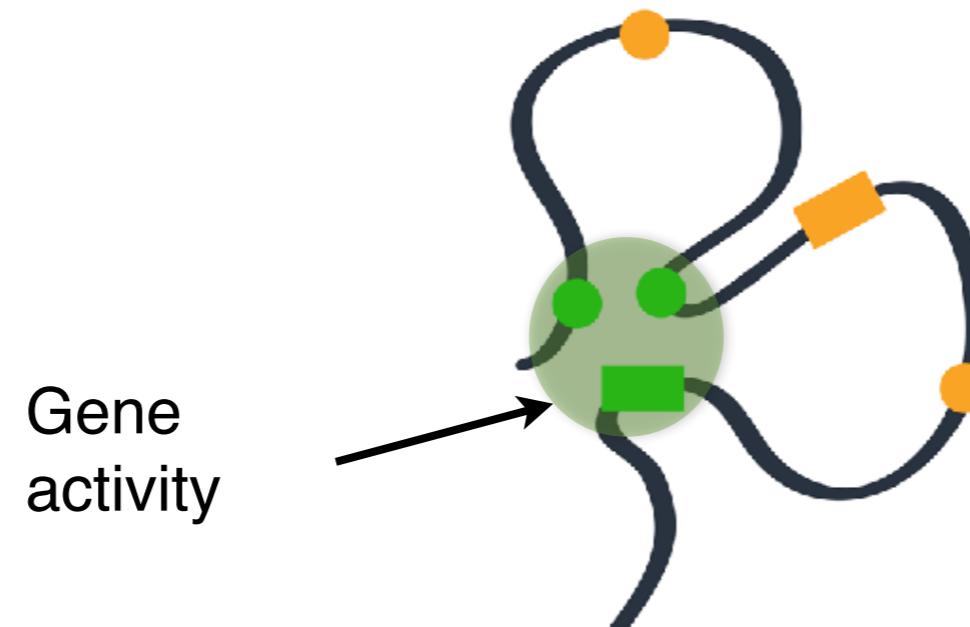
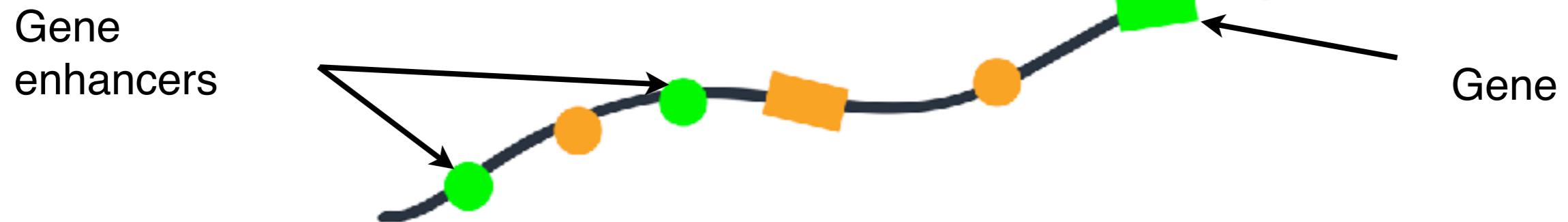


TADs are functional units

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

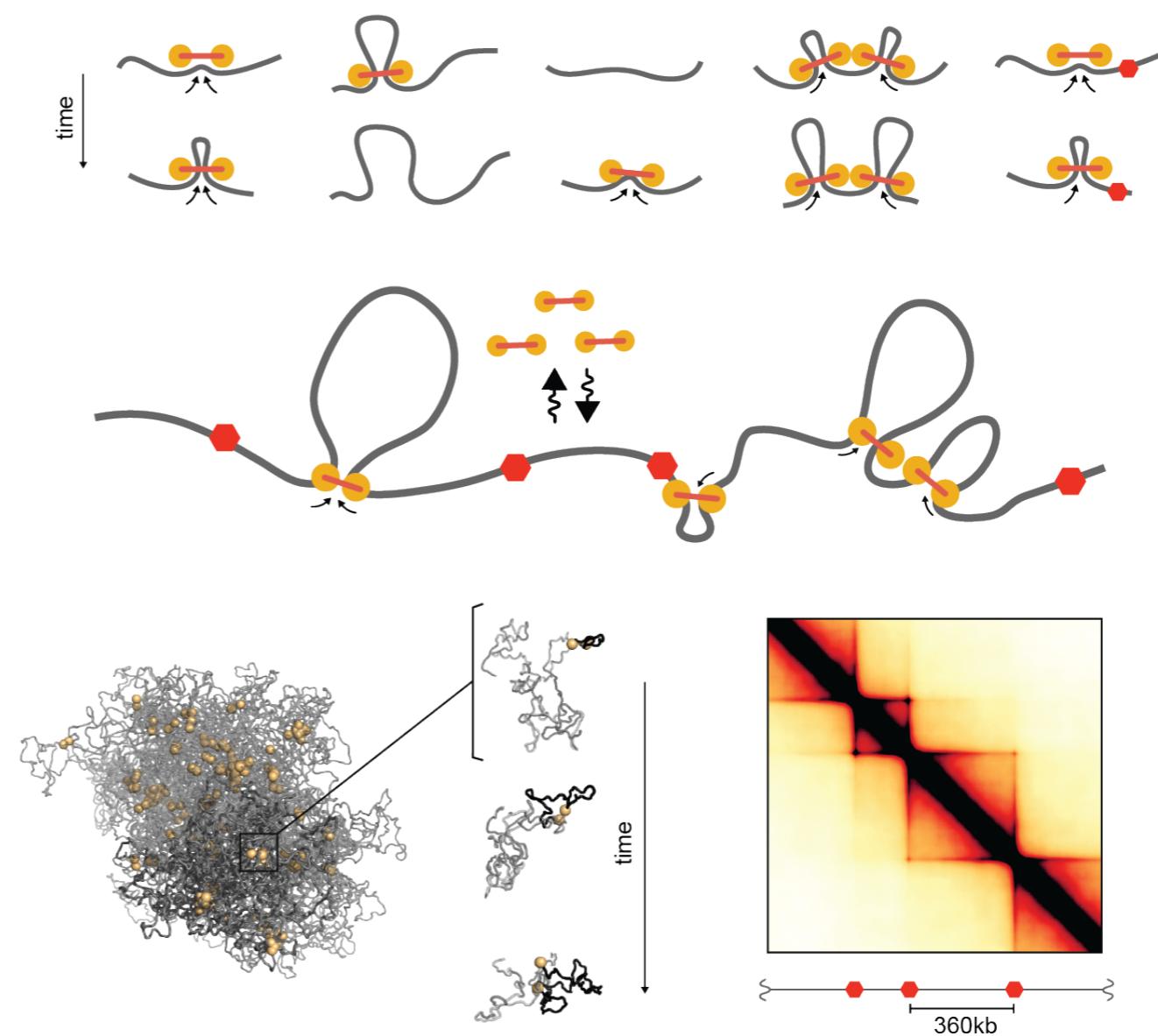
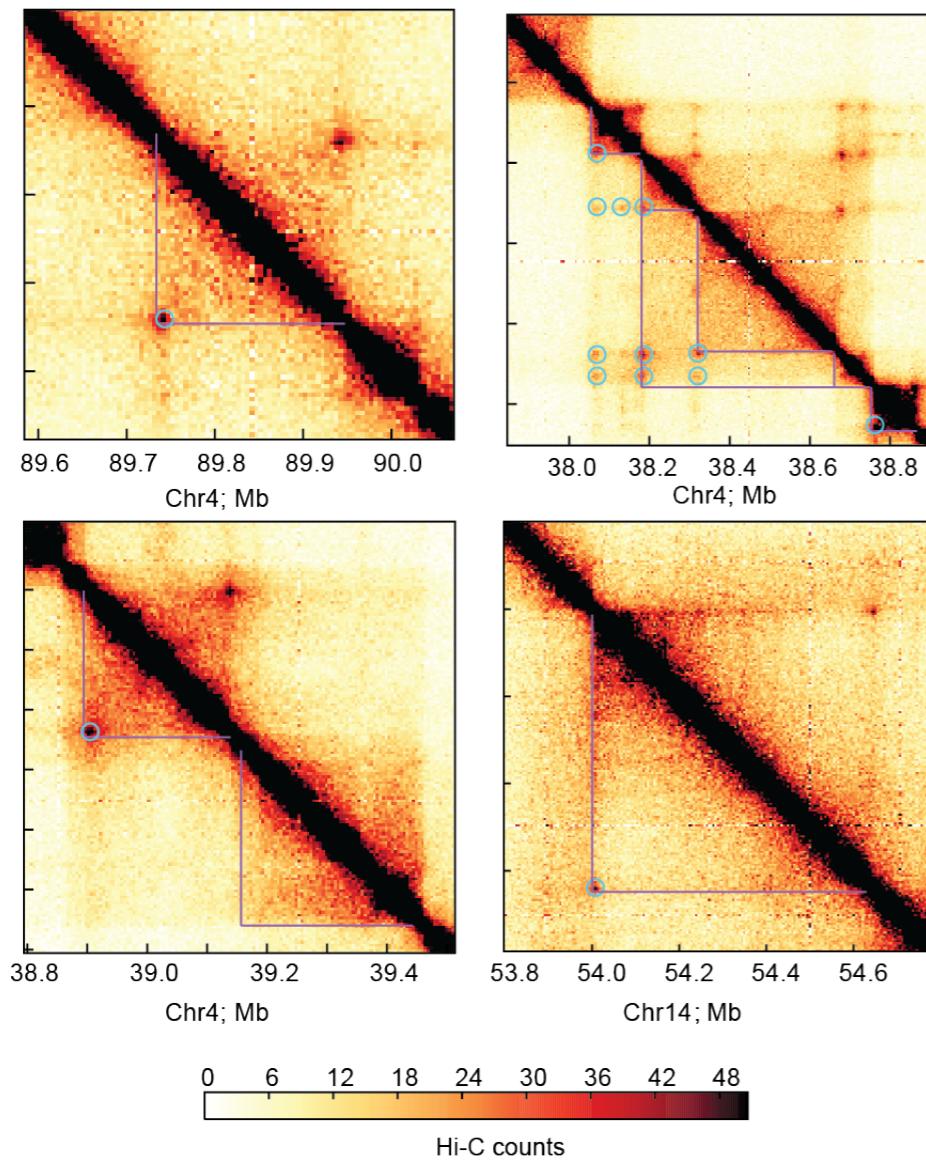


Level V: Chromatin loops

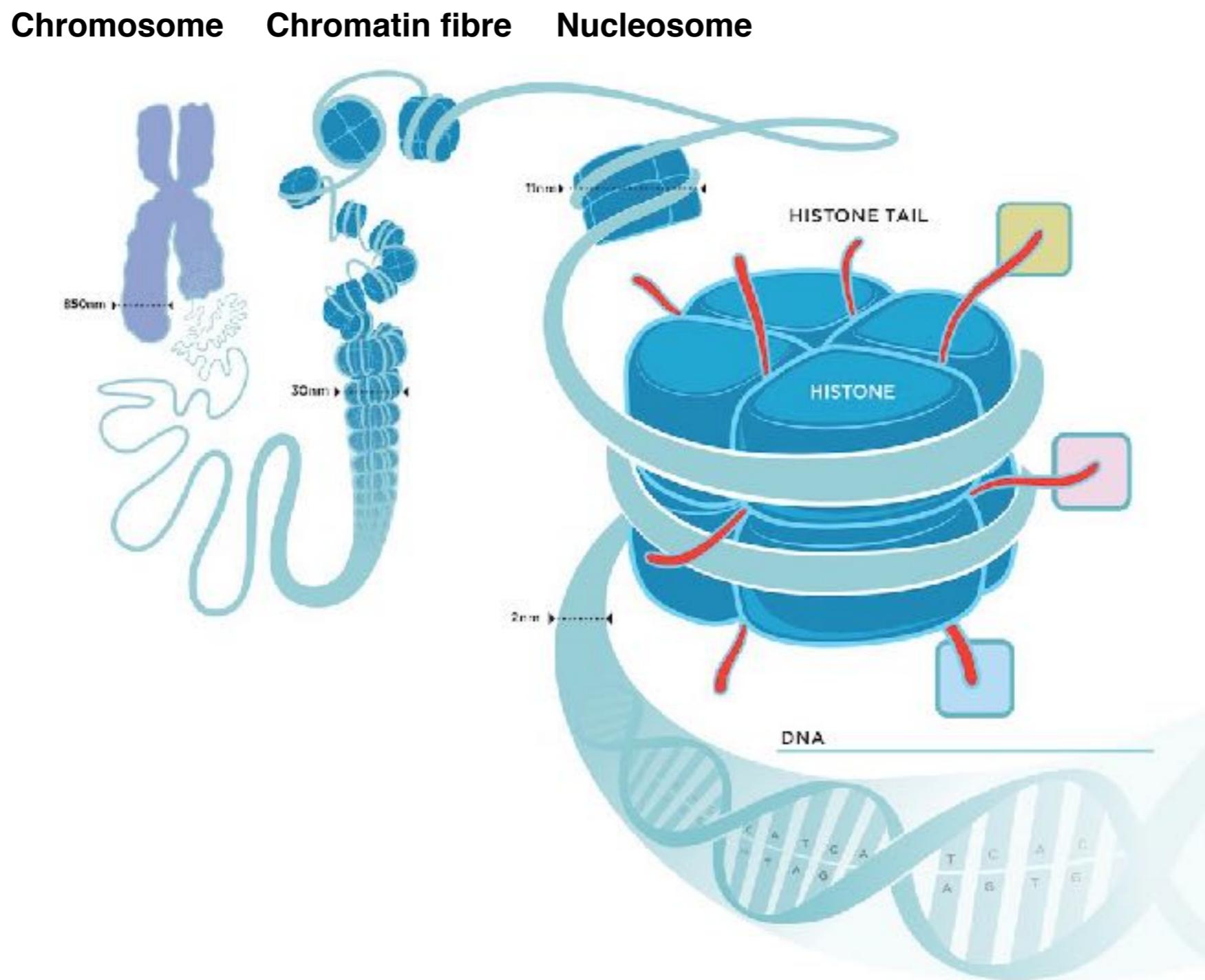


Level V: Loop-extrusion as a driving force

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



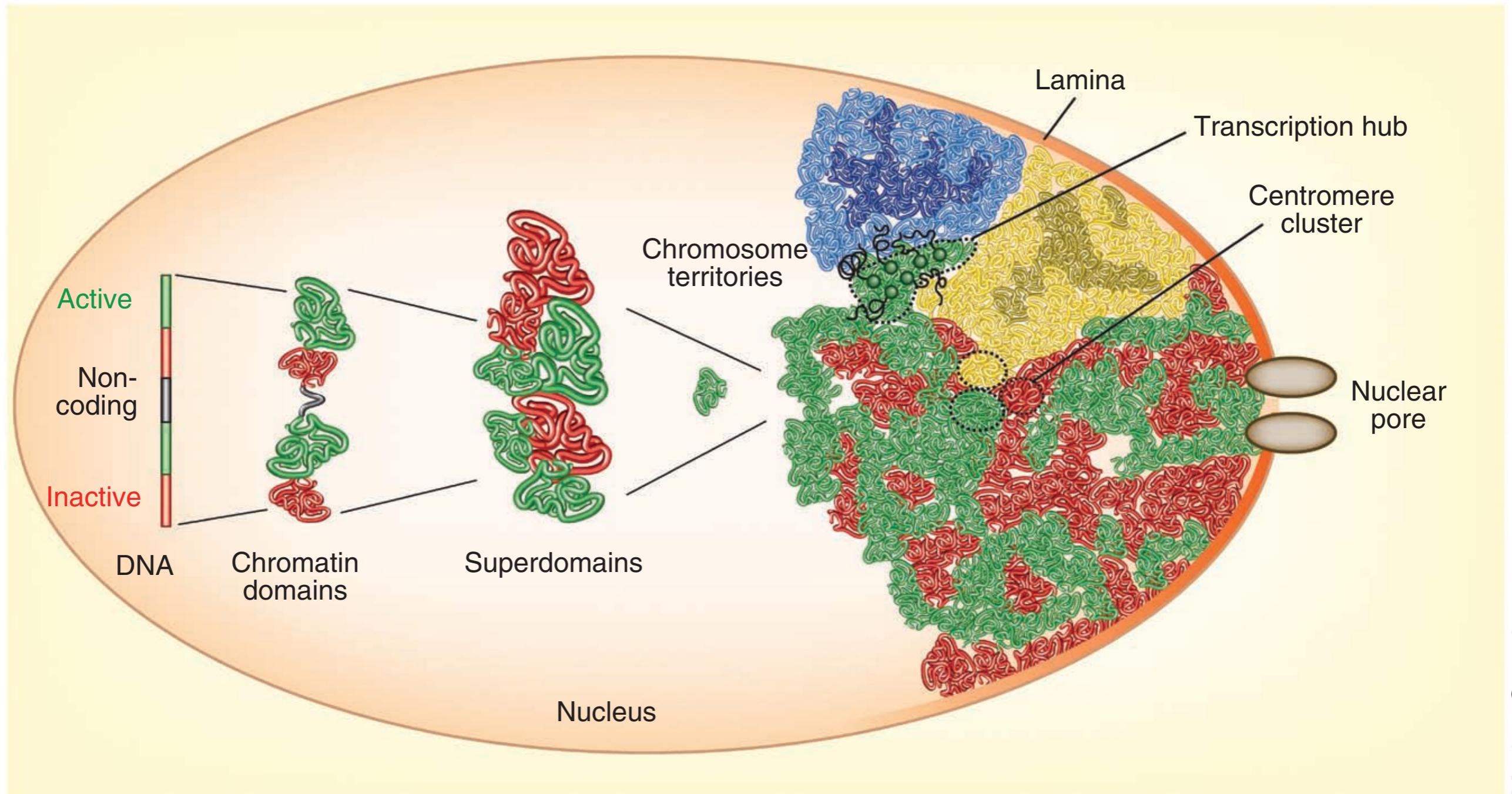
Level VI: Nucleosome



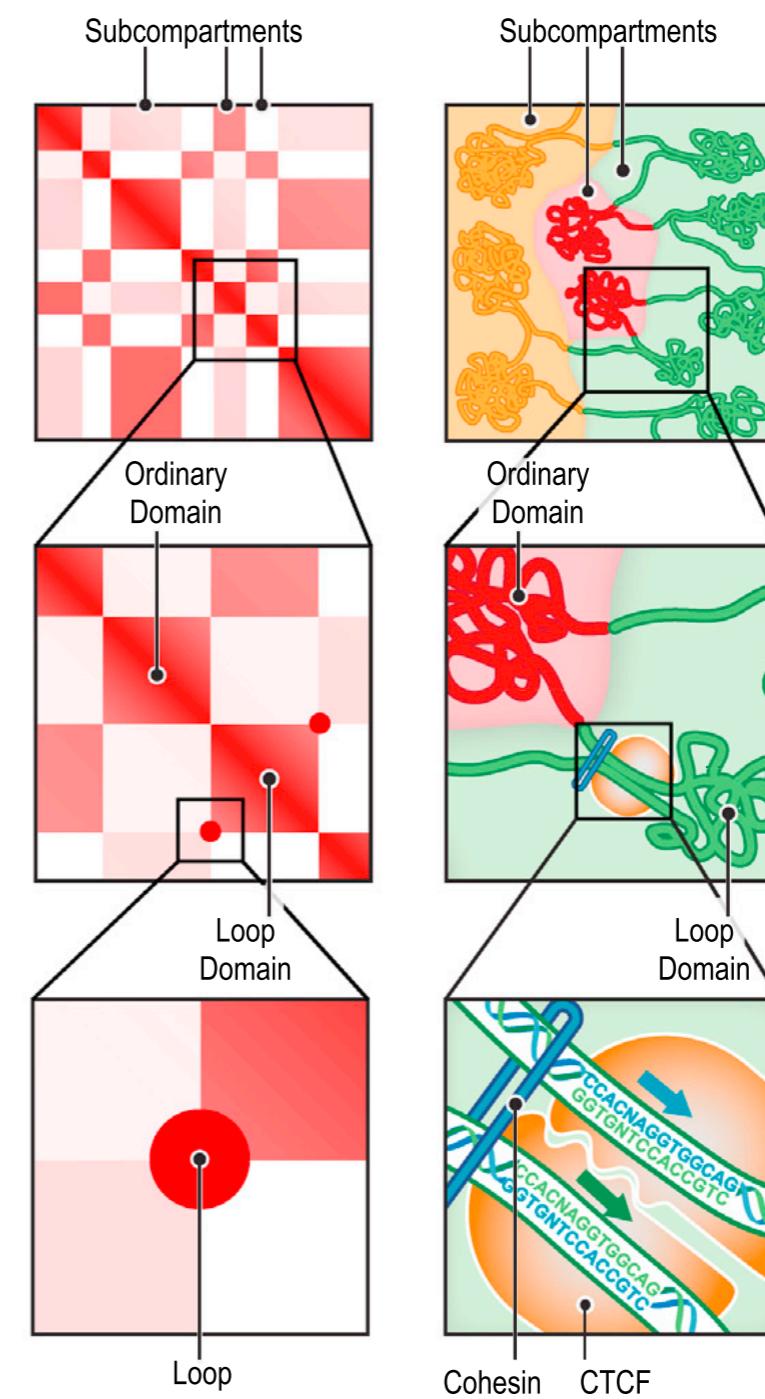
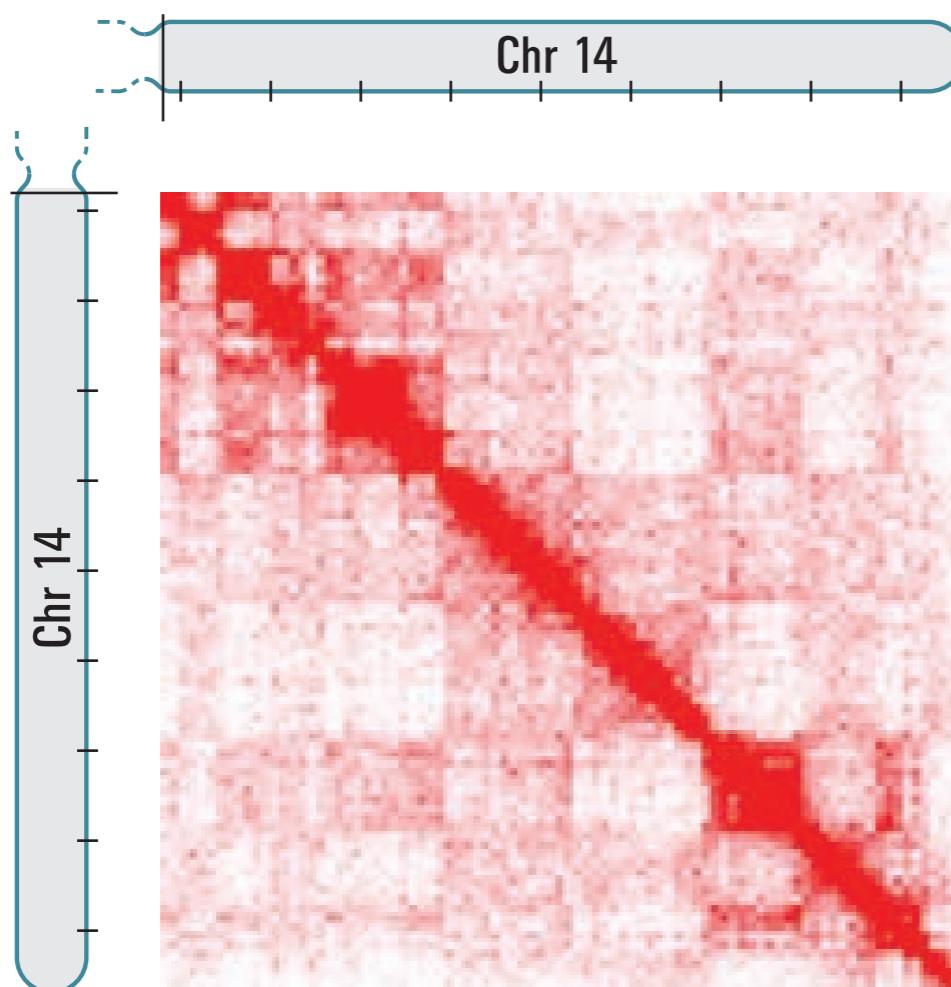
Adapted from Richard E. Ballermann, 2012

Complex genome organization

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



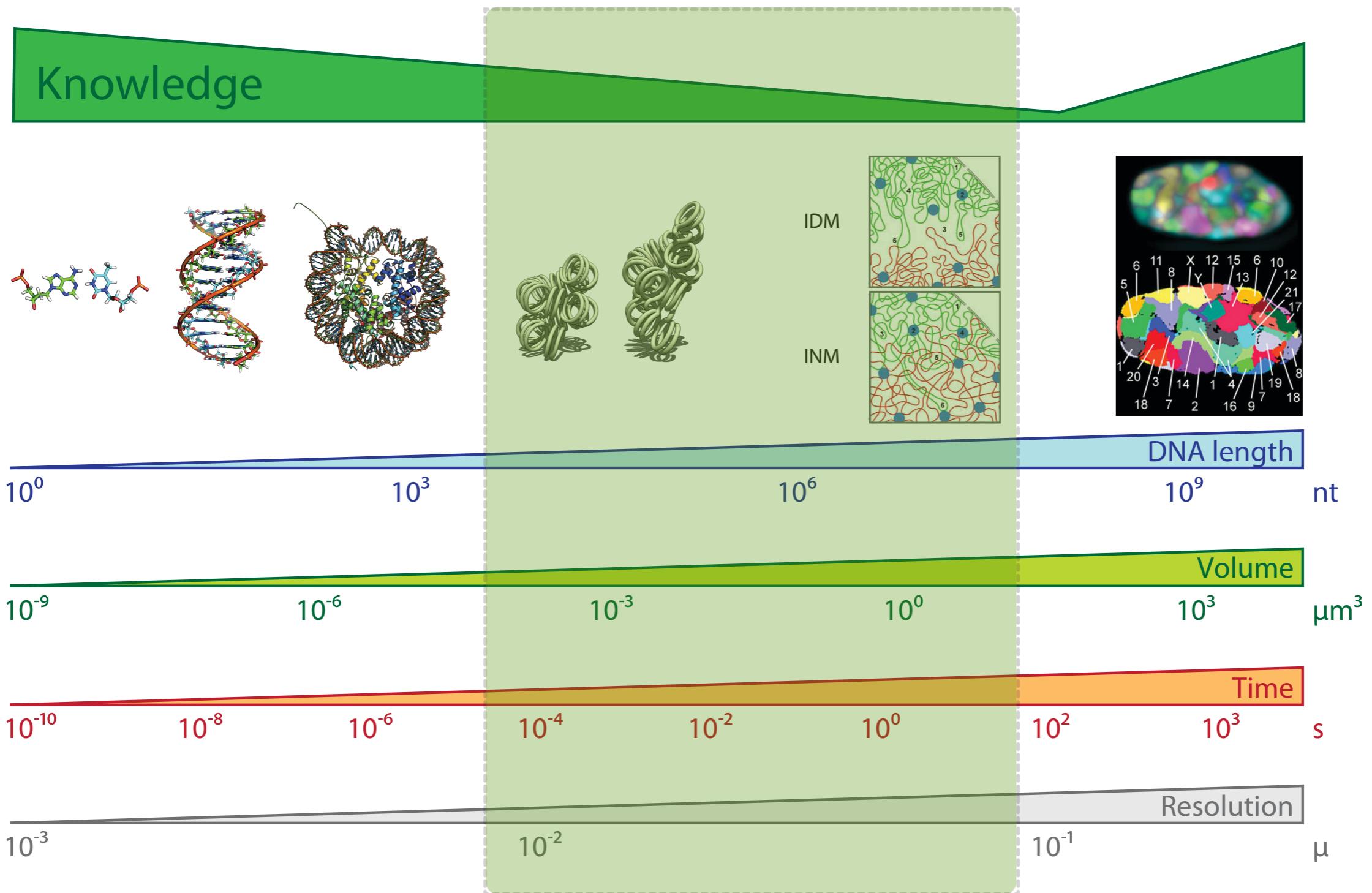
Hierarchical genome organisation



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

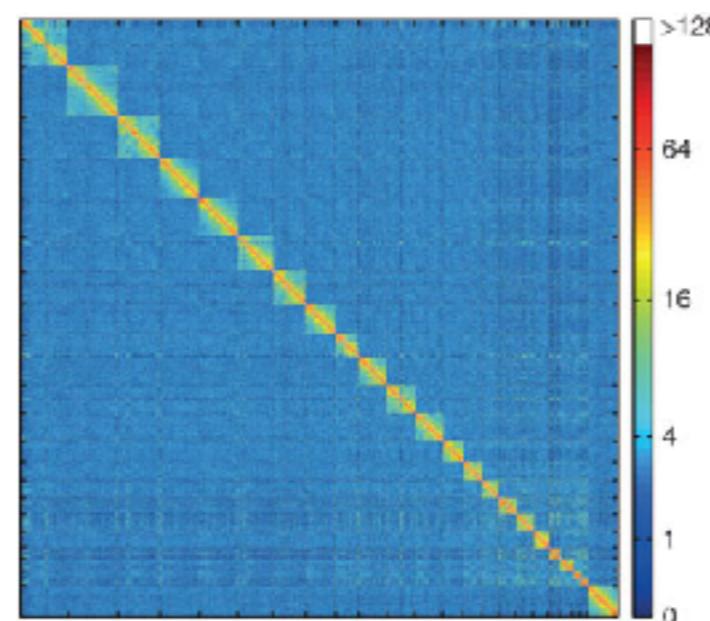
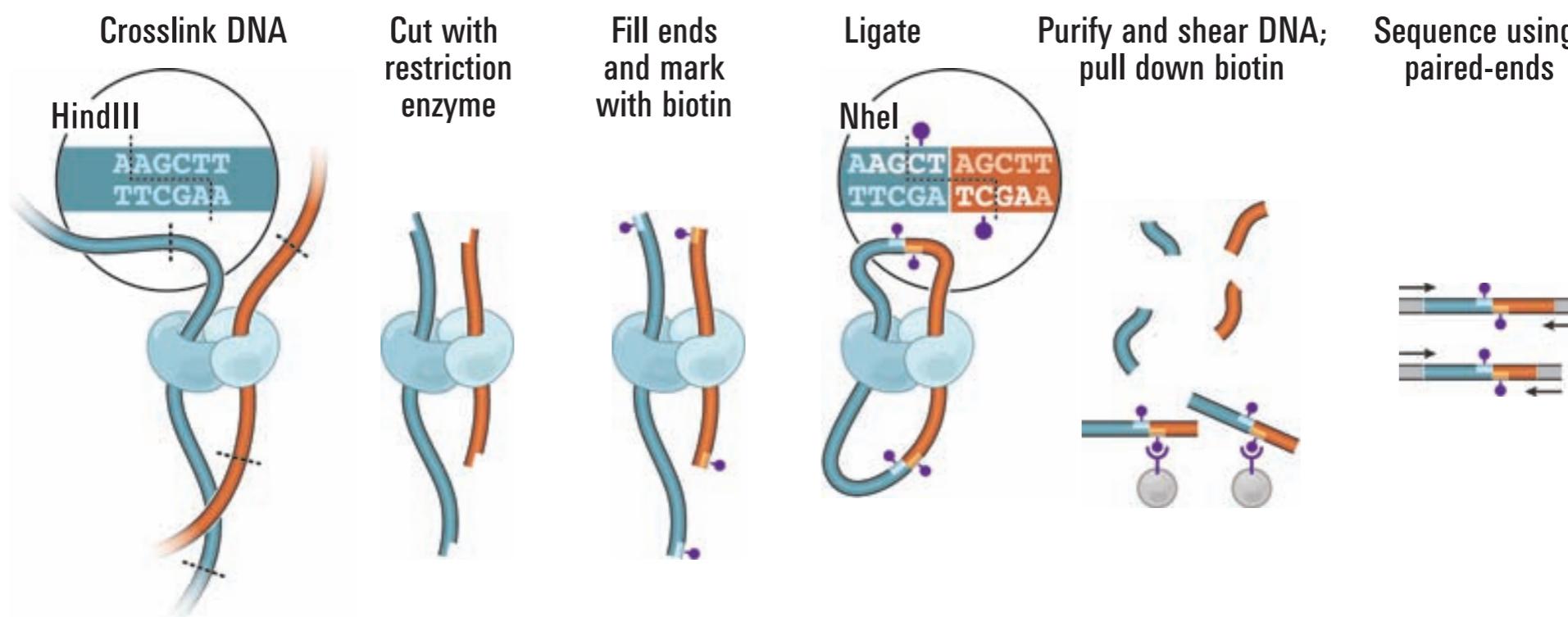
Resolution Gap

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

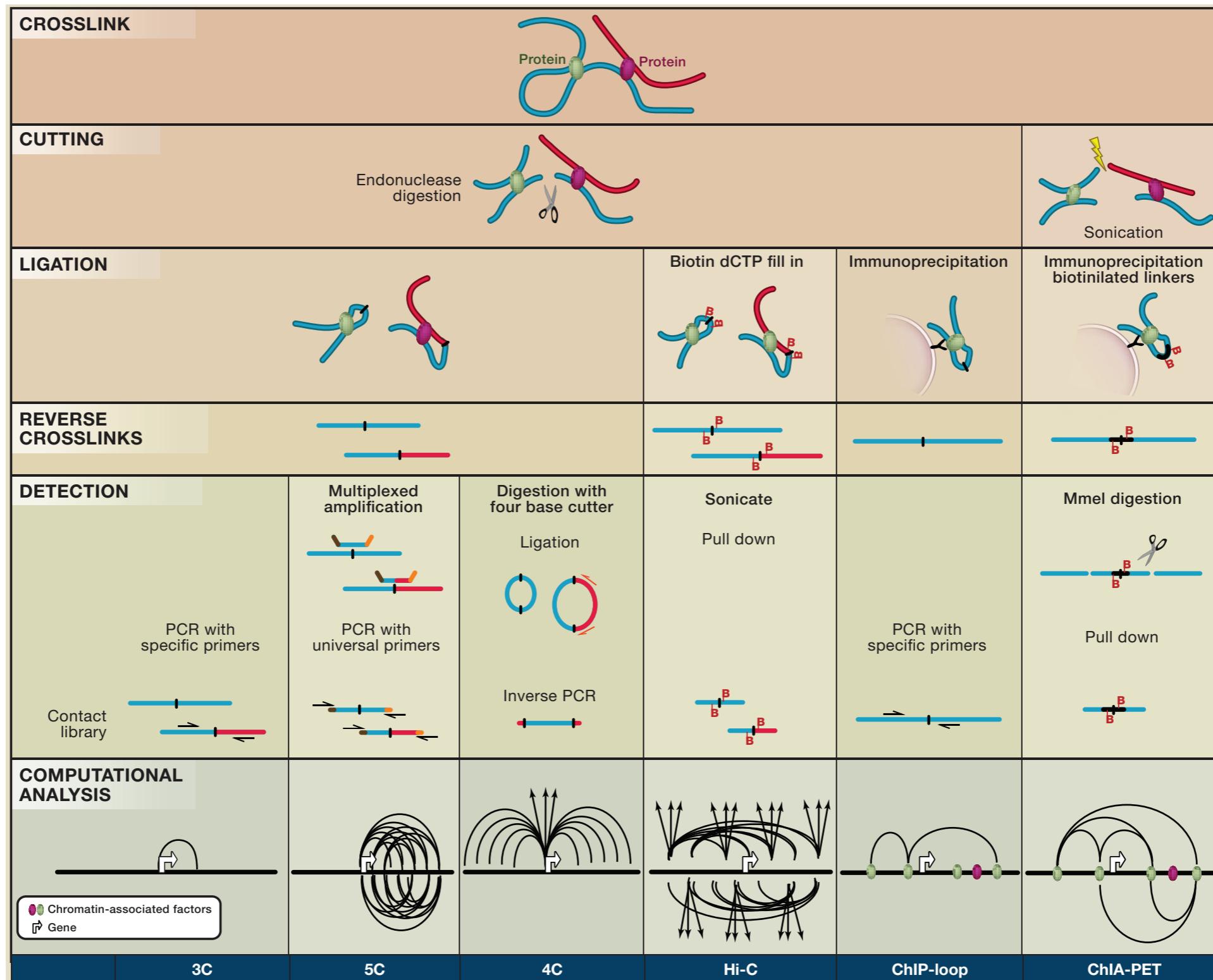


Chromosome Conformation Capture

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.

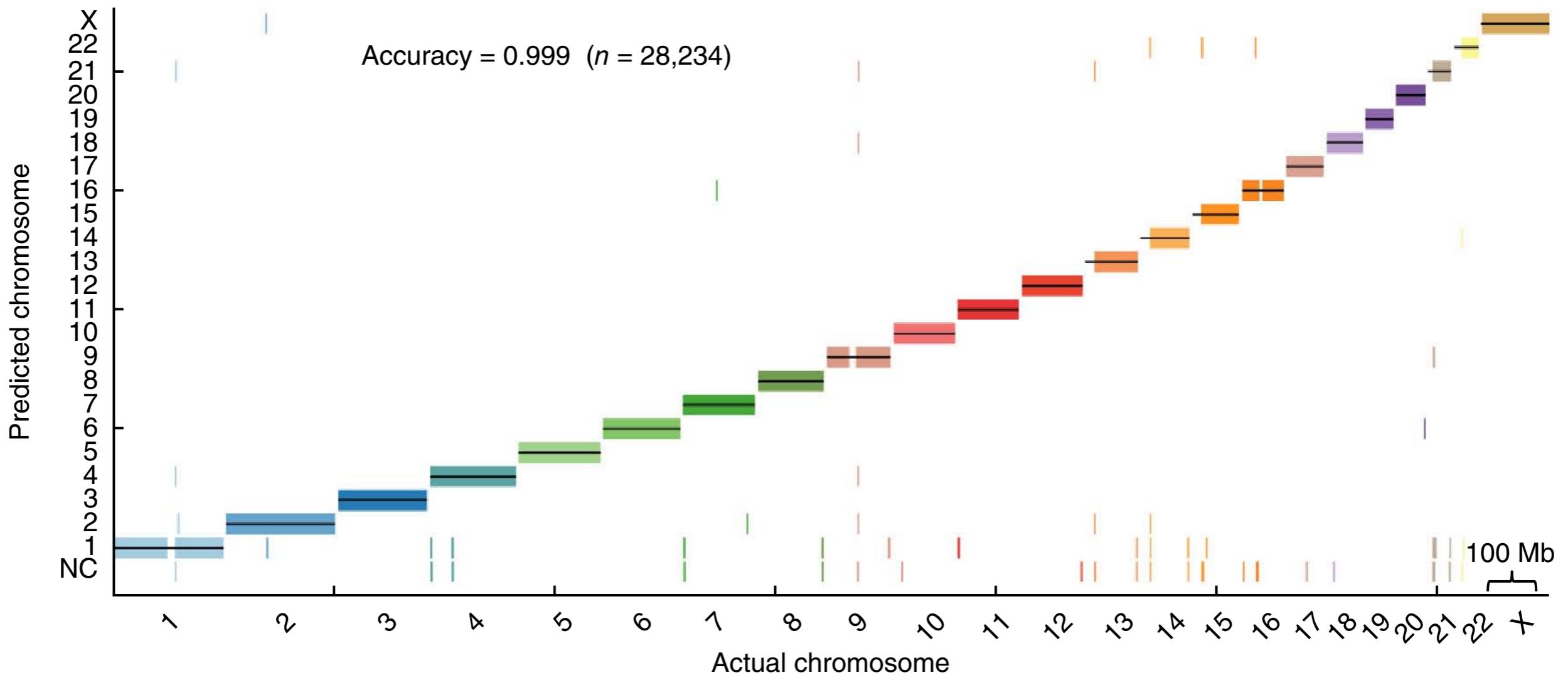


Chromosome Conformation Capture



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

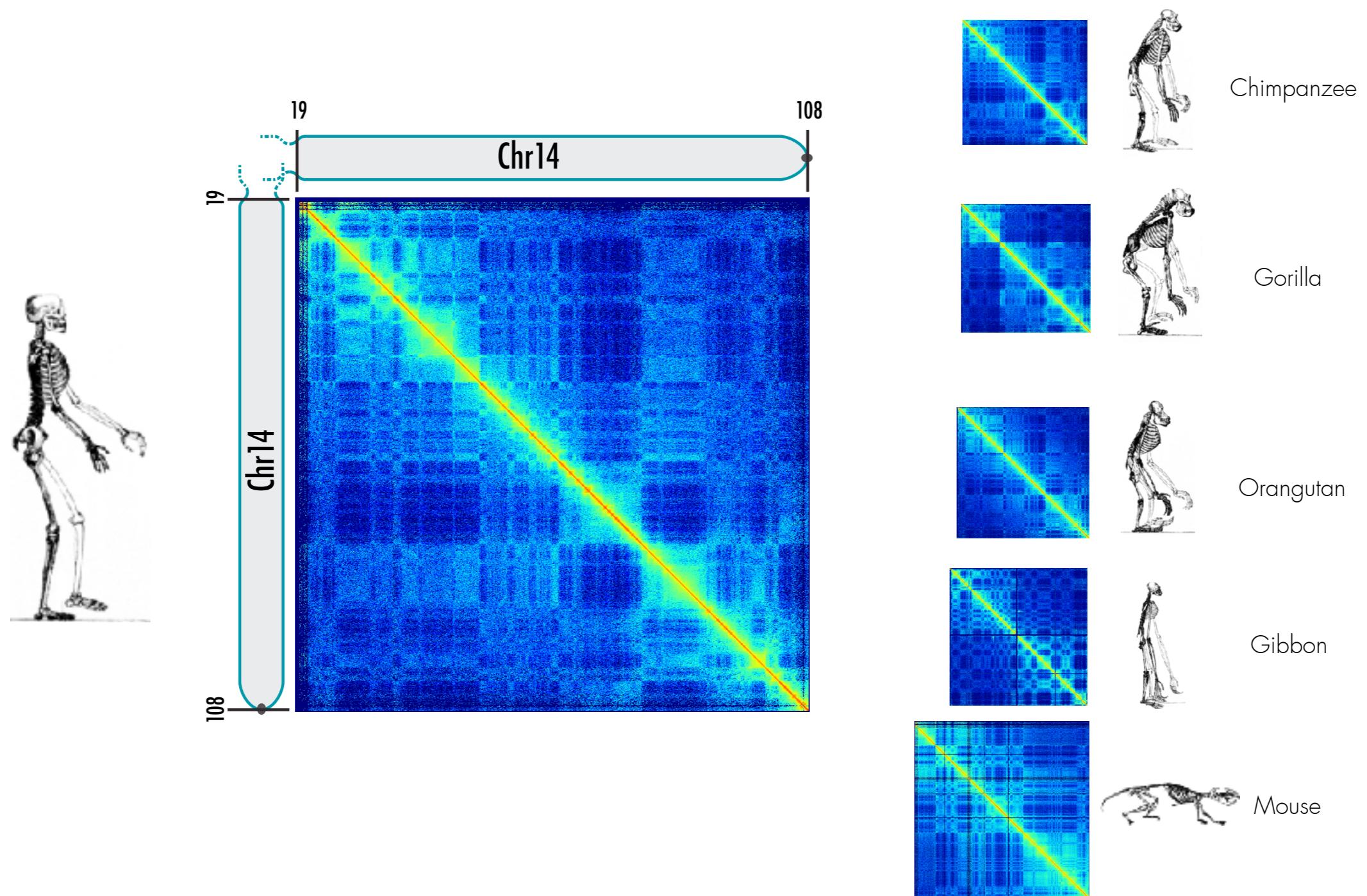
Chromosome Conformation Capture for de-novo assembly



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

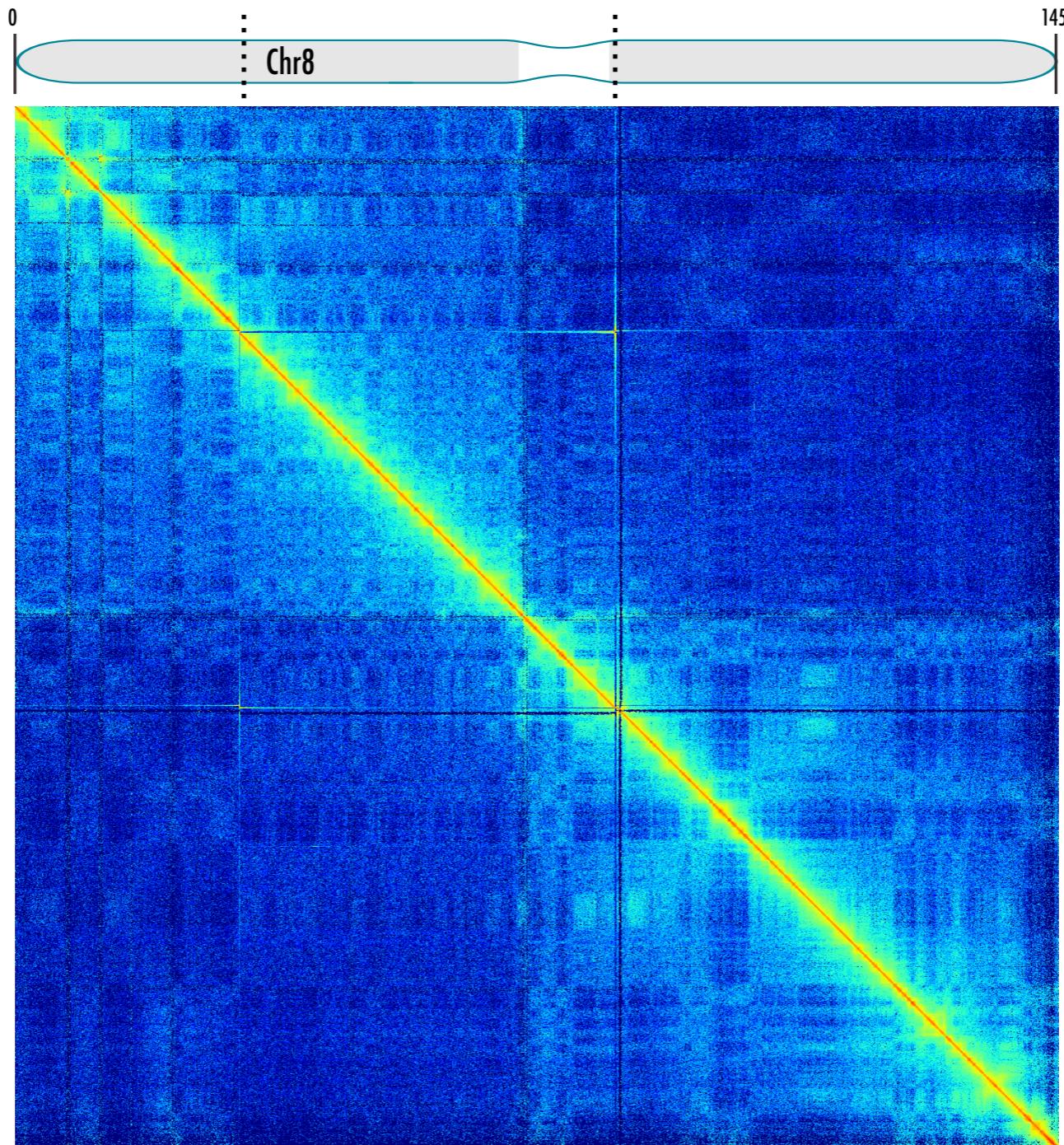
Great apes lymphoblast maps

Chromosome 14

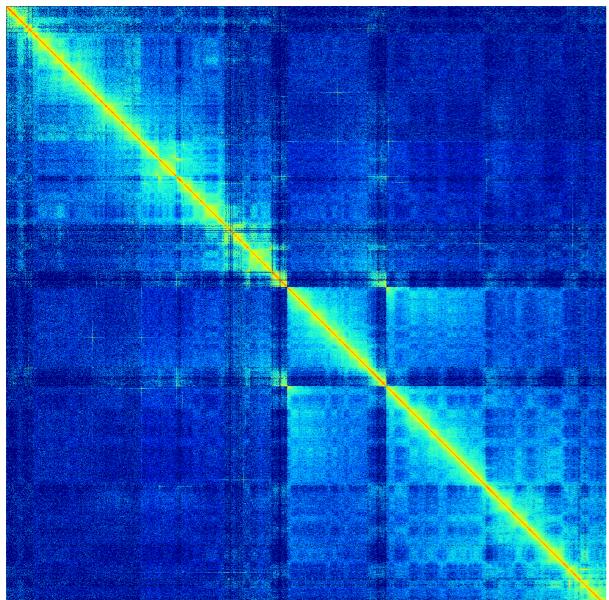


Assembly error detection

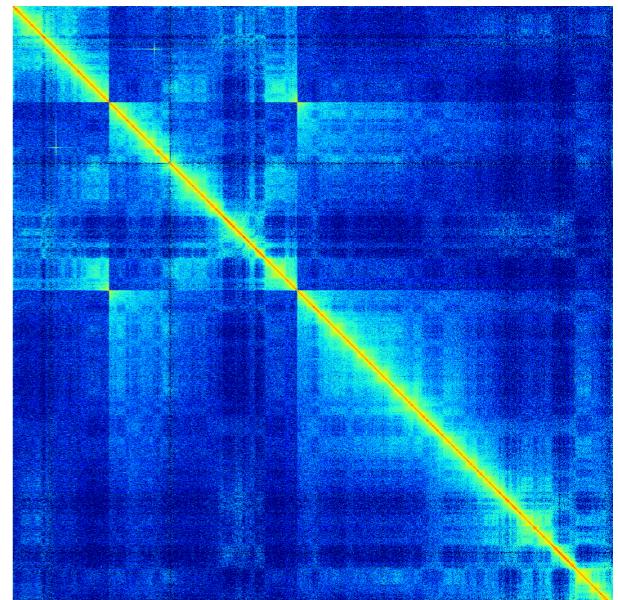
Chromosome 8 Gorilla



Chr 7

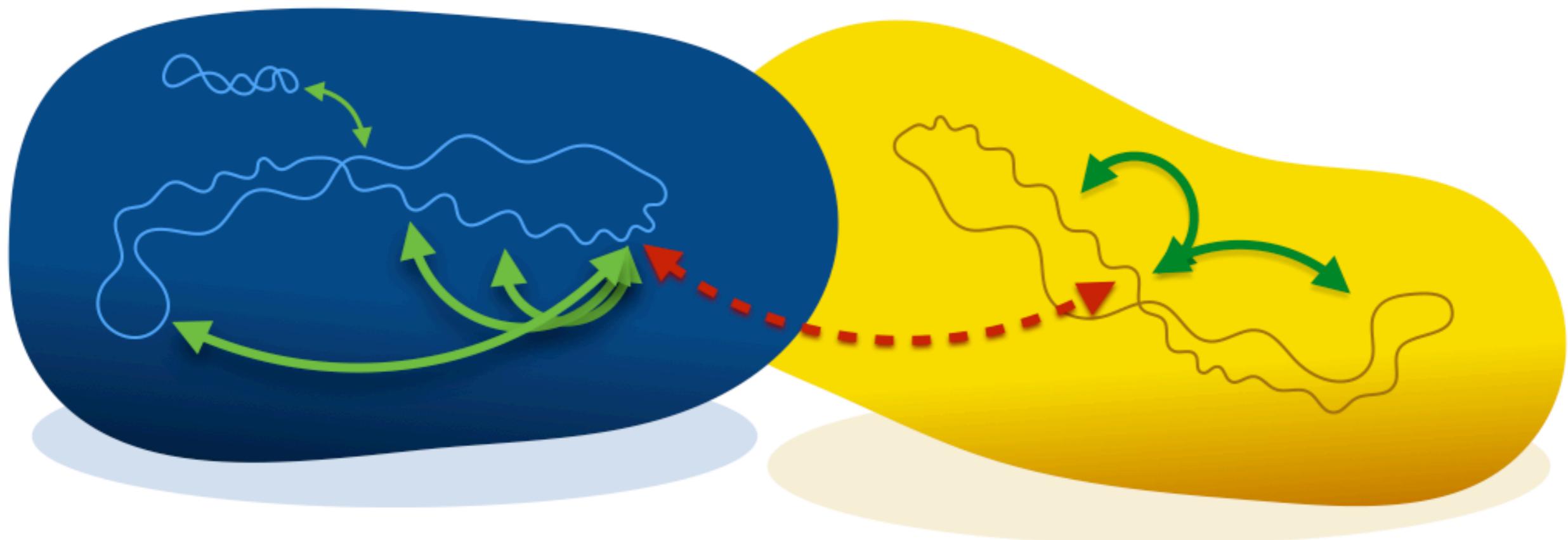


Chr 12



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

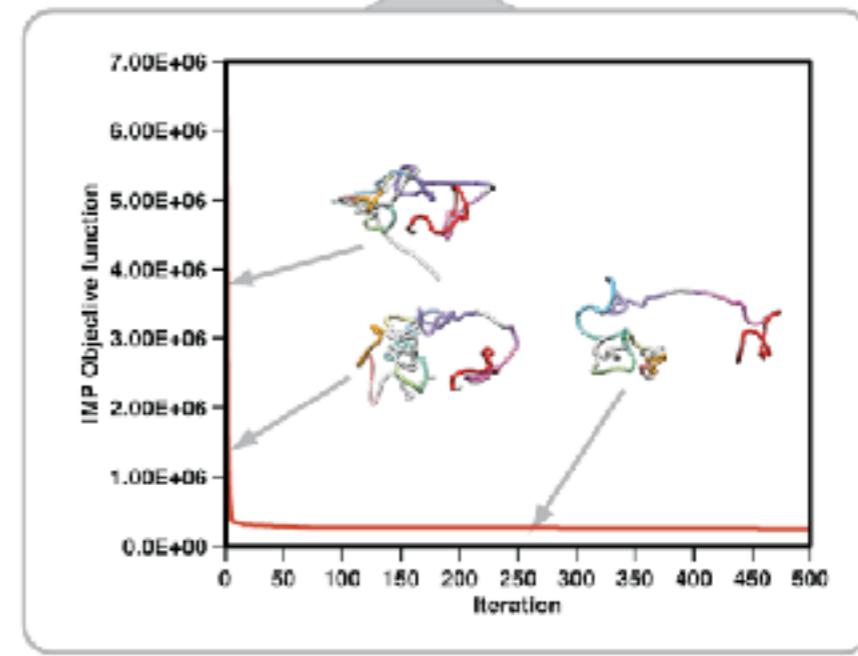
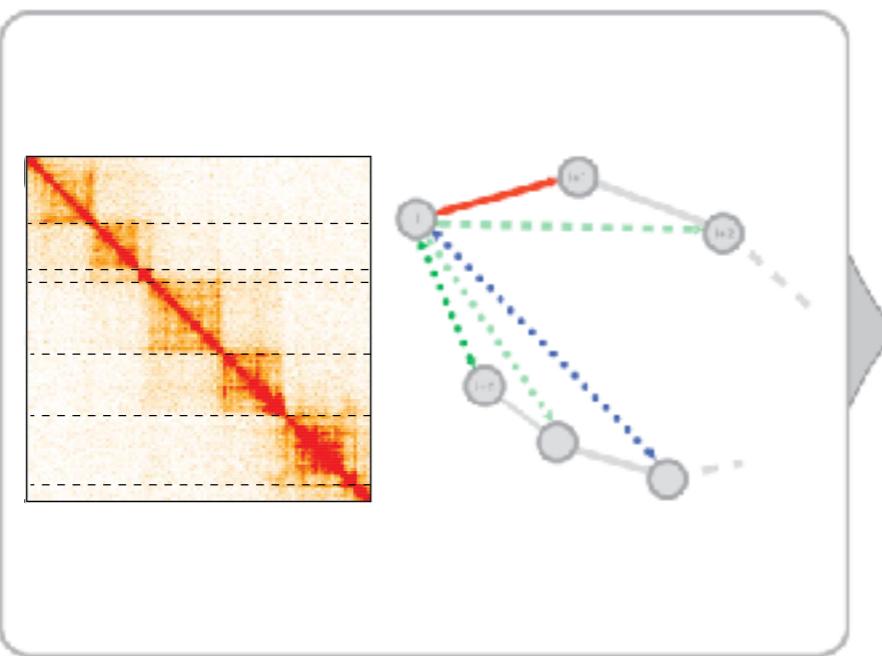
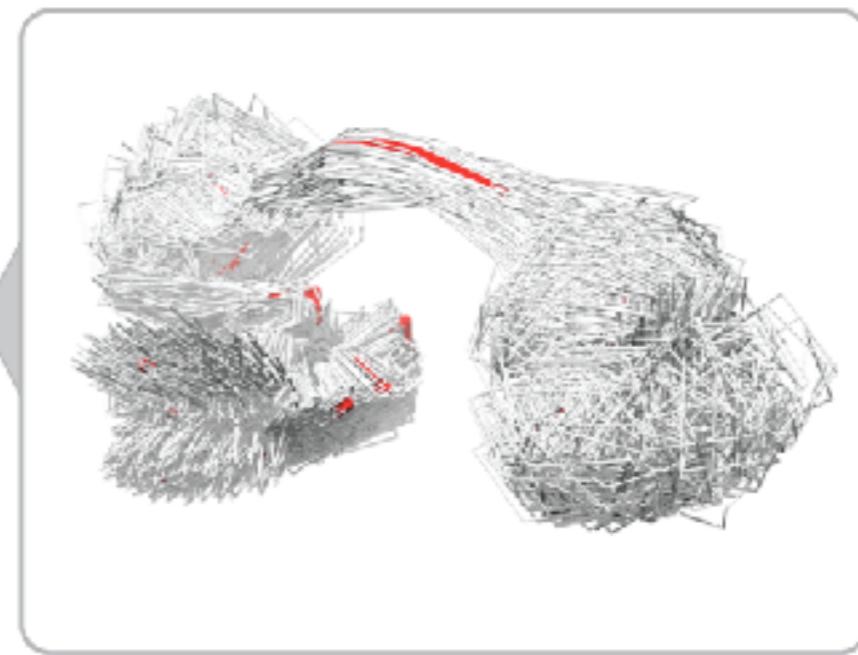
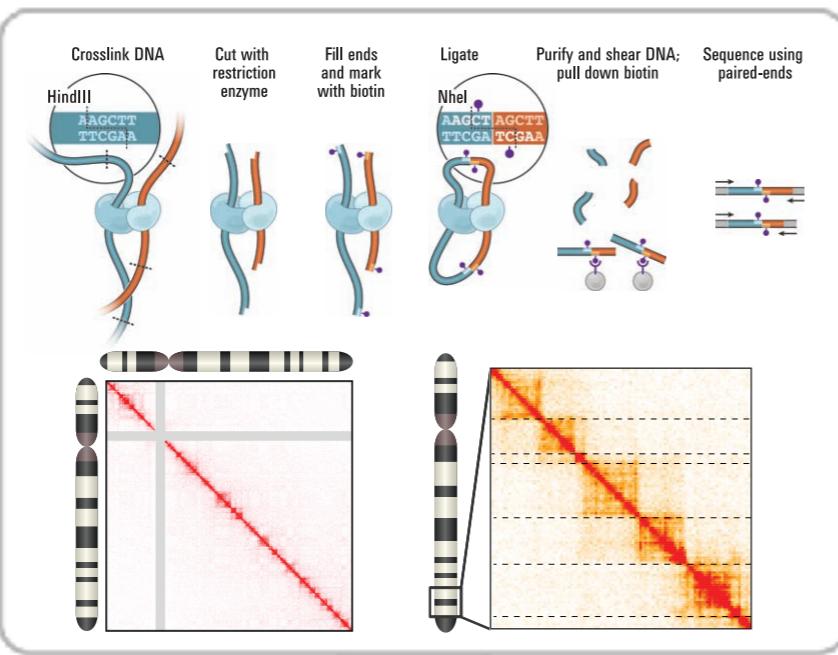


Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Michelmore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/peerj.preprints.260v1

Hybrid Method

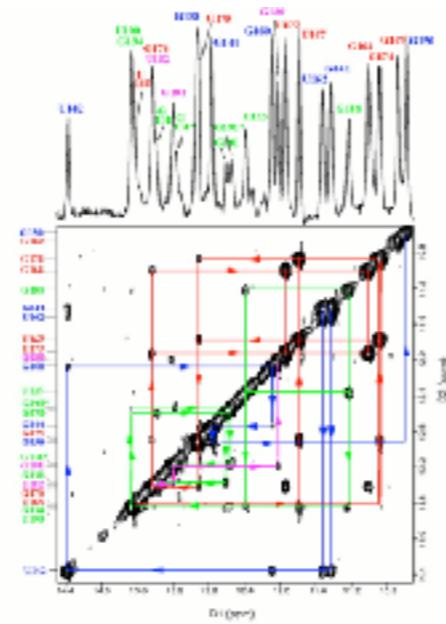
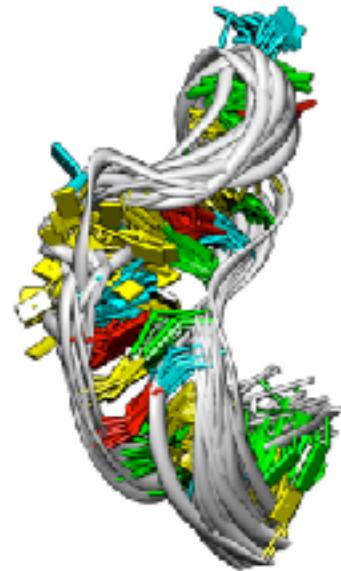
Baù, D. & Martí-Renom, M. A. Methods 58, 300–306 (2012).

Experiments

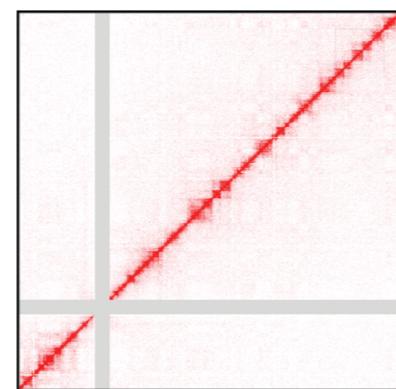
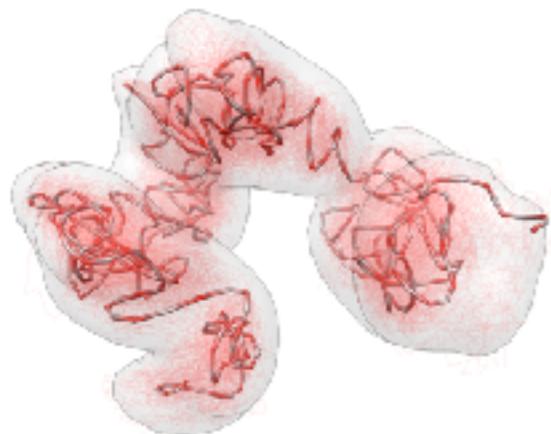


Computation

Structure determination using Hi-C data



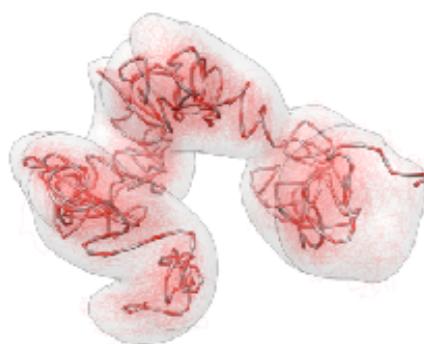
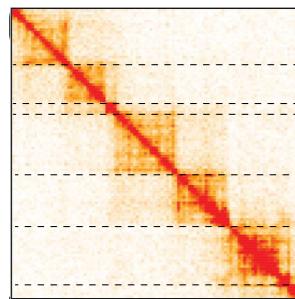
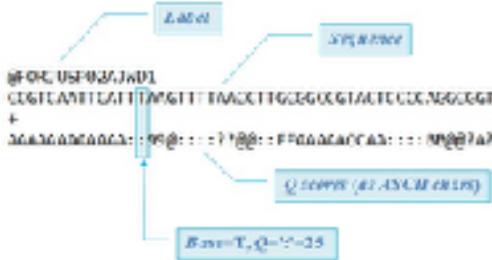
Biomolecular structure determination
2D-NOESY data



Chromosome structure determination
3C-based data



<http://3DGenomes.org>

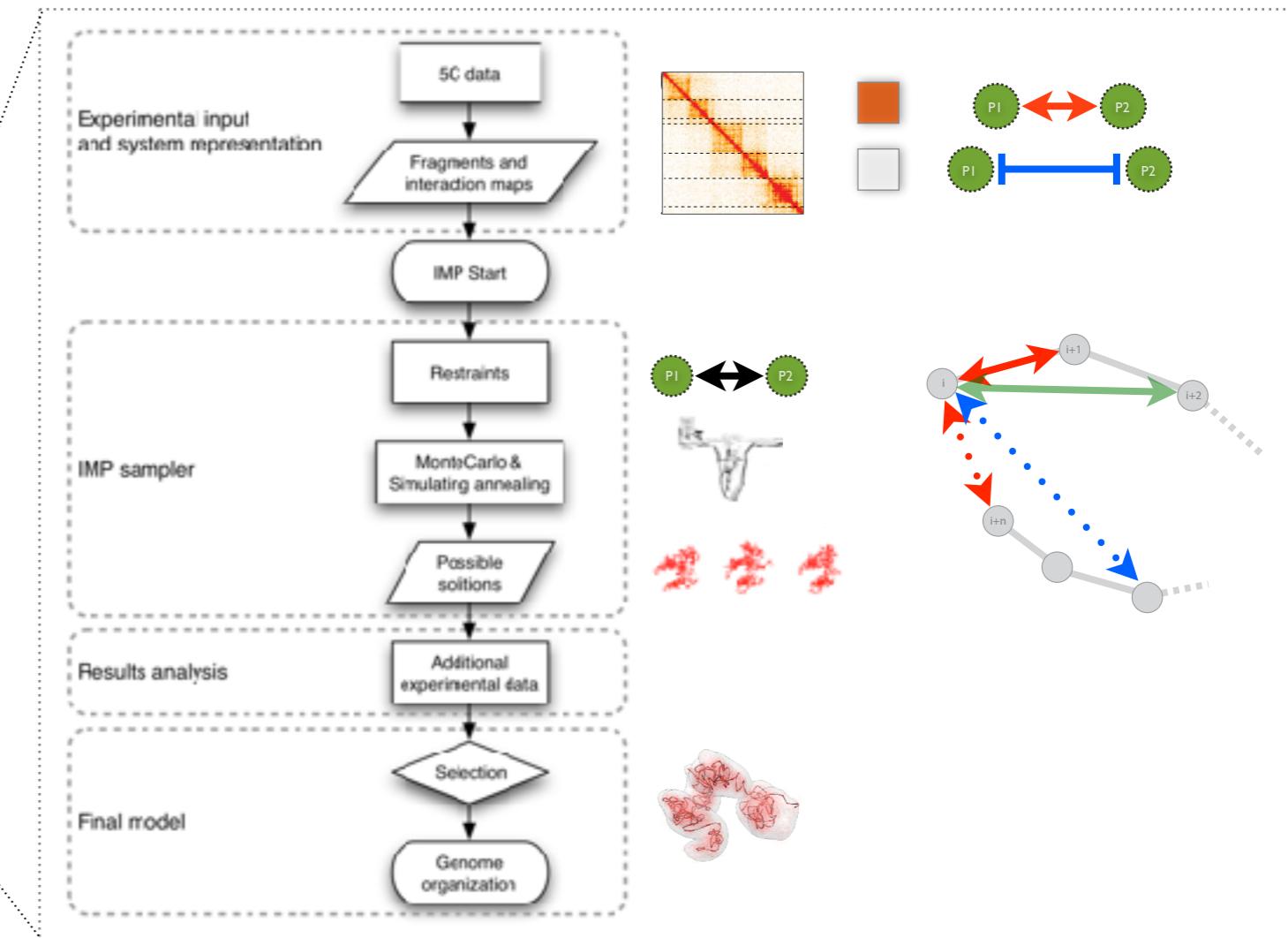


FastQ files to Maps

Map analysis

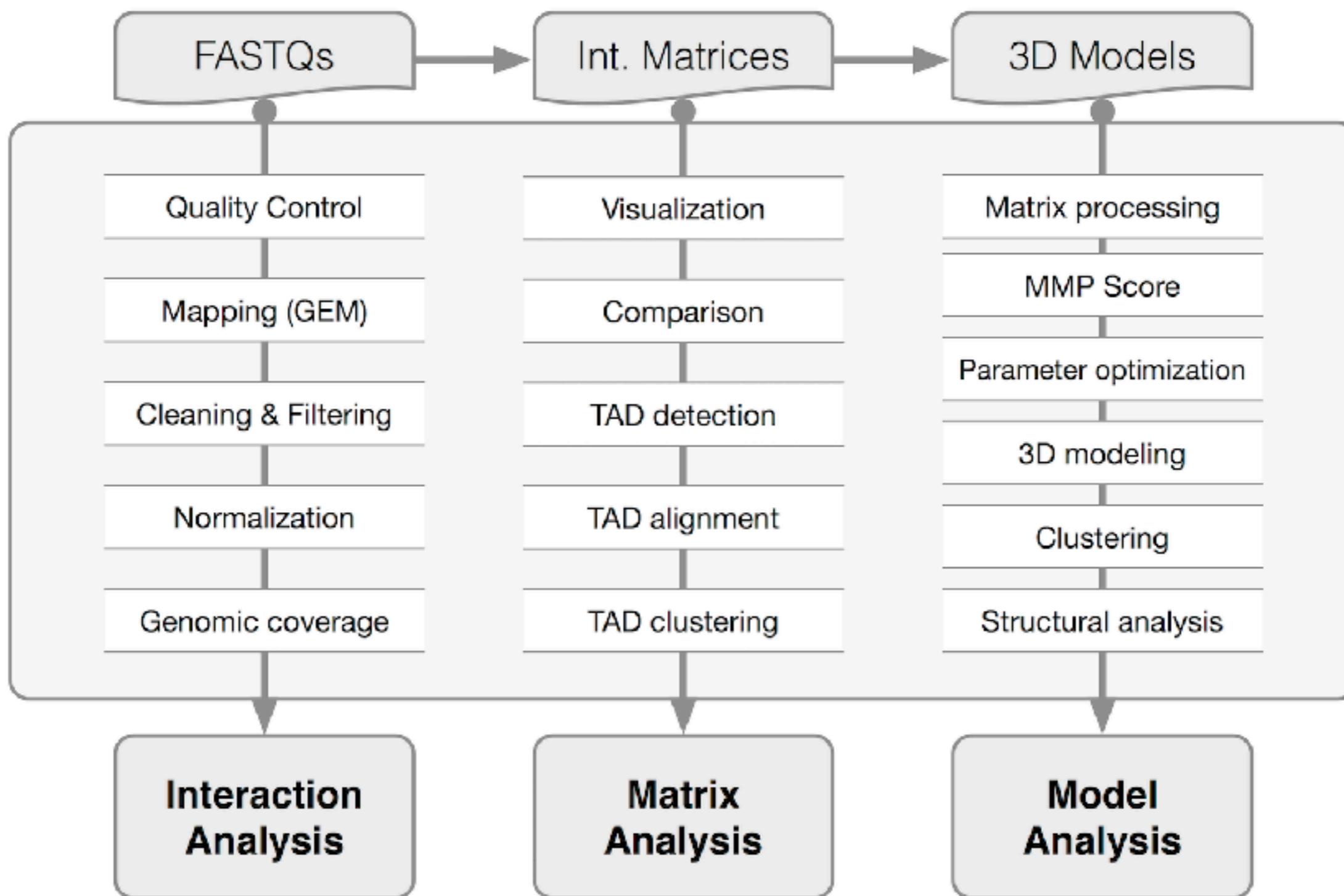
Model building

Model analysis



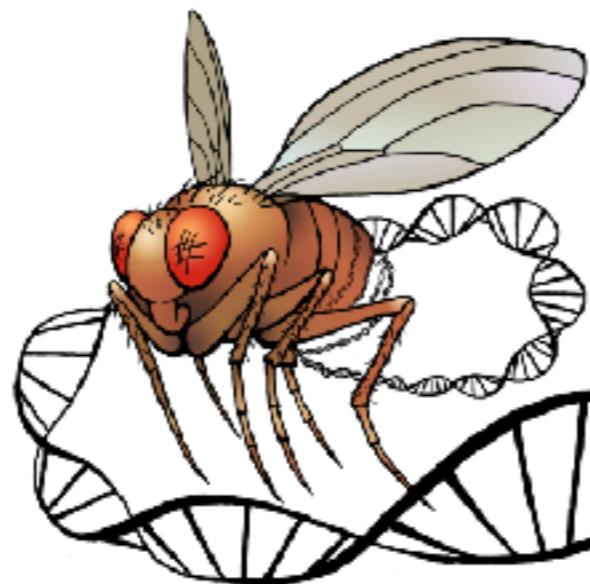


Serra, Baù, et al. (2017). PLOS CompBio



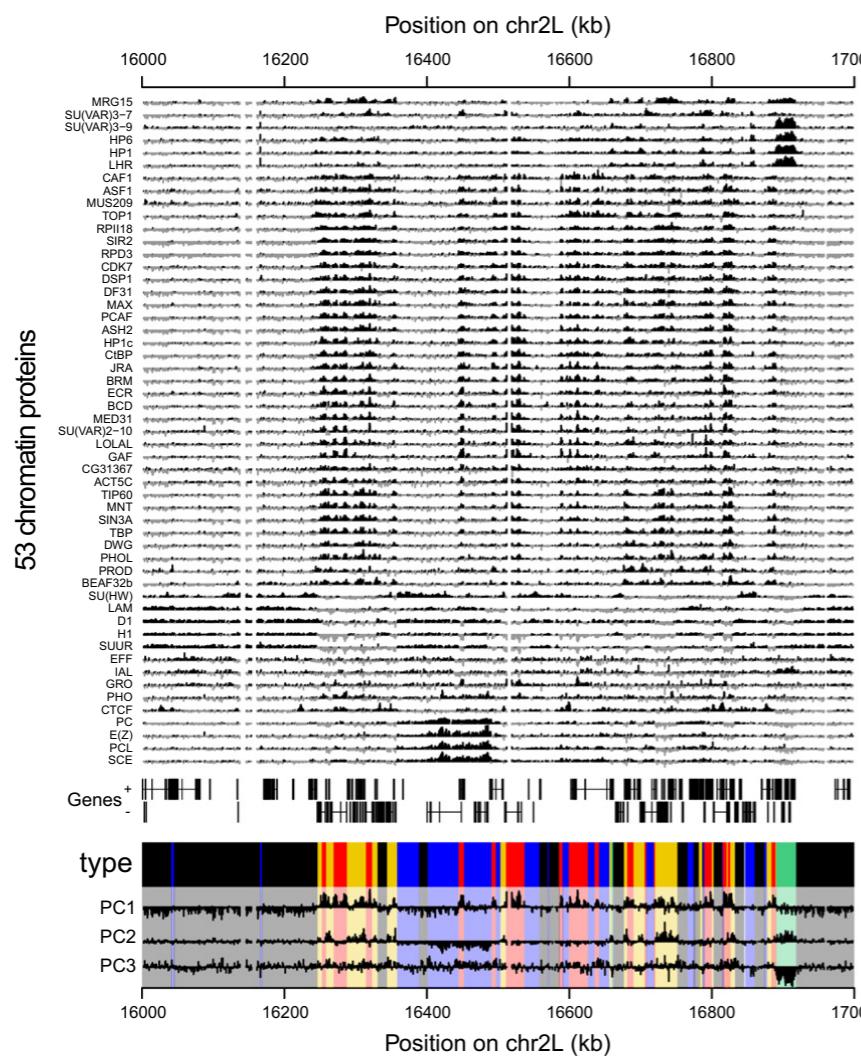
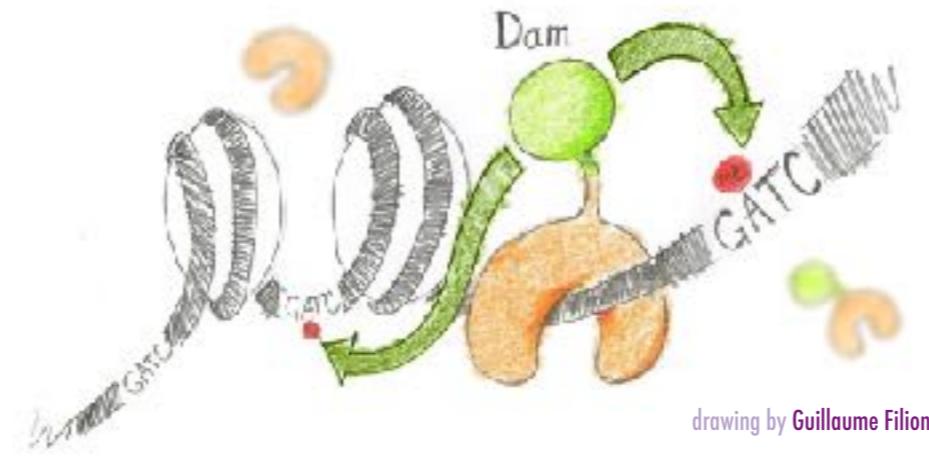
Structuring the **COLORs** of chromatin

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

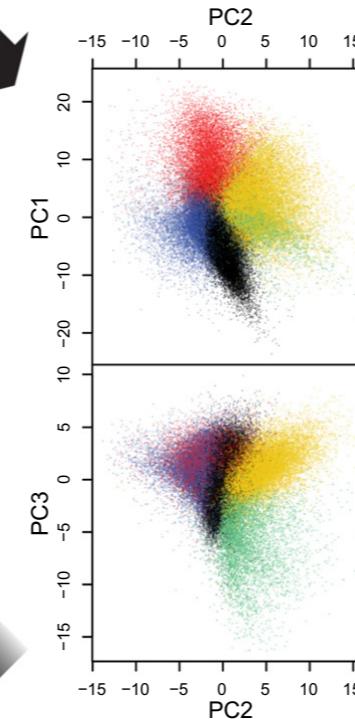


Fly Chromatin **COLORs**

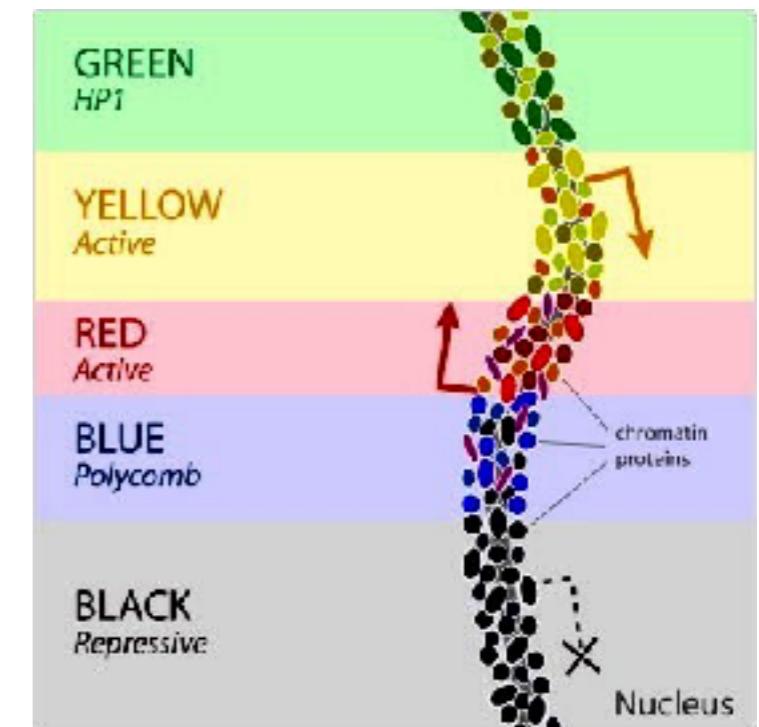
Filion et al. (2010). Cell, 143(2), 212–224.



Principal component analysis

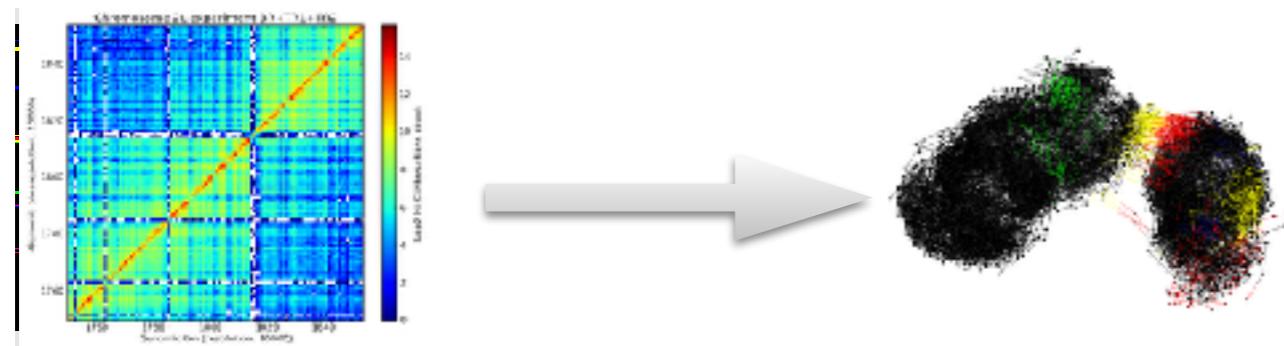
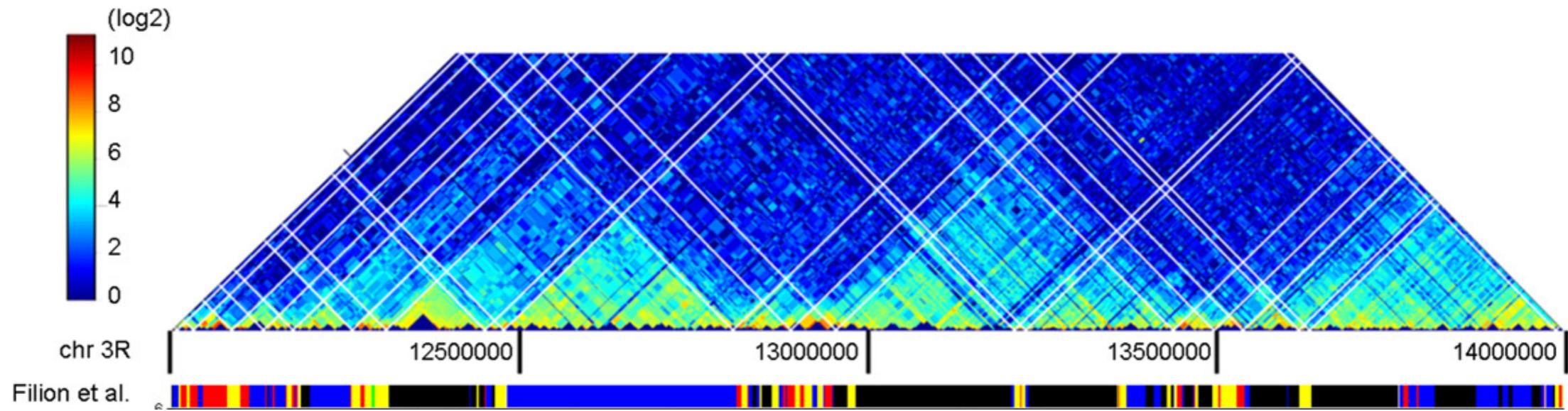


Hidden Markov model



Fly Chromatin **COLORs**

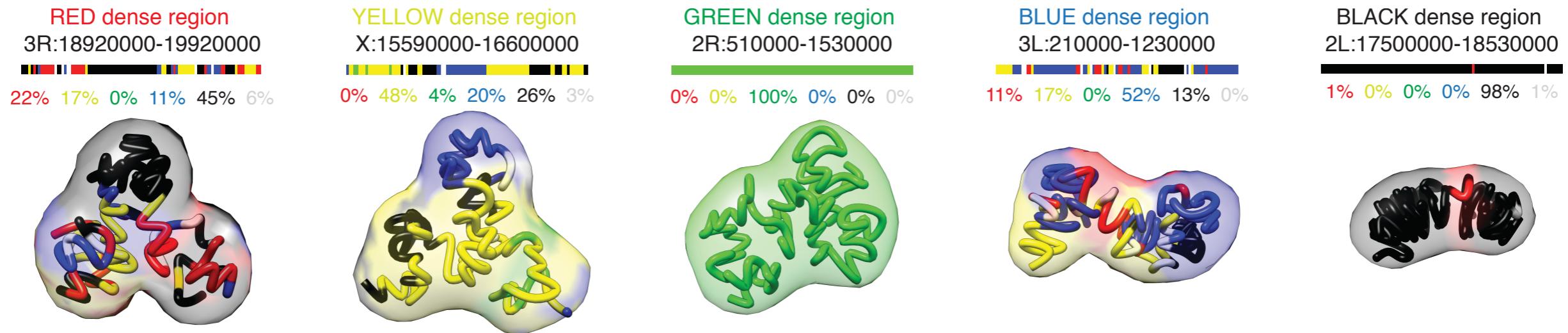
Hou et al. (2012). Molecular Cell, 48(3), 471–484.



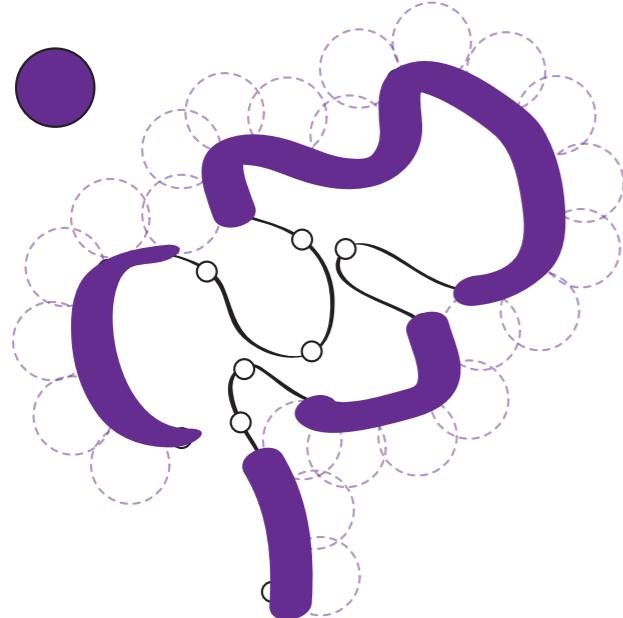
~200 regions of ~5Mb each
2Kb resolution

Structural properties

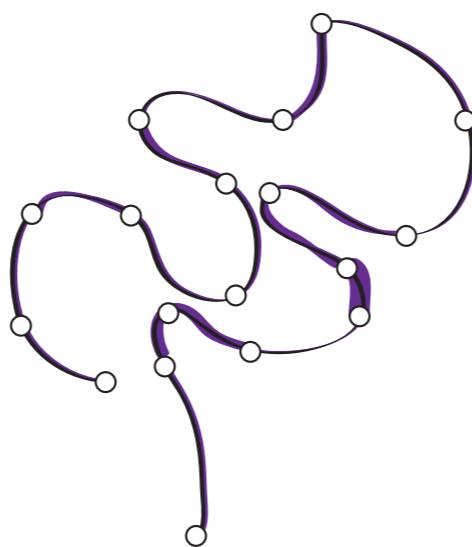
50 1Mb regions. 10 enriched for each color.



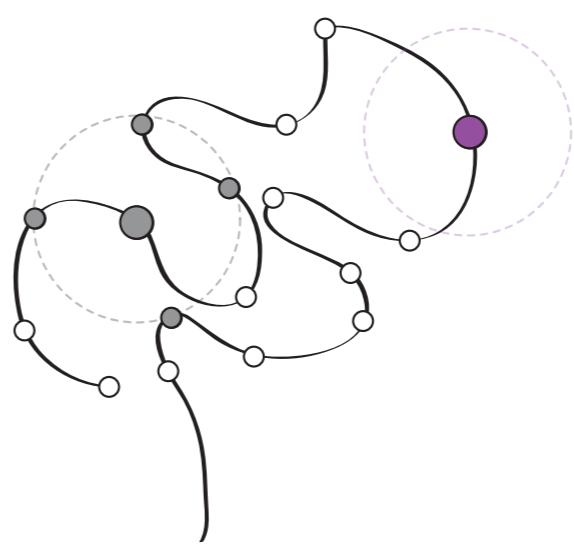
Accessibility (%)



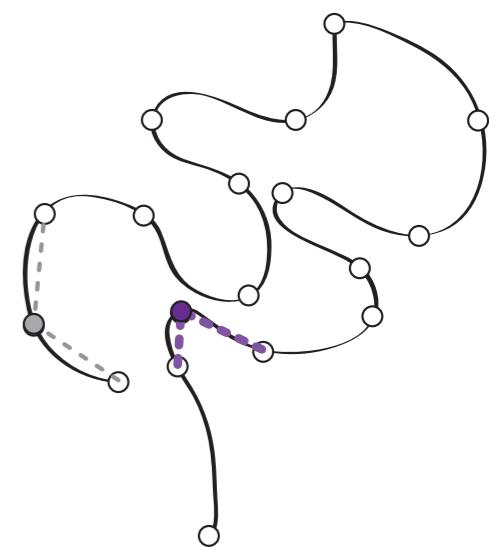
Density (bp/nm)



Interactions



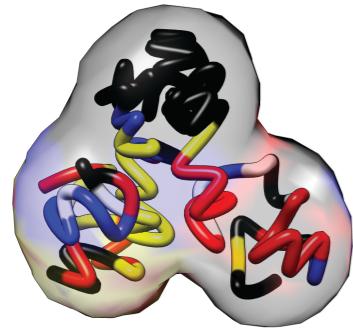
Angle



Structural COLORs

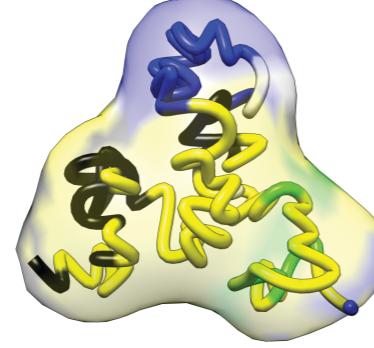
RED dense region
3R:18920000-19920000

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



YELLOW dense region
X:15590000-16600000

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



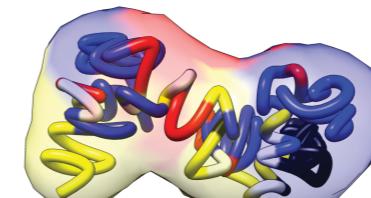
GREEN dense region
2R:510000-1530000

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



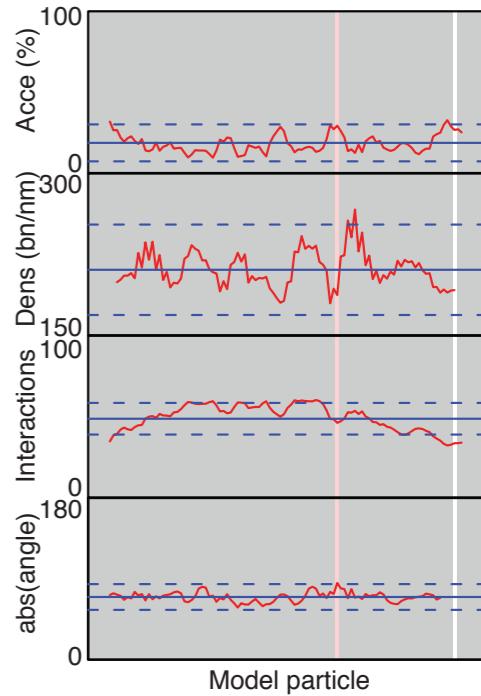
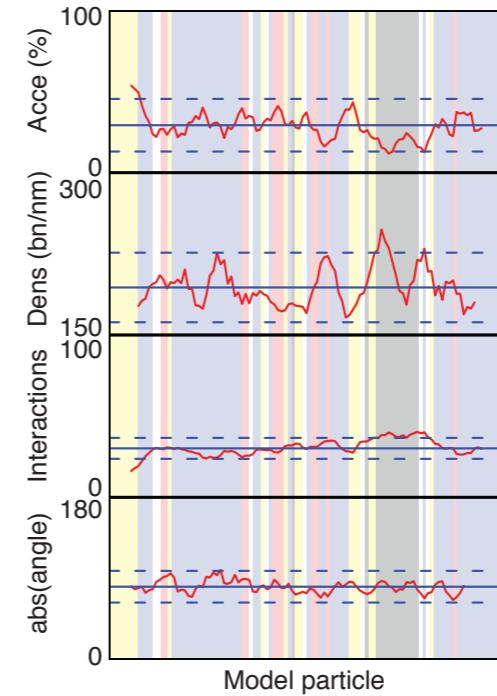
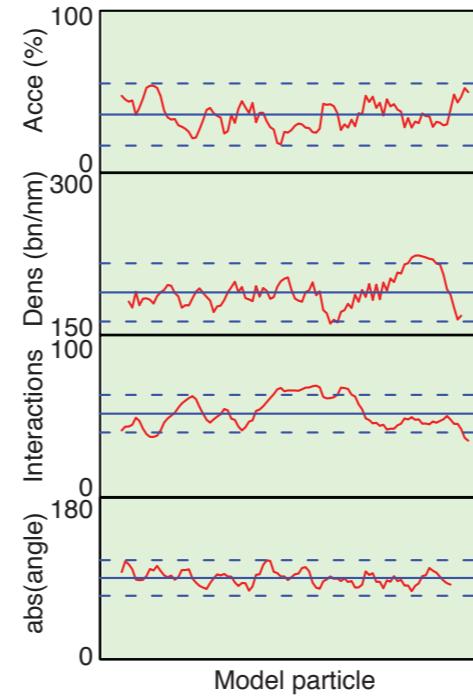
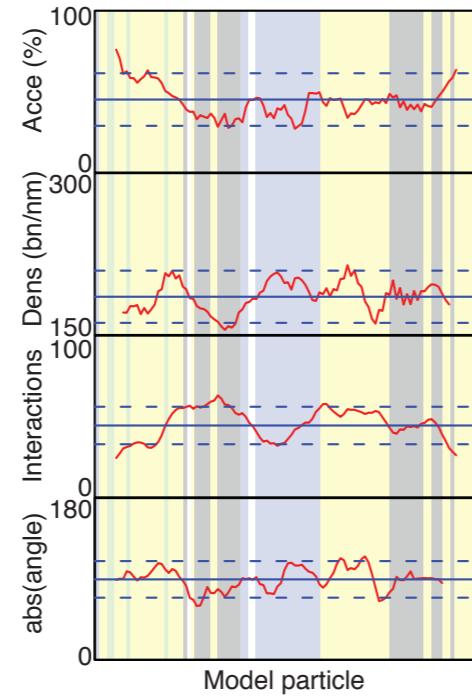
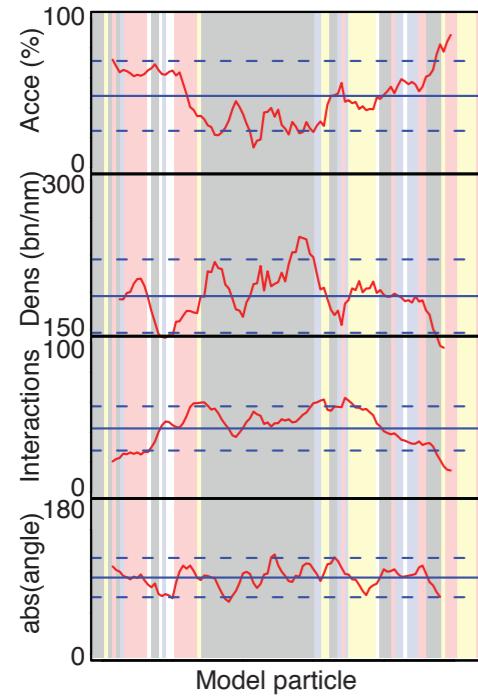
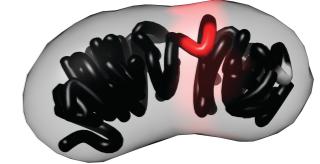
BLUE dense region
3L:210000-1230000

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

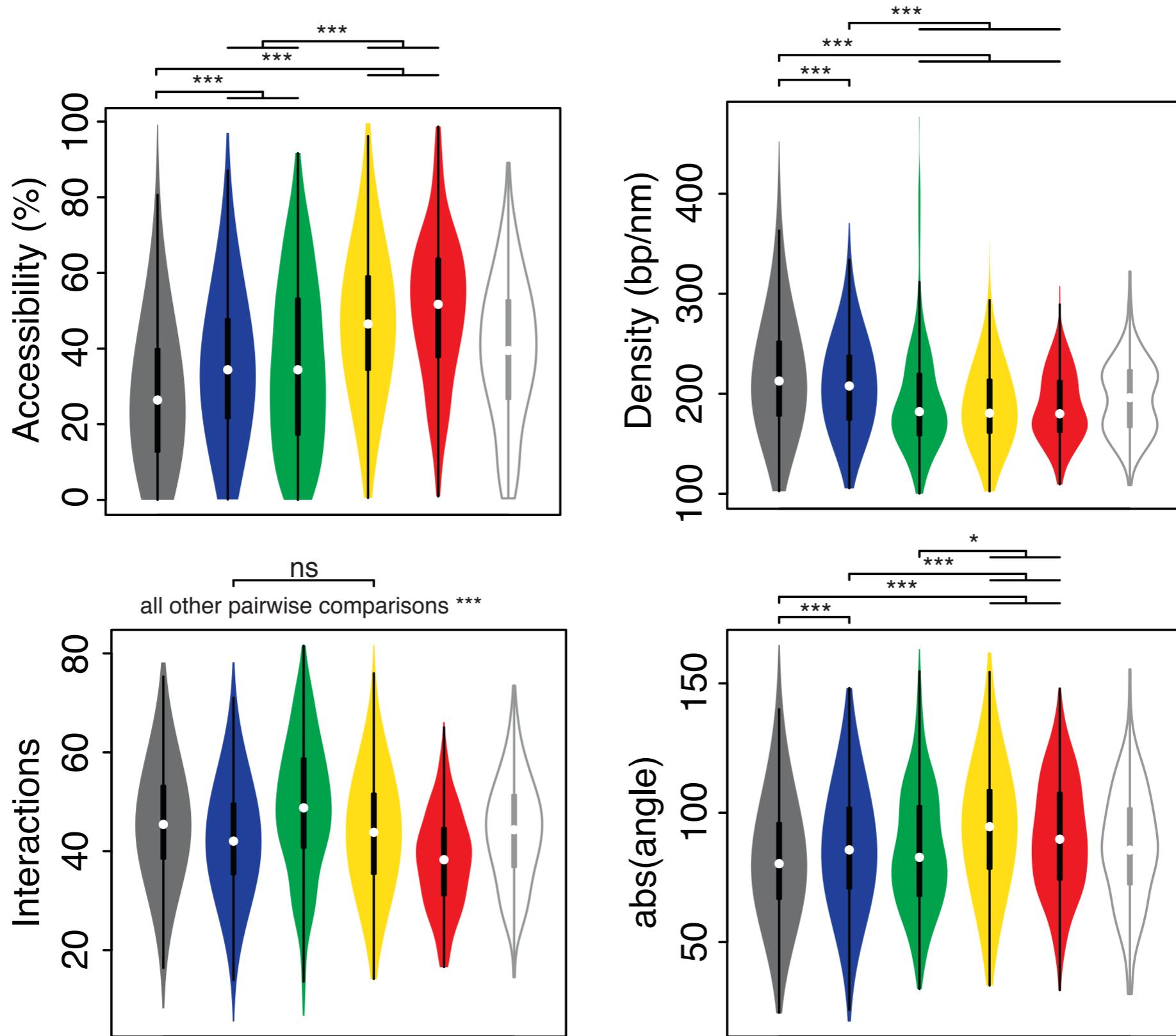


BLACK dense region
2L:17500000-18530000

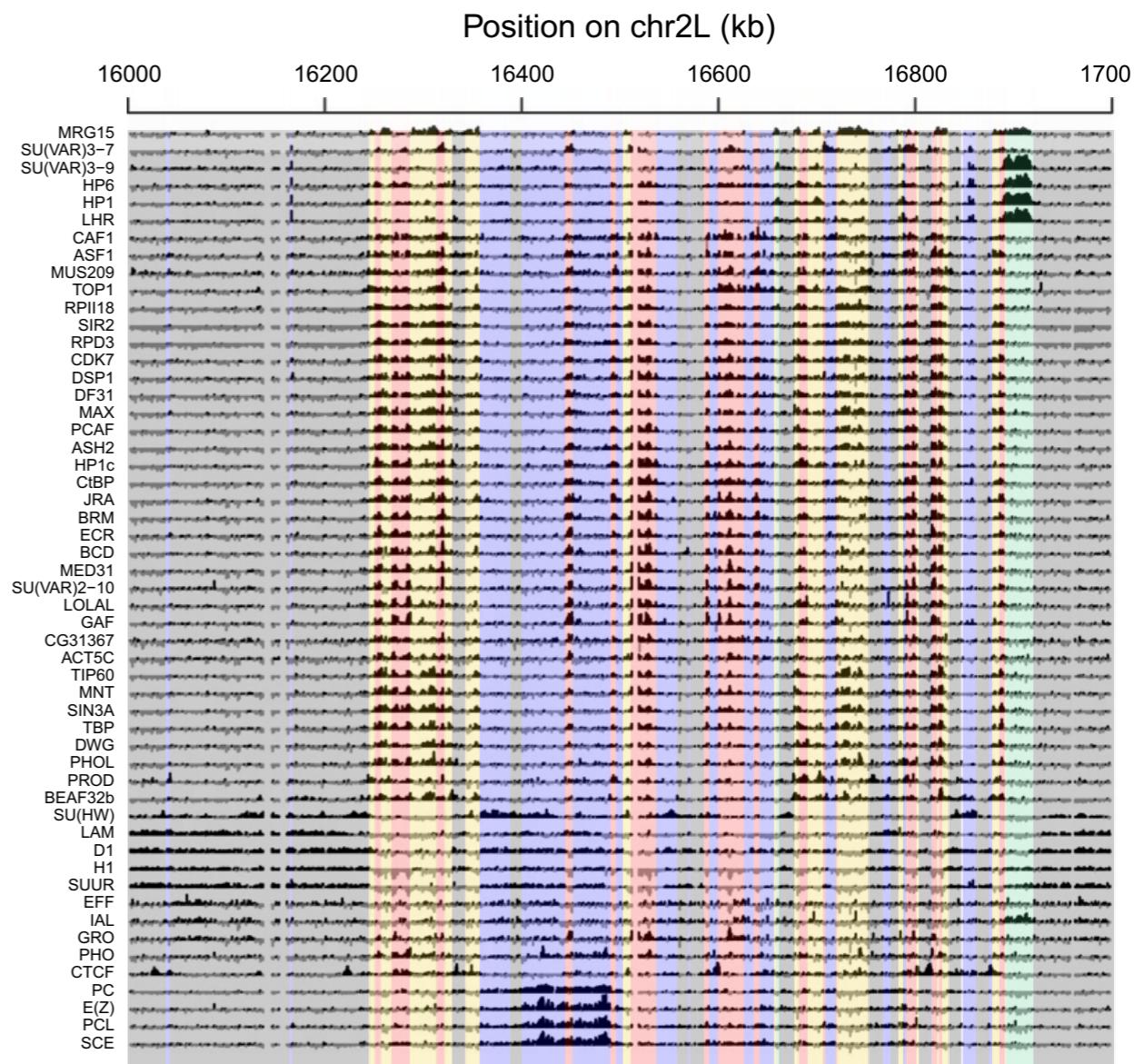
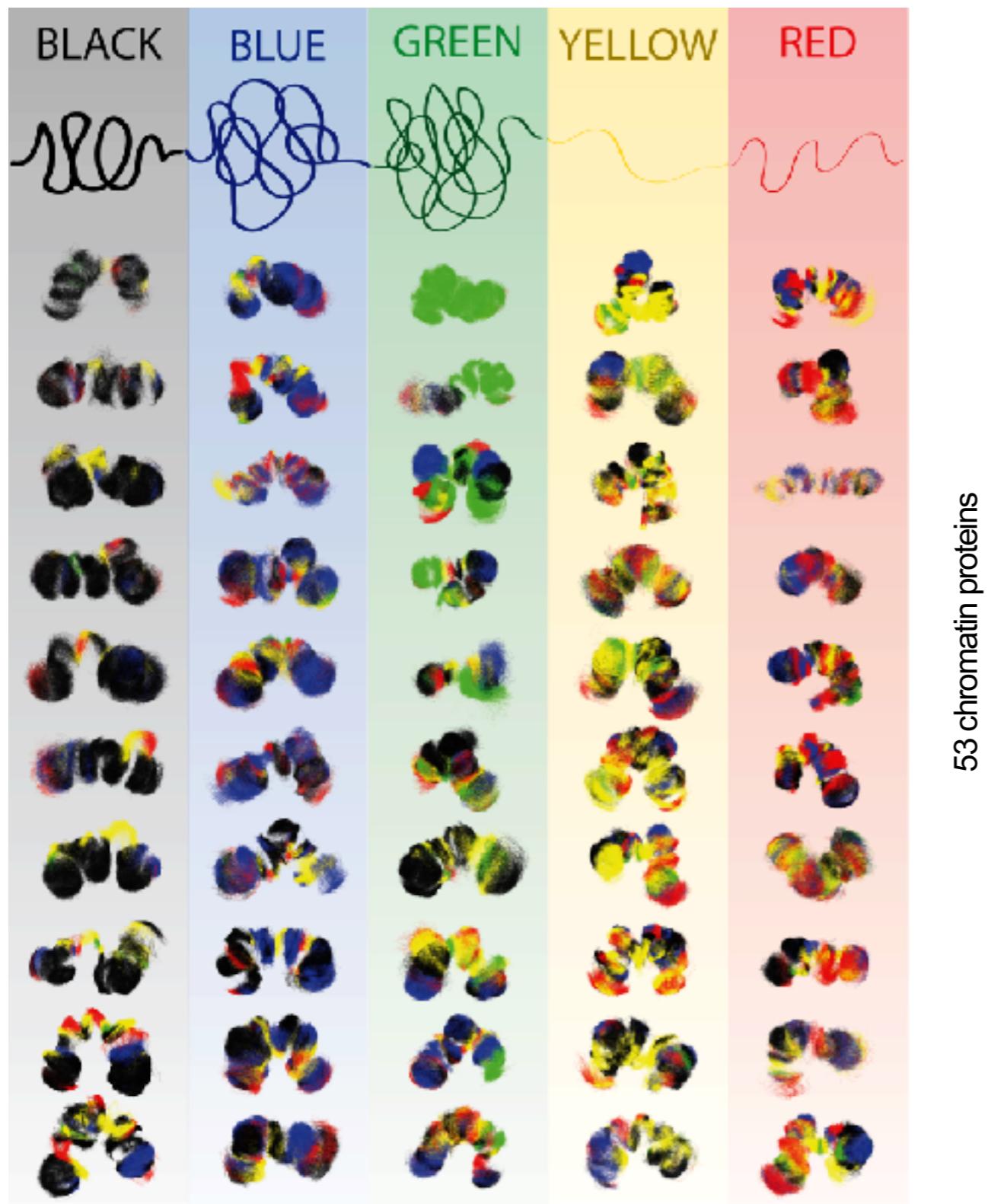
 1% 0% 0% 0% 98% 1%



Structural COLORs



Structural COLORs



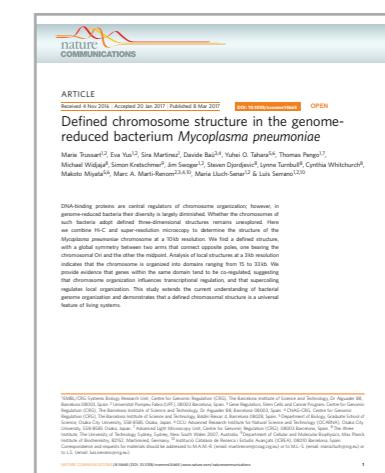
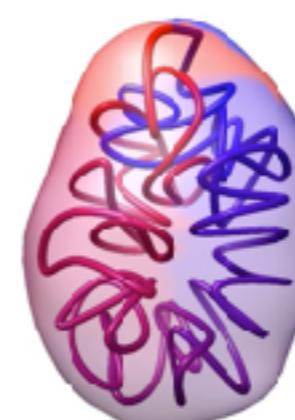
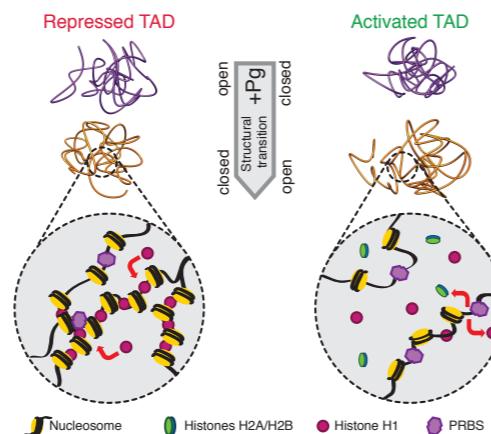
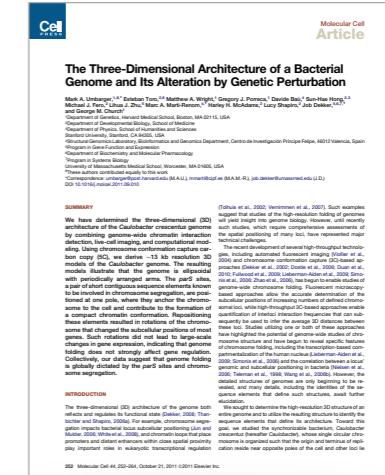
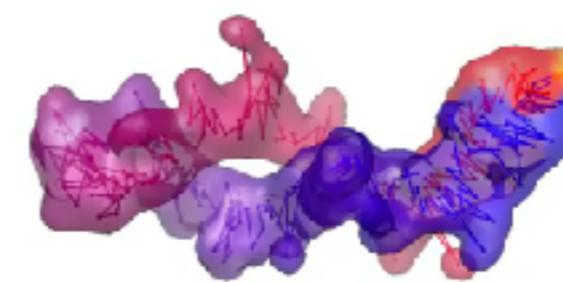
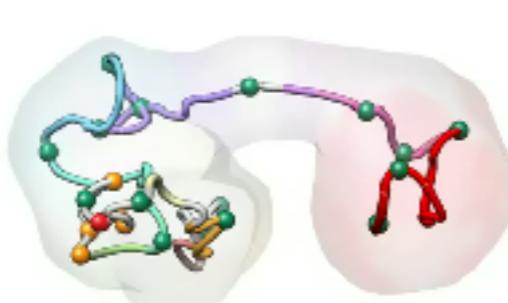
TADbit other applications...

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
Julen Mendieta
Francesca Mugianesi
Juan Rodríguez
François Serra
Paula Soler
Aleksandra Sparavier
Marco di Stefano

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

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



cnag

CRG
Centre
for Genomic
Regulation

ICREA