Chromatin structure and Hi-C data

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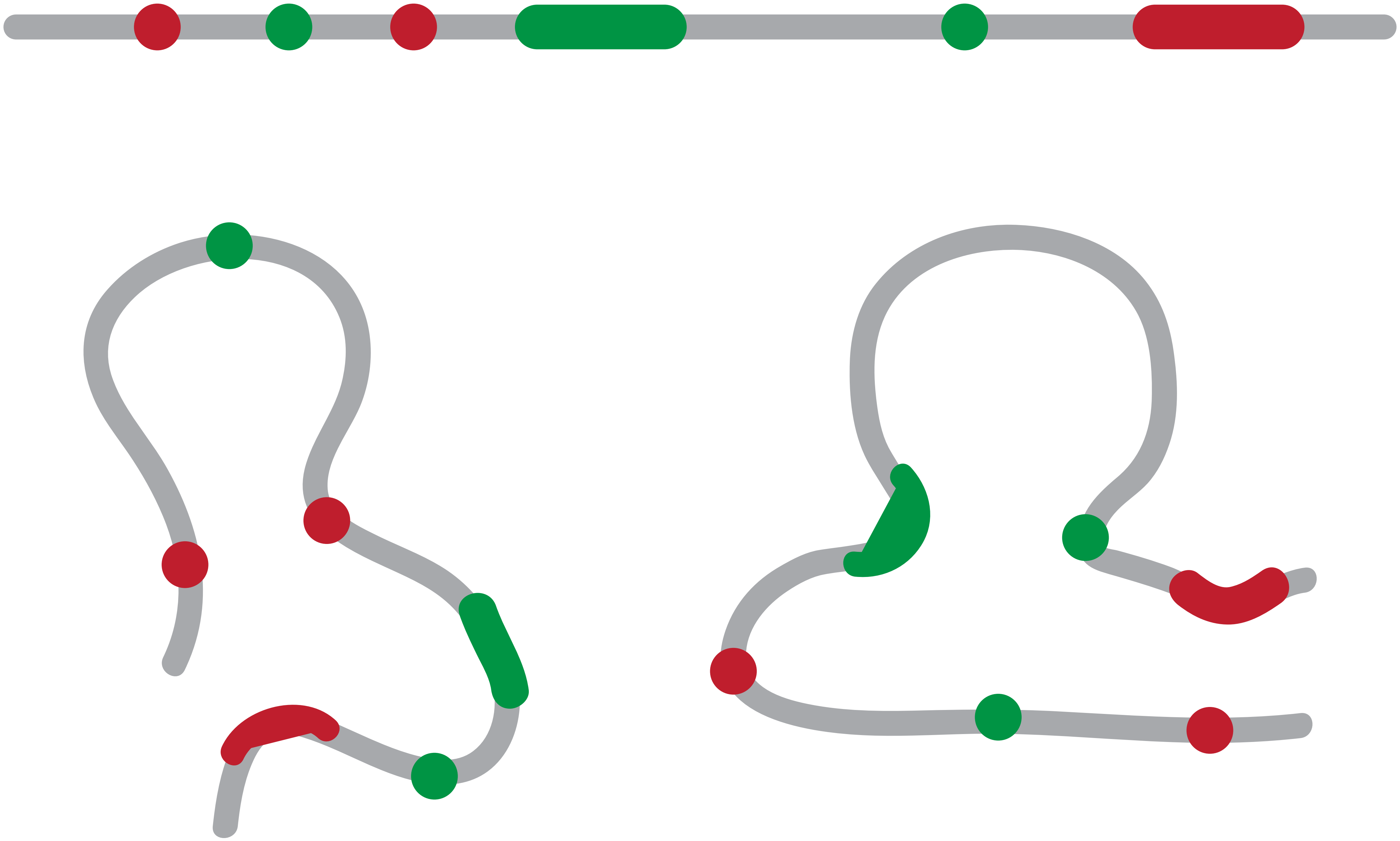
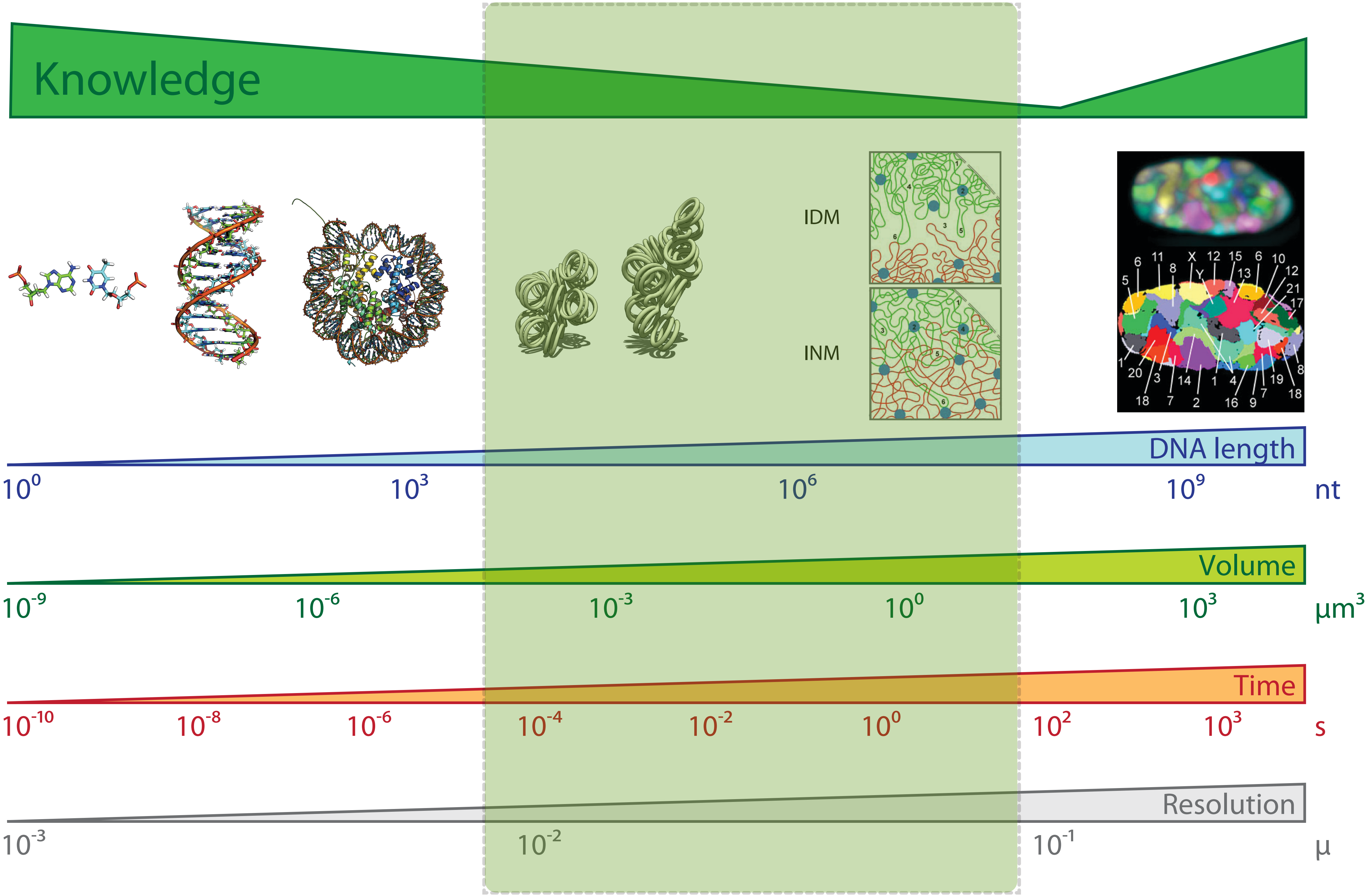
Structural Genomics Group (CNAG-CRG)

cnag CRG Centre for Genomic Regulation



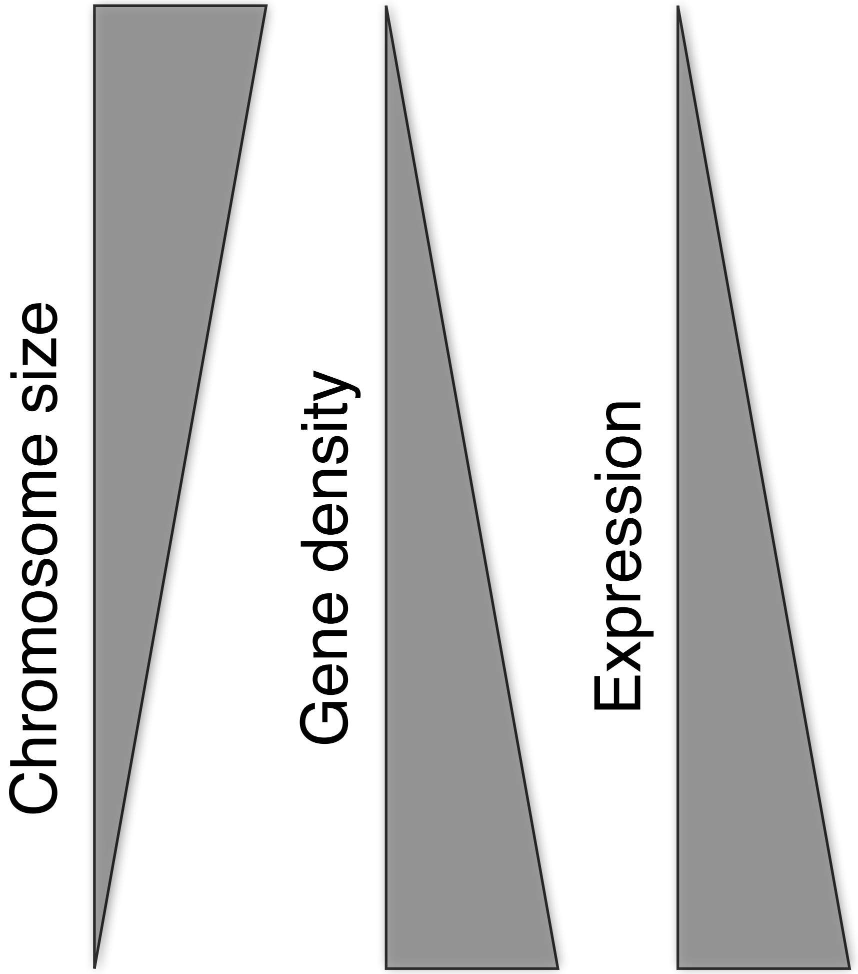
Resolution Gap

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



Level I: Radial genome organization

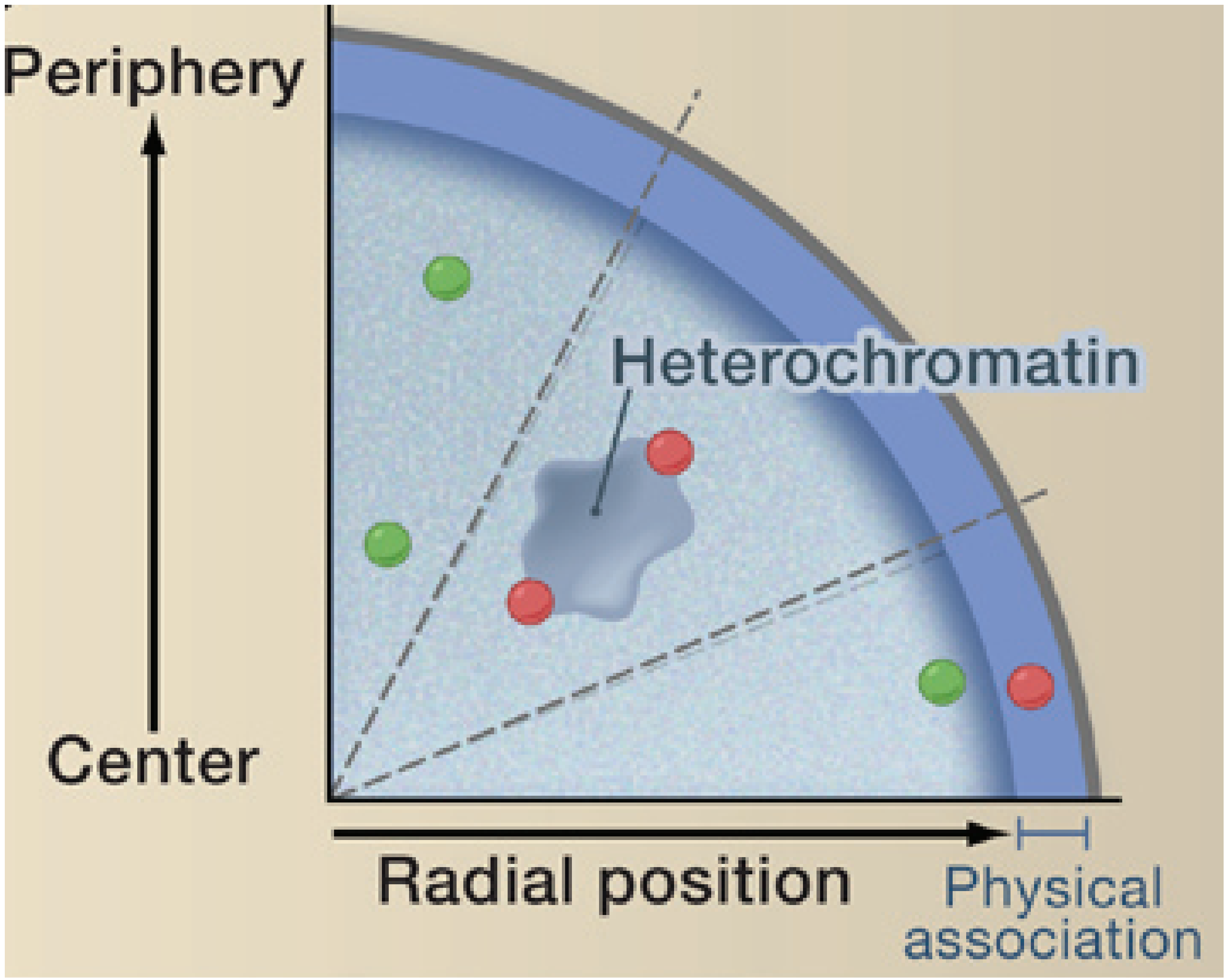
Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



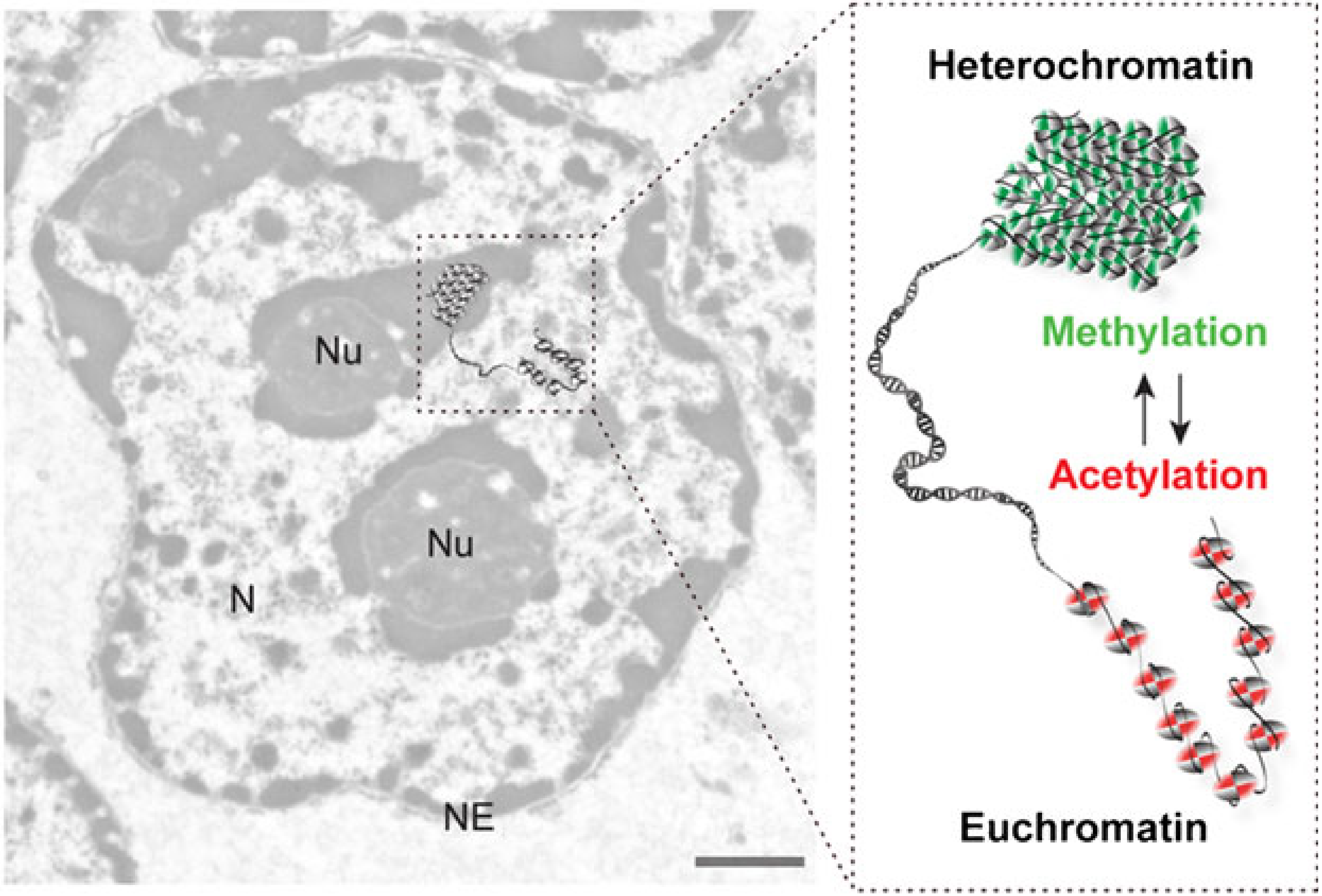
Chromosome size

Gene density

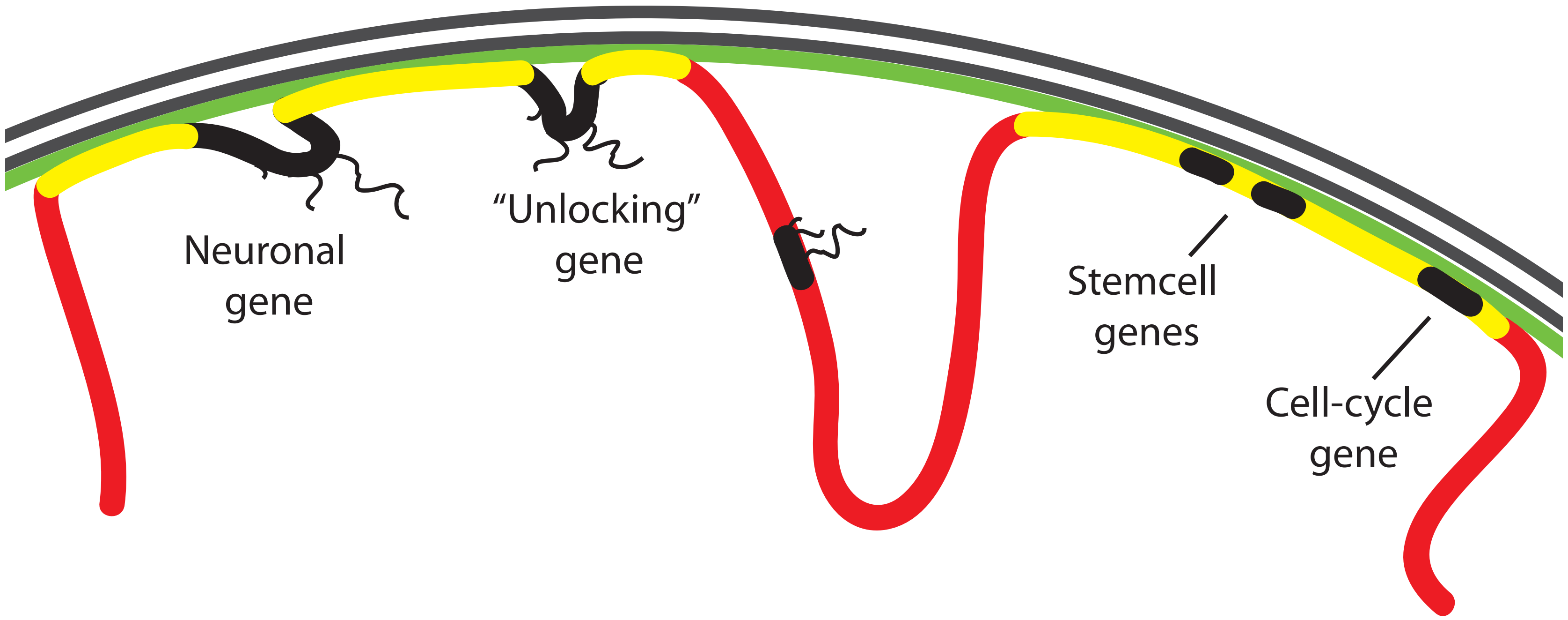
Expression



Level II: Euchromatin vs heterochromatin



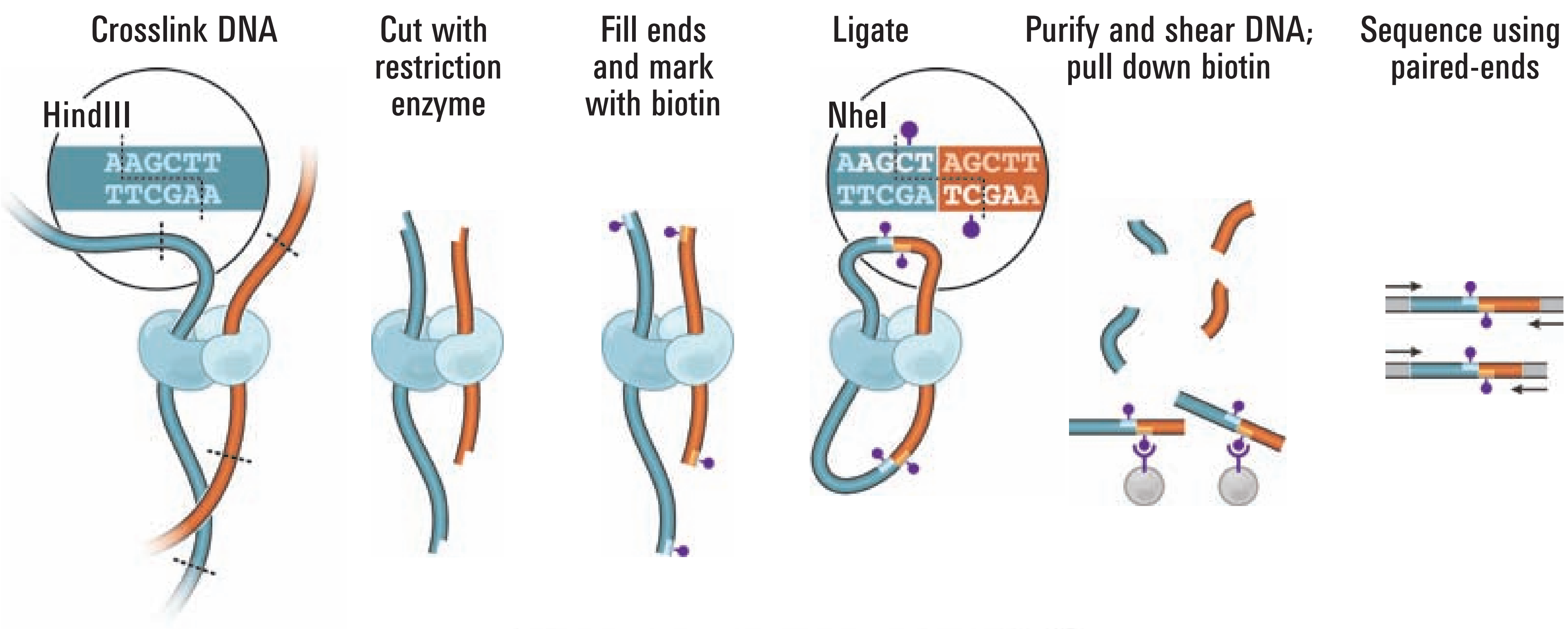
Level III: Lamina-genome interactions

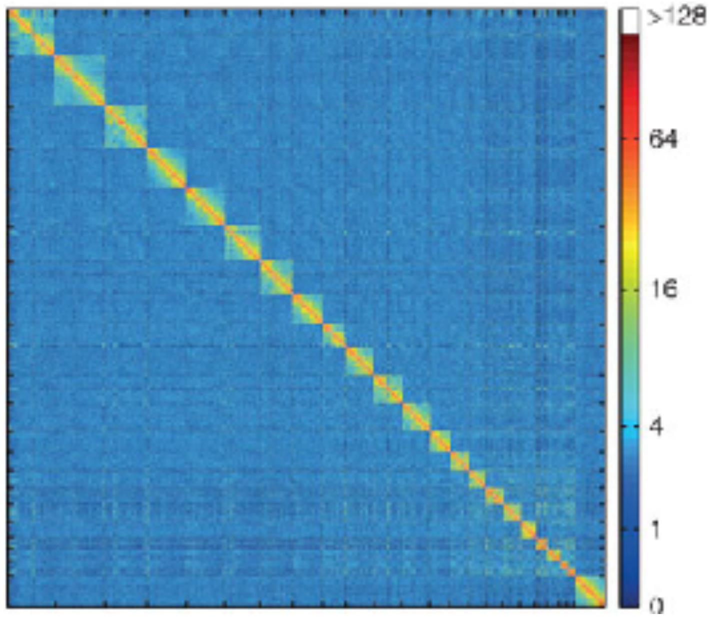


- = nuclear membrane
- 🟩 nuclear lamina
- 🟥 internal chromatin (mostly active)
- 🟨 lamina-associated domains (repressed)
- ▬ Genes
- ~ mRNA

Adapted from Molecular Cell 38, 603-613, 2010

Level IV: Higher-order organization

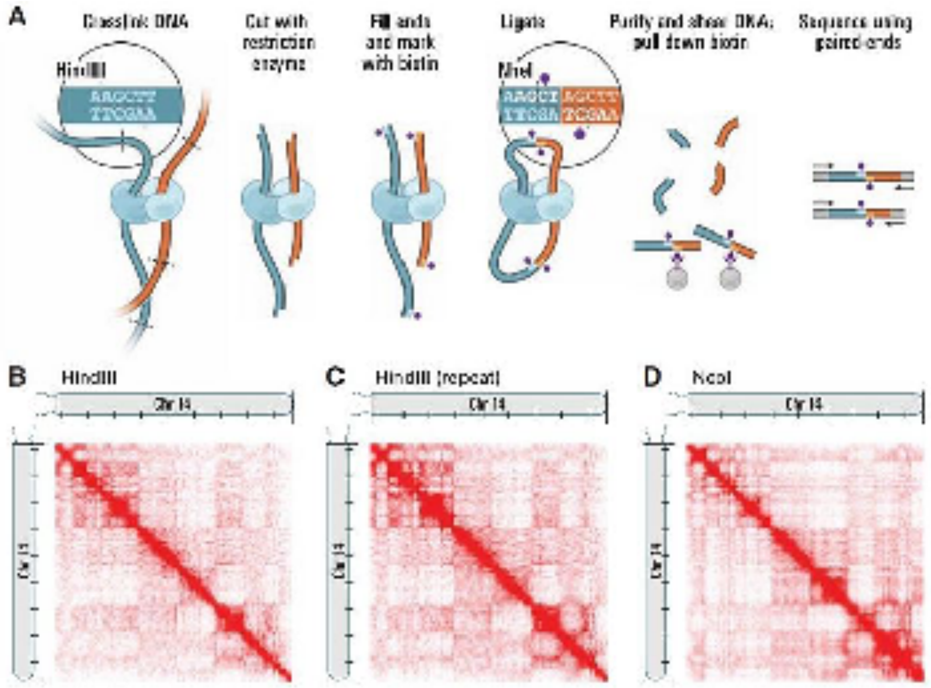


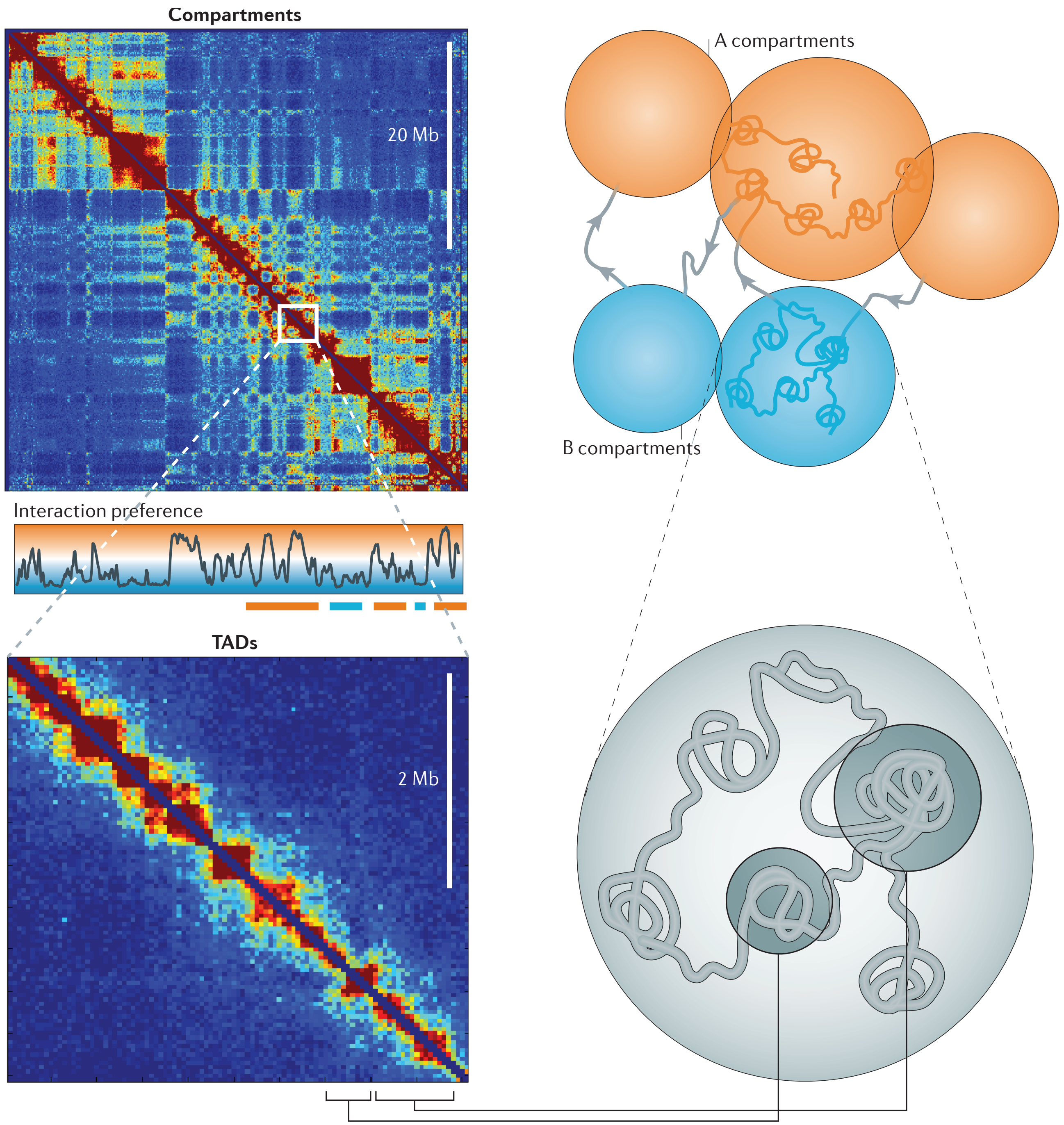


Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311.
Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.

Level IV: Higher-order organization

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

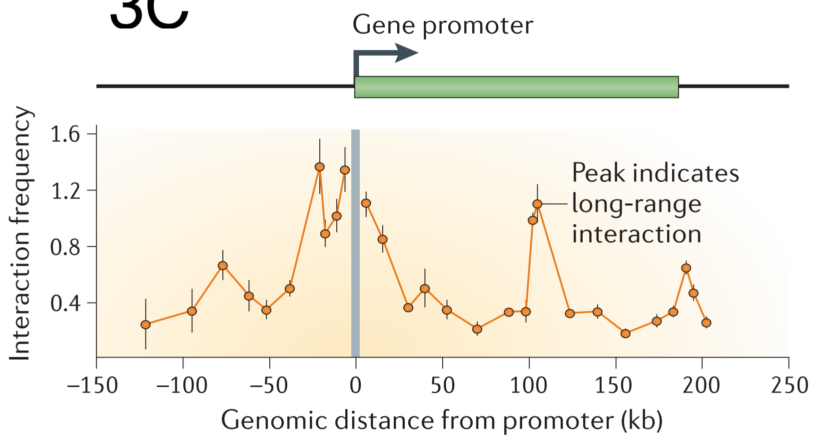




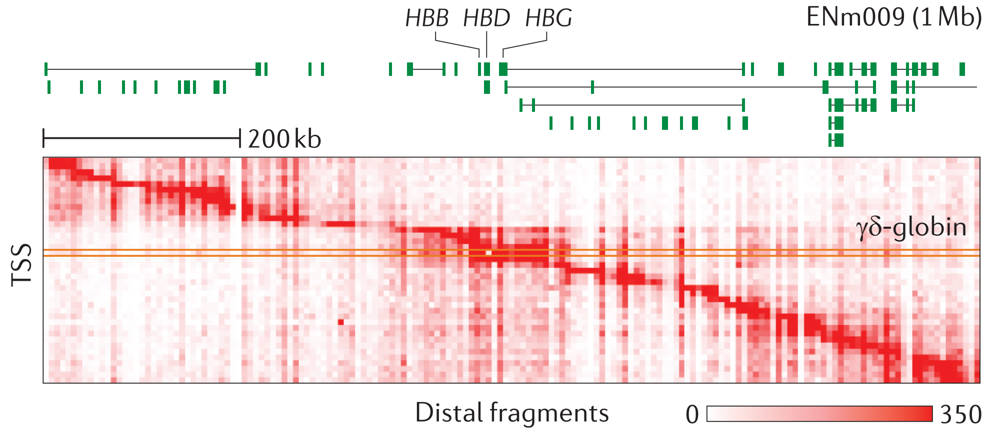
Level IV: Higher-order organization

Insights from 3C-based technologies

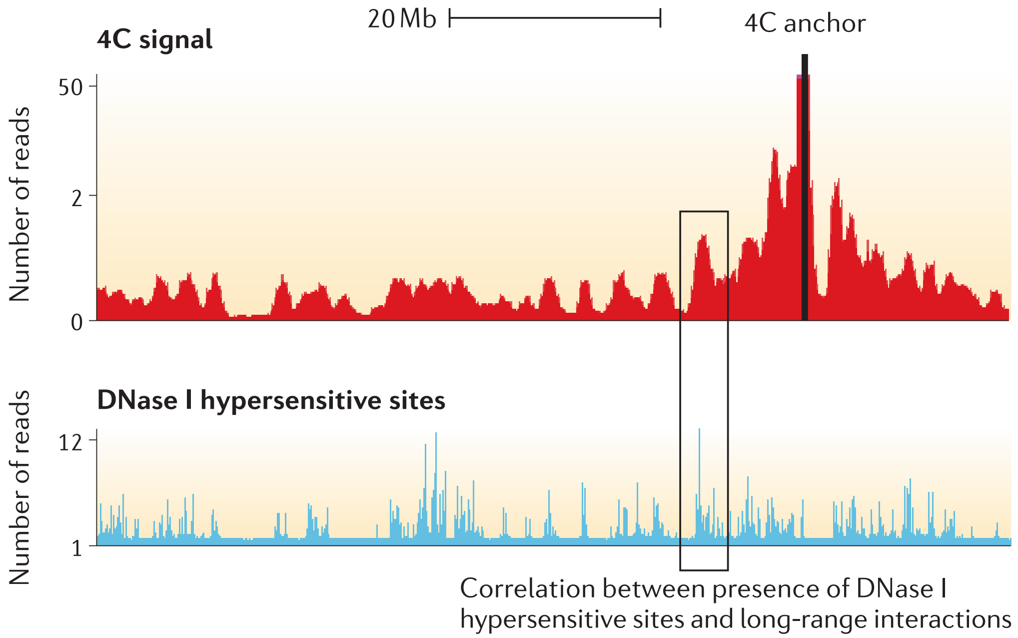
3C



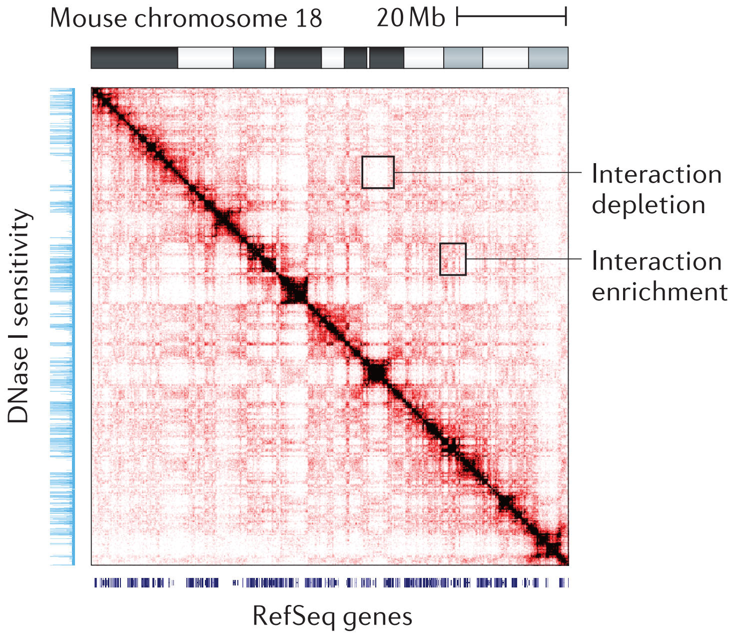
5C



4C



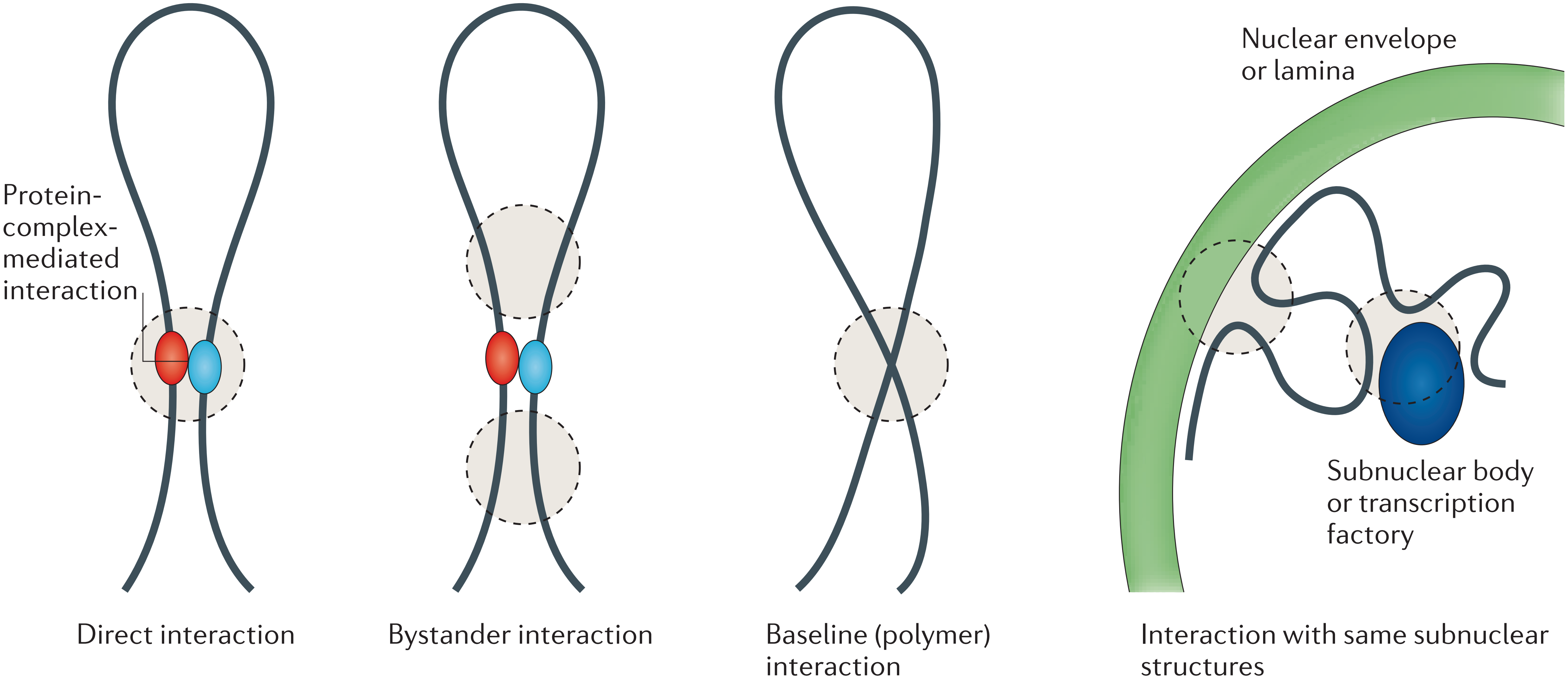
Hi-C



Adapted from Dekker et all, (2013) Nat Rev Genetics

Level IV: Higher-order organization

Interpreting chromatin interaction data



Protein-complex-mediated interaction

Direct interaction

Bystander interaction

Baseline (polymer) interaction

Nuclear envelope or lamina

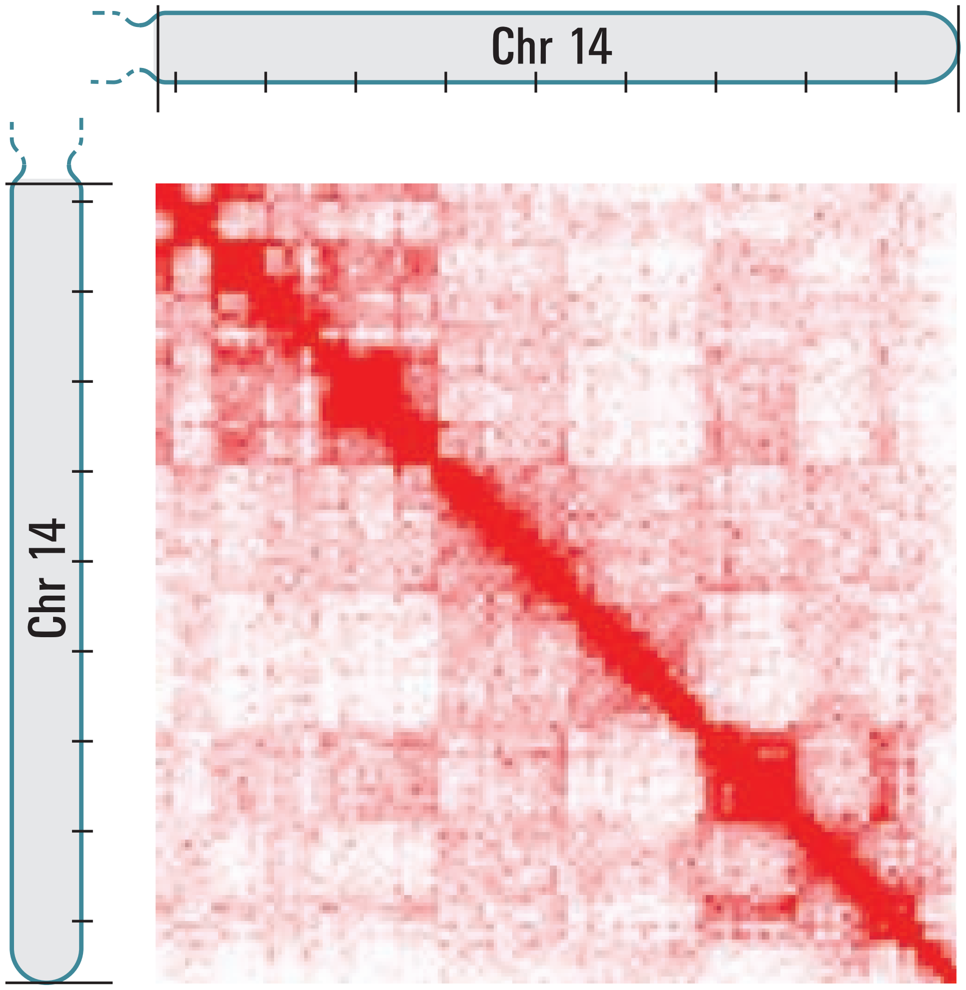
Subnuclear body or transcription factory

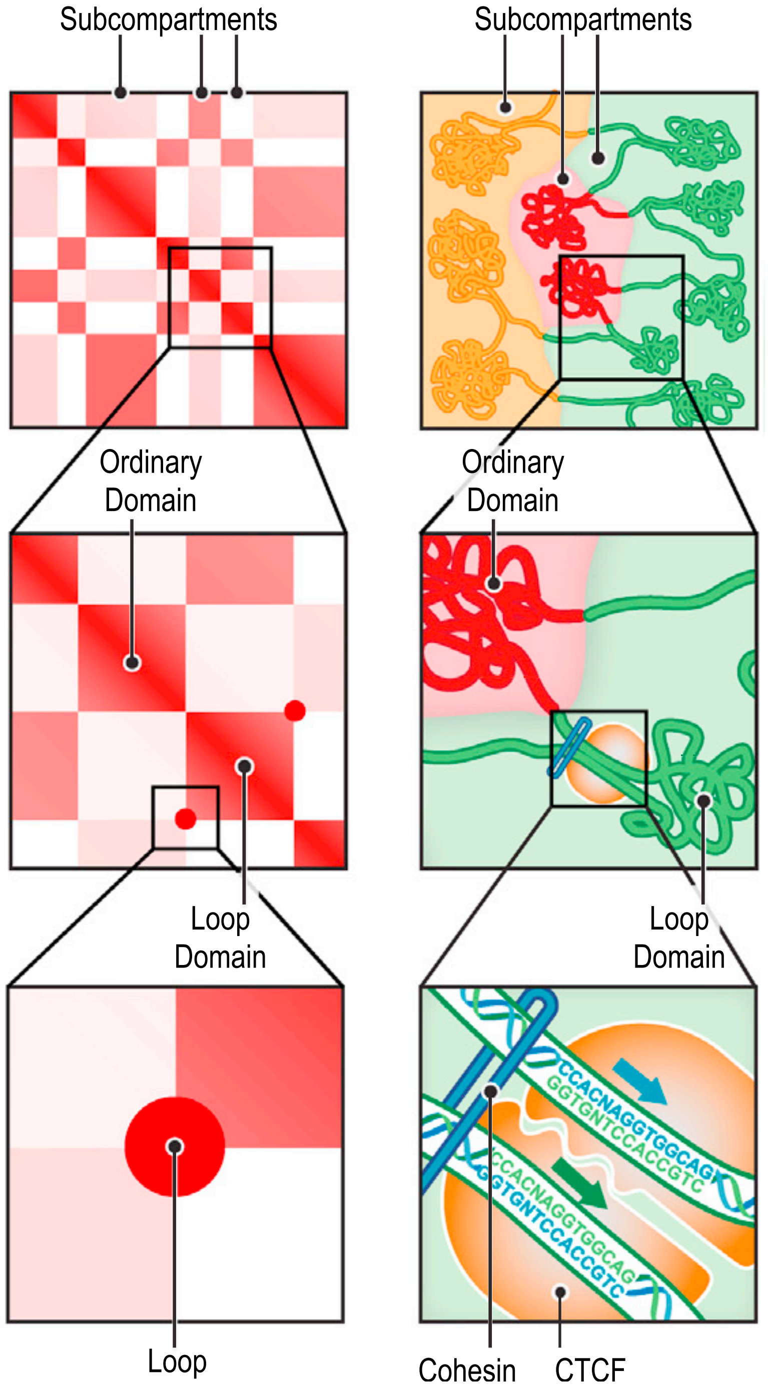
Interaction with same subnuclear structures

Adapted from Dekker et all, (2013) Nat Rev Genetics

Level IV: Higher-order organization

Hierarchical genome organisation

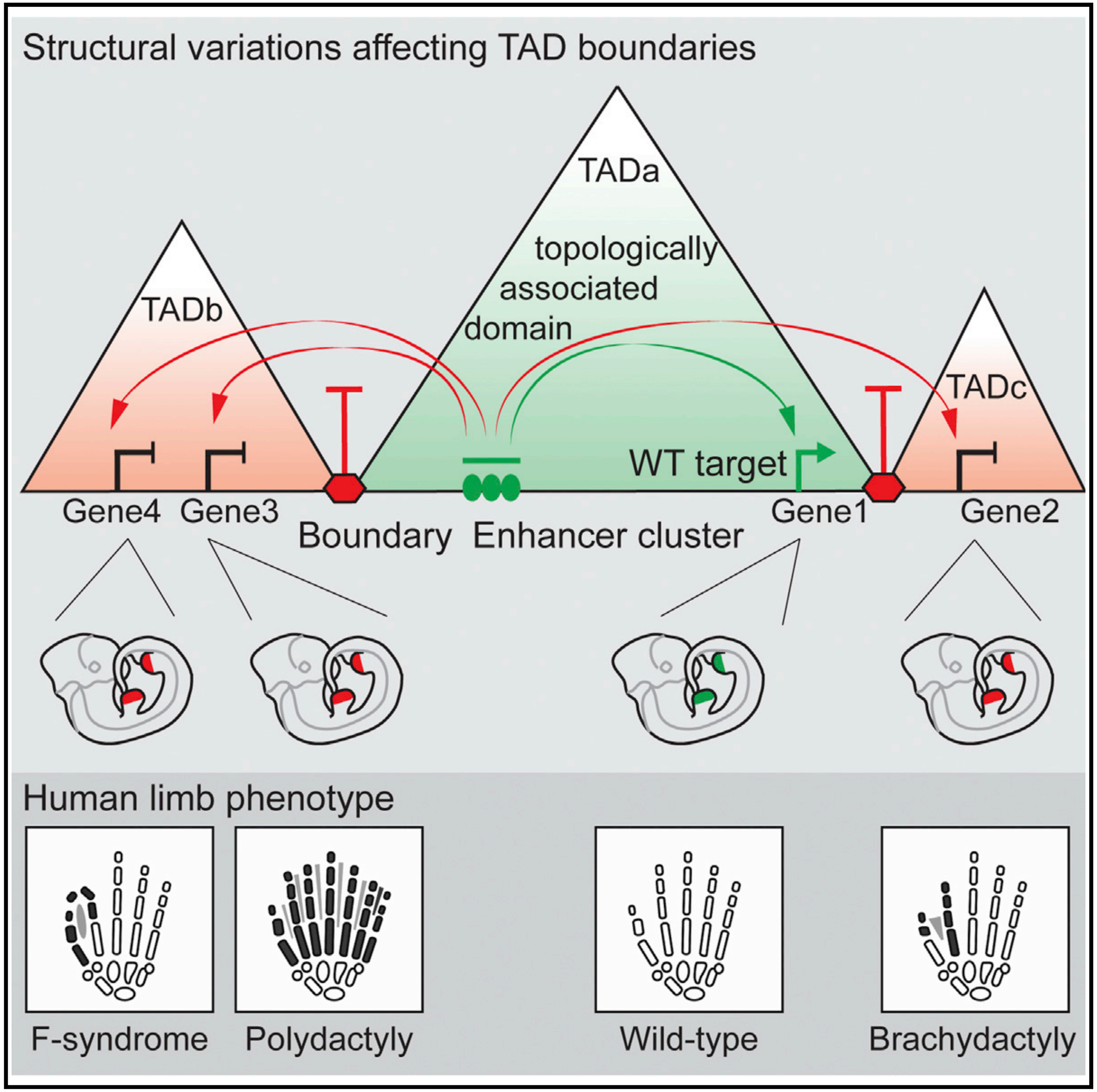




Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.
Rao, S. S. P., et al. (2014). Cell, 1–29.

Level IV: Higher-order organization

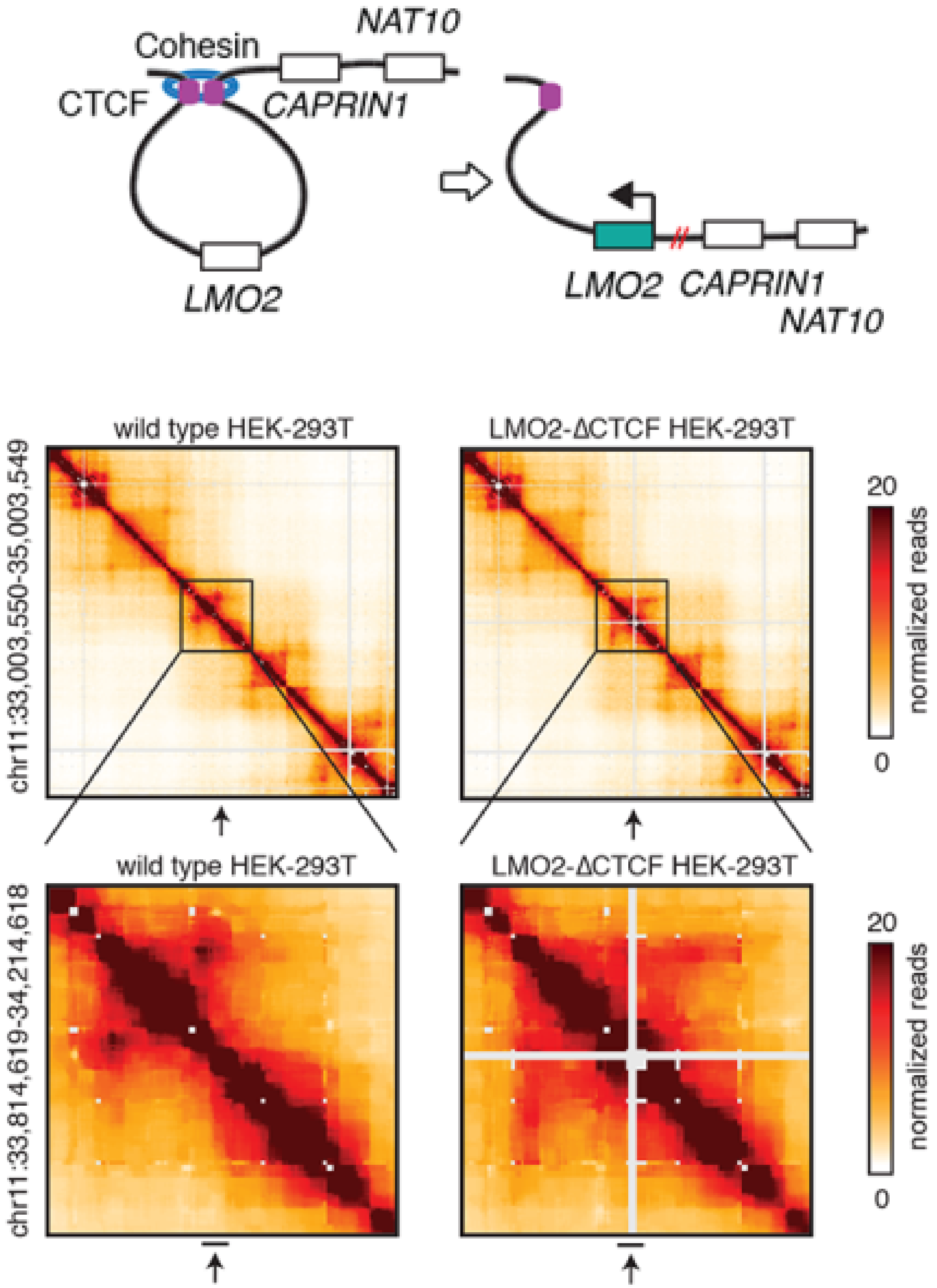
TADs are functional units



Lupiáñez, et al. (2015). Cell, 1–15.

Level IV: Higher-order organization

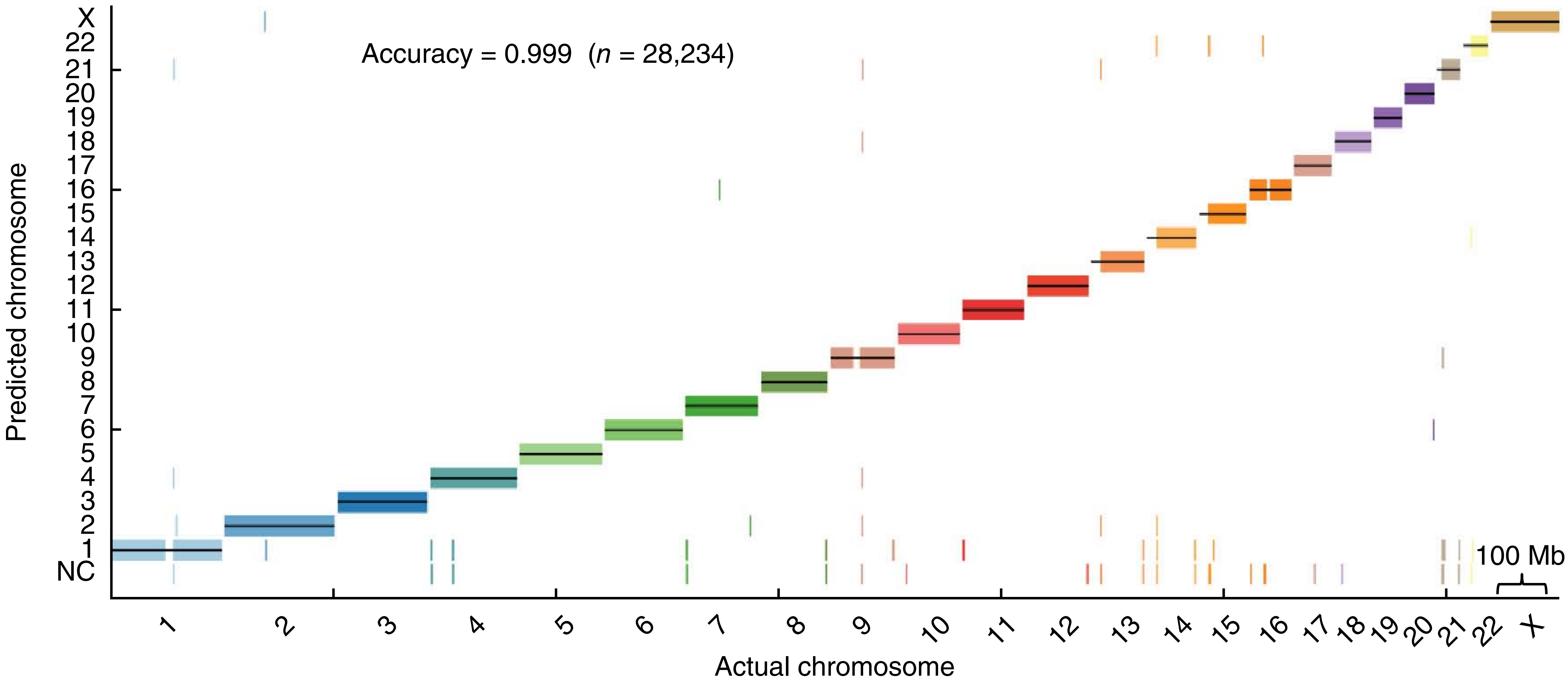
TADs are functional units



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

3C Detour…
desirable side effects

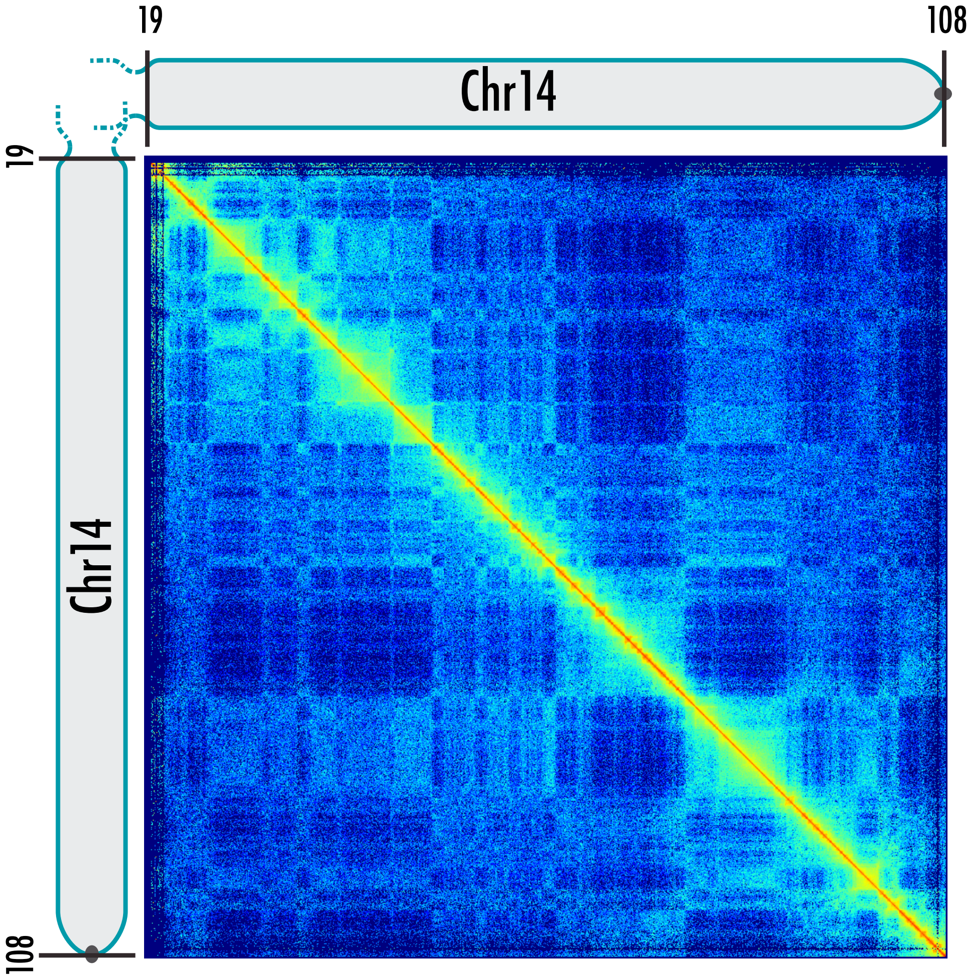
Chromosome Conformation Capture for de-novo assembly

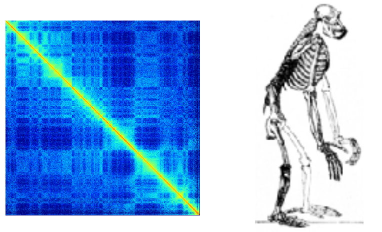


Kaplan, N., & Dekker, J. (2013). High-throughput genome scaffolding from in vivo DNA interaction frequency. Nature Biotechnology, 31(12), 1143–1147.

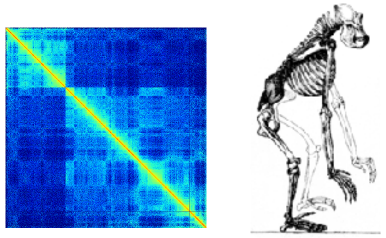
Great apes lymphoblast maps

Chromosome 14

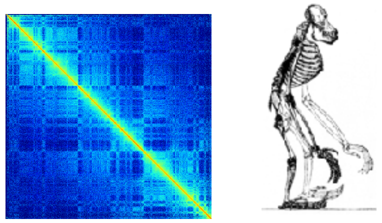




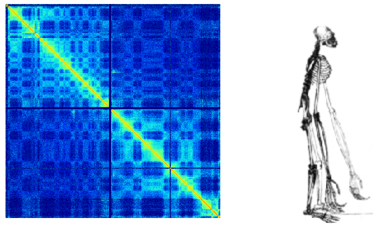
Chimpanzee



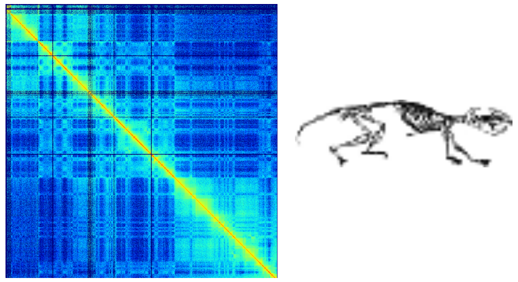
Gorilla



Orangutan



Gibbon

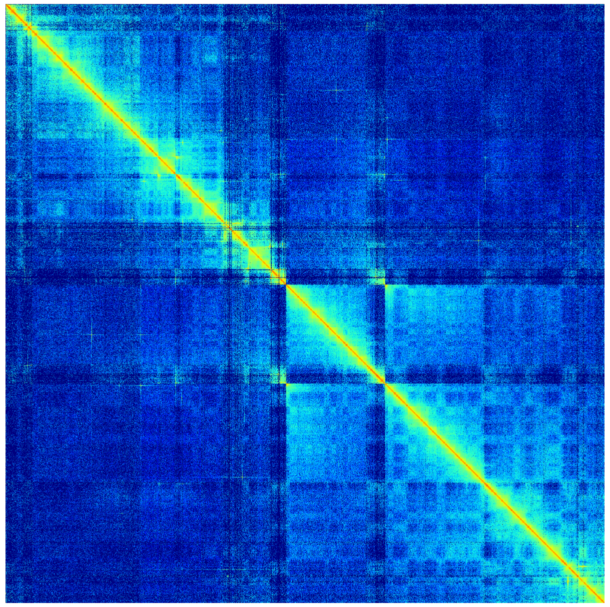


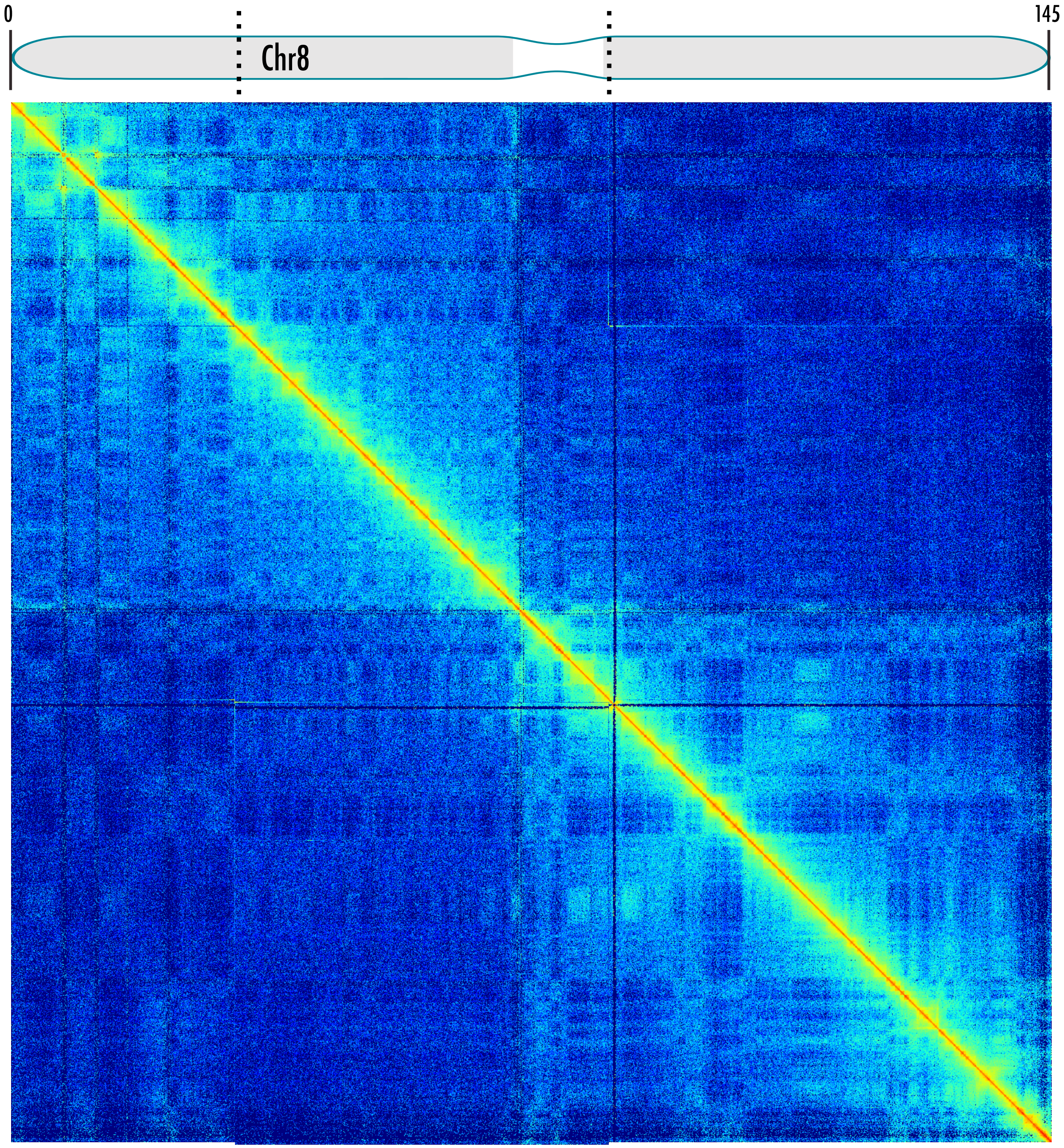
Mouse

Assembly error detection

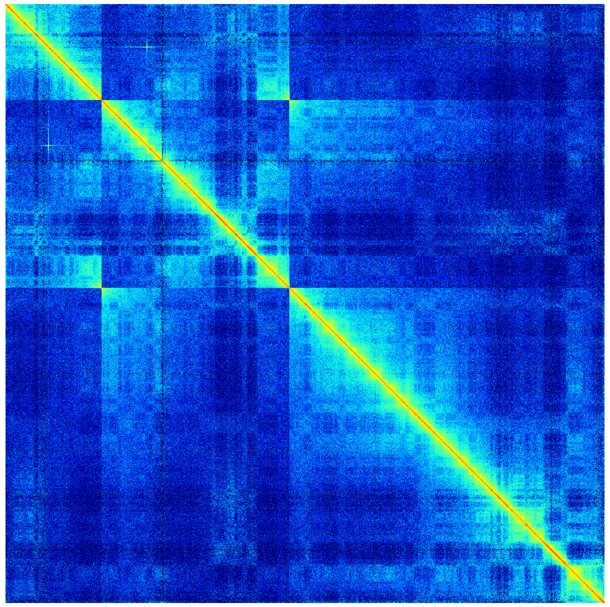
Chromosome 8 Gorilla

Chr 7



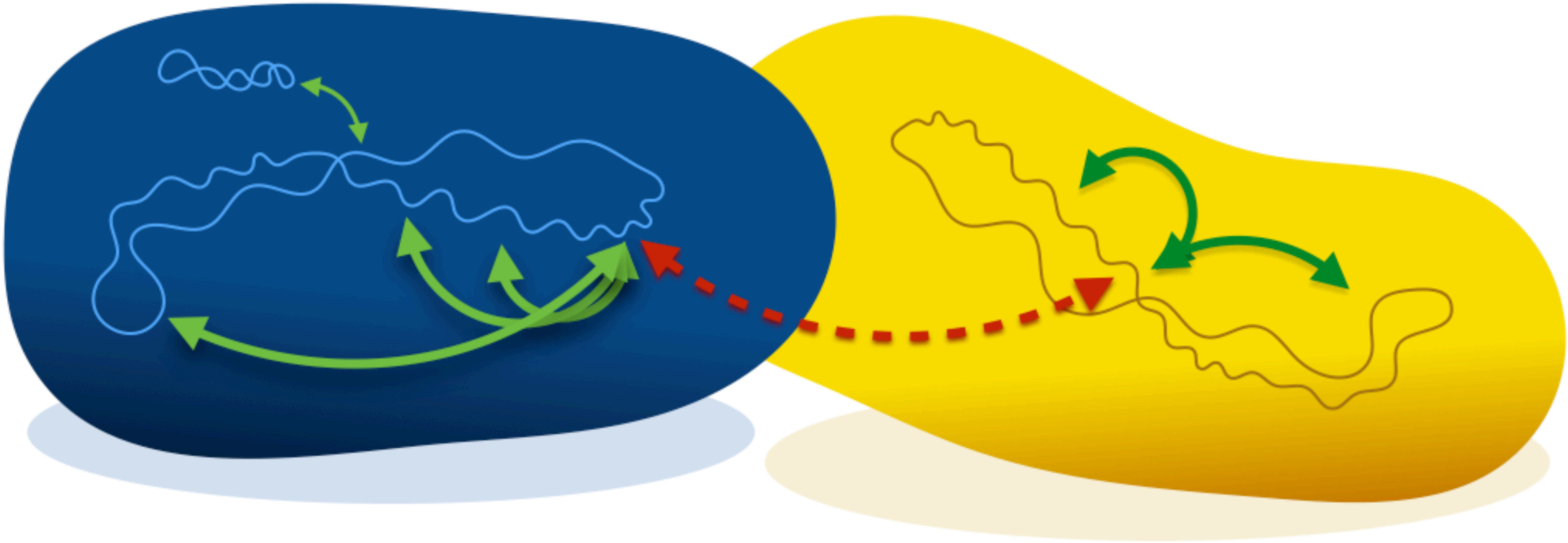


Chr 12



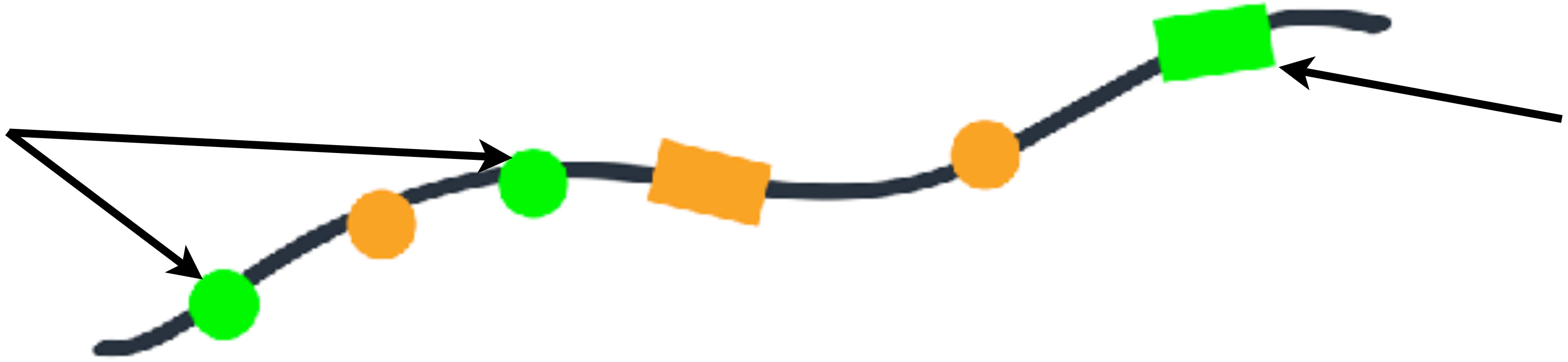
GGO8 has an inversion of the region corresponding to HSA8:30.0-86.9Mb
Aylwyn Scally (Department of Genetics, University of Cambridge)

Chromosome Conformation Capture for meta genomics



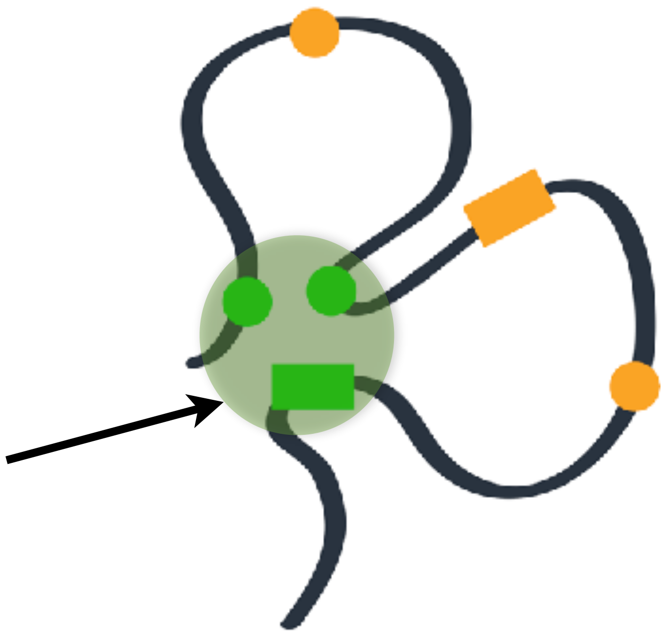
Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Michelmore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/peerj.preprints.260v1

Level V: Chromatin loops



Gene enhancers

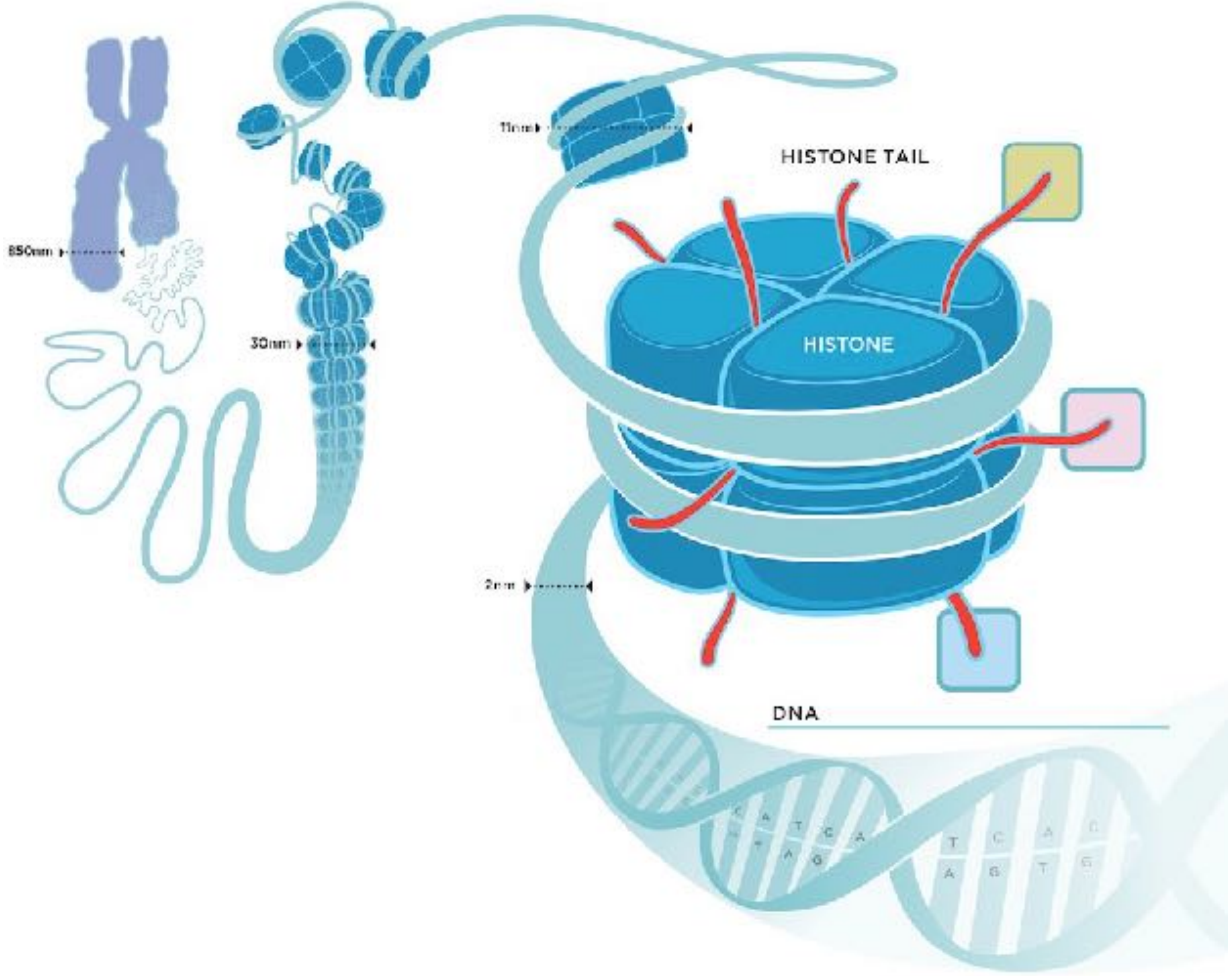
Gene



Gene activity

Level VI: Nucleosome

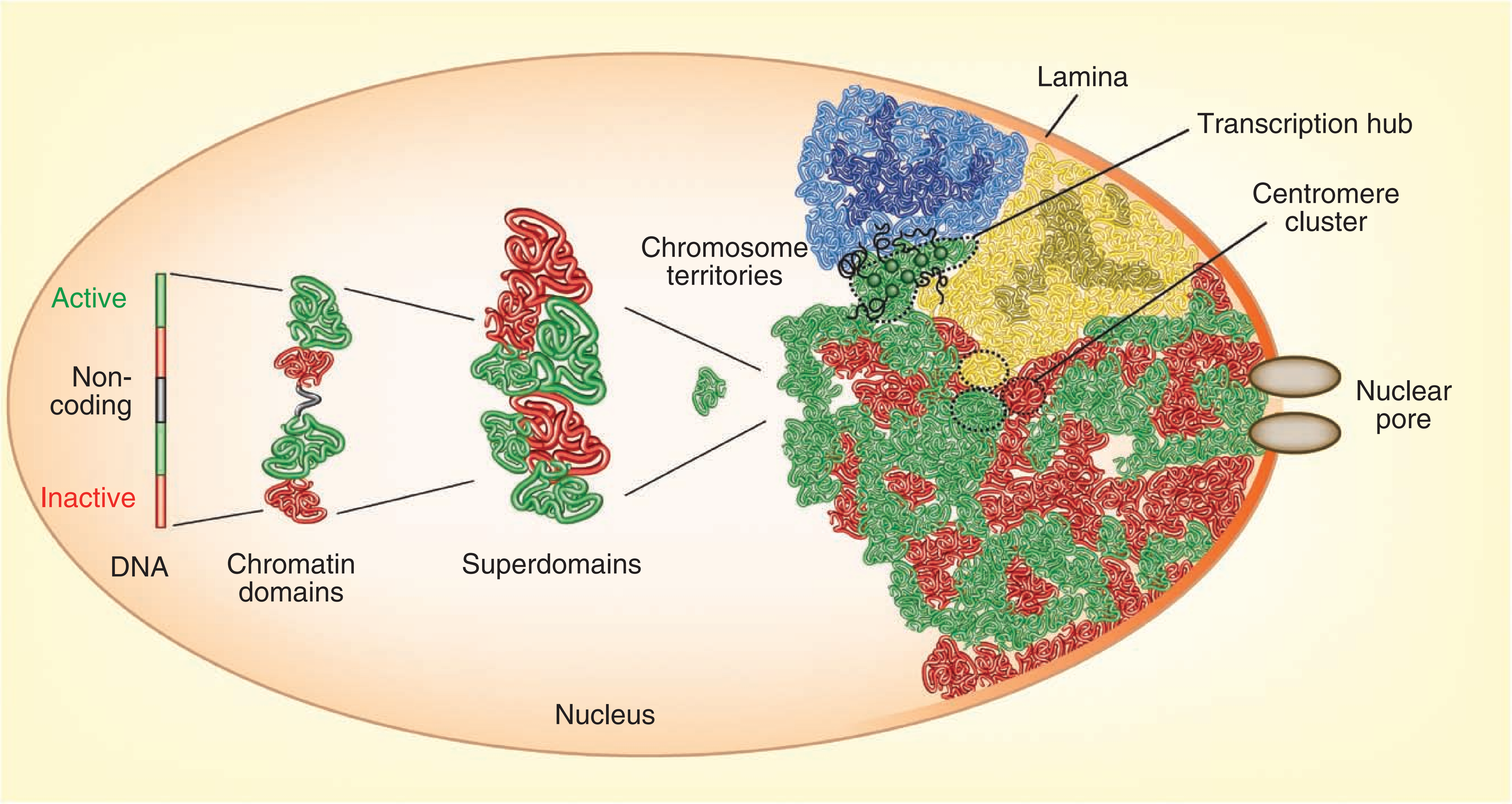
Chromosome **Chromatin fibre** **Nucleosome**



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).



Marina Corral