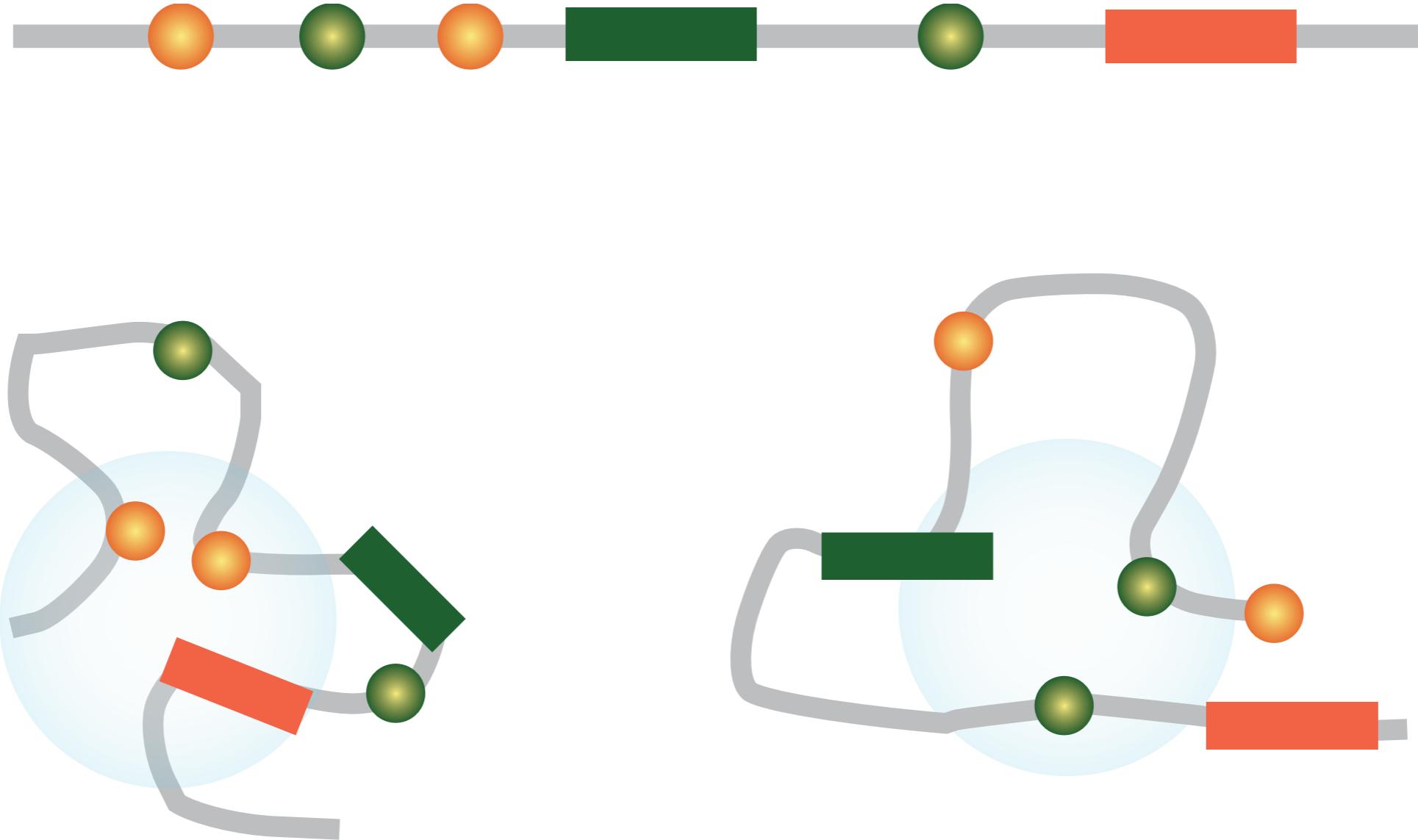


# Chromatin structure and Hi-C data

François Serra, Marco Di Stefano & Marc A. Martí-Renom  
Structural Genomics Group (CNAG-CRG)

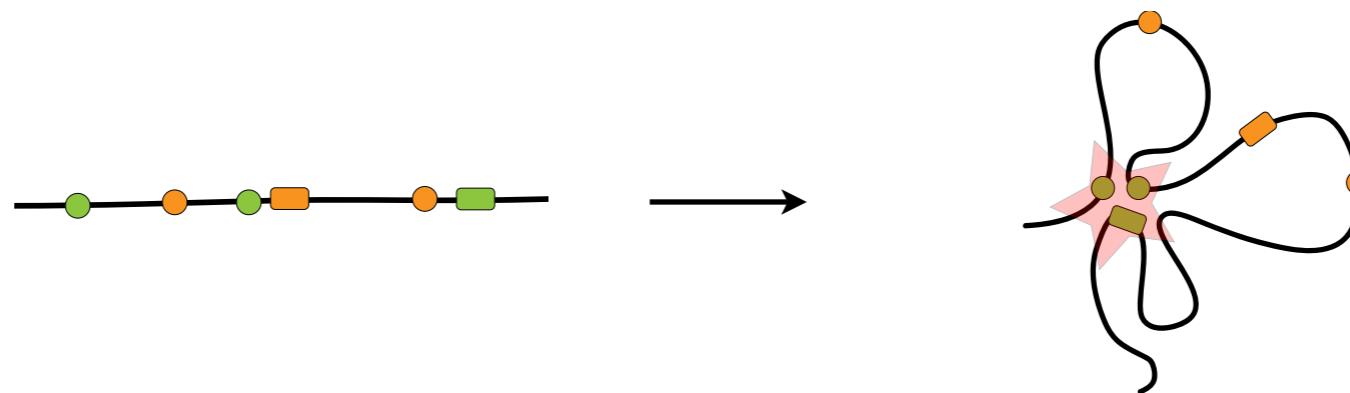


# Complex genome organization



# The role of chromatin structure

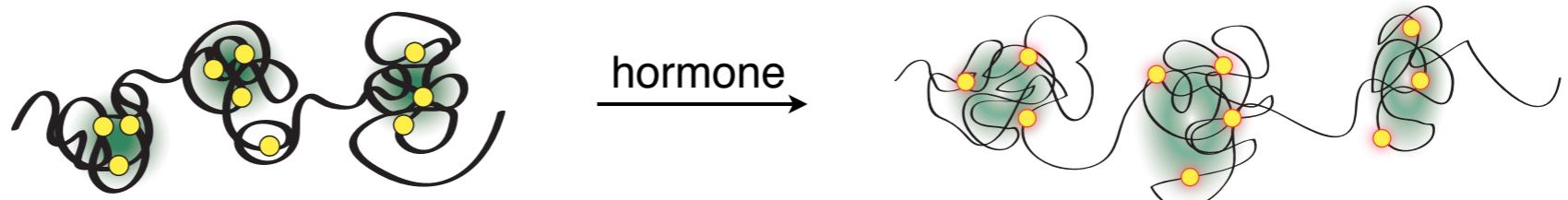
Activity



Organization

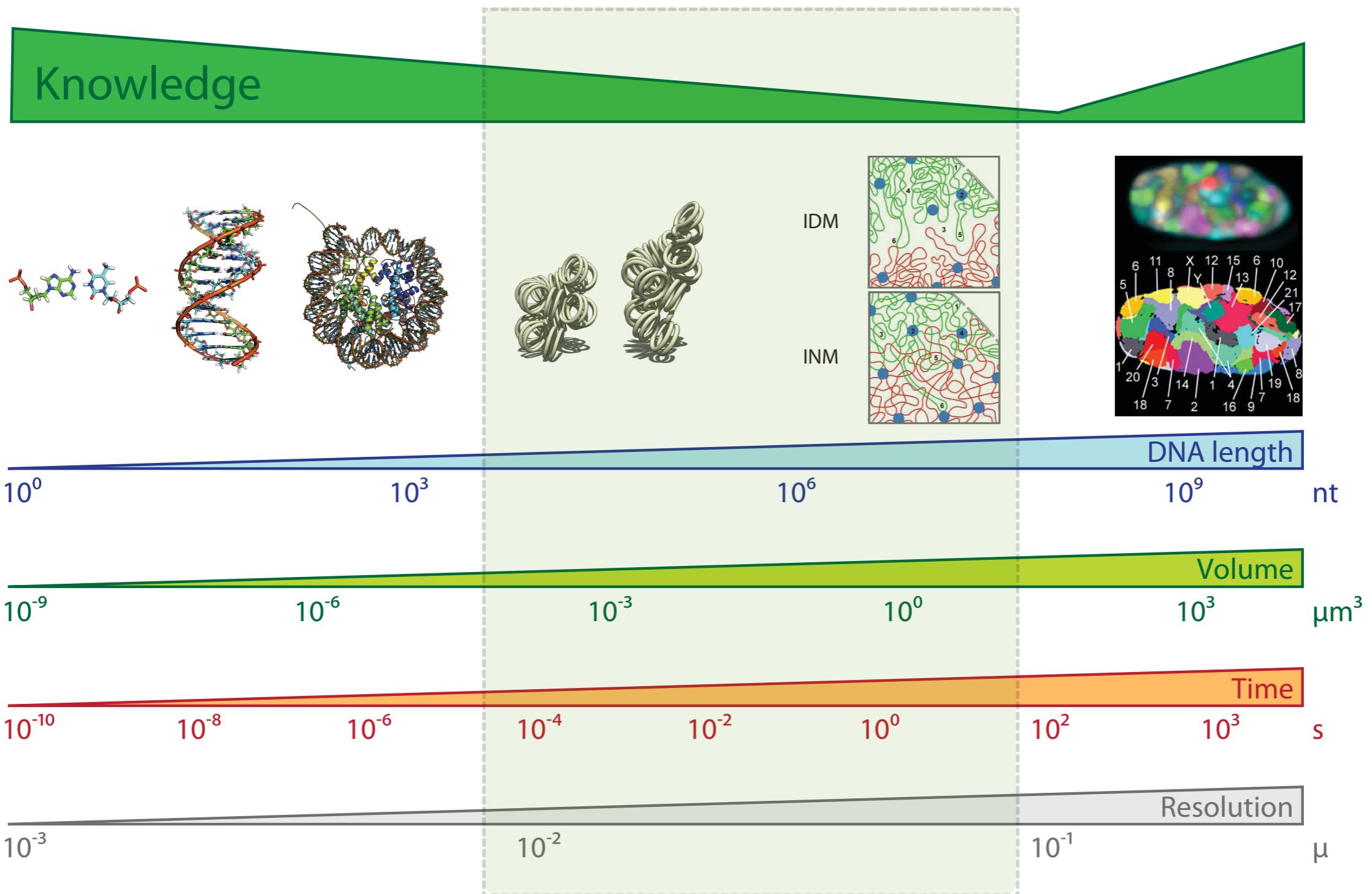


Processes



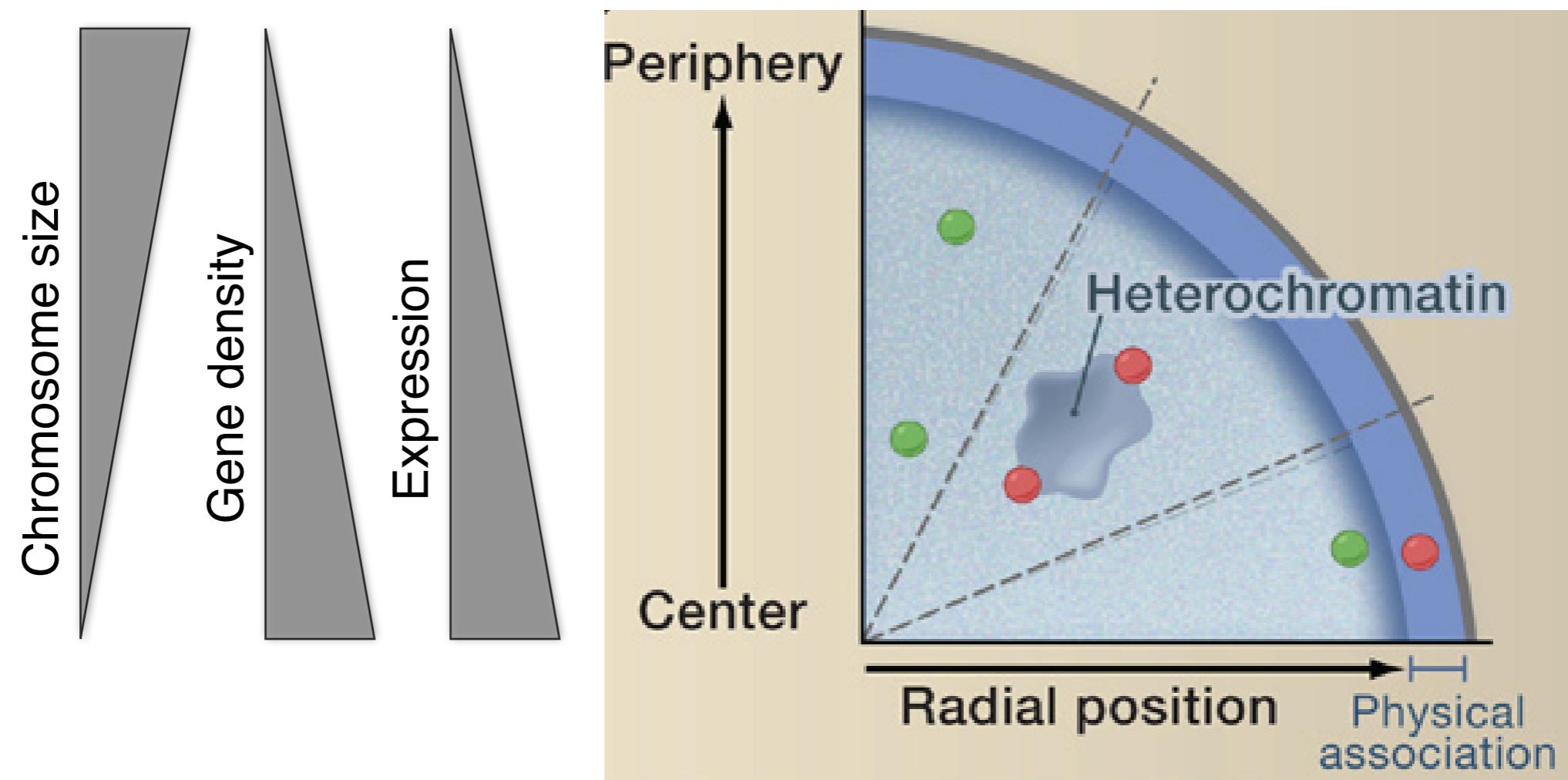
# Resolution Gap

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



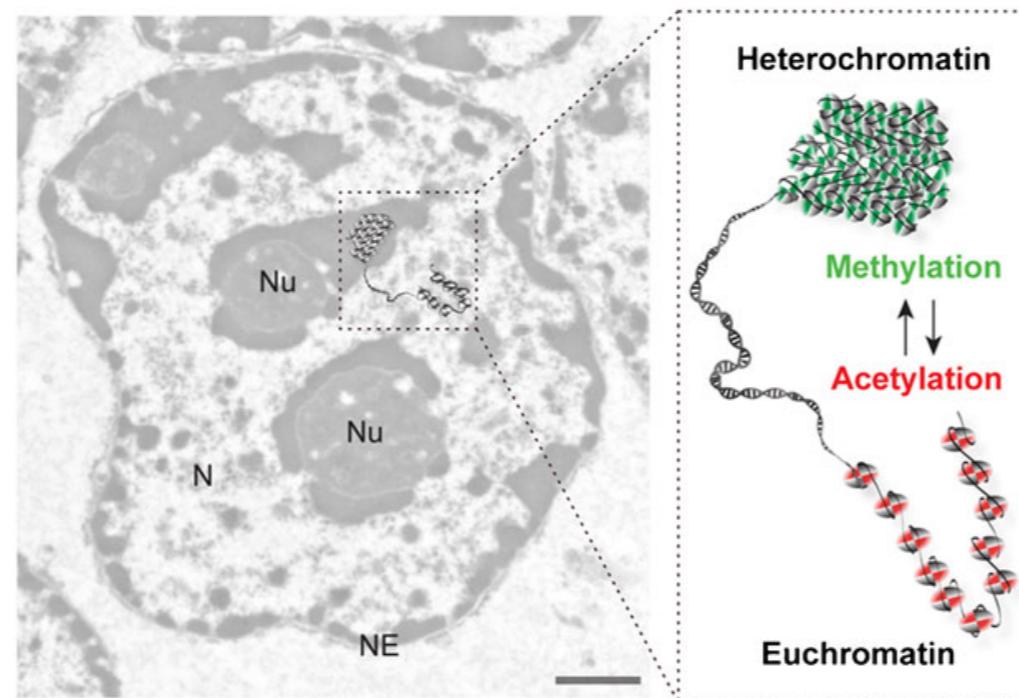
# Level I: Radial genome organization

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



# Level II: Euchromatin vs heterochromatin

Electron microscopy



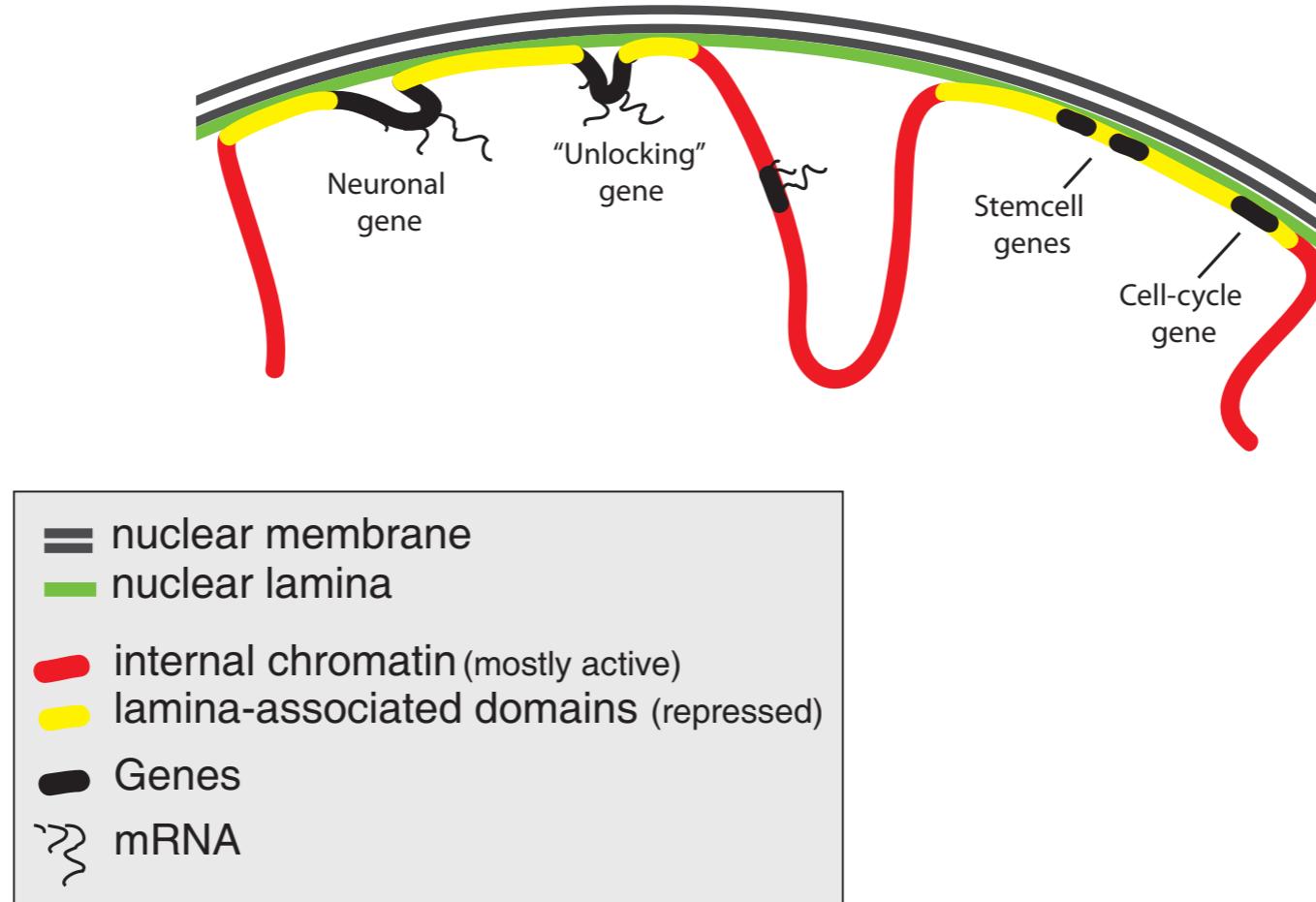
## Euchromatin:

chromatin that is located away from the nuclear lamina, is generally less densely packed, and contains actively transcribed genes

## Heterochromatin:

chromatin that is near the nuclear lamina, tightly condensed, and transcriptionally silent

# Level III: Lamina-genome interactions

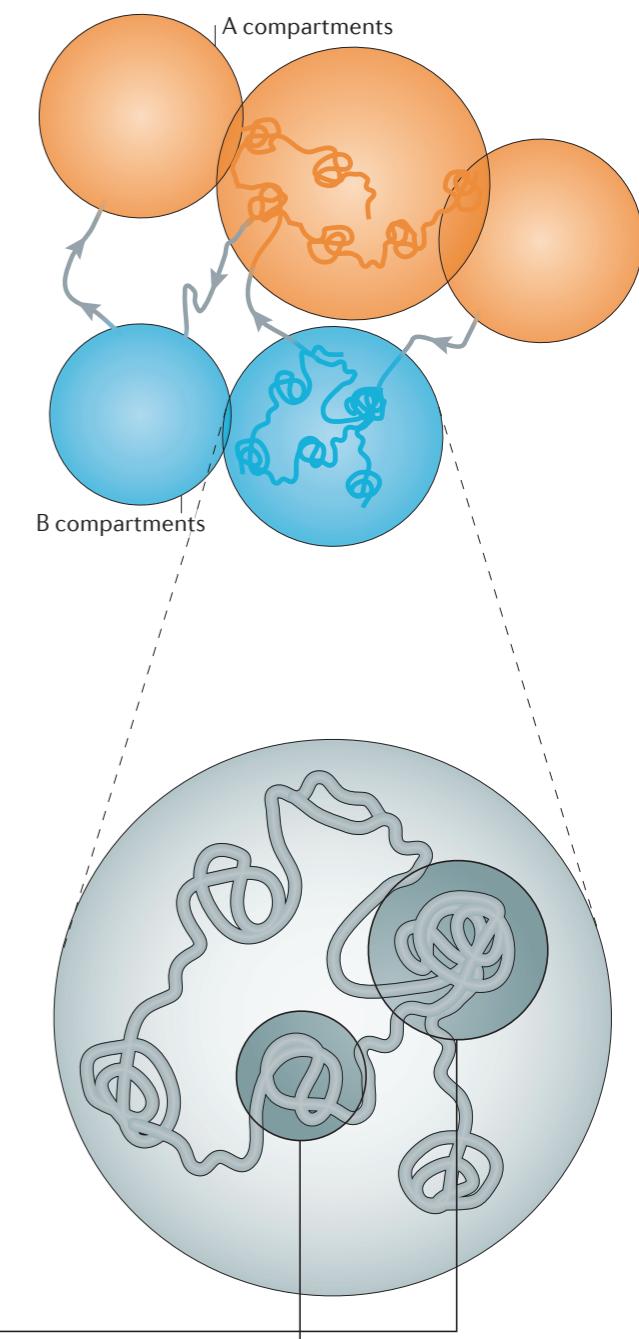
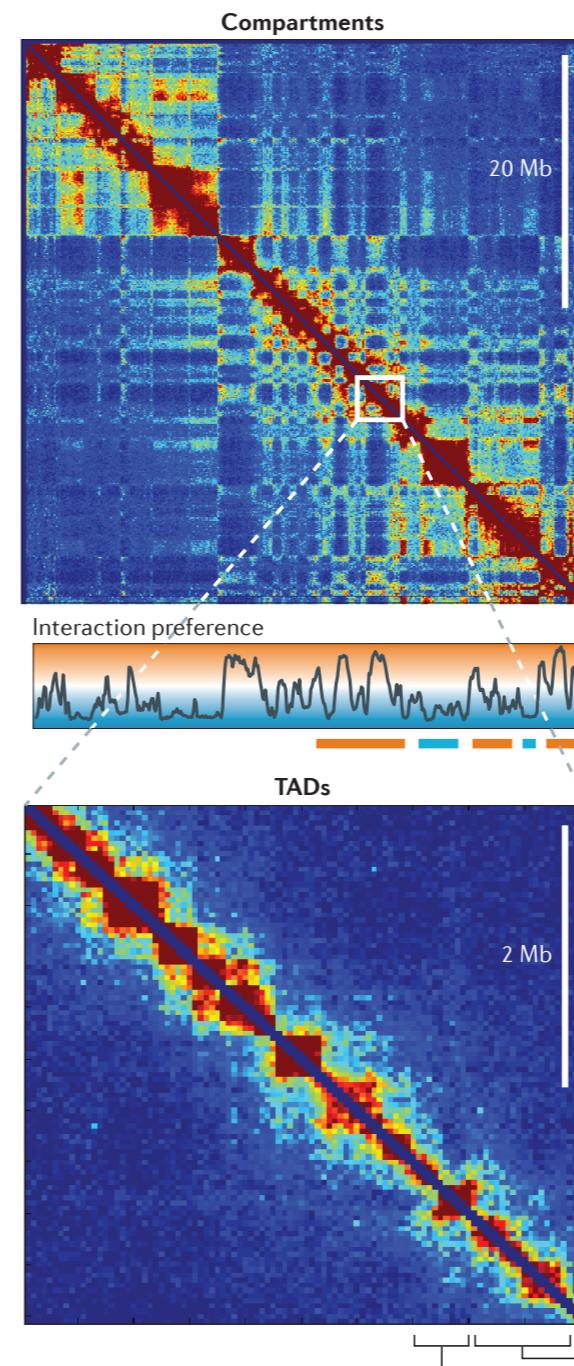
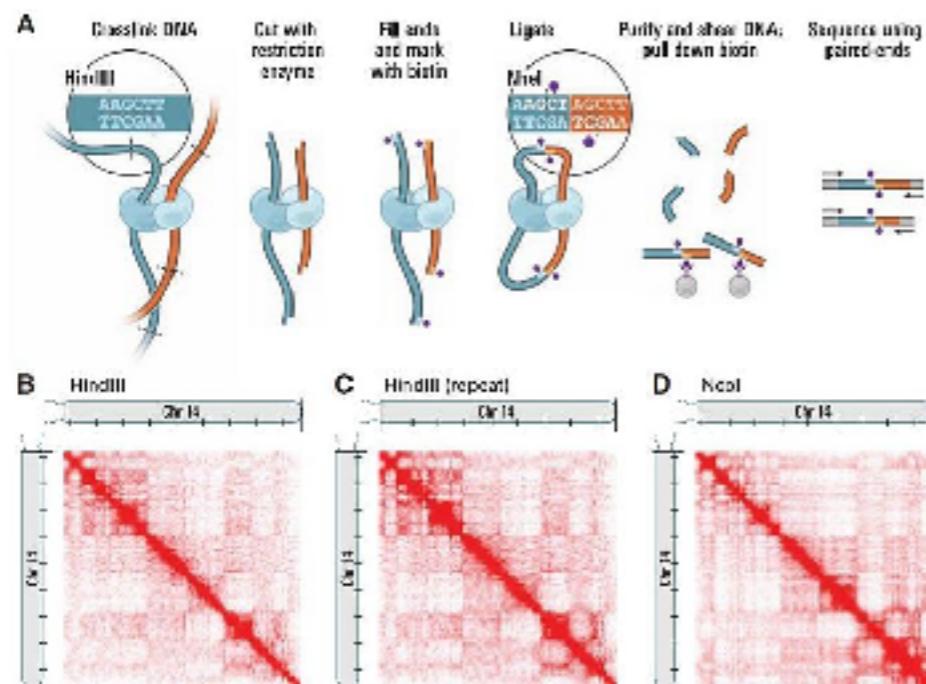


Most genes in Lamina Associated Domains are transcriptionally silent, suggesting that **lamina-genome interactions** are widely involved in the control of **gene expression**

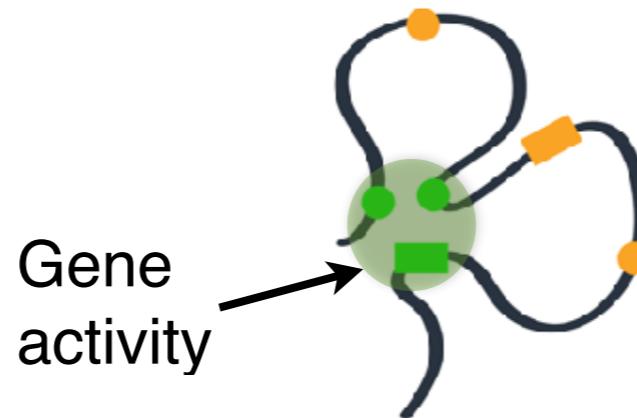
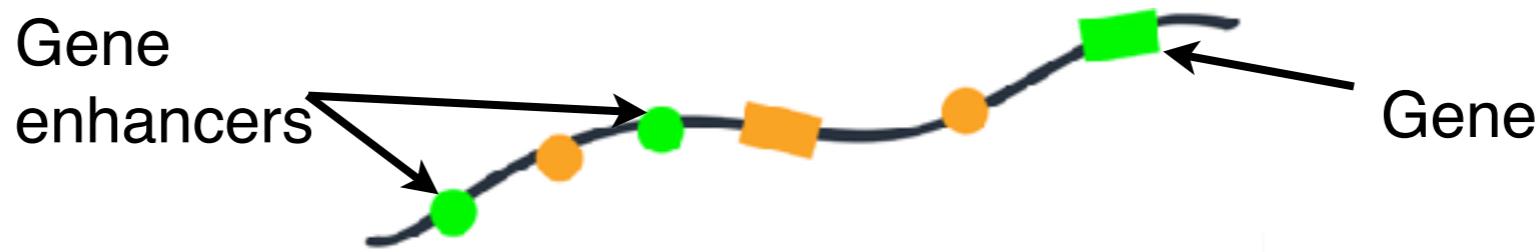
Adapted from Molecular Cell 38, 603-613, 2010

# Level IV: Higher-order organization

Dekker, J., Marti-Renom, M. A. & Mirny, L. A. Exploring the three-dimensional organization of genomes: interpreting chromatin interaction data. Nat Rev Genet 14, 390–403 (2013).



# Level V: Chromatin loops



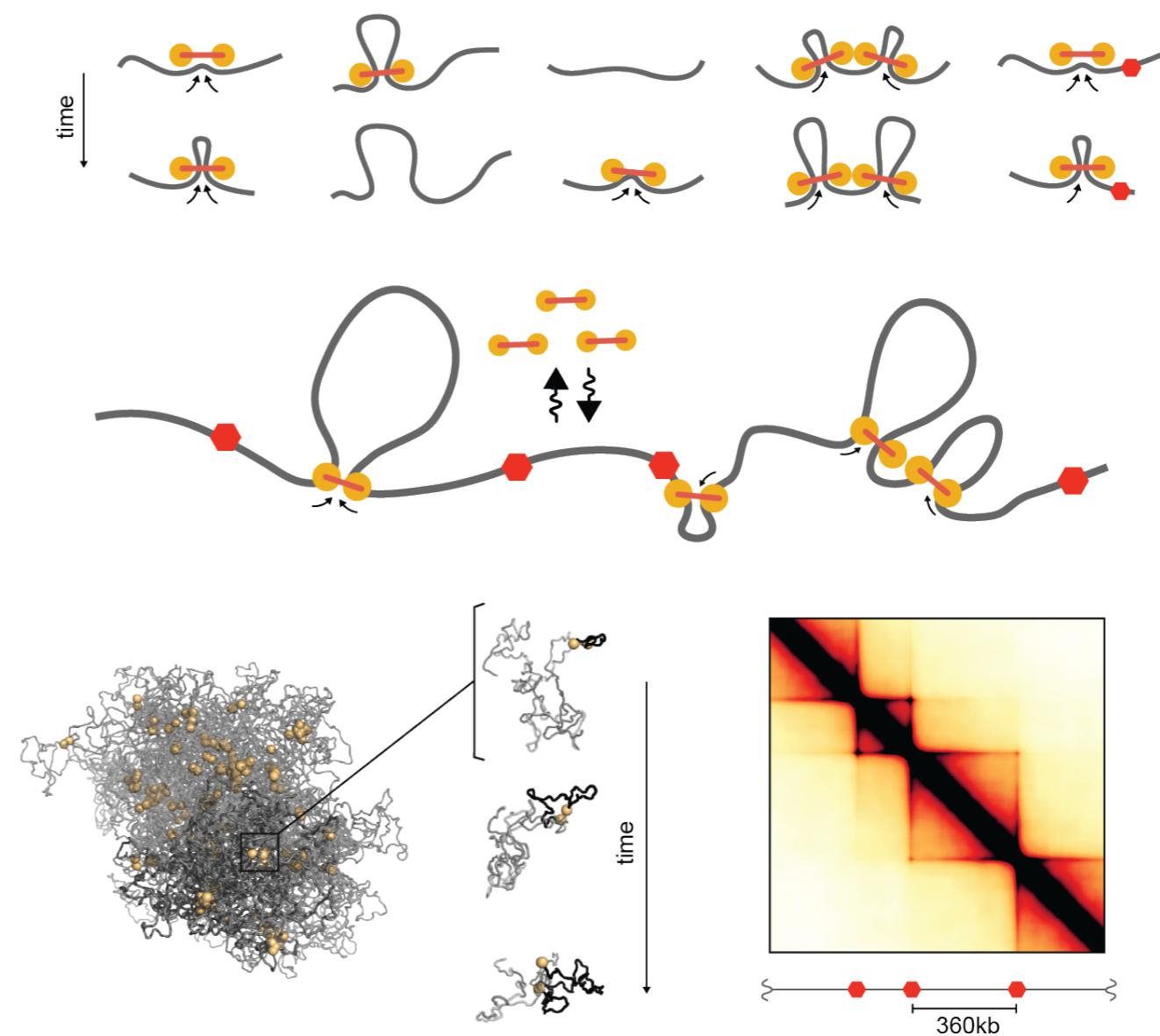
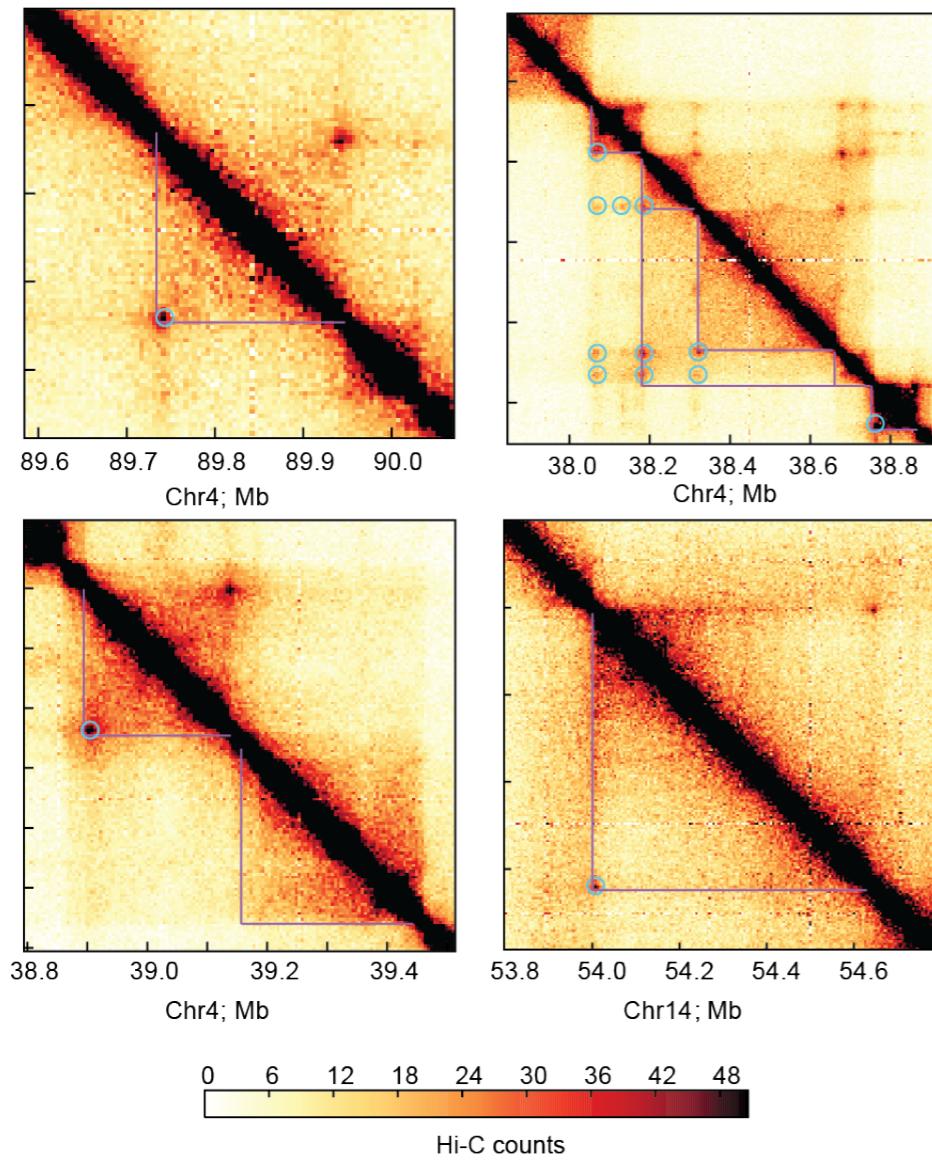
**Loops bring distal genomic regions in close proximity to one another**

**This in turn can have profound effects on gene transcription**

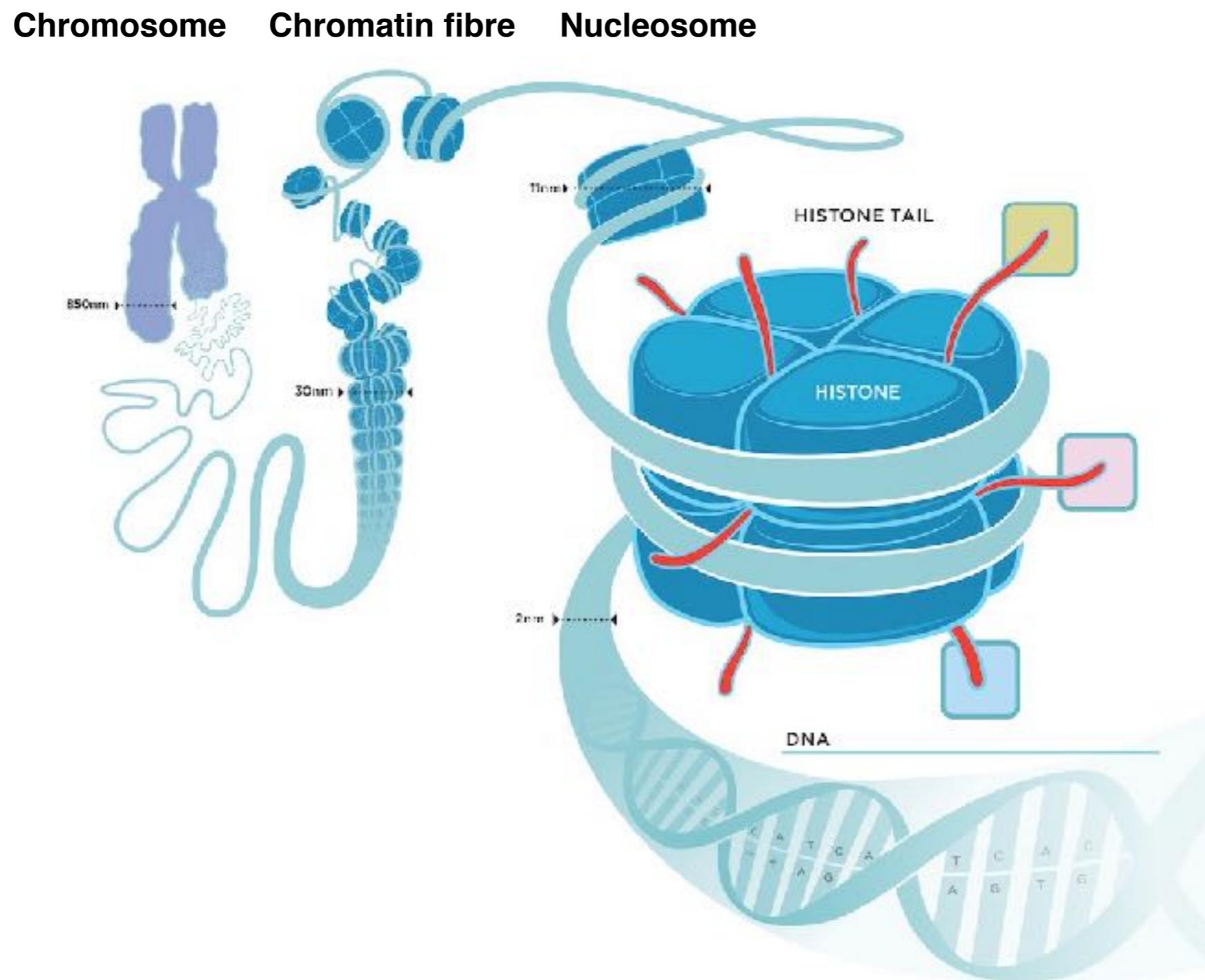
**Enhancers can be thousands of kilobases away from their target genes in any direction (or even on a separate chromosome)**

# 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*.

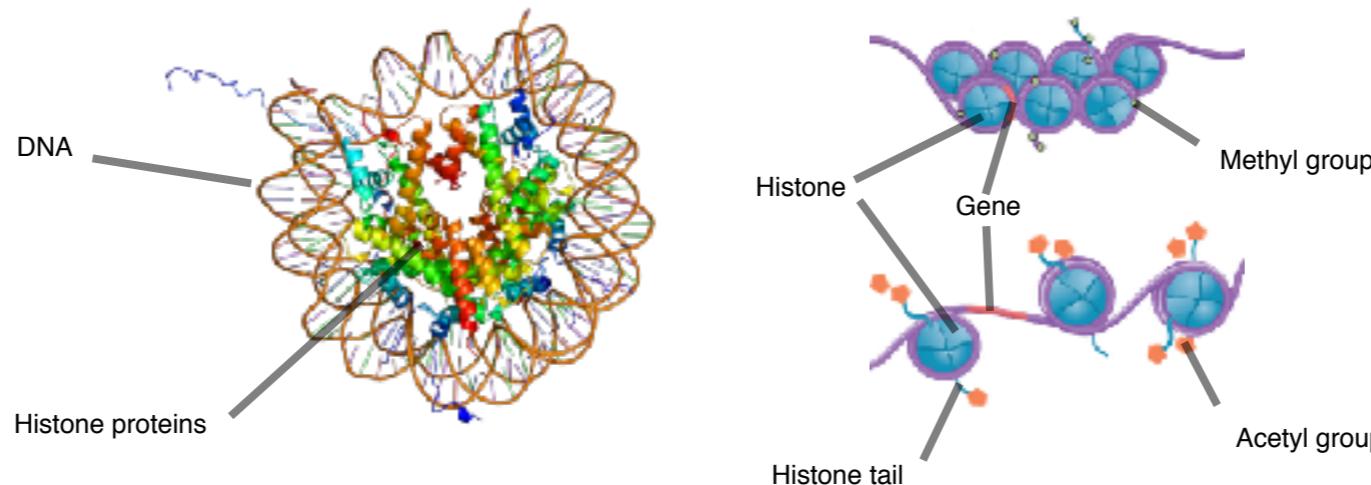


# Level VI: Nucleosome



Adapted from Richard E. Ballermann, 2012

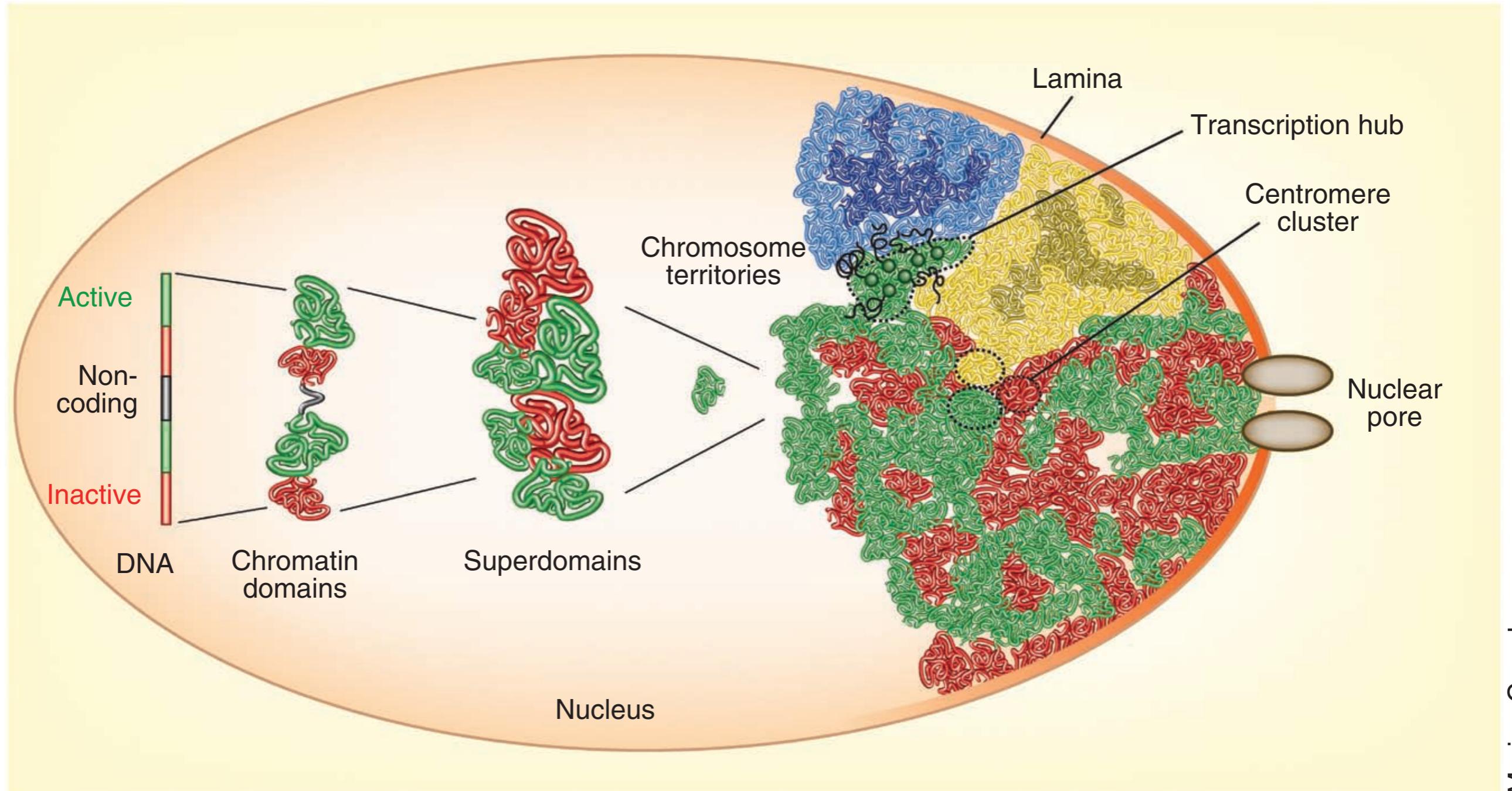
# Level VI: Nucleosome modifications



Modification	H3K4	H3K9	H3K14	H3K27	H3K79	H4K20	H2BK5
<b>mono-methylation</b>	activation	activation		activation	activation	activation	activation
<b>di-methylation</b>	activation	repression		repression	activation		
<b>tri-methylation</b>	activation	repression		repression	activation, repression		repression
<b>acetylation</b>		activation	activation				

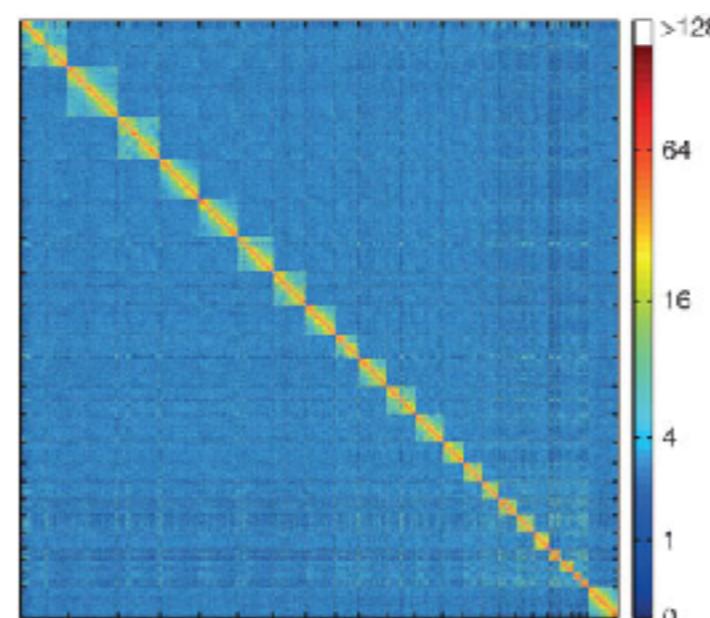
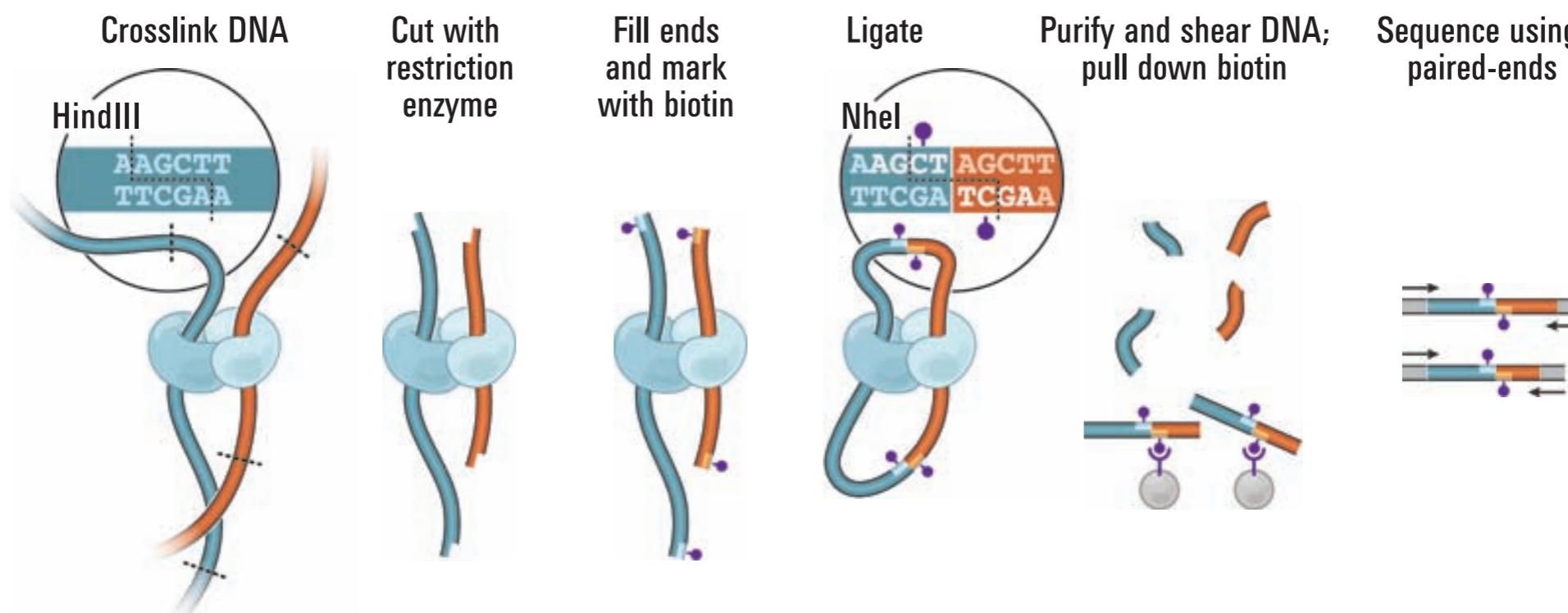
# Complex genome organization

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

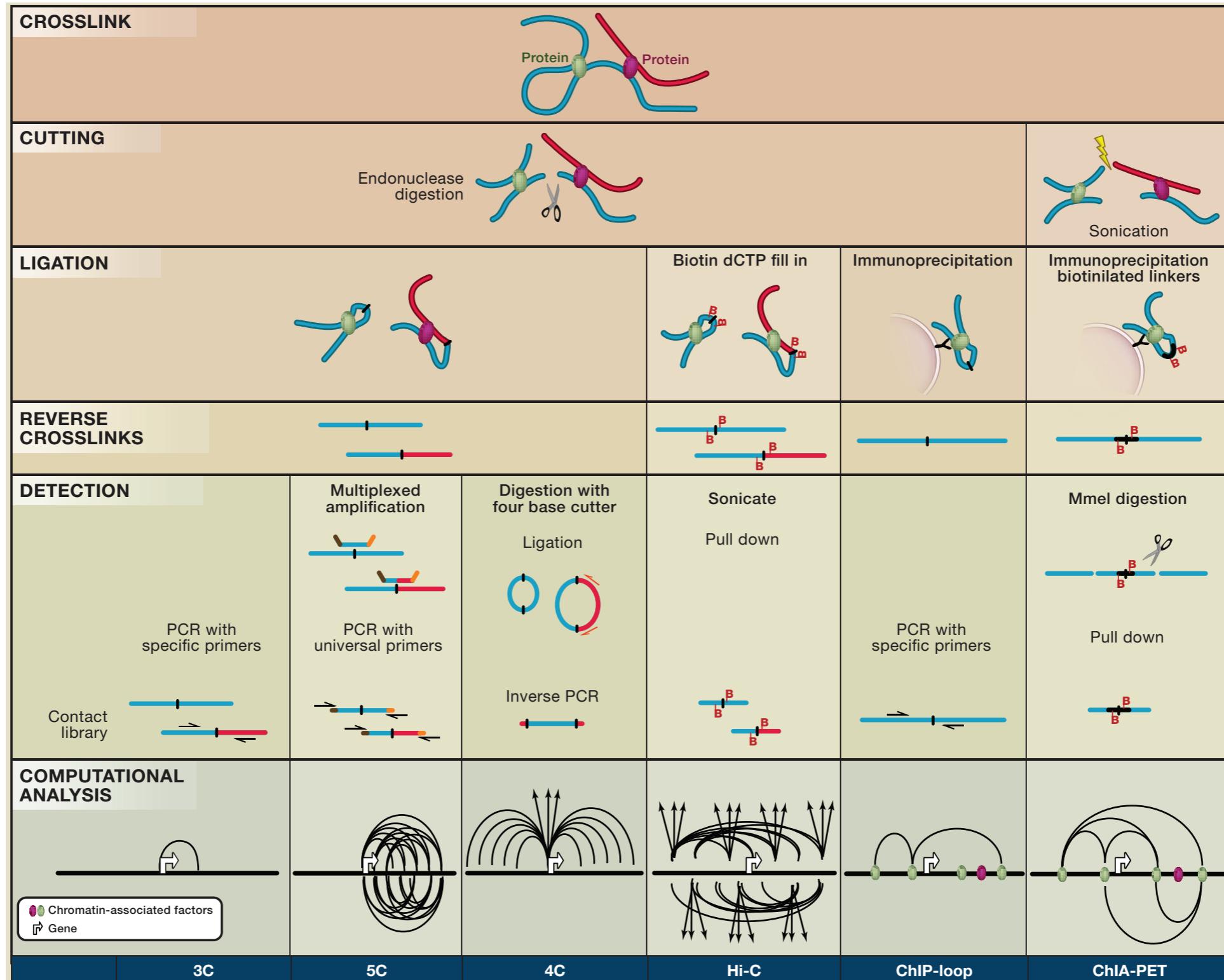


# Chromosome Conformation Capture

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.

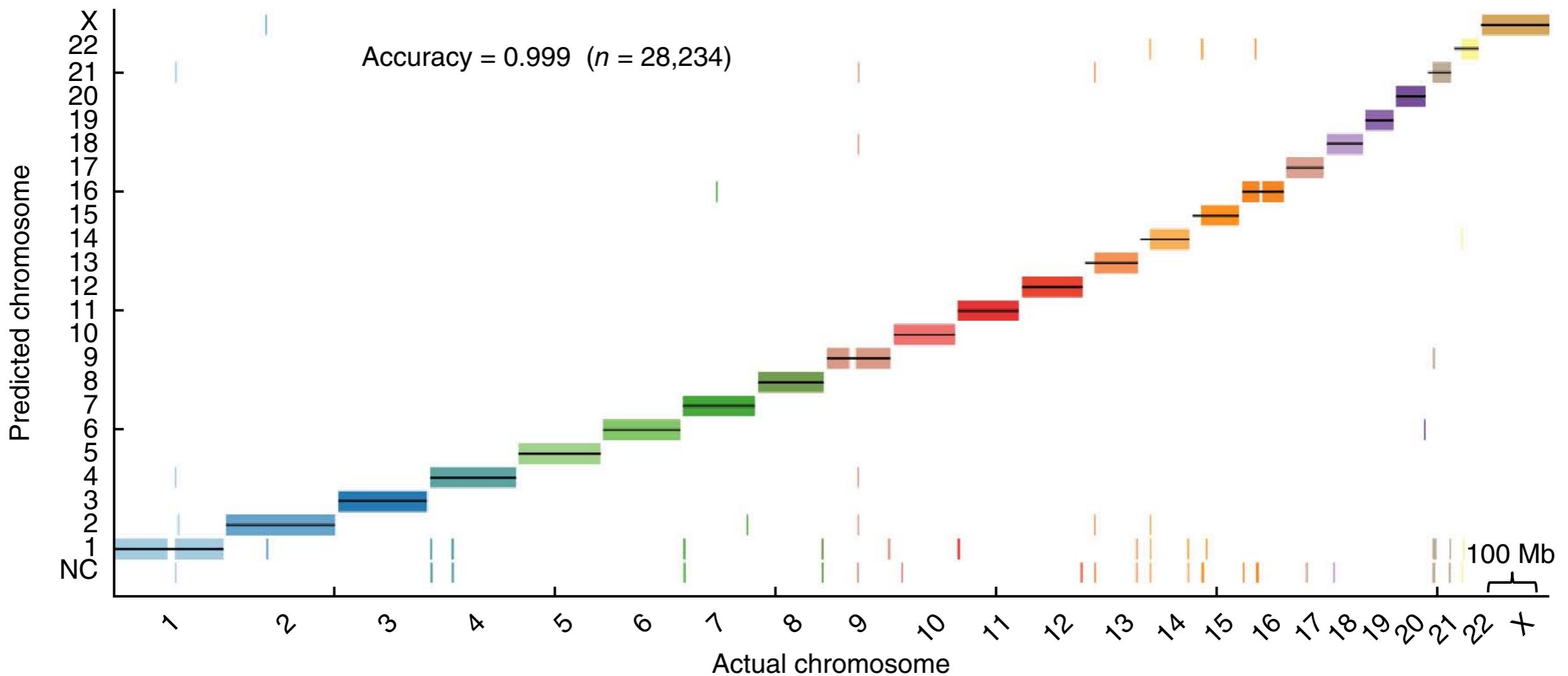


# Chromosome Conformation Capture



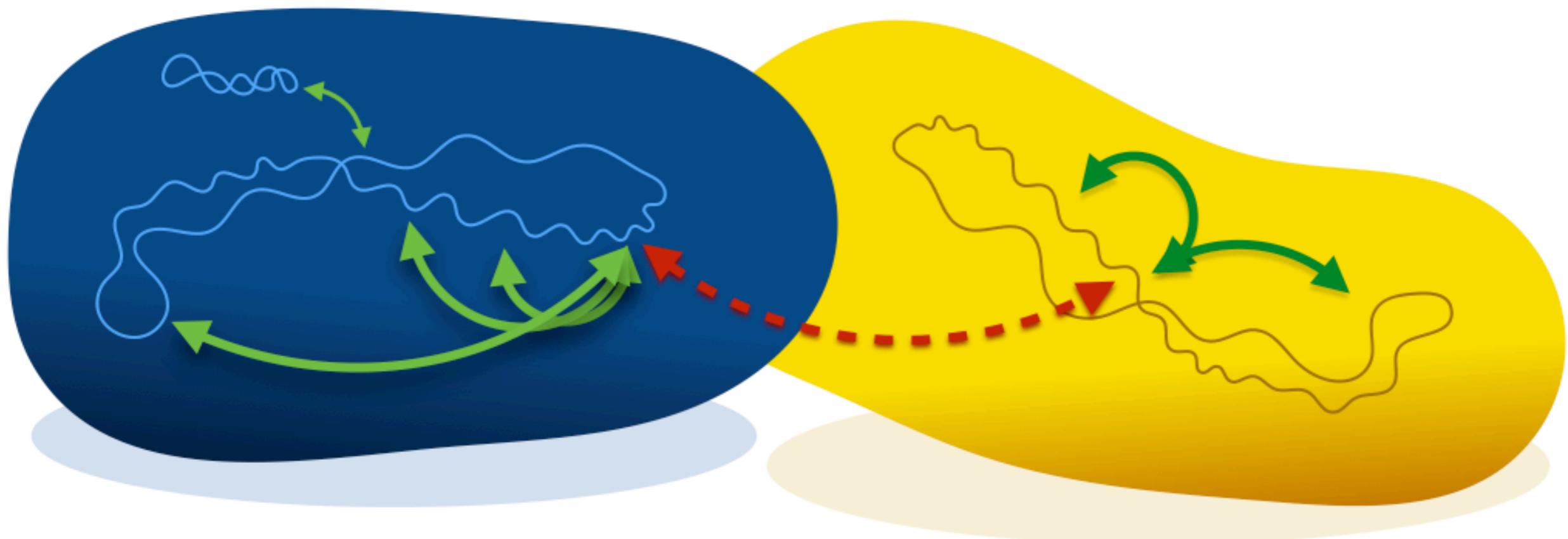
Hakim, O., & Misteli, T. (2012). SnapShot: Chromosome Confirmation Capture. *Cell*, 148(5), 1068–1068.e2.

# 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.

# 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