Structure determination of genomes and genomic domains by satisfaction of spatial restraints.

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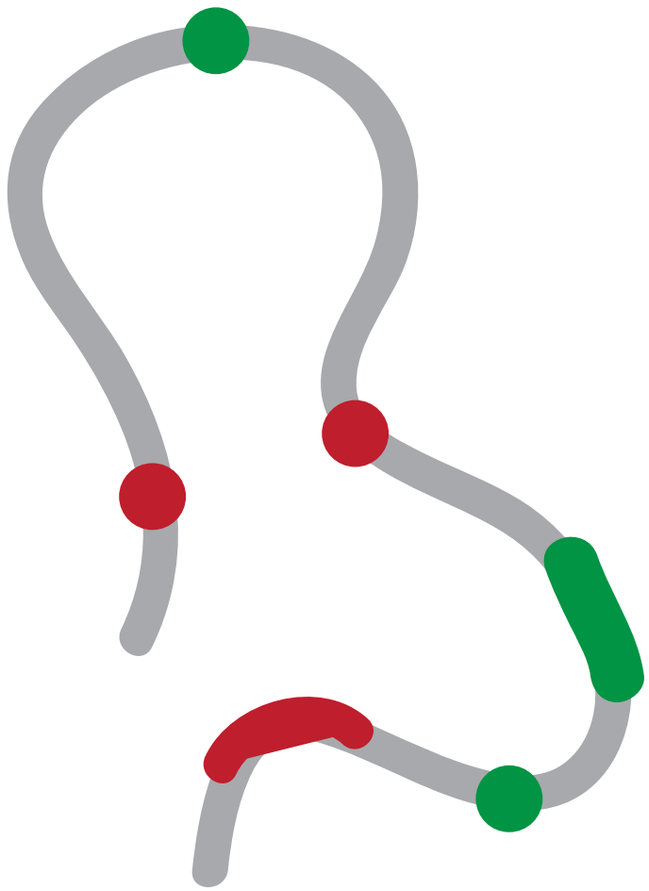
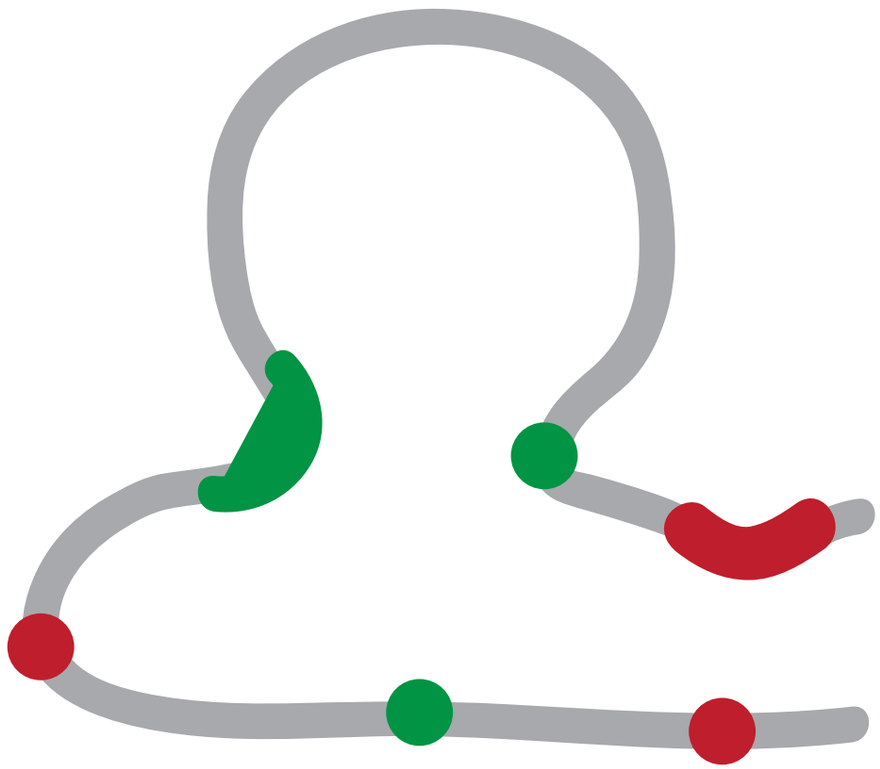
Structural Genomics Group (ICREA, CNAG-CRG)

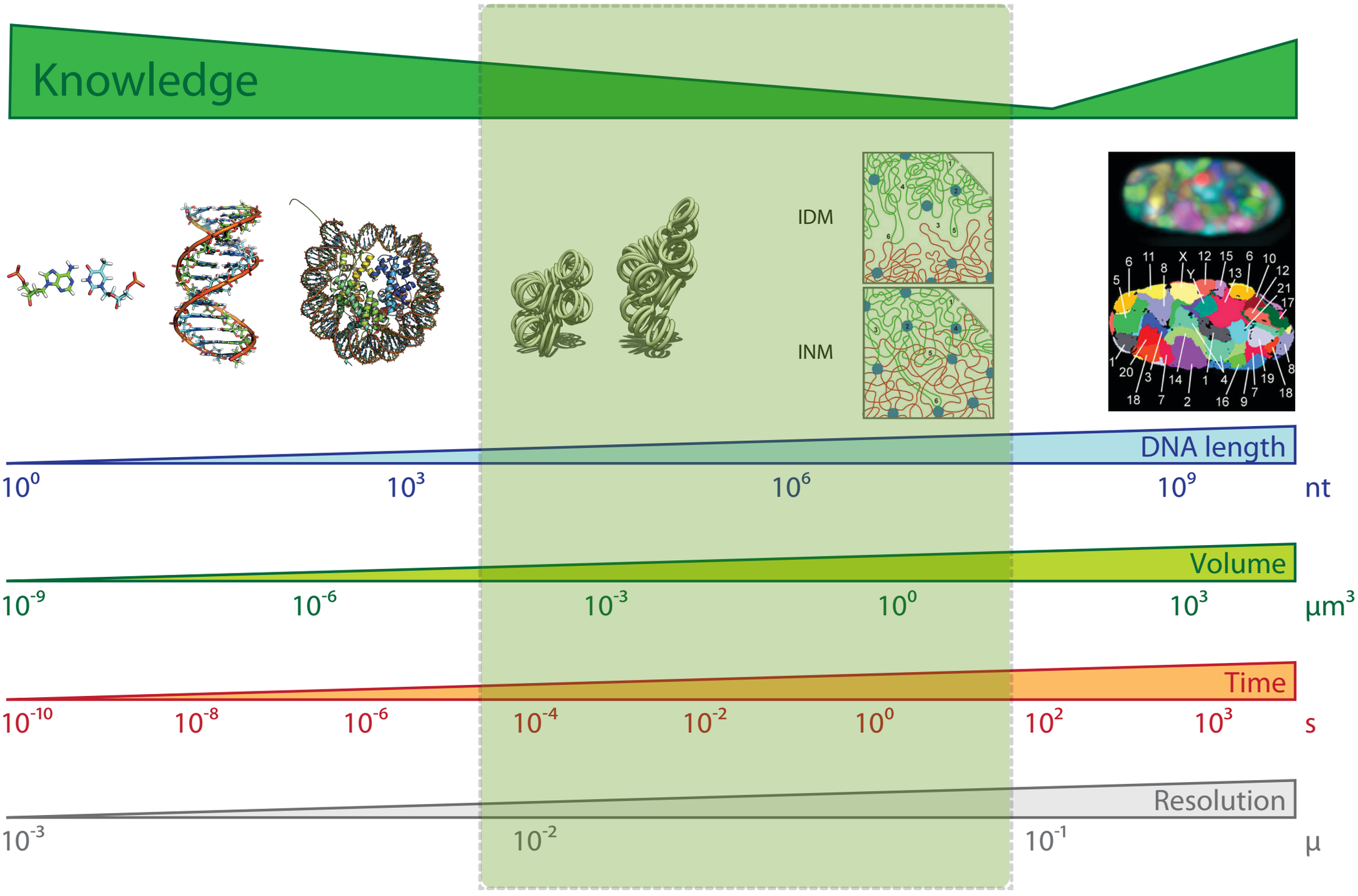
http://marciuslab.org
http://3DGenomes.org
http://cnag.crg.eu





Resolution Gap

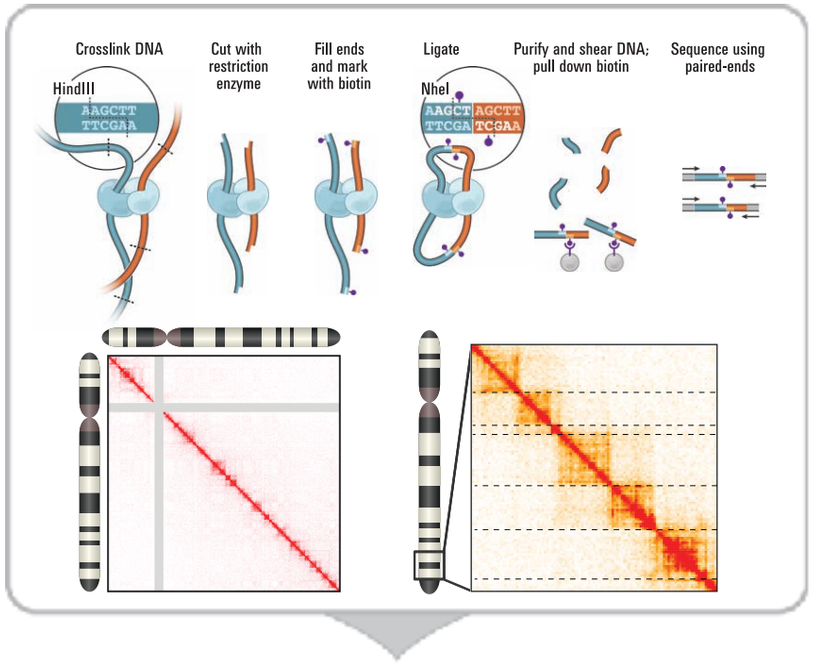
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol *7*, e1002125 (2011)

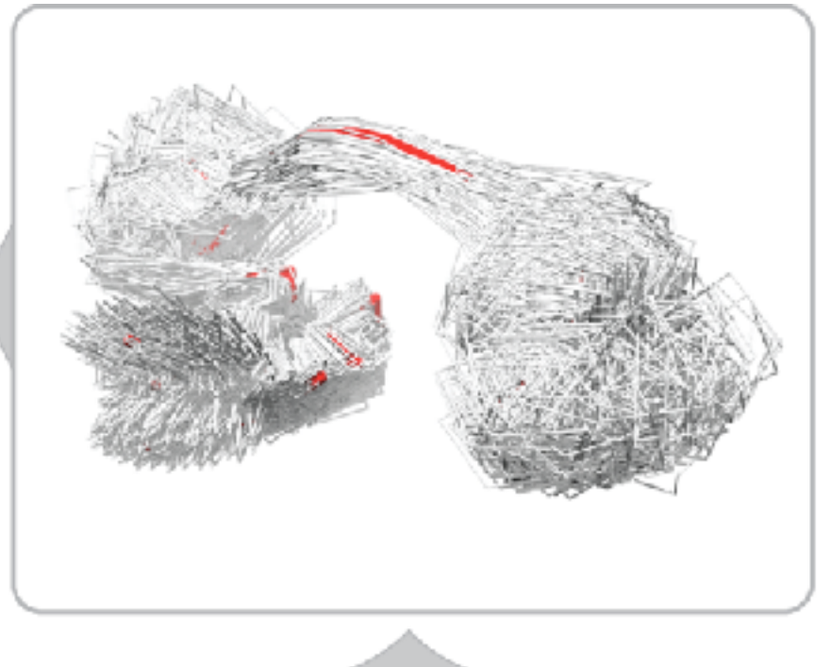


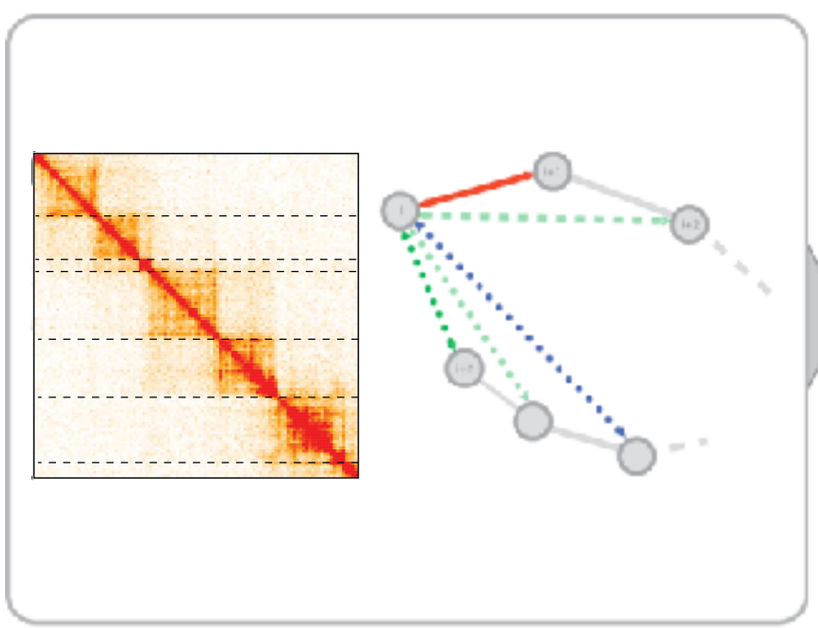
Hybrid Method

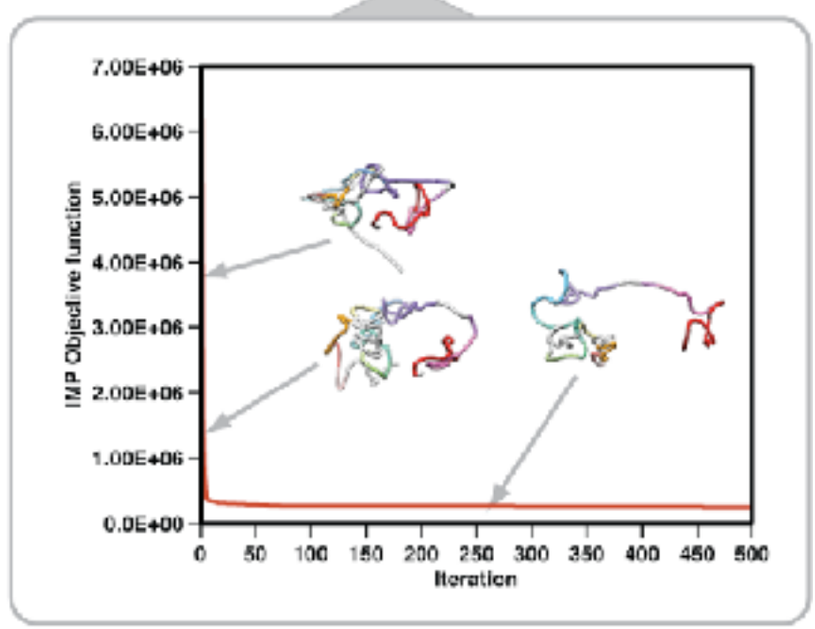
Baù, D. & Marti-Renom, M. A. Methods 58, 300–306 (2012).

Experiments





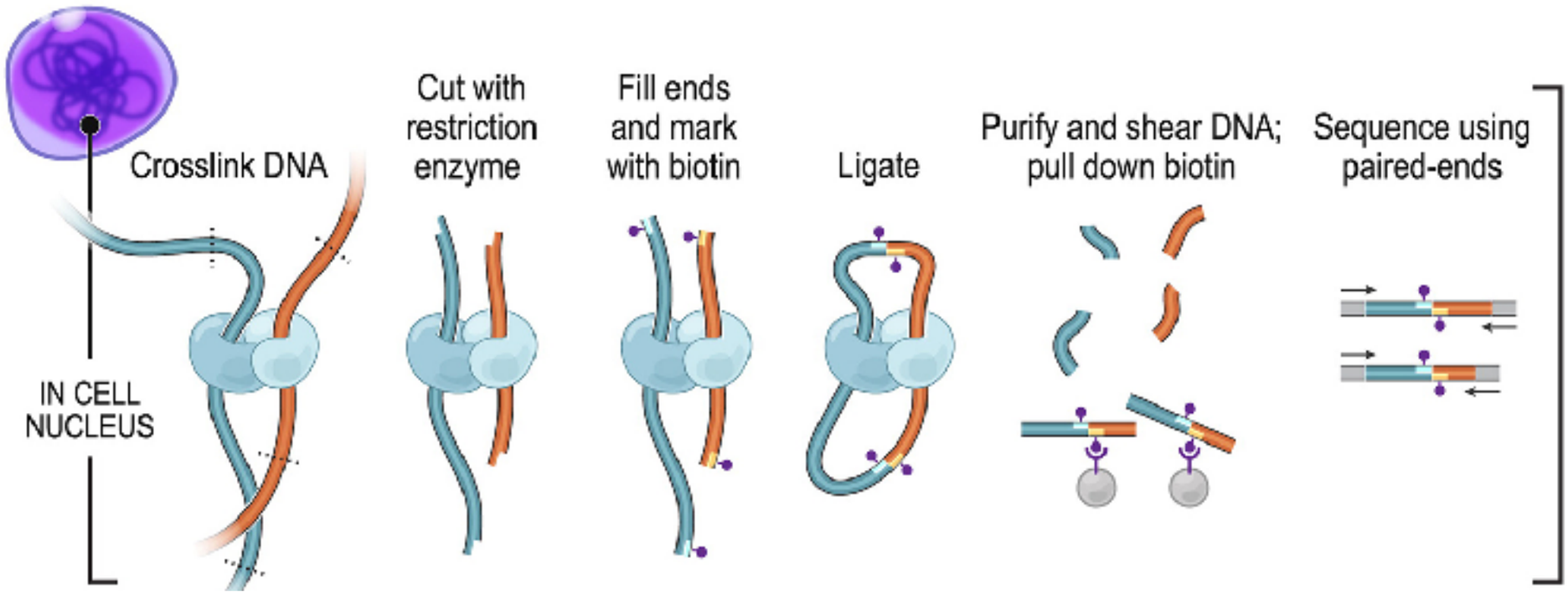


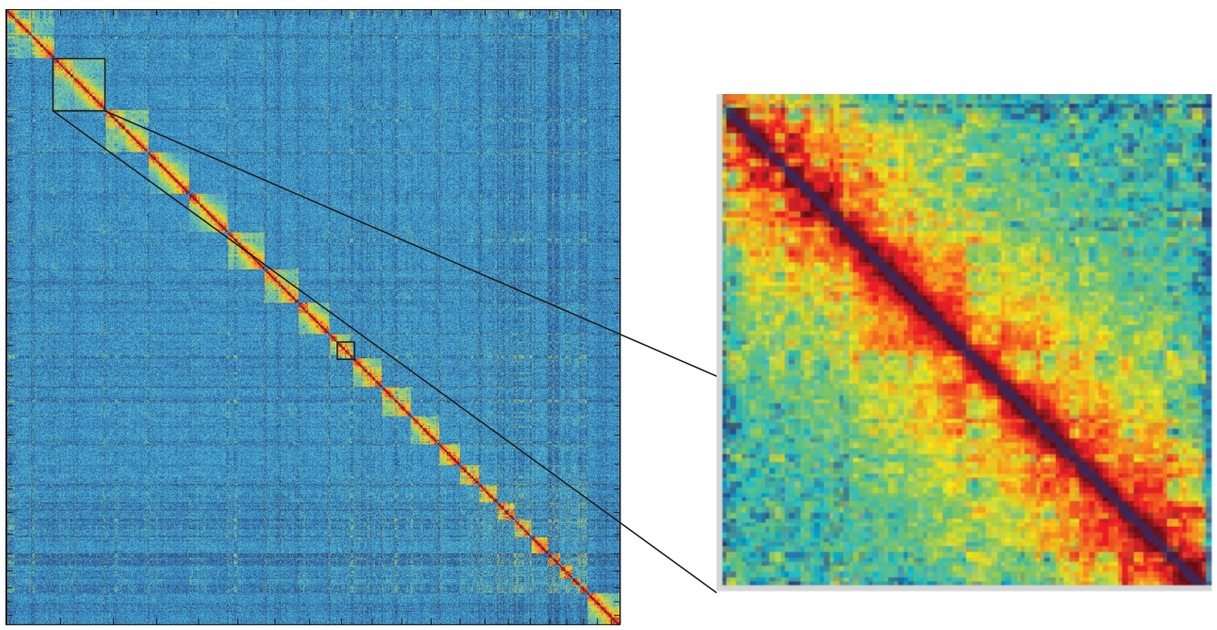


Computation

Chromosome Conformation Capture

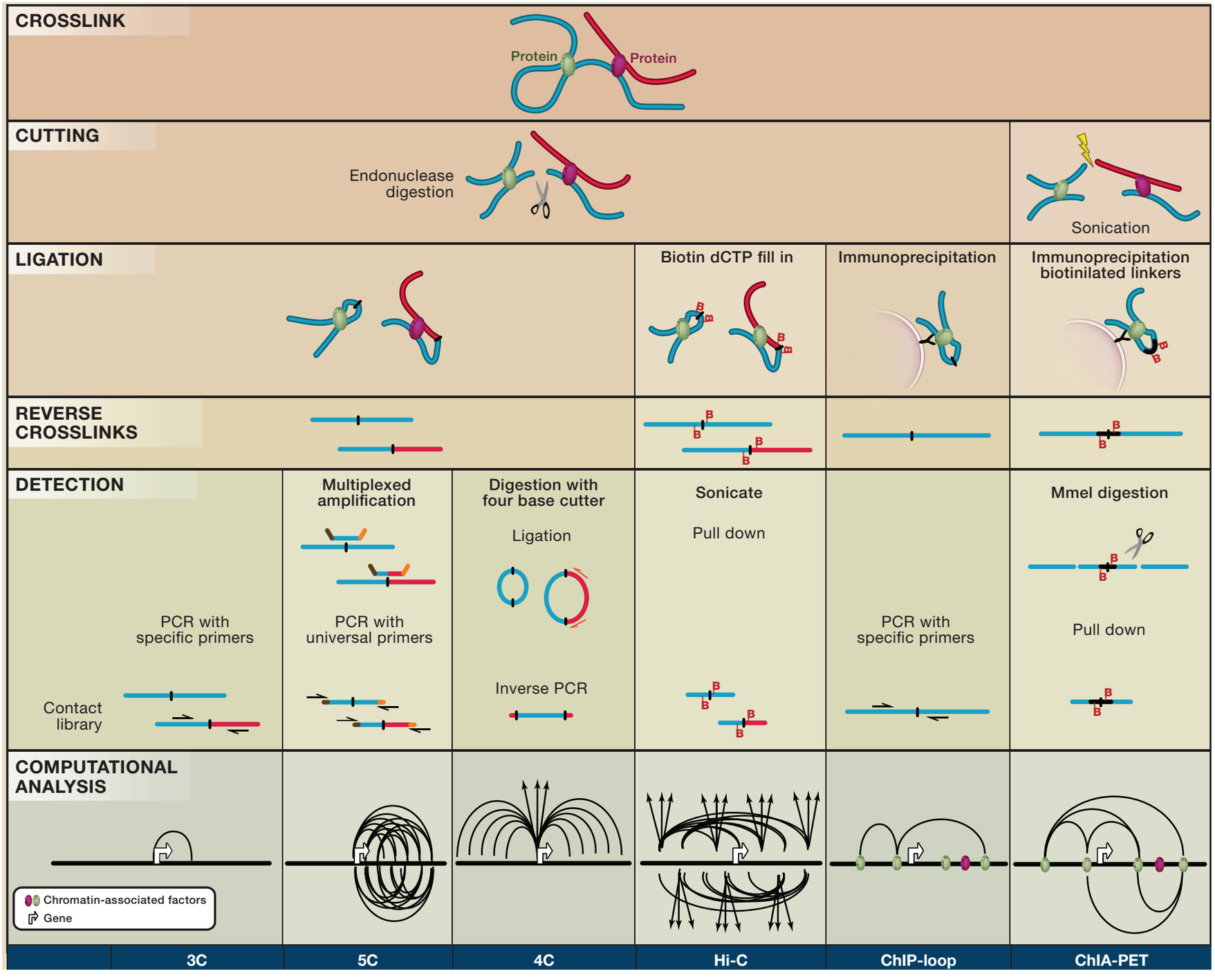
Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311.
Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.





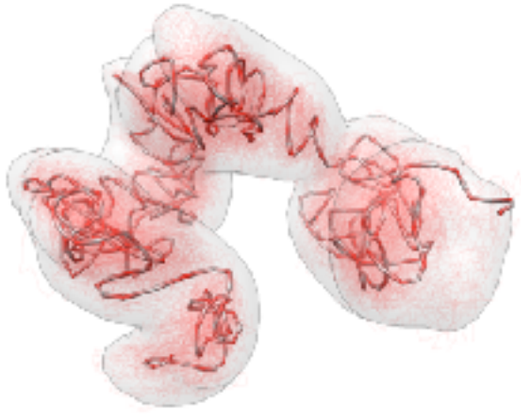
Chromosome Conformation Capture

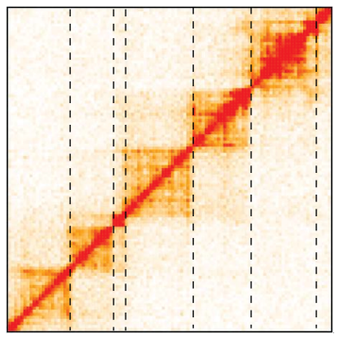
Hakim, O., & Misteli, T. (2012). Cell, 148(5), 1068–1068.e2



Restraint-based Modeling

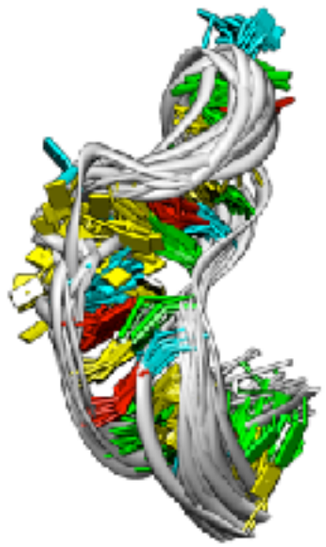
Baù, D. & Marti-Renom, M. A. Methods 58, 300–306 (2012).

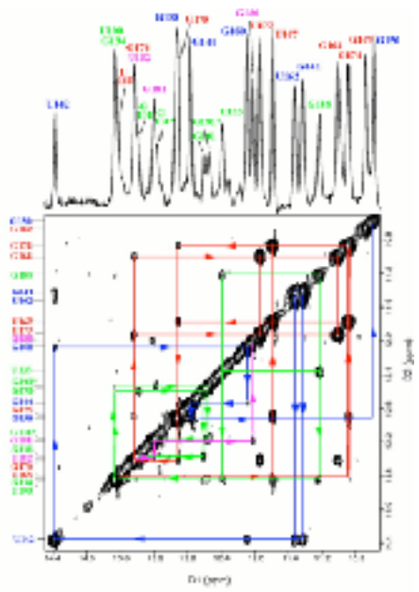




Chromosome structure determination

3C-based data





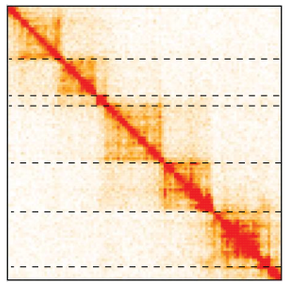
Biomolecular structure determination

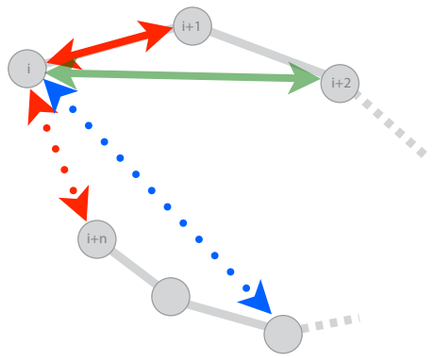
2D-NOESY data

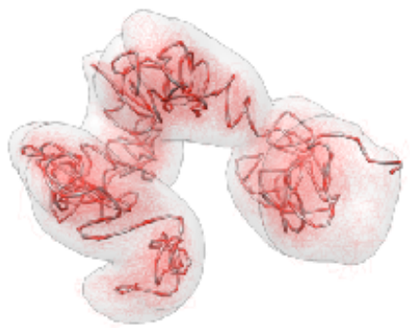
TADbit

http://3DGenomes.org

Serra, F., Baù, D. et al. PLOS CB (2017)







FastQ files to Maps

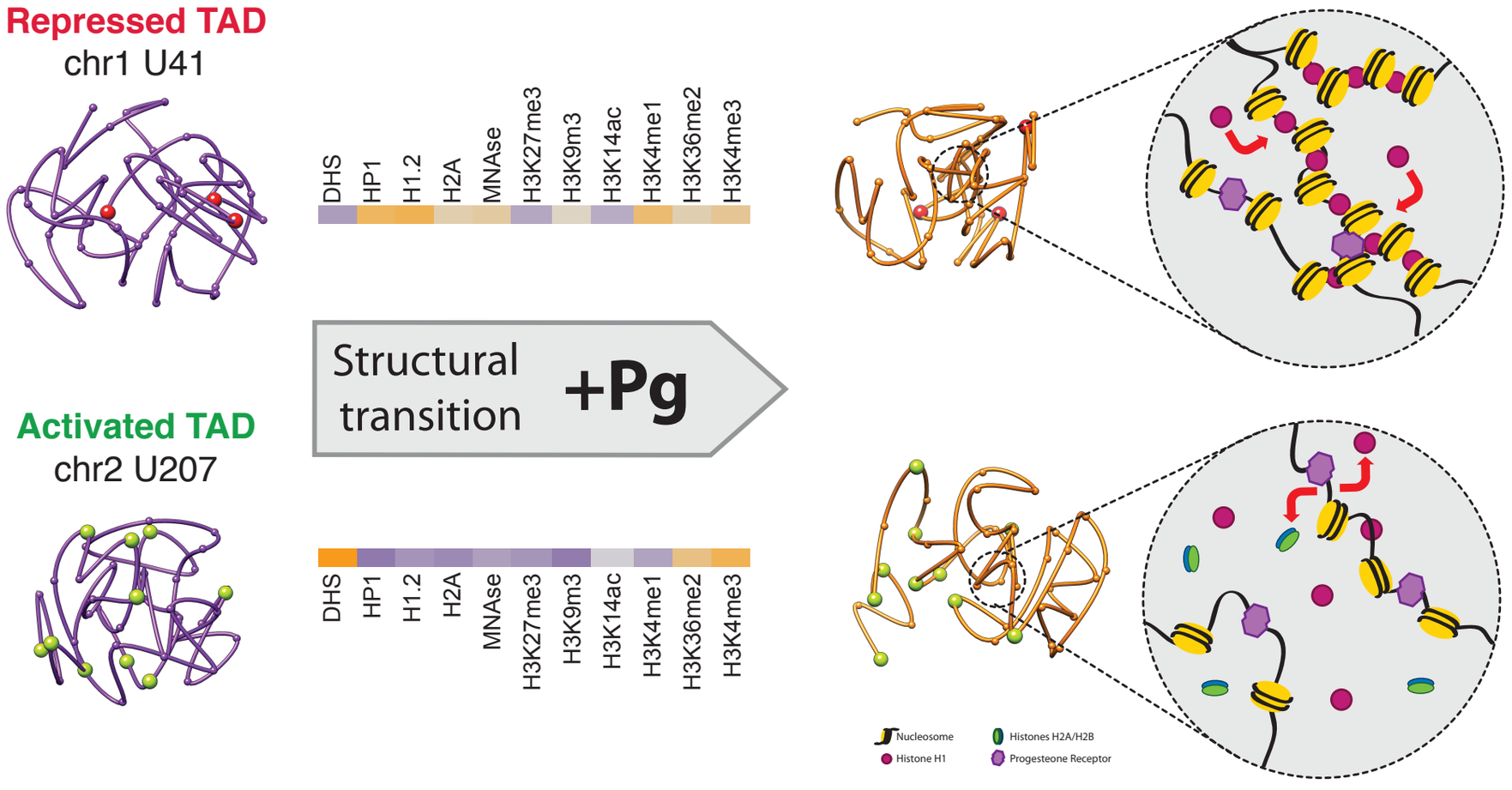
Map analysis

Model building

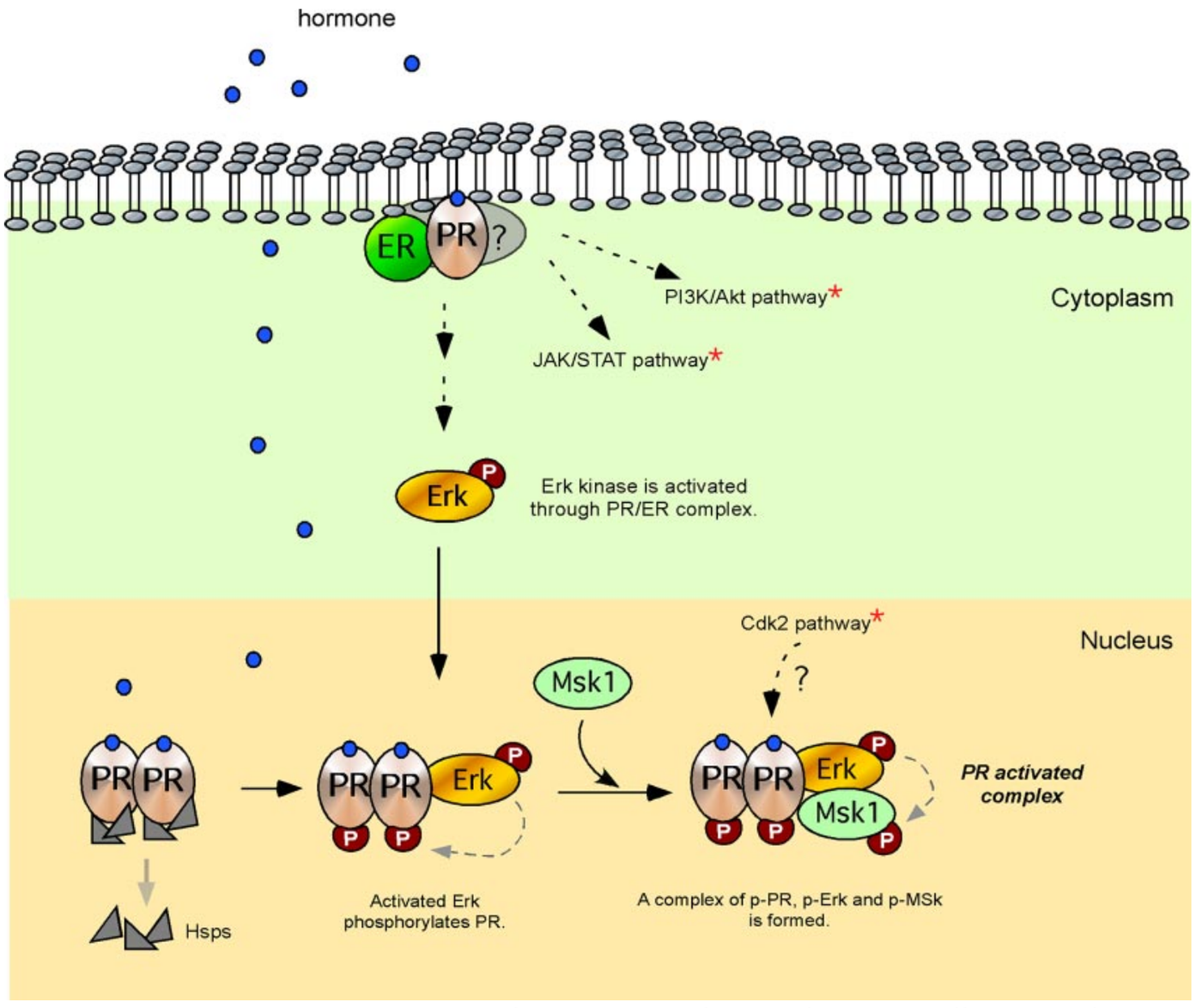
Model analysis

TADbit previous 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)
Belton, J.M. et al. Cell Reports (2015)
Trussart M. et al. Nature Communication (2017)
Cattoni et al. Nature Communication (2017)
Stadhouders R. et al. Nature Genetics (2017) in press



Progesterone-regulated transcription in breast cancer



Vicent *et al* 2011, Wright *et al* 2012, Ballare *et al* 2012

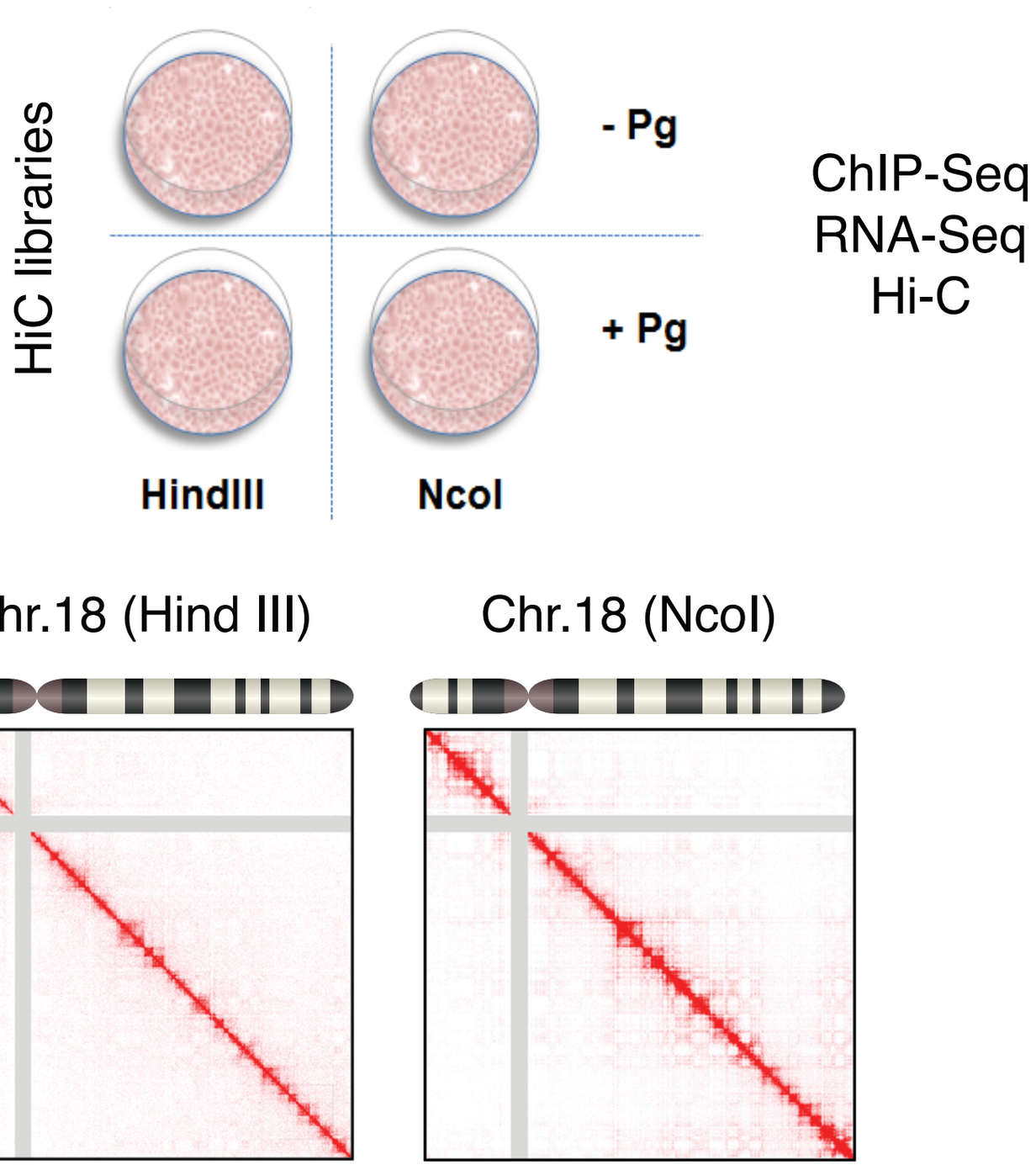
> 2,000 genes **Up**-regulated

> 2,000 genes **Down-**

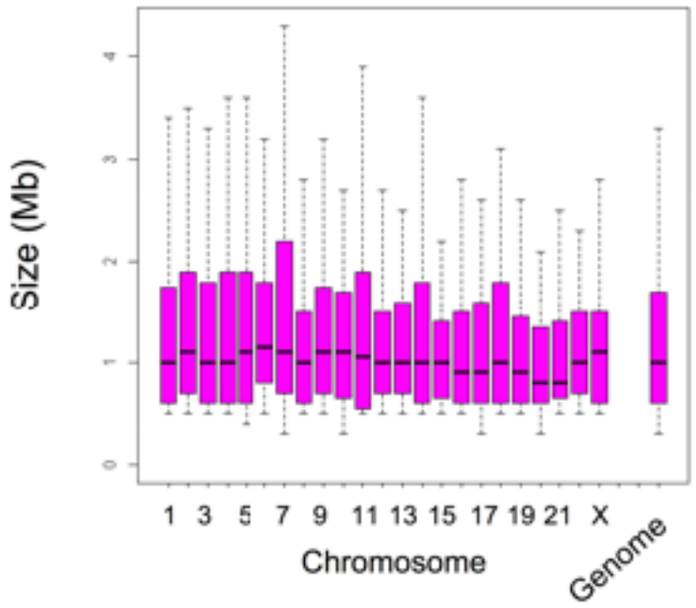
Regulation in 3D?

Le Dily, F. et al. Genes & Dev (2014)

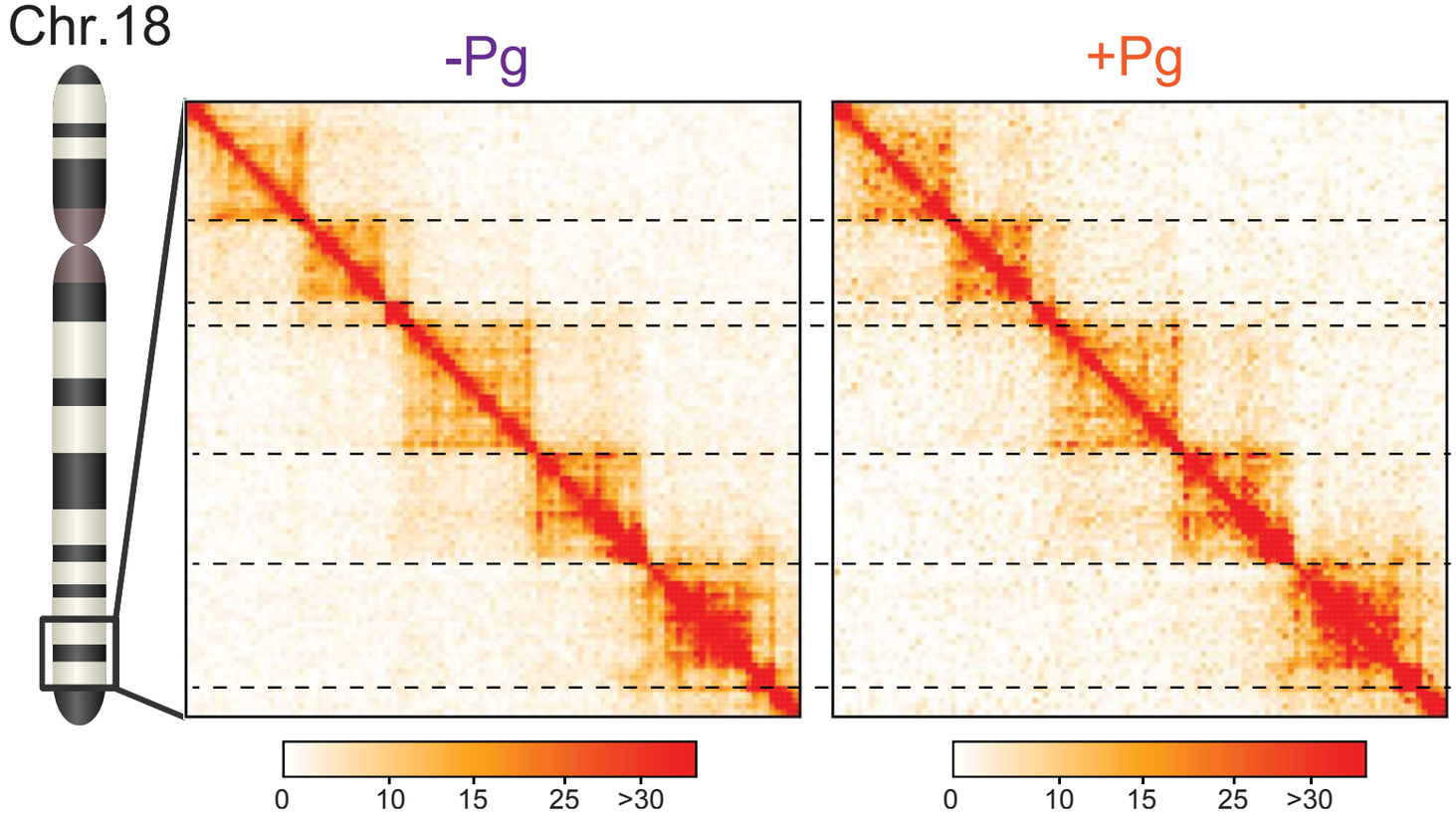
Experimental design

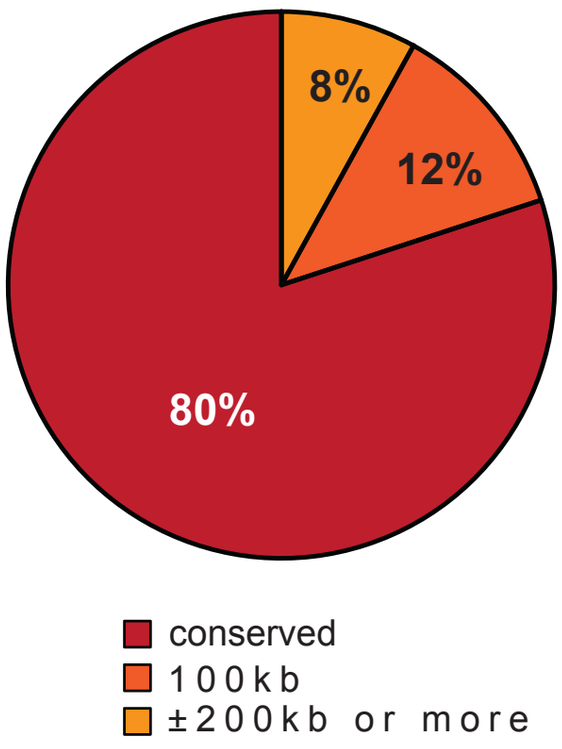


Are there TADs? how robust?

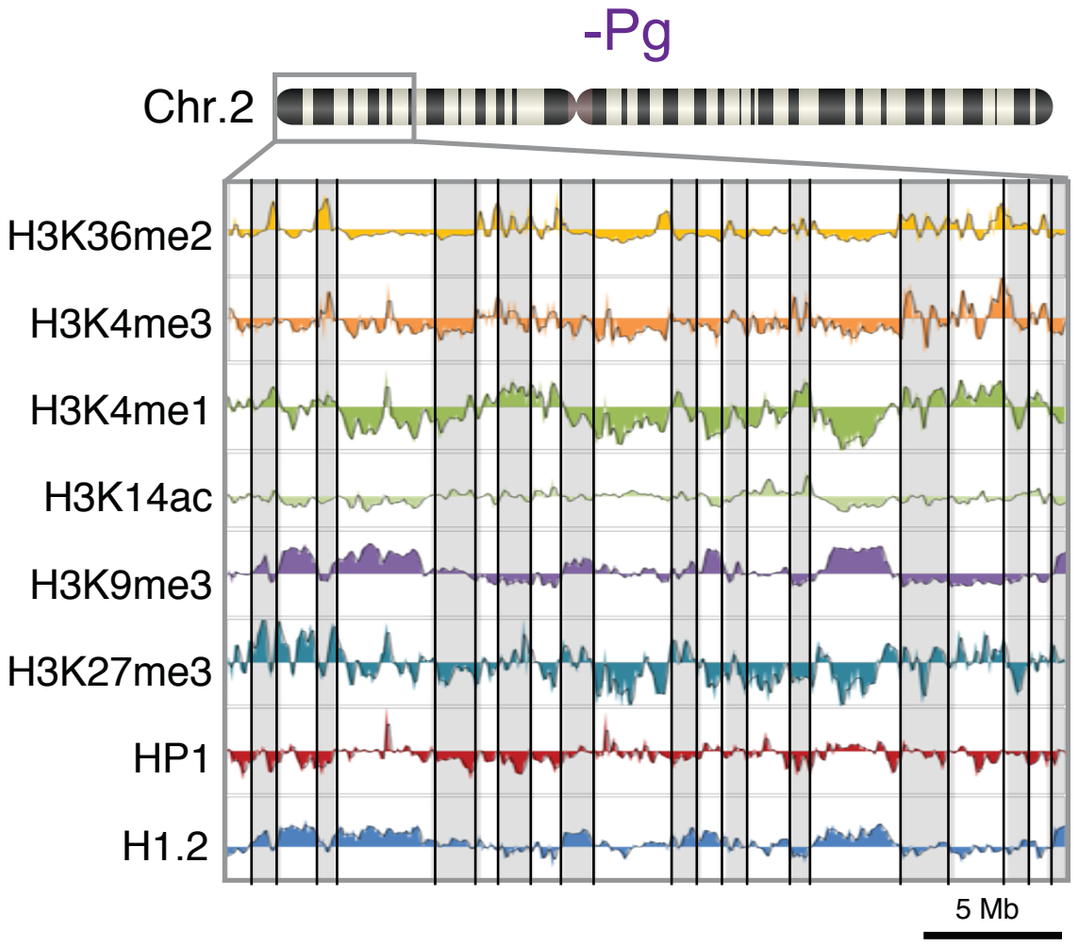


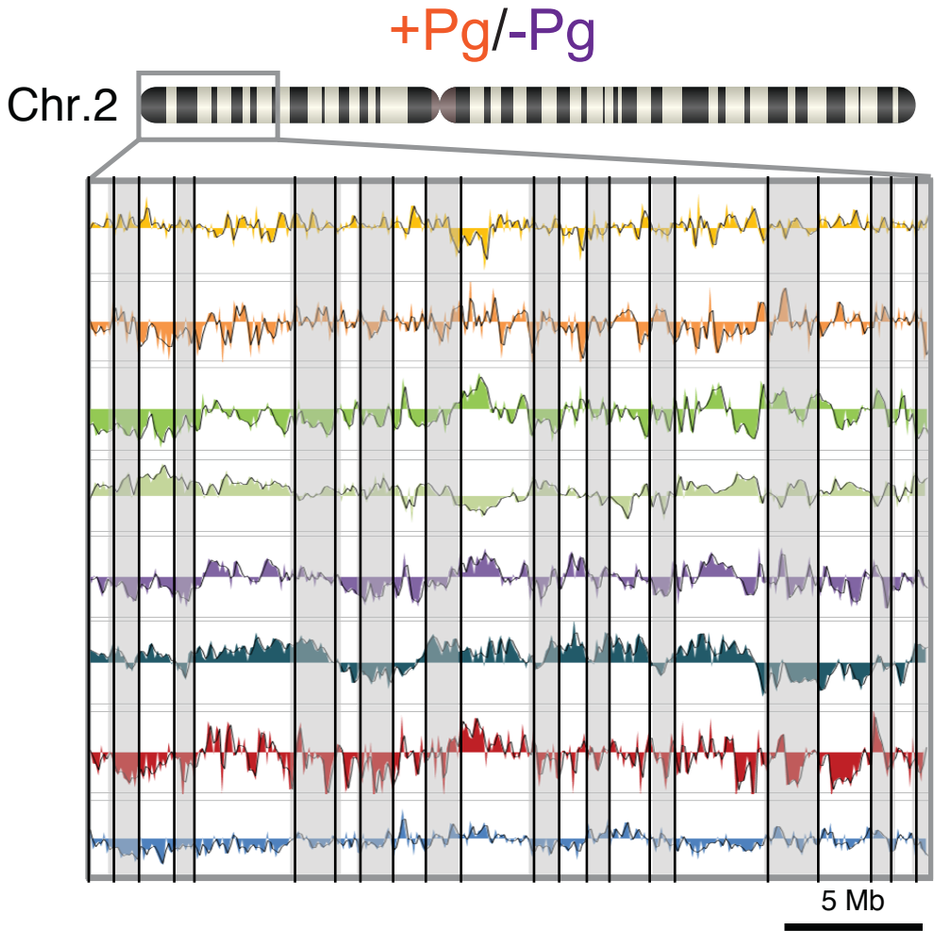
>2,000 detected TADs

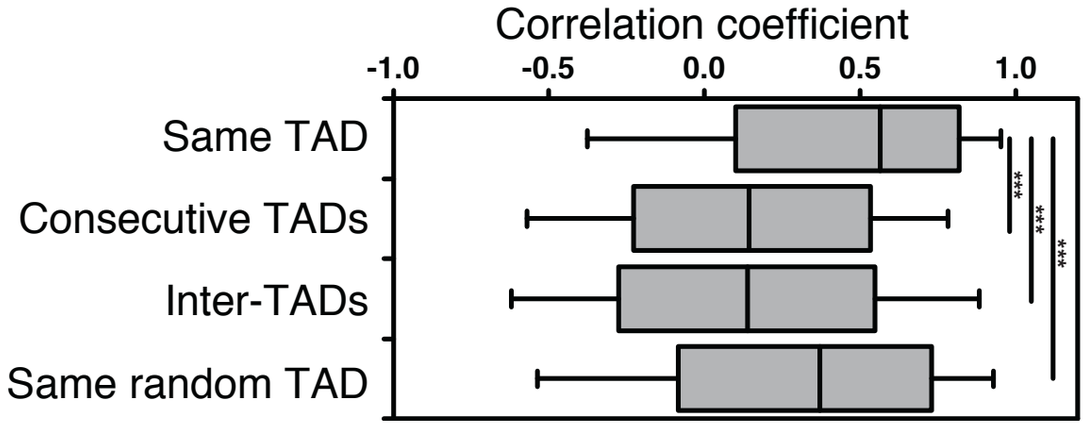


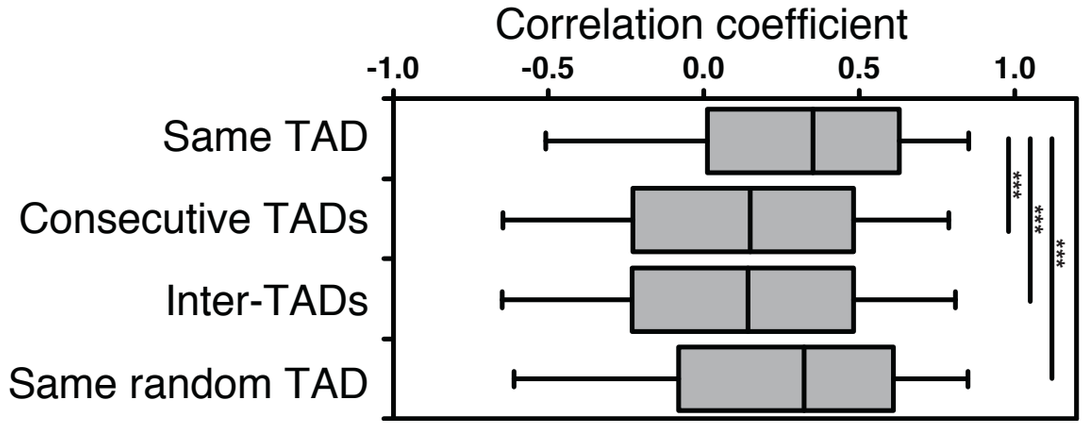


Are TADs homogeneous?

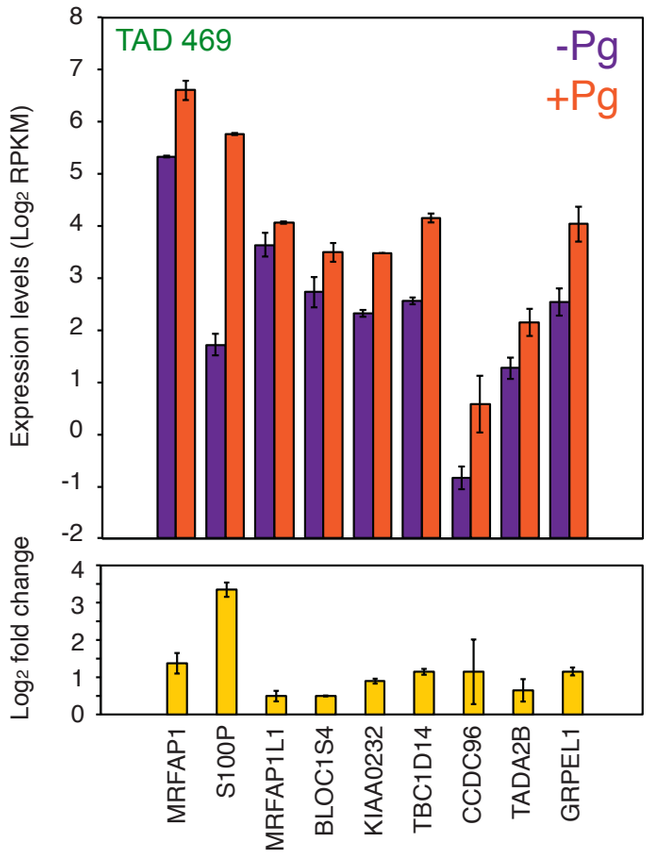


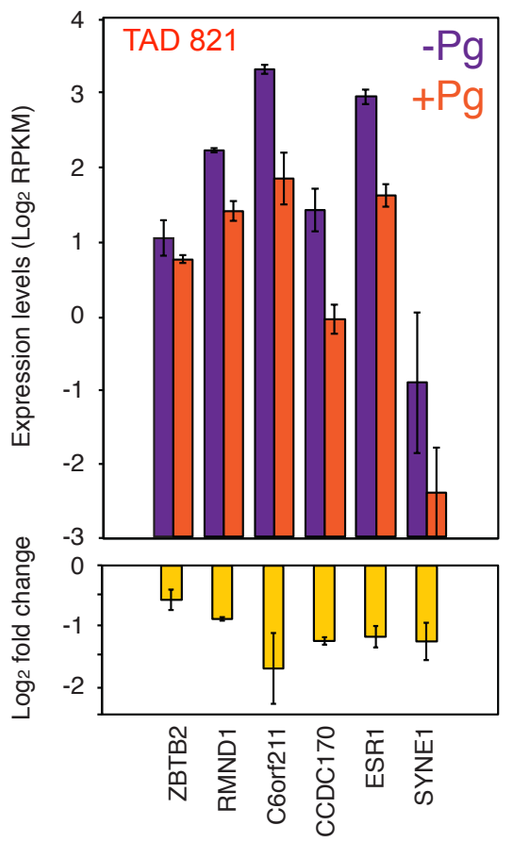


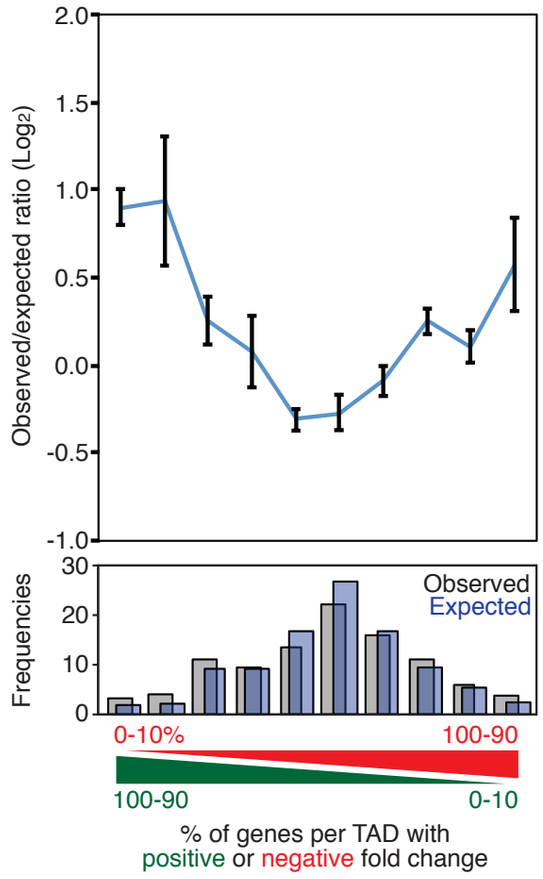




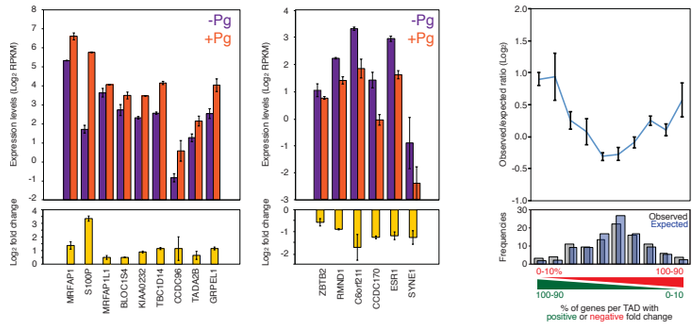
Do TADs respond differently to Pg treatment?





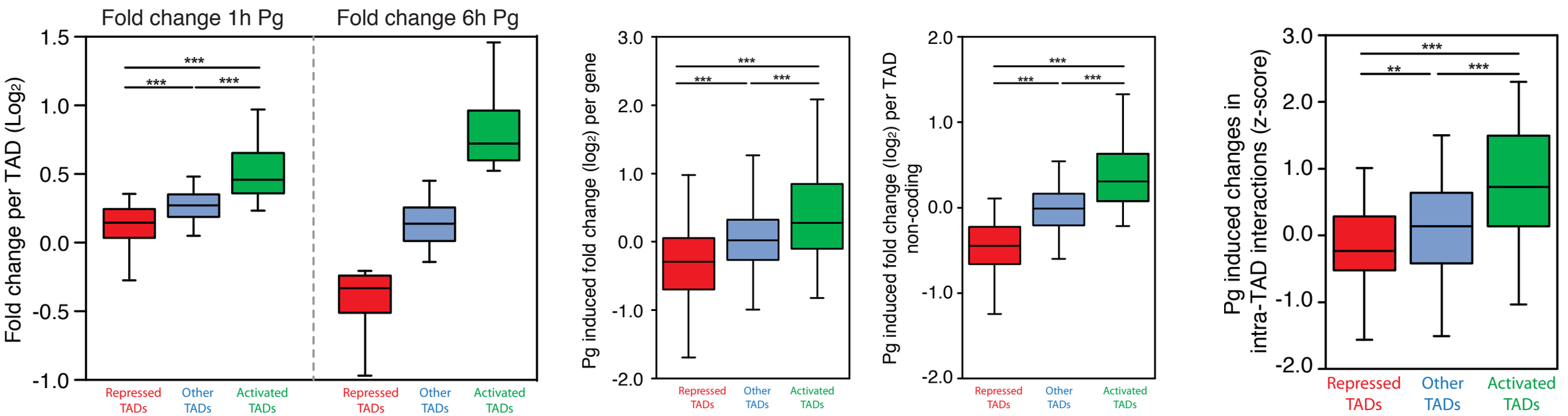


Do TADs respond differently to Pg treatment?

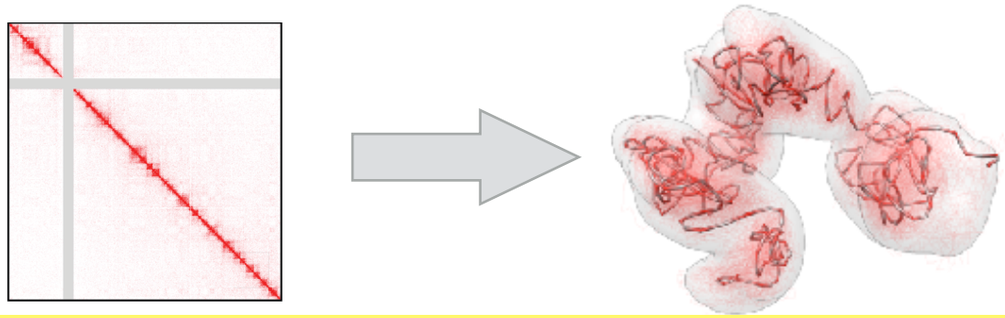


Pg induced fold change per TAD (6h)

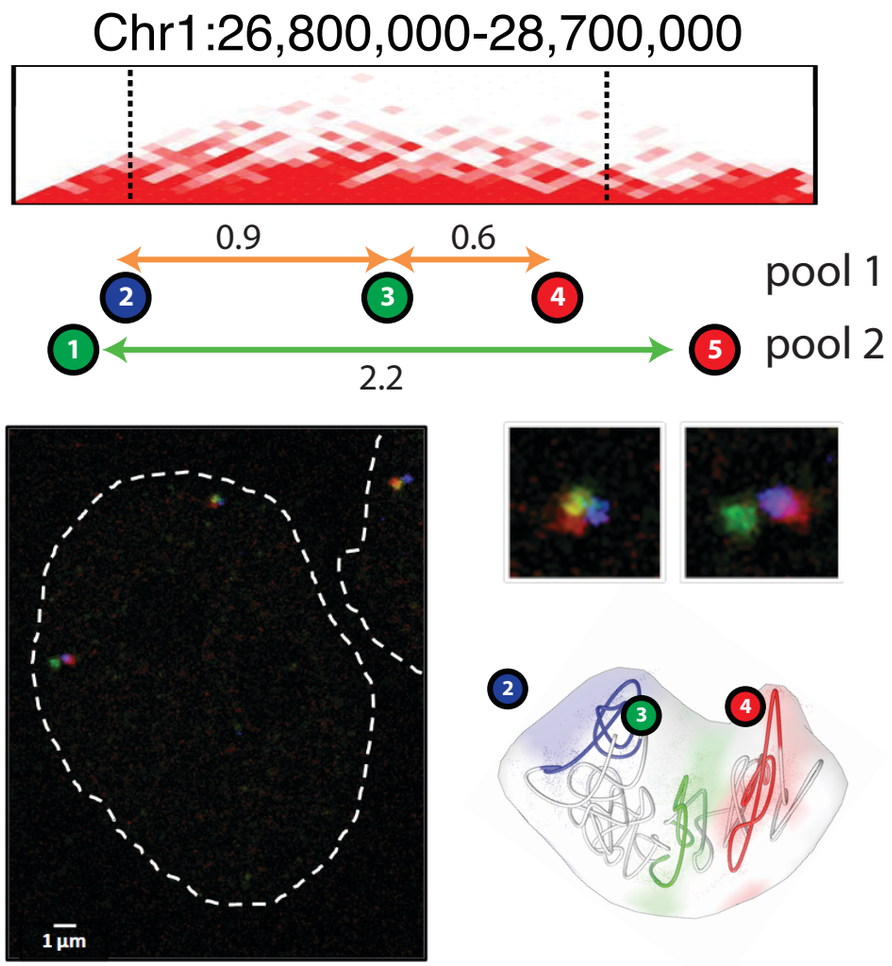
Repressed TADs | Other TADs | Activated TADs

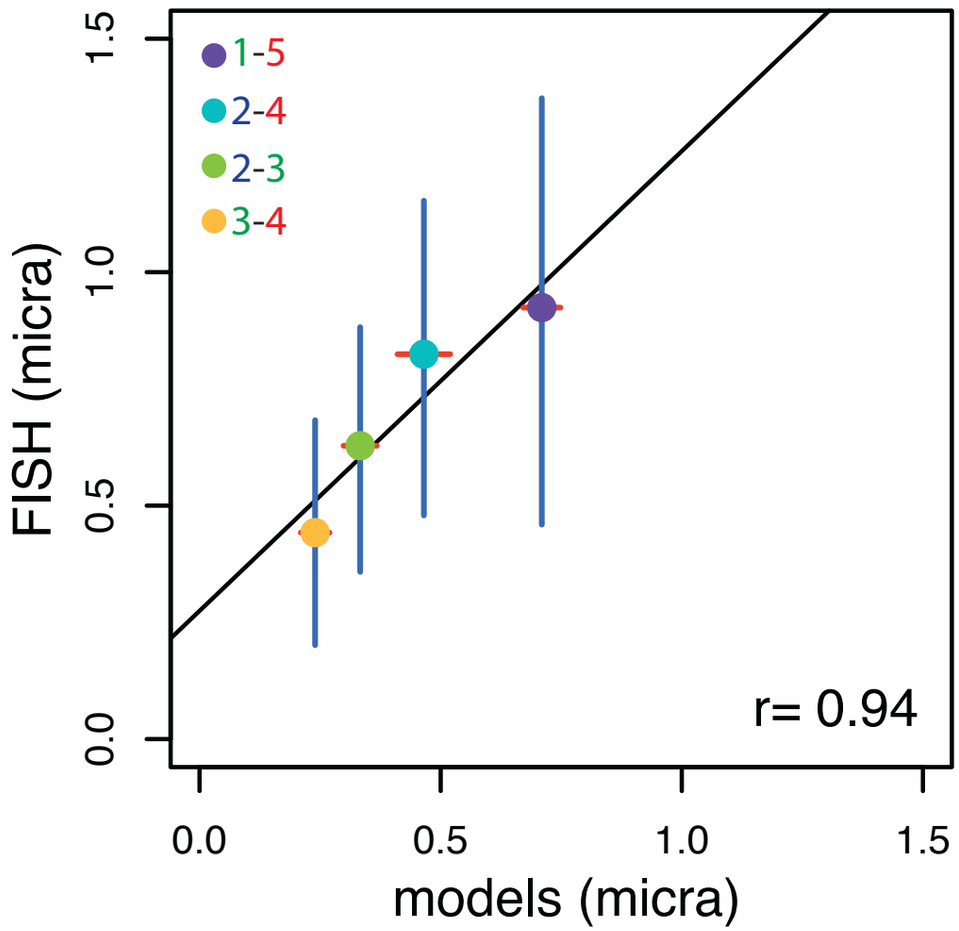


Modeling 3D TADs



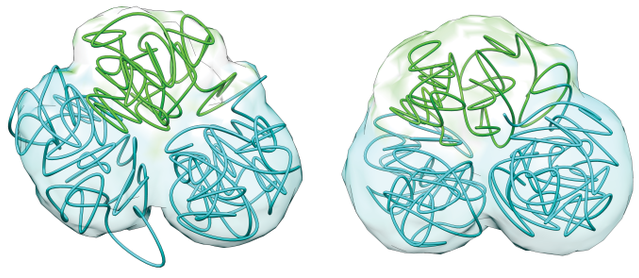
61 genomic regions containing 209 TADs covering 267Mb

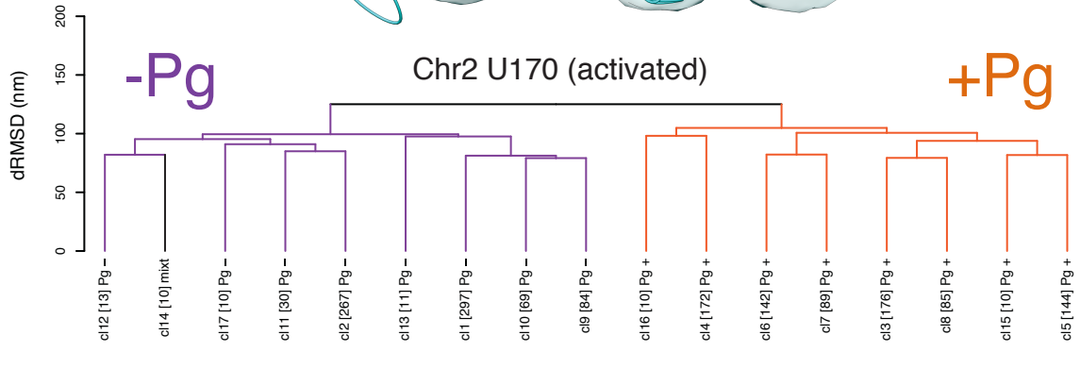




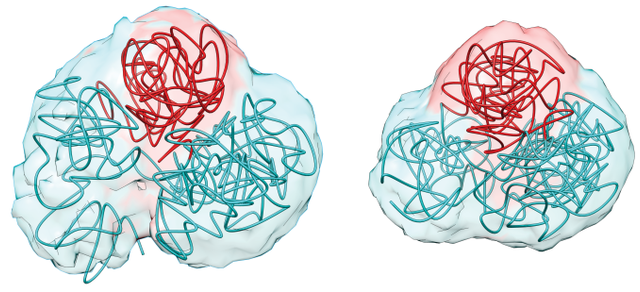
How TADs respond structurally to Pg?

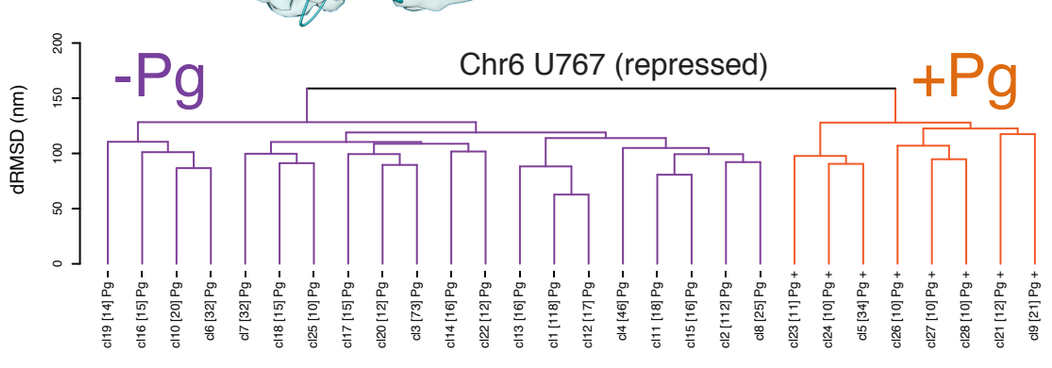
Chr2:9,600,000-13,200,000

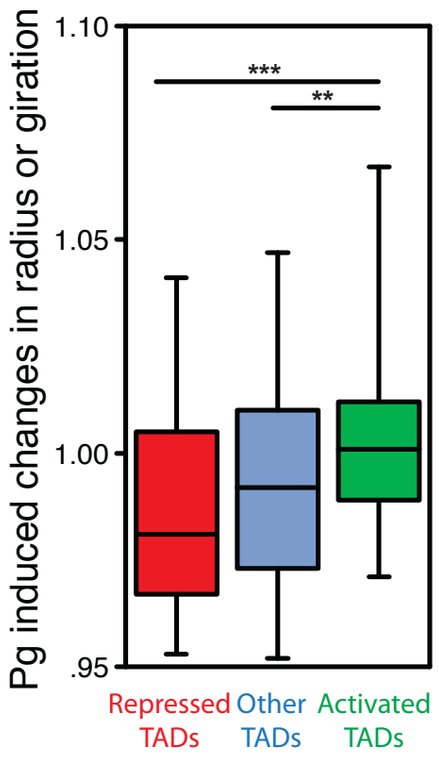


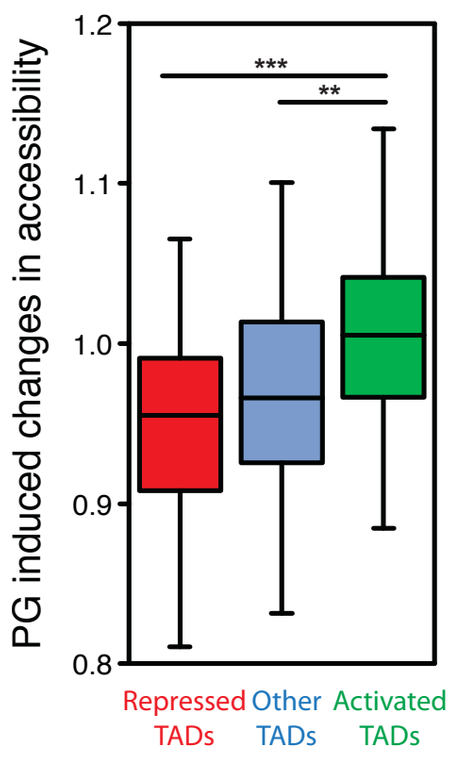


Chr6:71,800,000-76,500,000

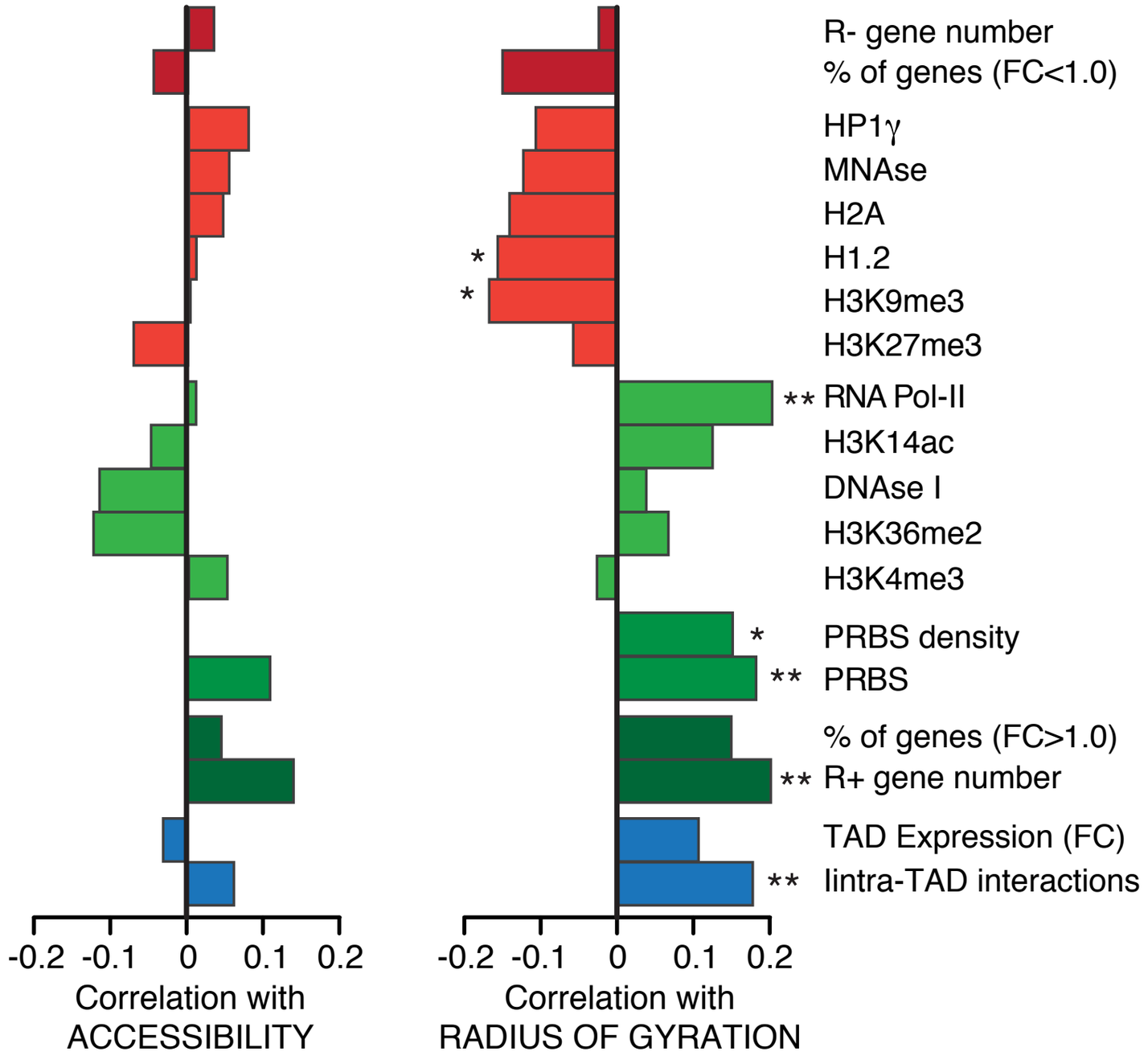




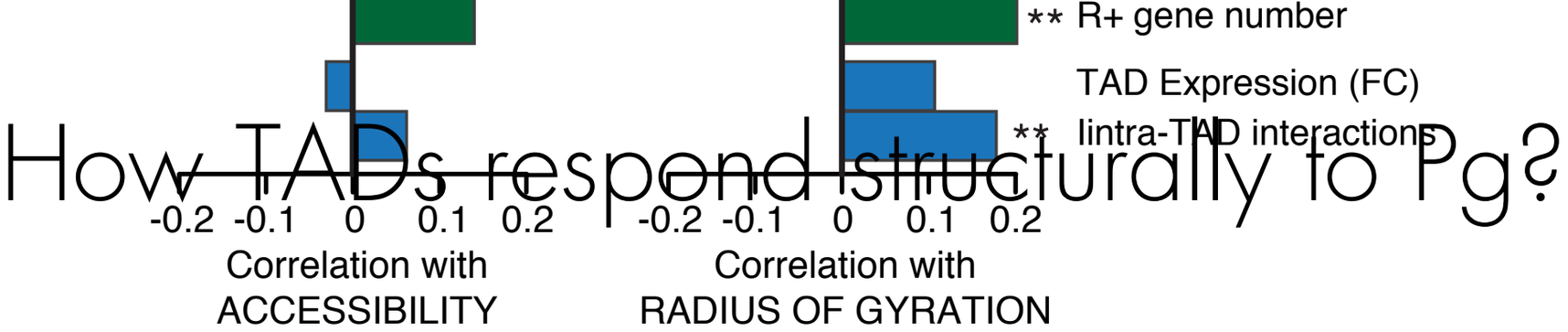


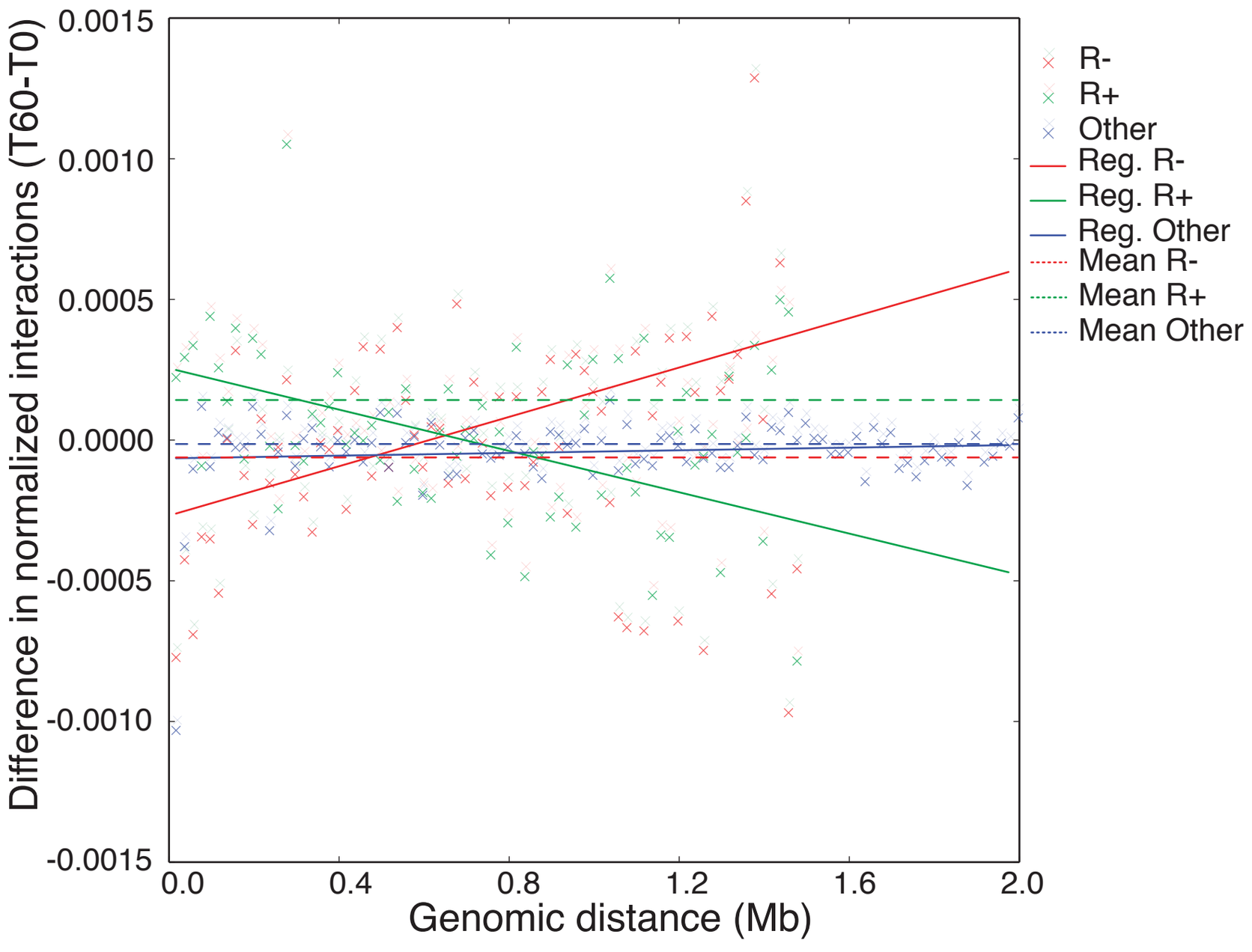


How TADs respond structurally to Pg?



How TADs respond structurally to Pg?

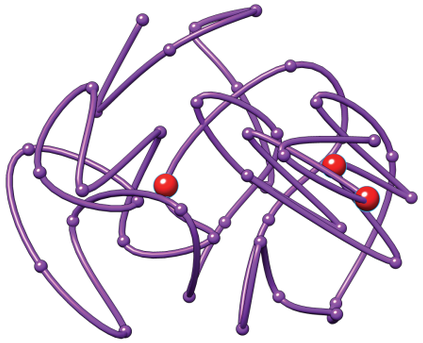


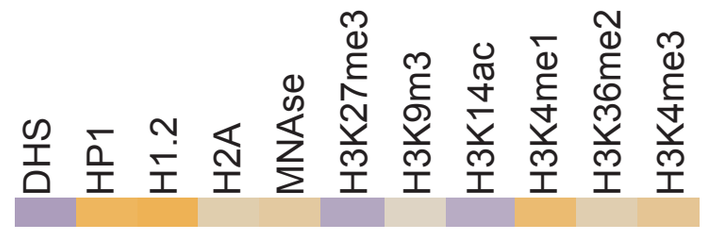


Model for TAD regulation

Repressed TAD

chr1 U41

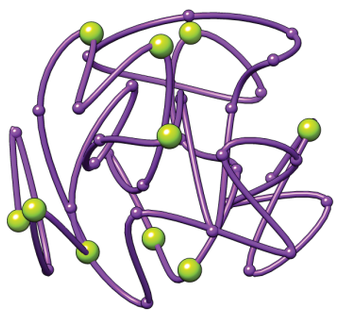


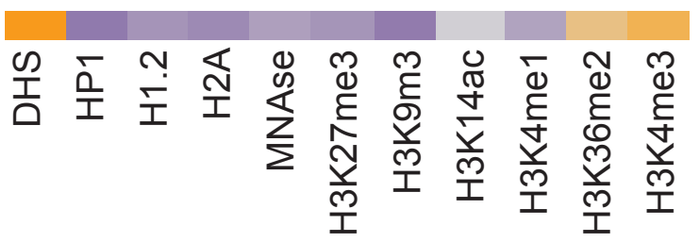


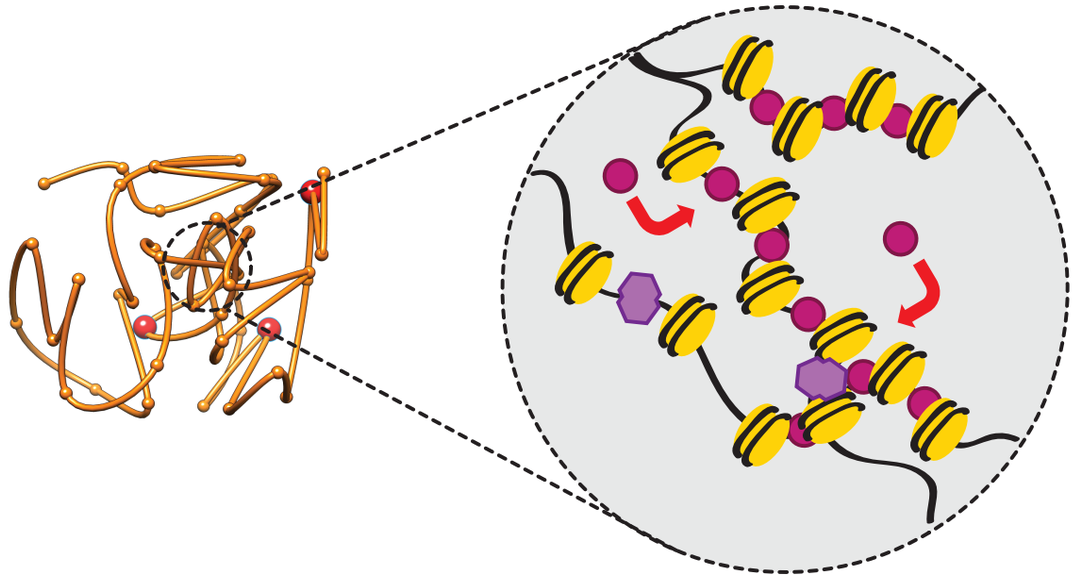
Structural transition **+Pg**

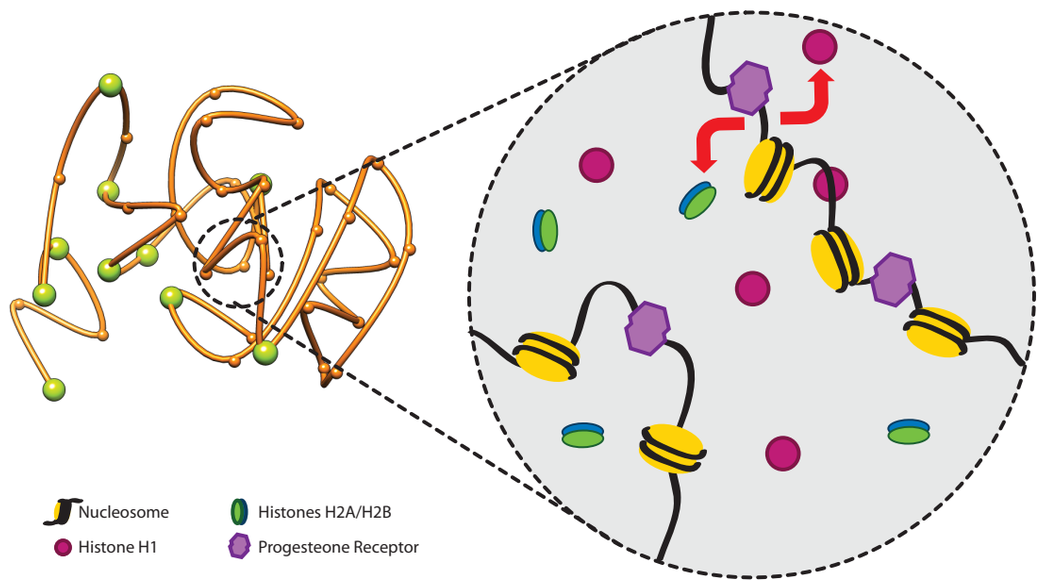
Activated TAD

chr2 U207









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Aleksandra Sparavier
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In collaboration with François Le Dily and Miguel Beato

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