

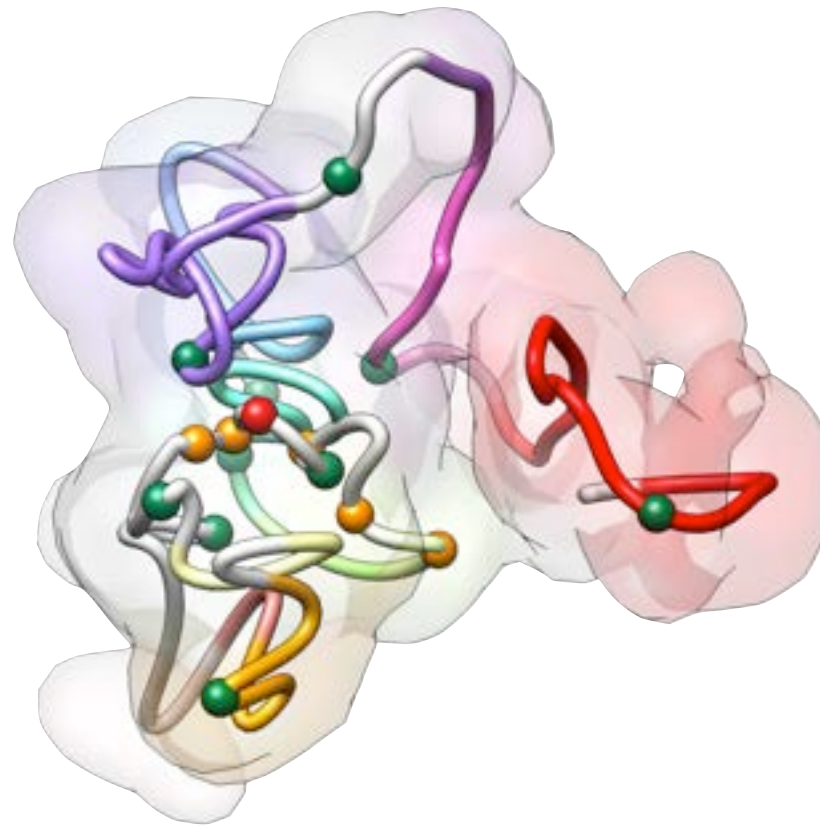
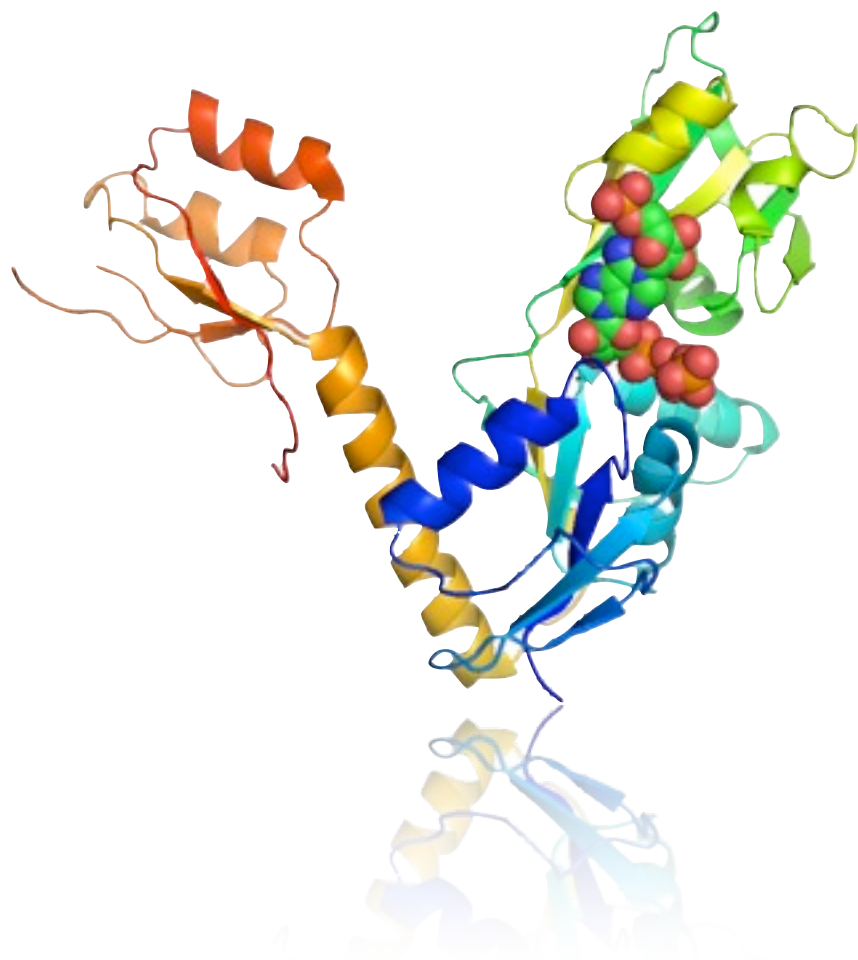
Modeling 3D genomes:
**Hormone induced structural
reorganization of TADs in the
breast cancer genome**

Marc A. Marti-Renom

*Genome Biology Group (CNAG)
Structural Genomics Group (CRG)*

Structural Genomics Group

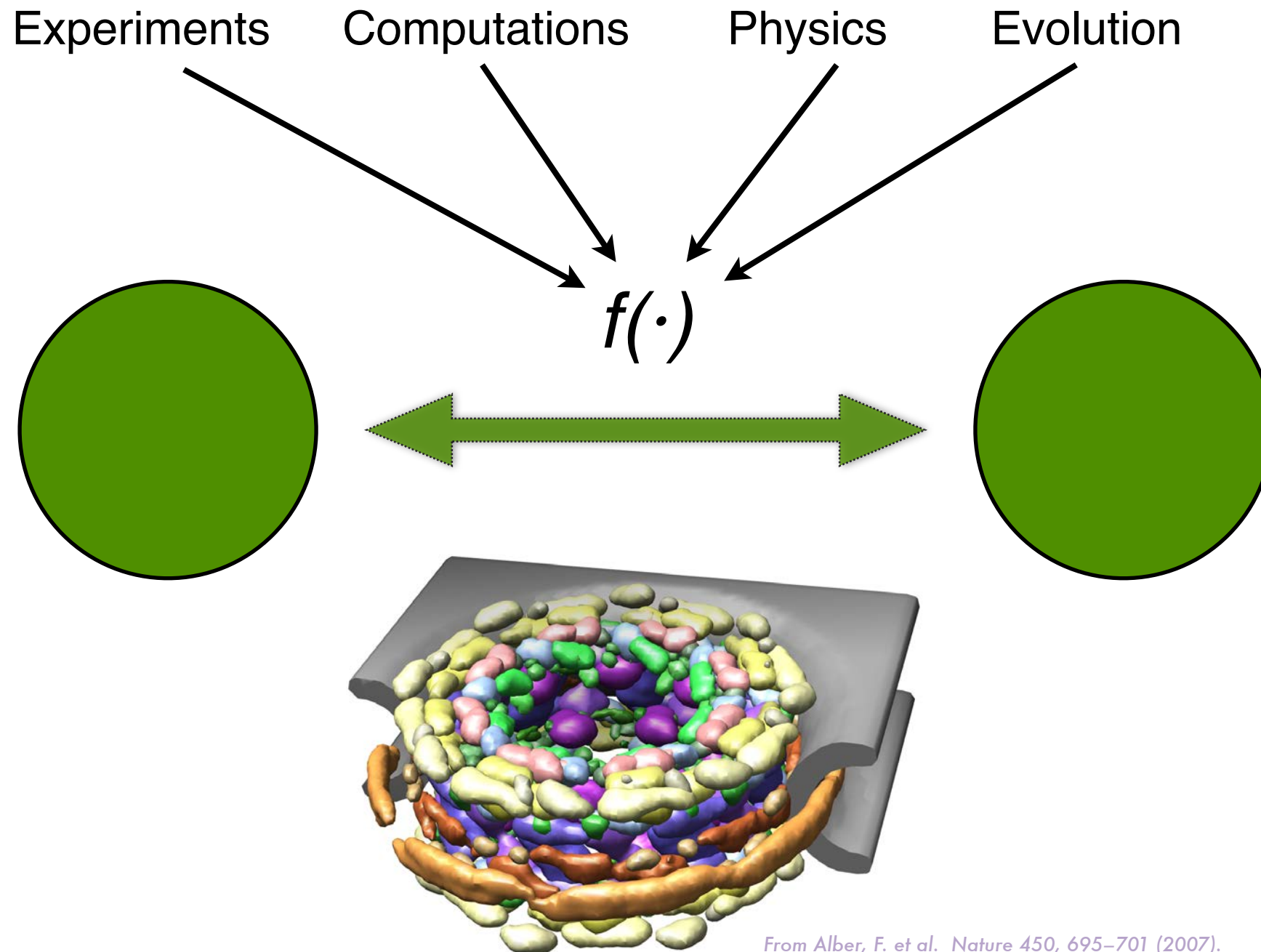
<http://www.marciuslab.org>



Integrative Modeling Platform

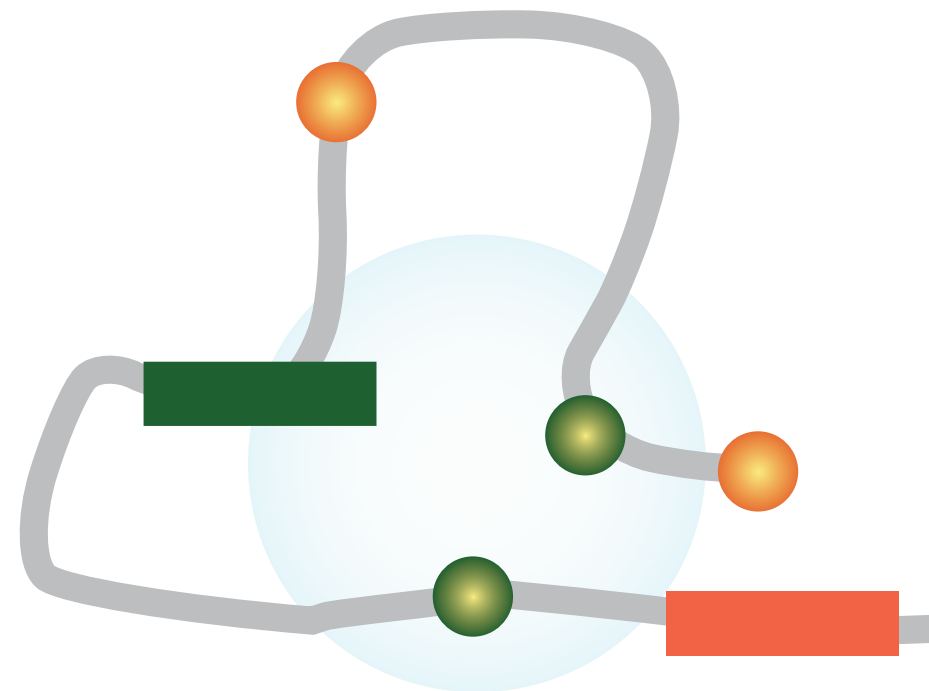
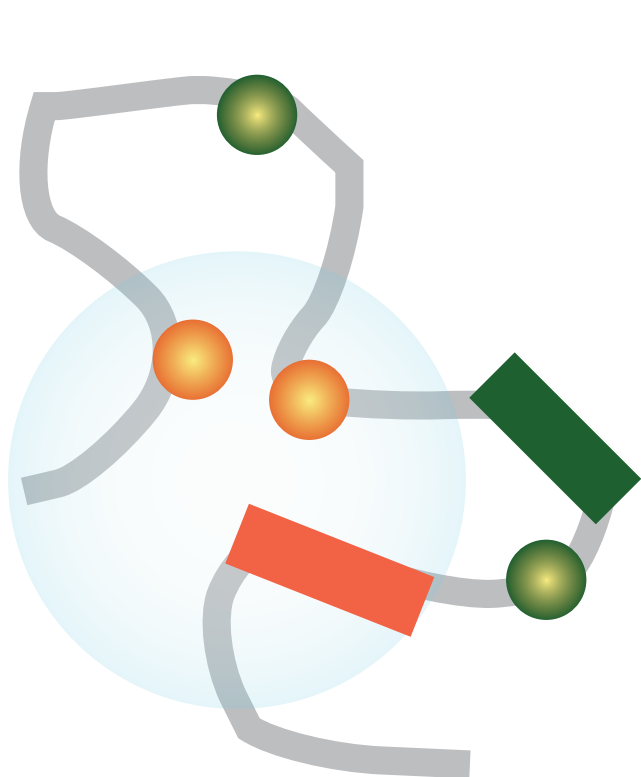
<http://www.integrativemodeling.org>

Russel, D. et al. PLOS Biology 10, e1001244 (2012).



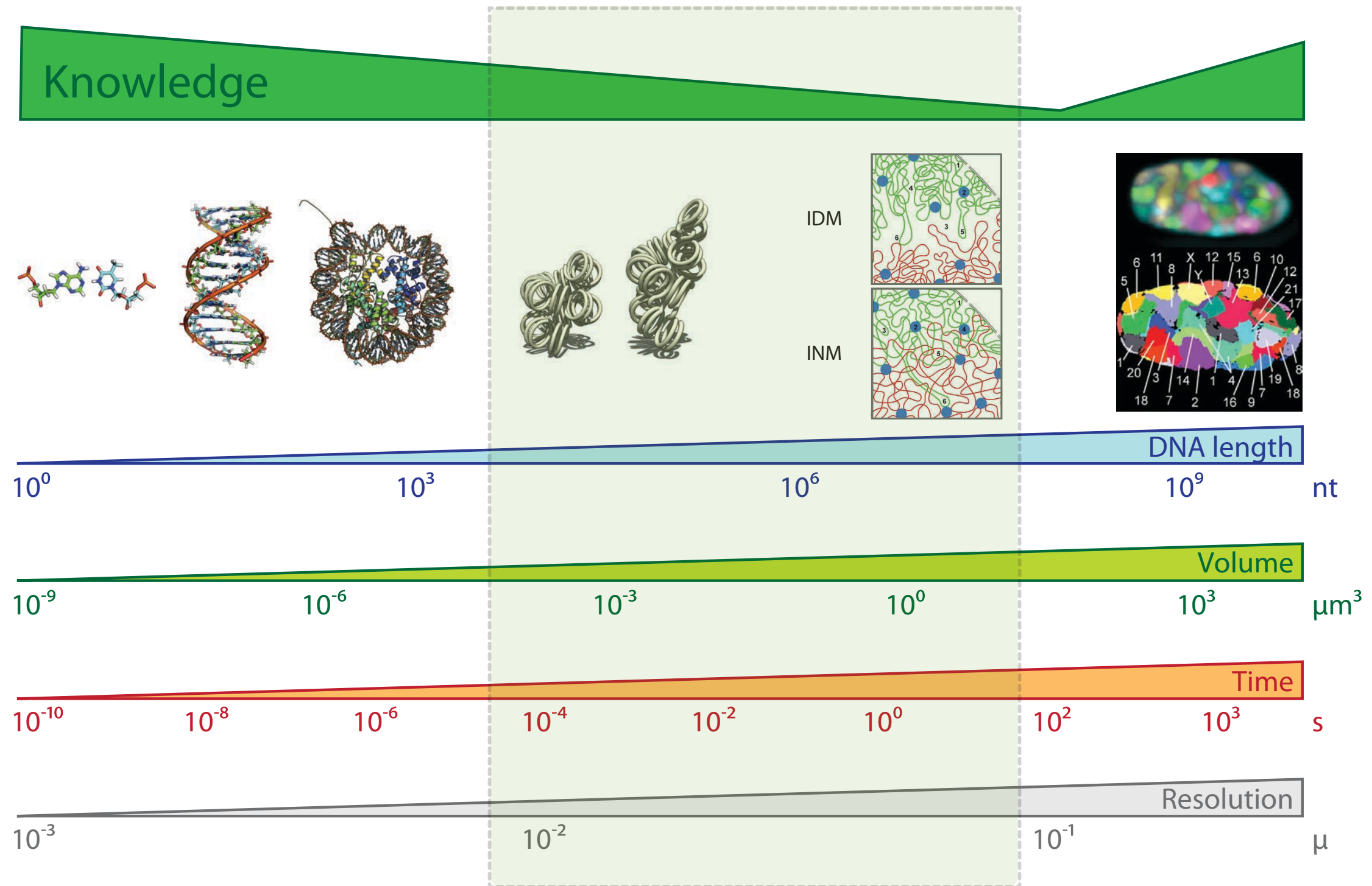
From Alber, F. et al. Nature 450, 695–701 (2007).

Complex genome organization



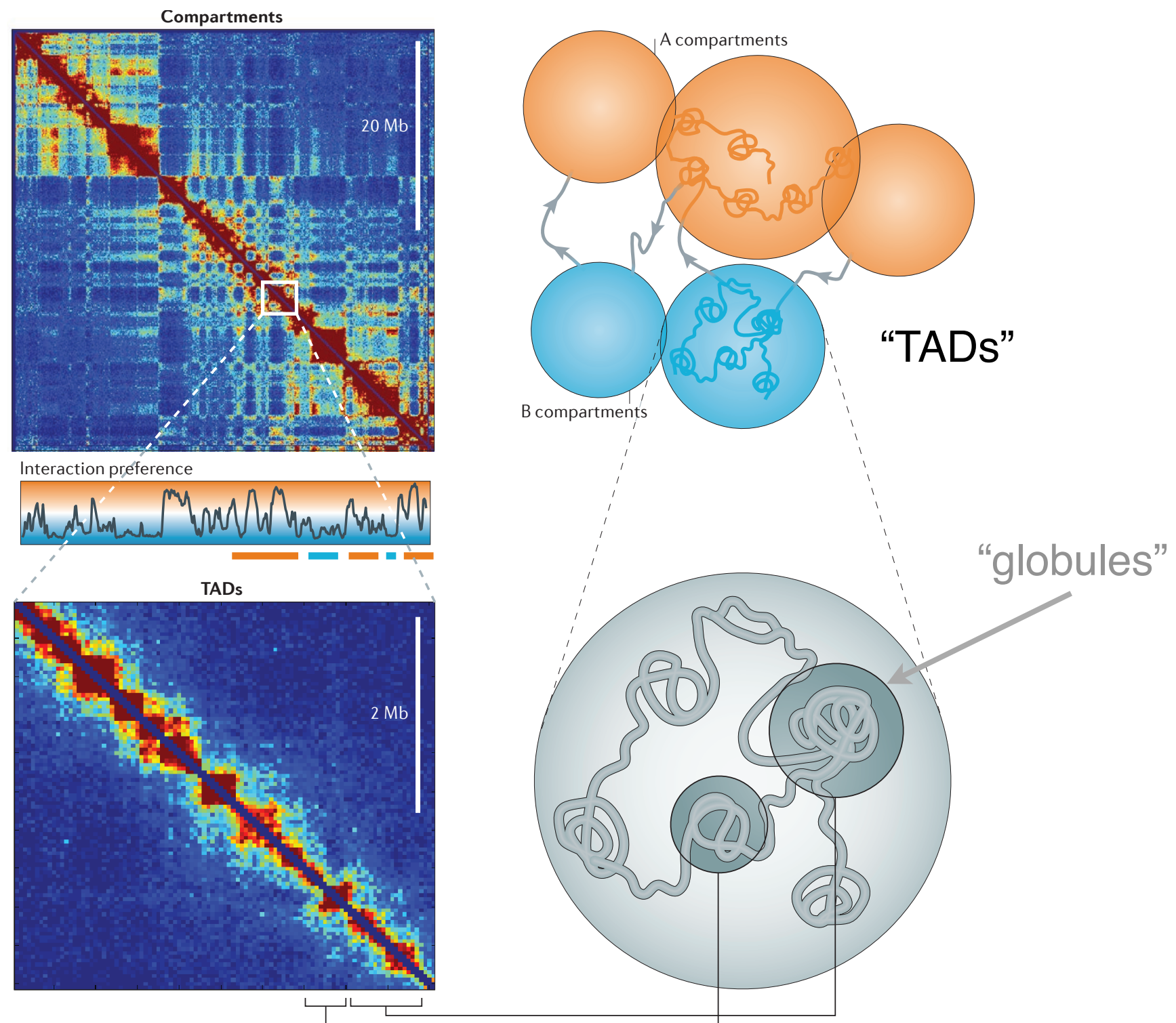
Resolution Gap

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



Genome Organization

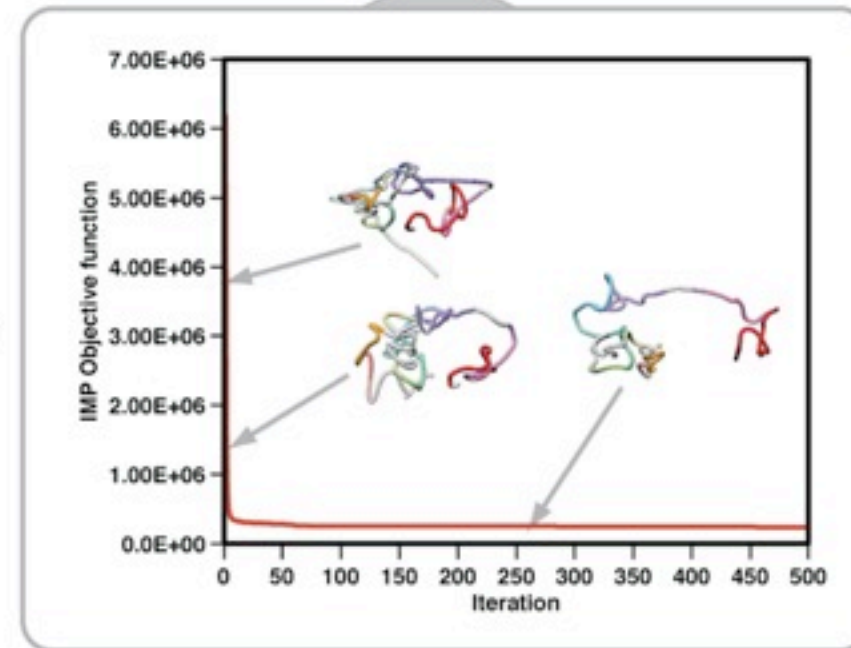
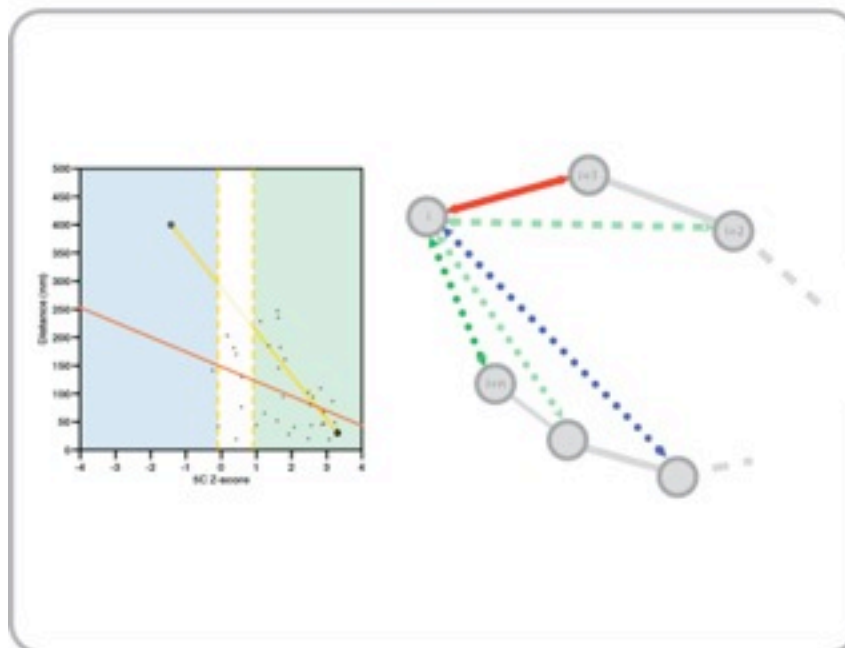
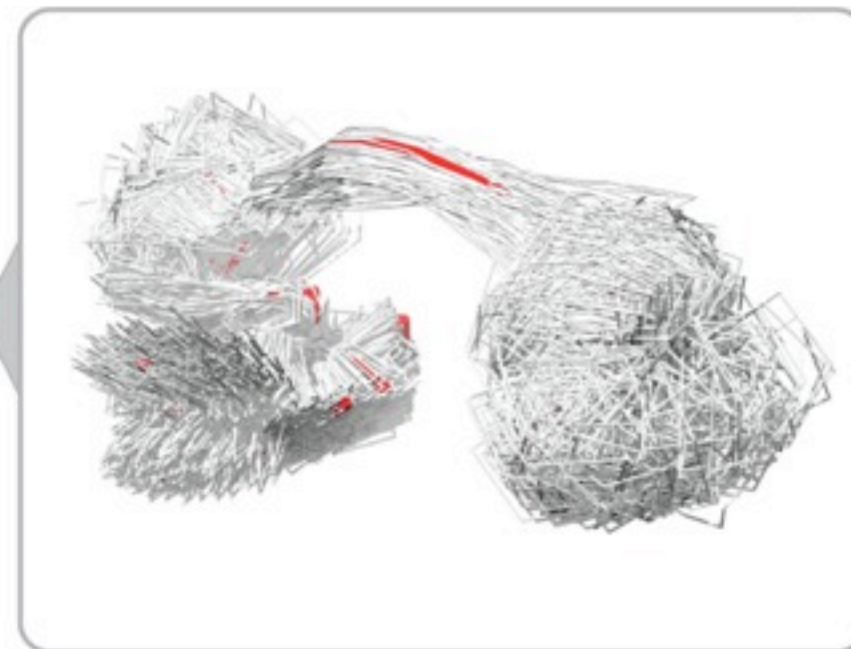
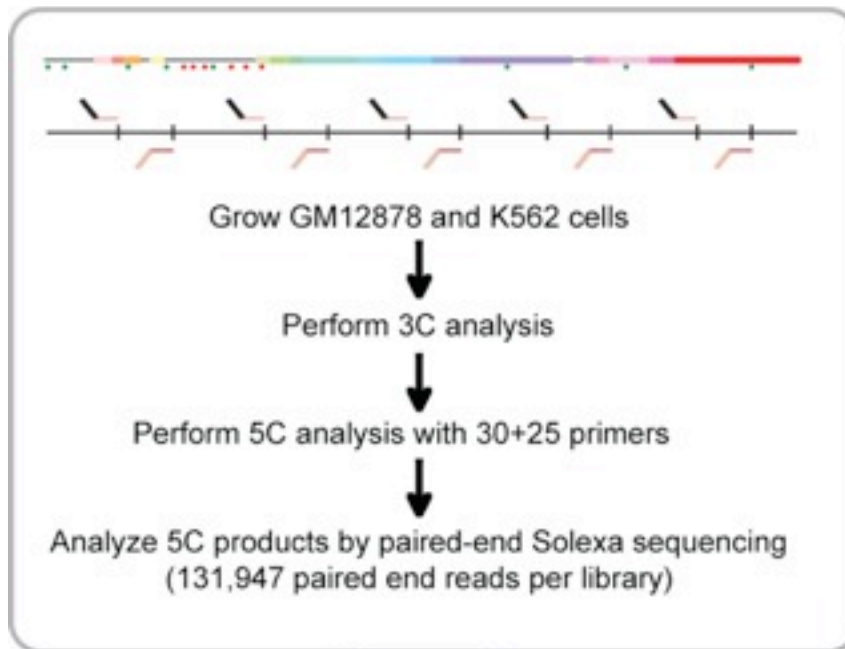
Dekker, J., Marti-Renom, M. A. & Mirny, L. A. Nat Rev Genet (2013)



Hybrid Method

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

Experiments

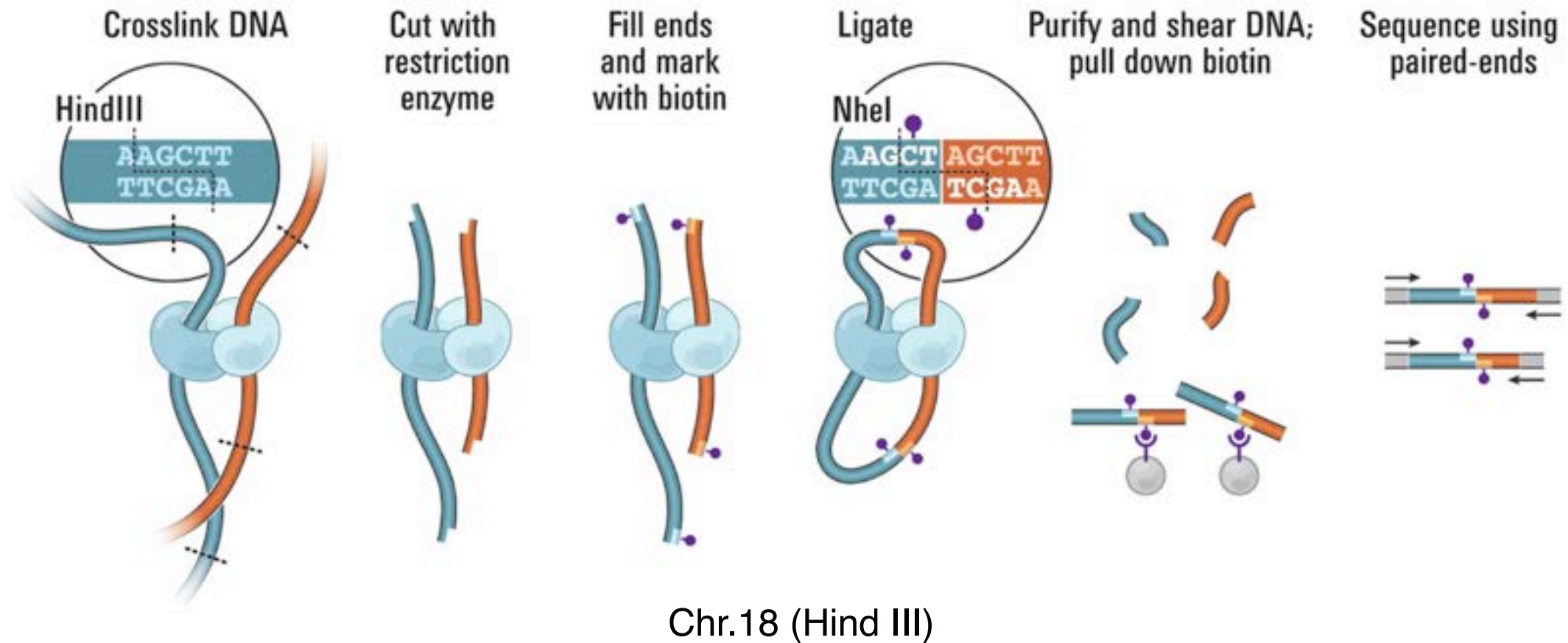


Computation

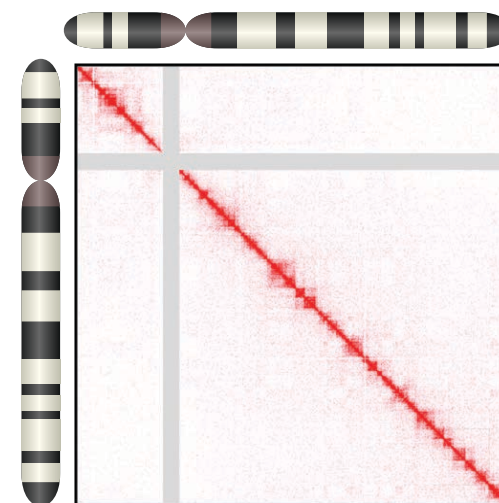
Hi-C technology

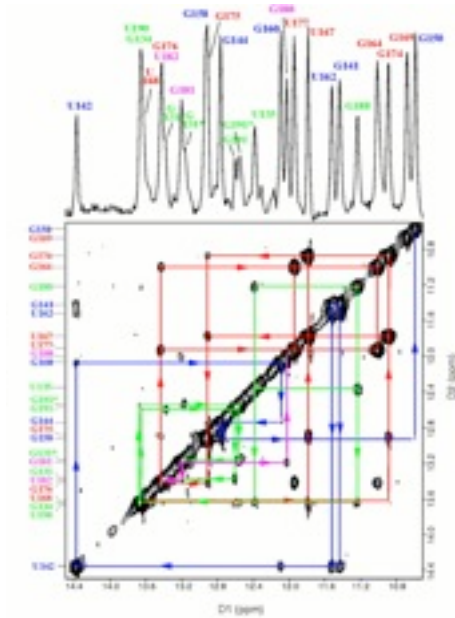
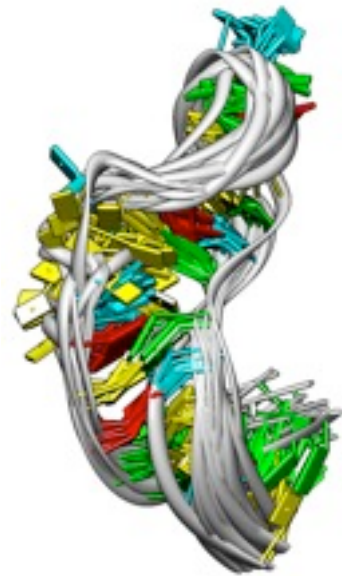
Lieberman-Aiden, E. et al. Science 326, 289–293 (2009).

<http://3dg.umassmed.edu>

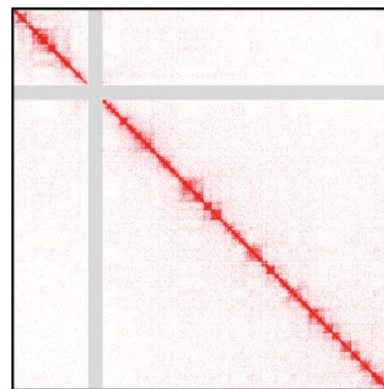
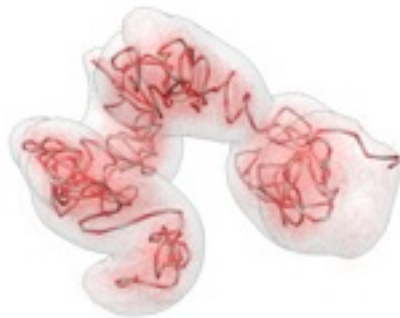


Chr.18 (Hind III)





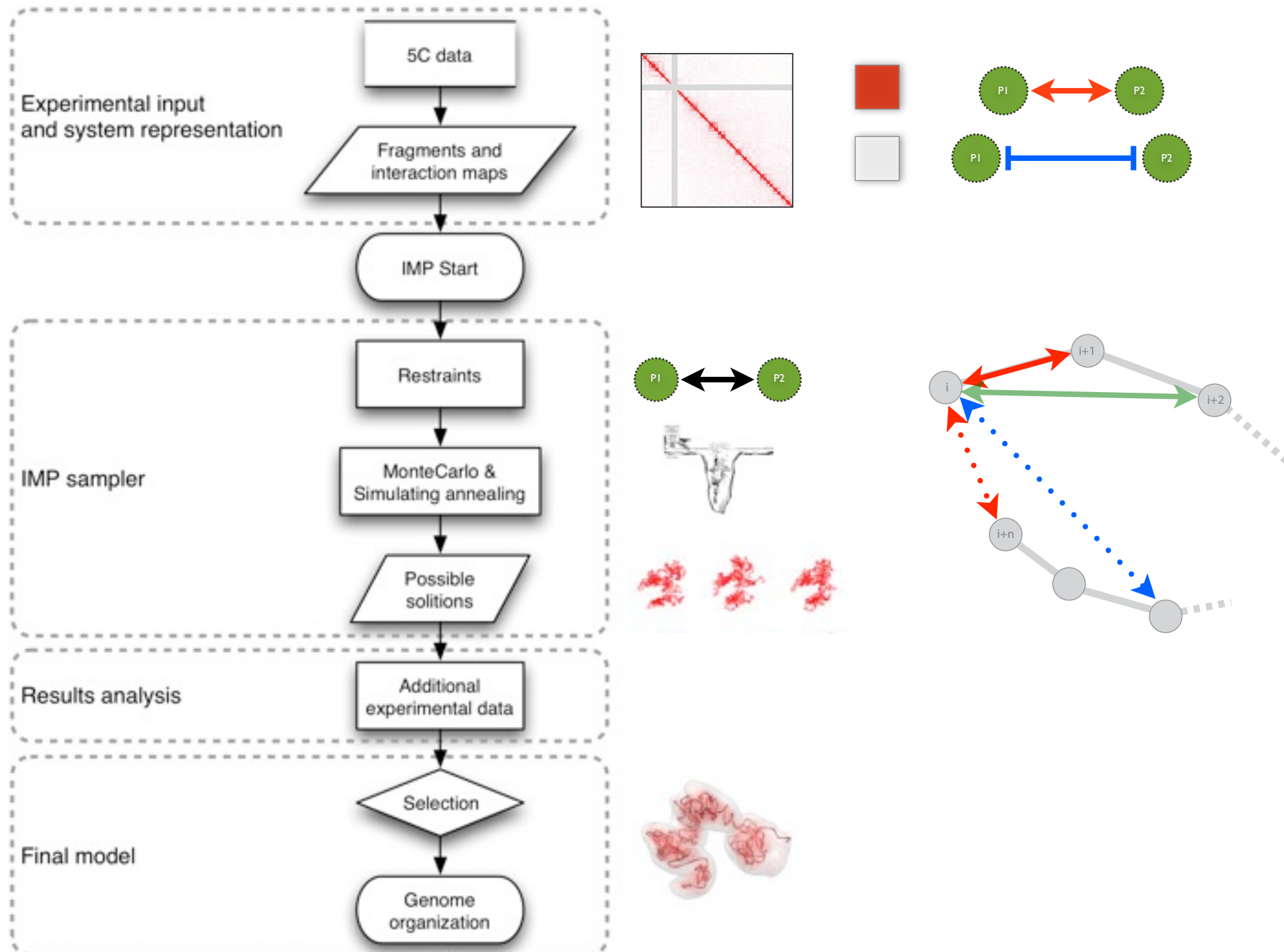
Biomolecular structure determination 2D-NOESY data



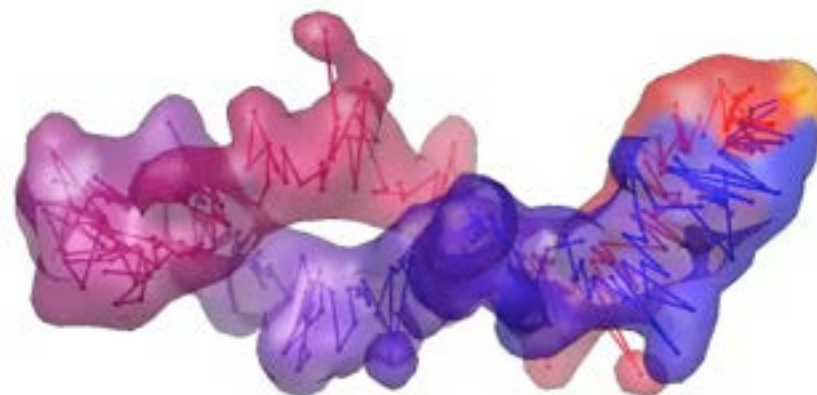
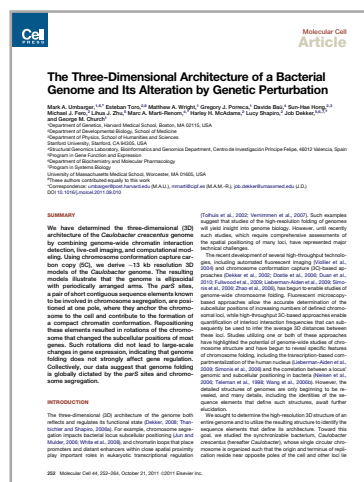
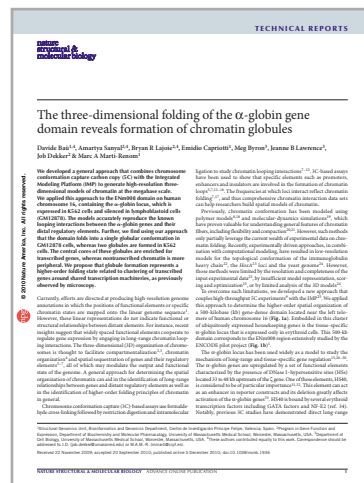
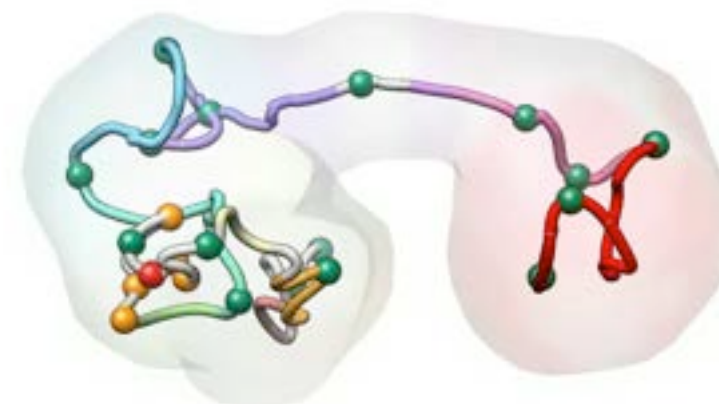
Chromosome structure determination 3C-based data

Integrative Modeling

<http://www.integrativemodeling.org>



Baù, D. et al. Nat Struct Mol Biol (2011).
Umberger, M. A. et al. Mol Cell (2011).



On TADs and hormones



Davide Baù



François le Dily



Miguel Beato

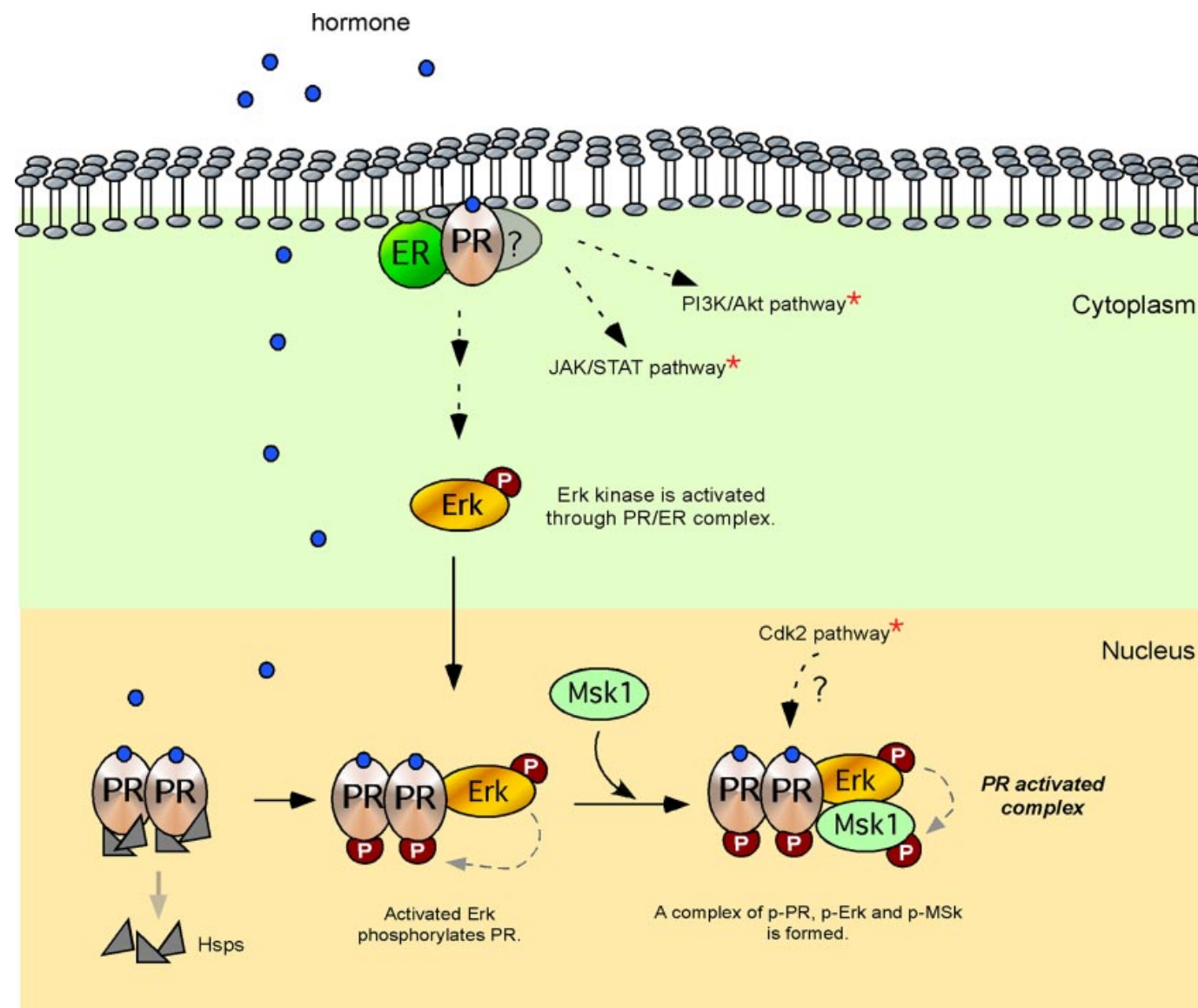
Chromatin and Gene Expression Group (CRG)



Guillaume Filion

Genome Architecture Group (CRG)

Progesterone-regulated transcription in breast cancer

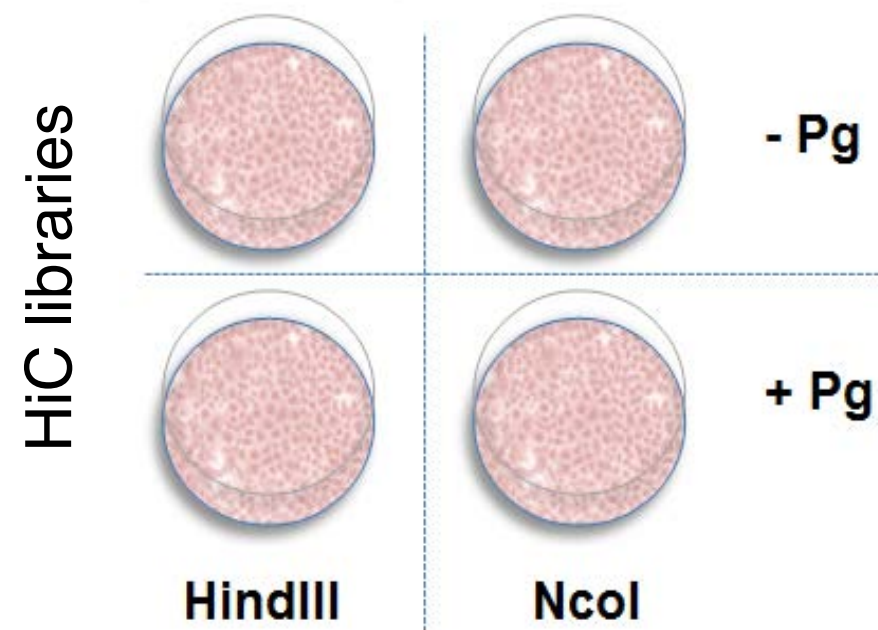


Vicent *et al* 2011, Wright *et al* 2012, Ballare *et al* 2012

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

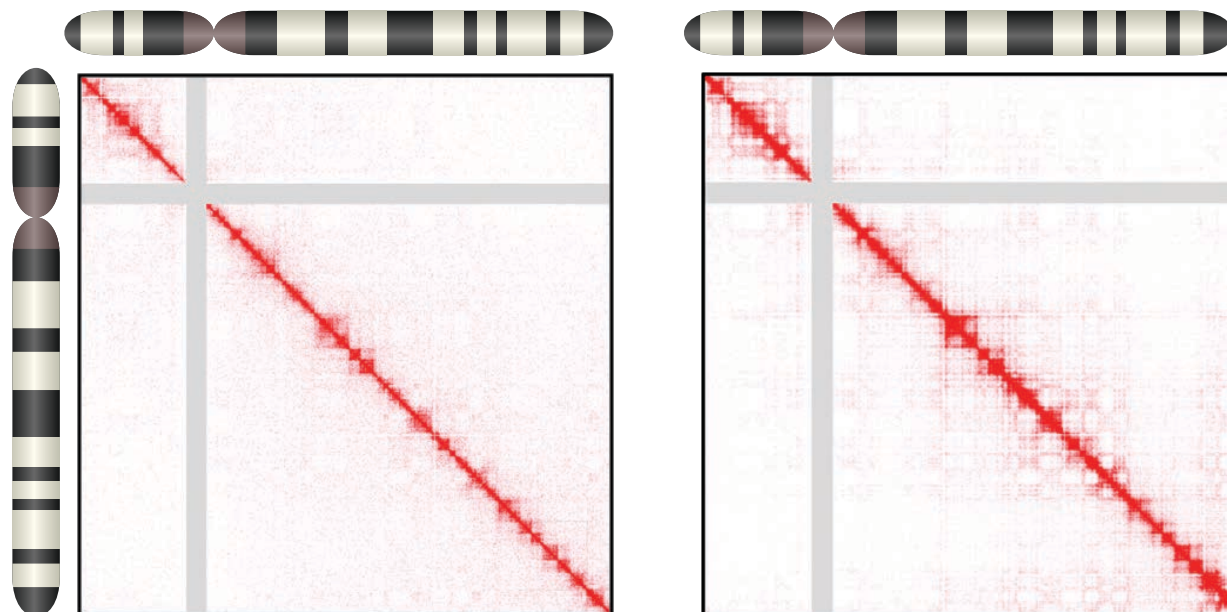
Regulation in 3D?

Experimental design



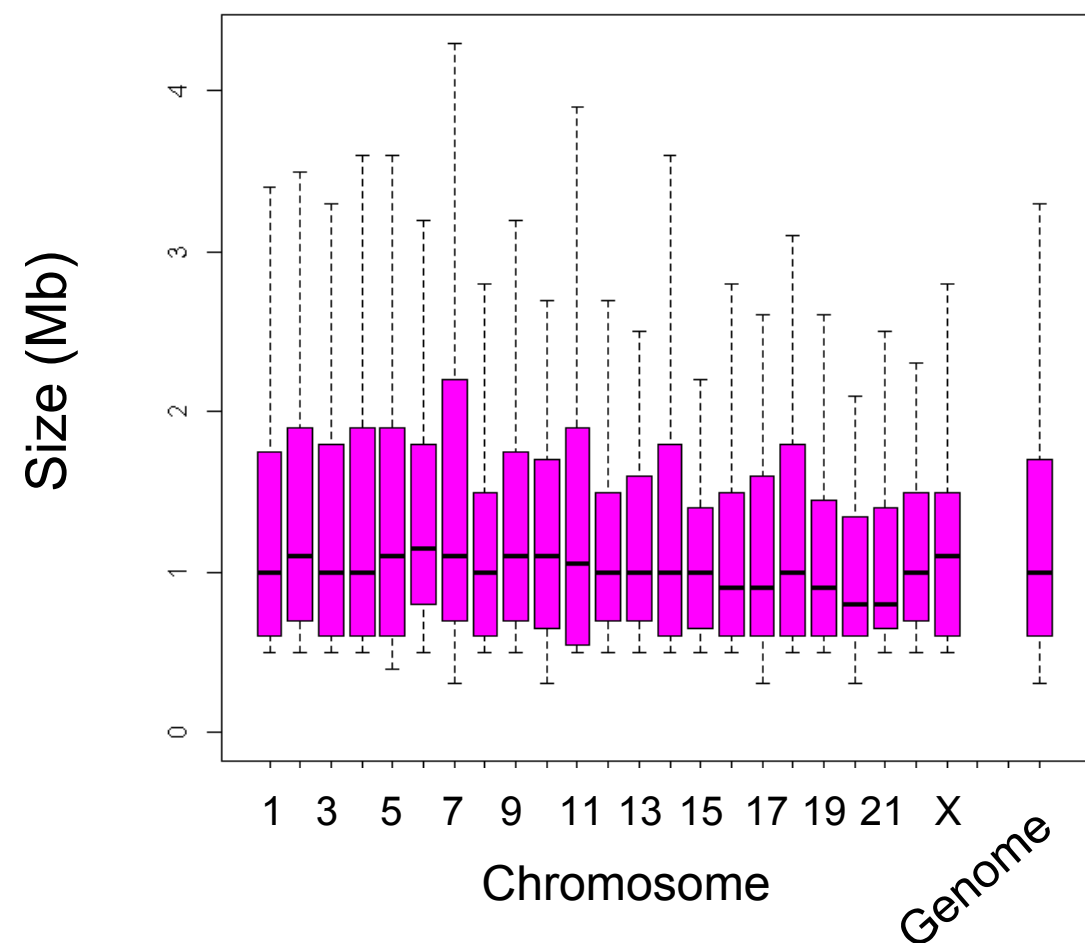
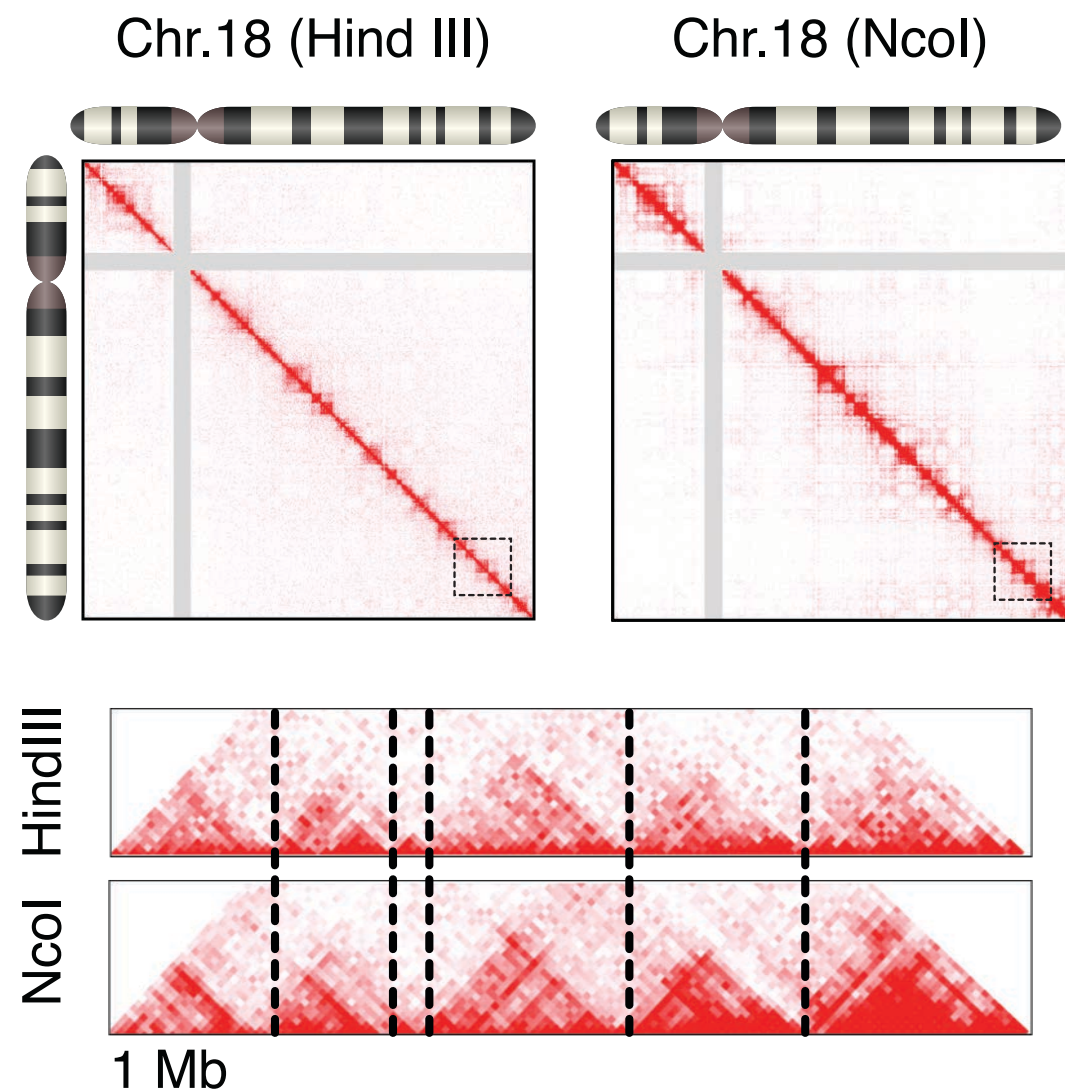
Chr.18 (Hind III)

Chr.18 (NcoI)



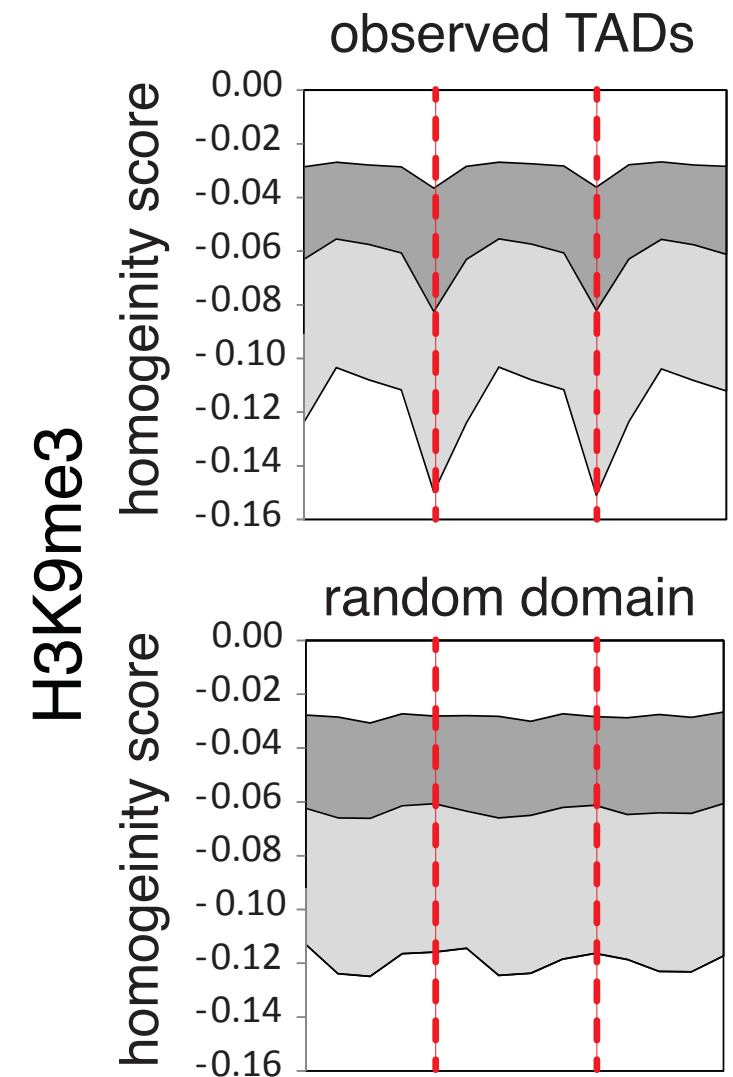
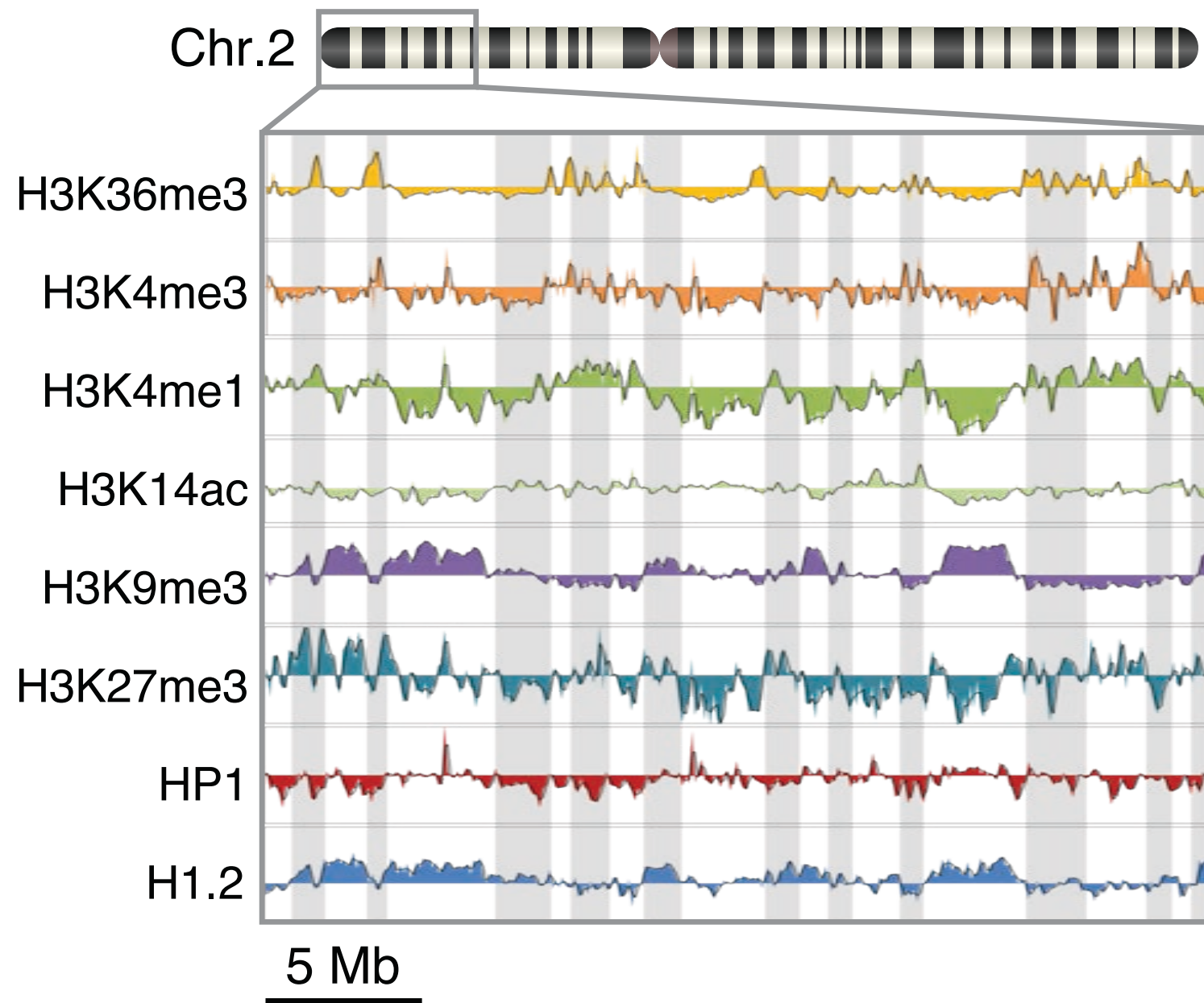


Chromosomes are organized into Topologically Associated Domains (TADs)

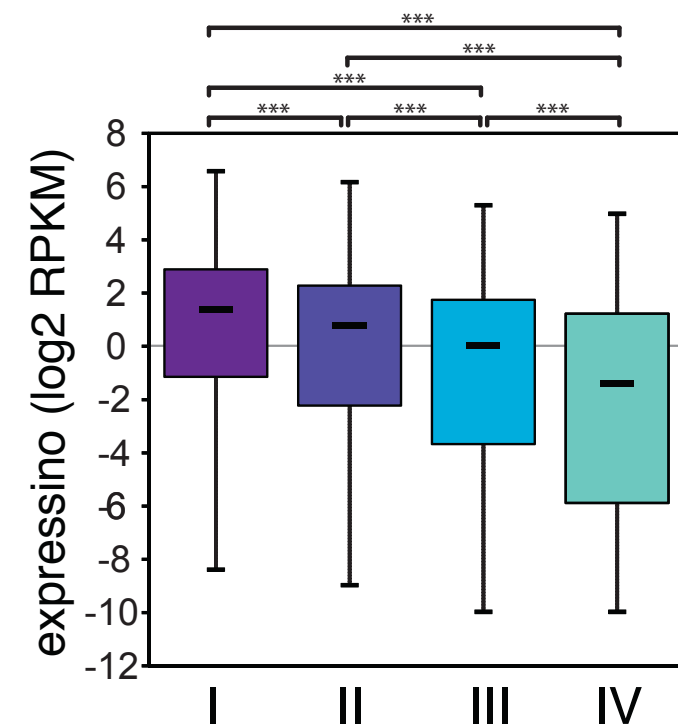
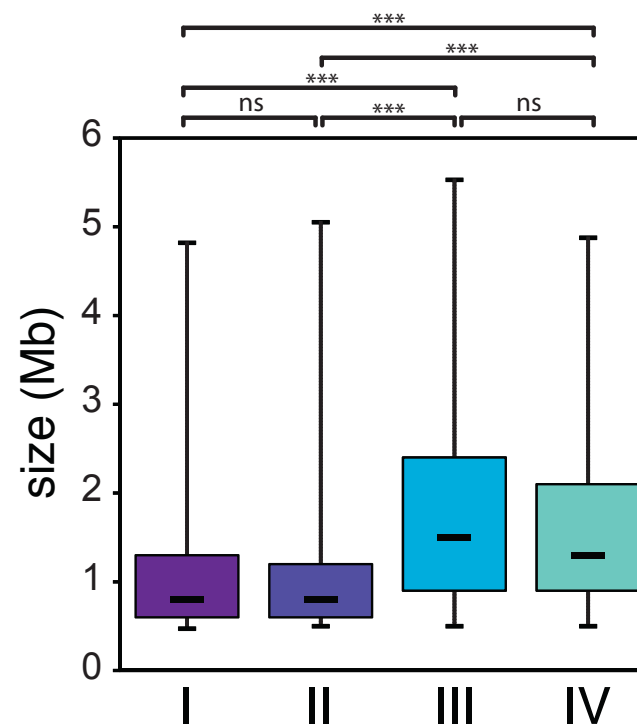
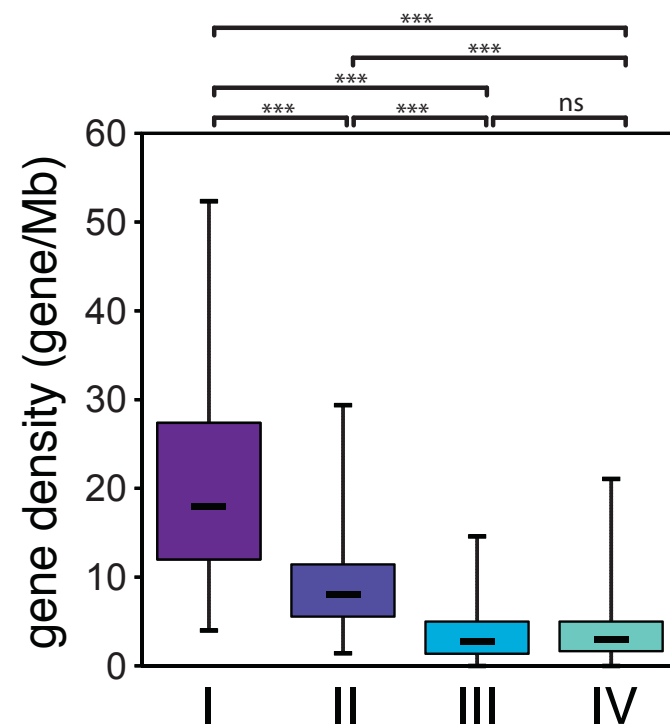
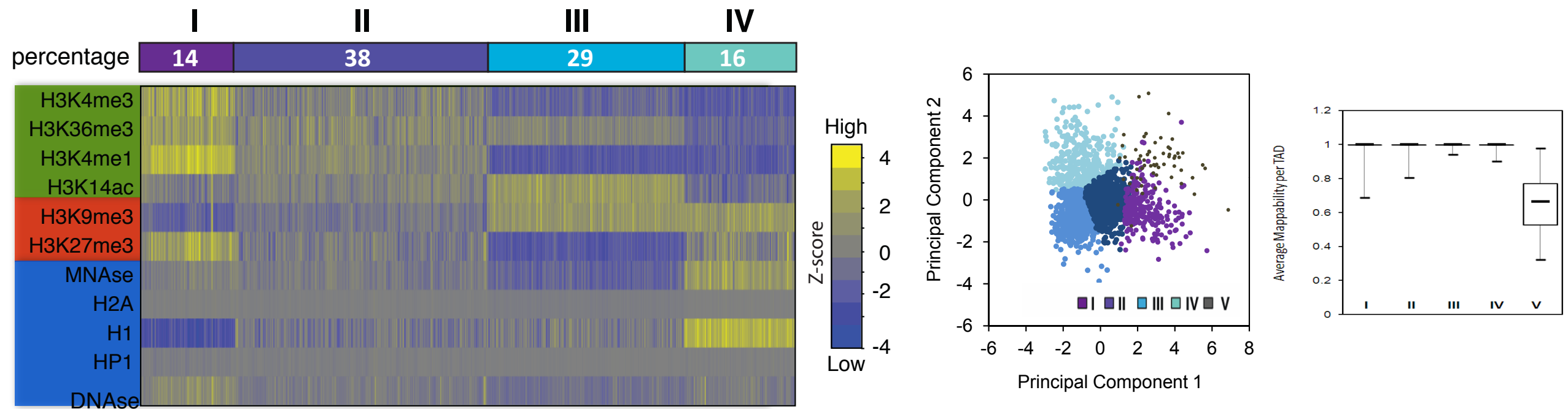




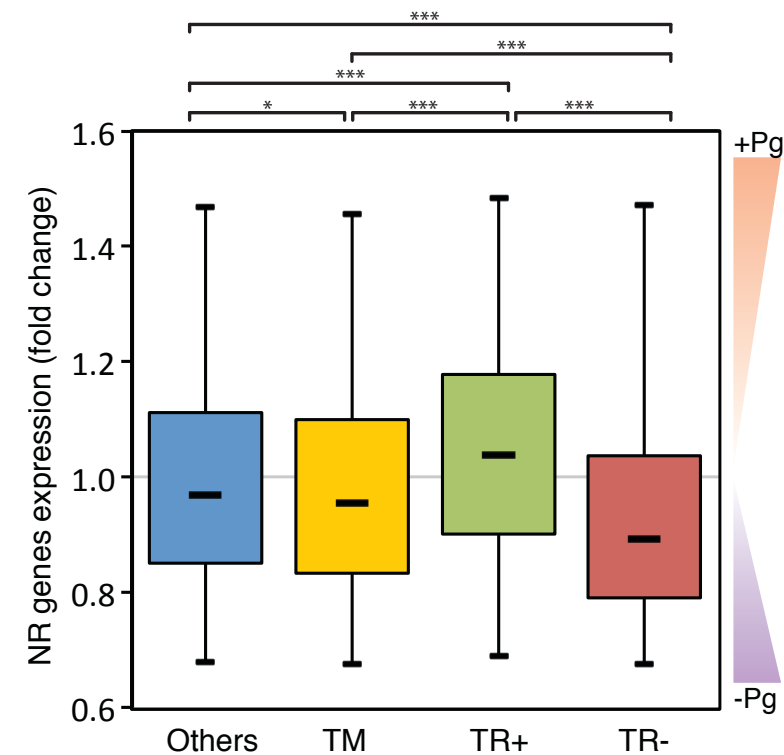
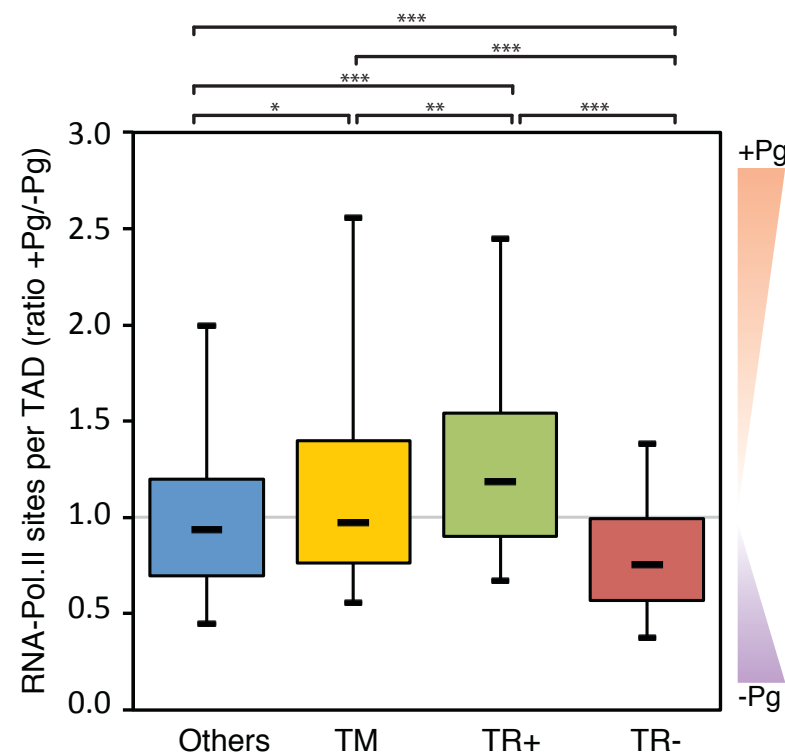
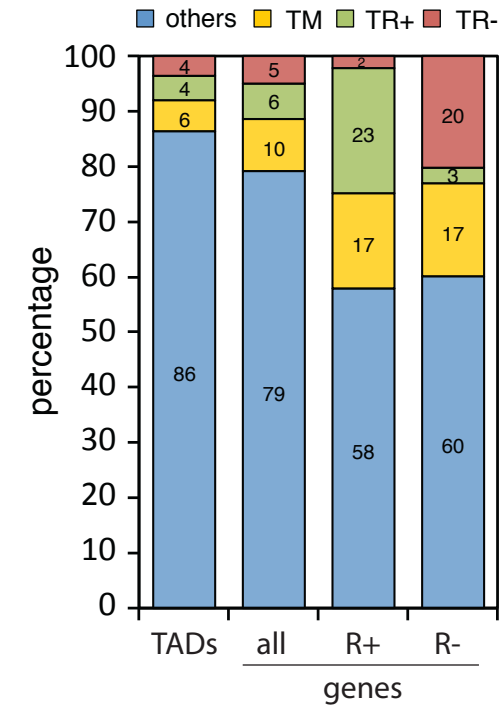
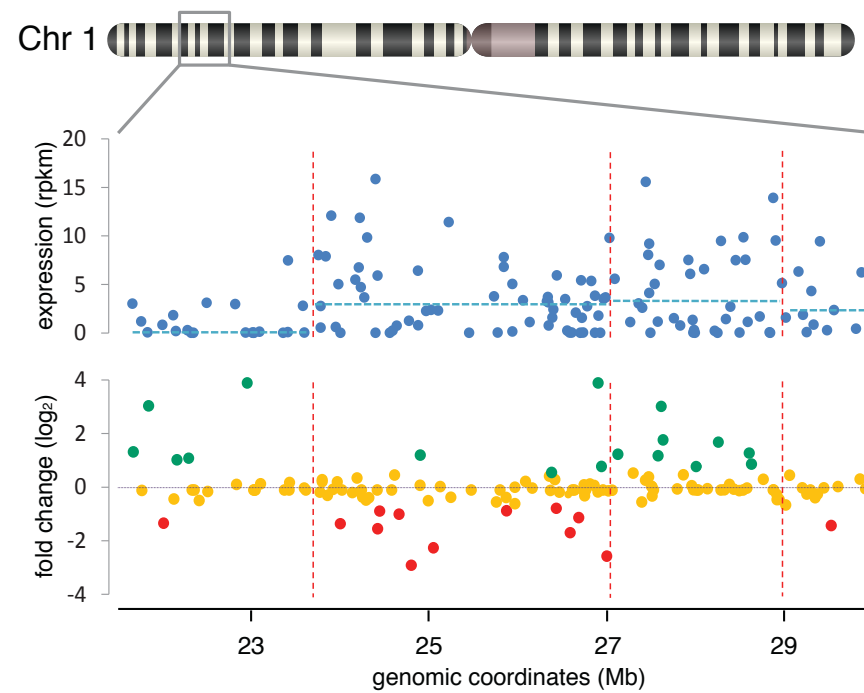
Are TADs homogeneous?



Do TADs have specific chromatin signatures?



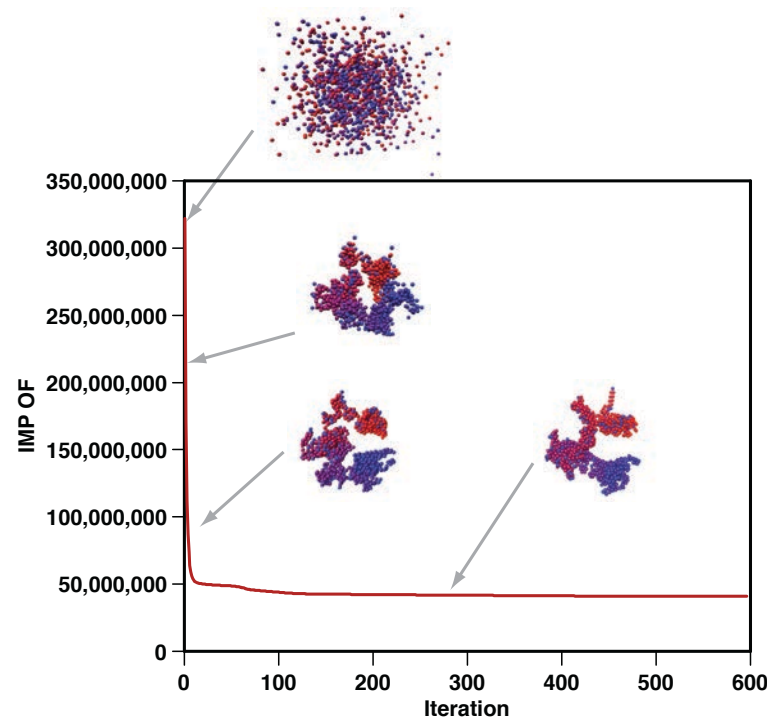
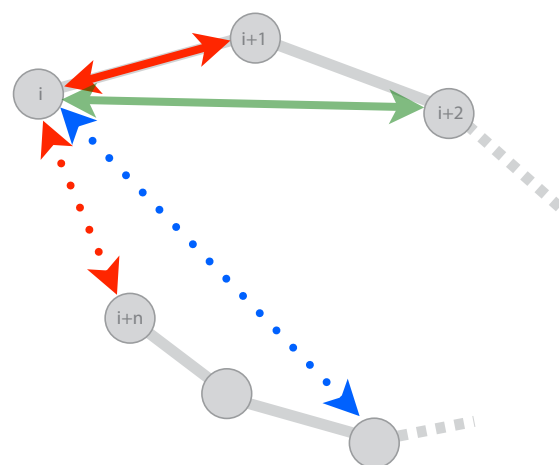
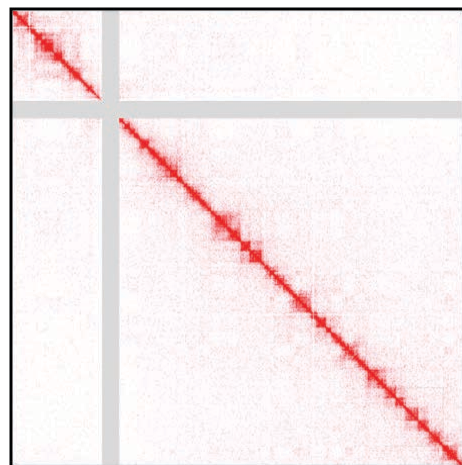
Do TADs respond differently to Pg treatment?



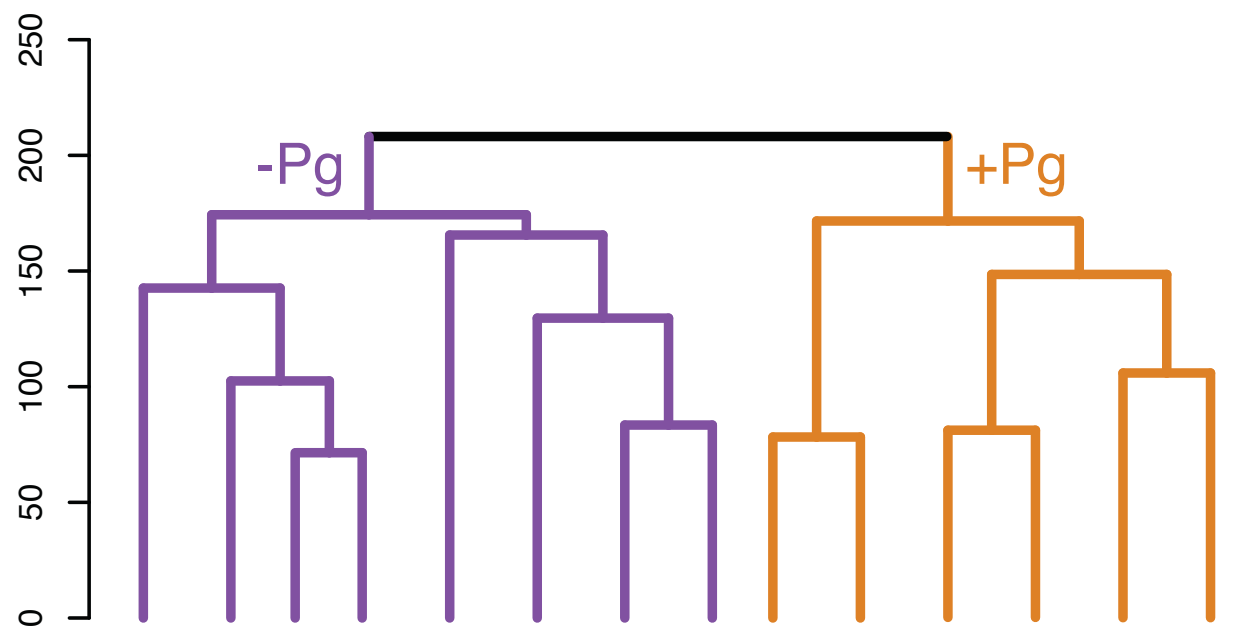


Modeling 3D TADs

15 genomic regions with 105 TADs in total



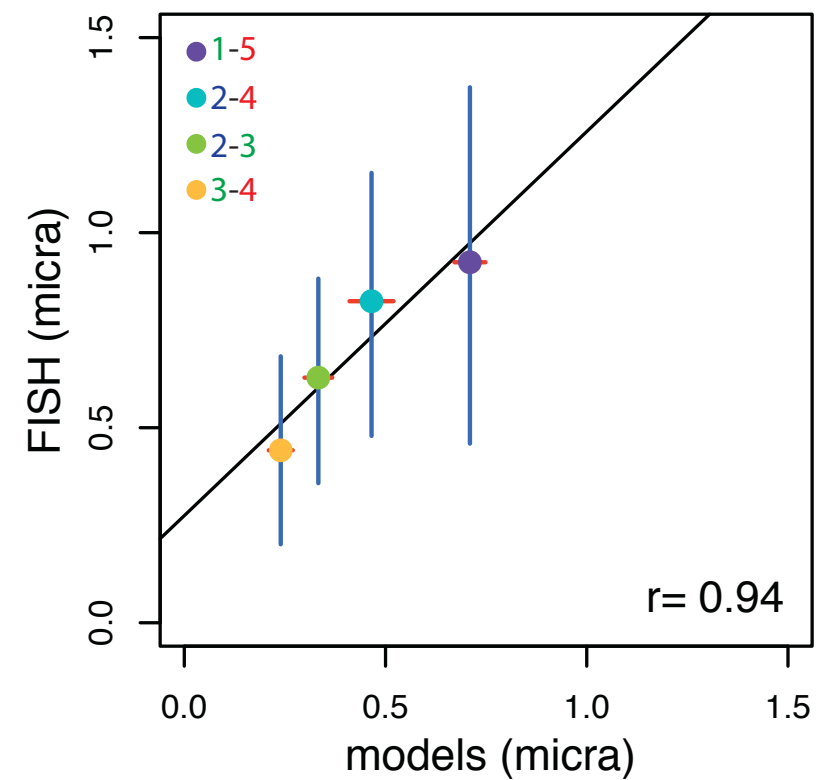
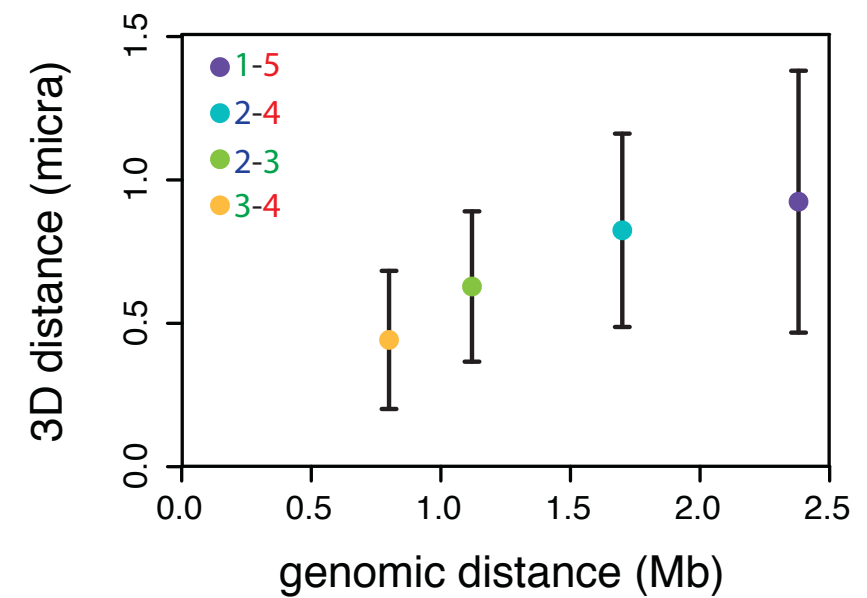
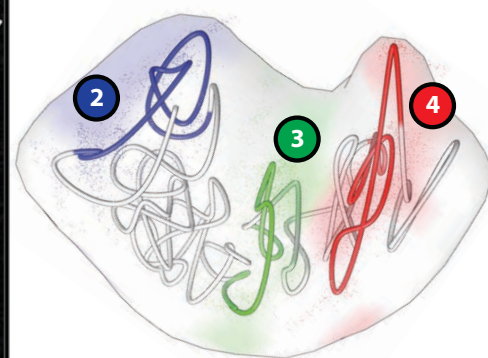
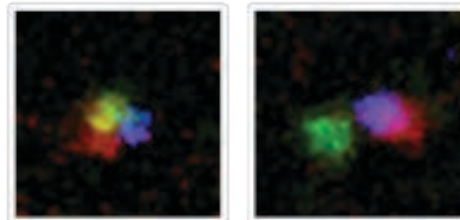
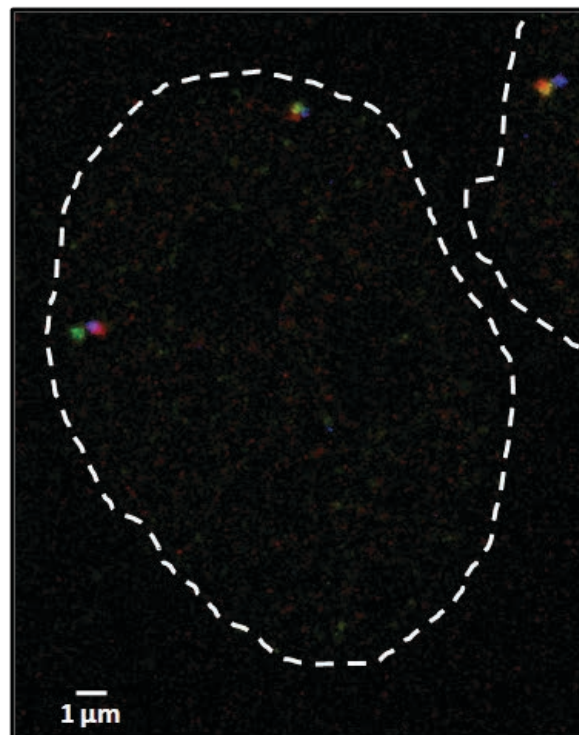
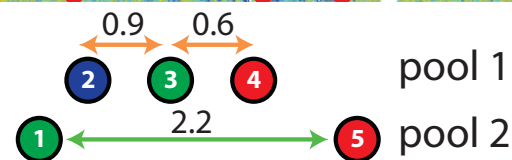
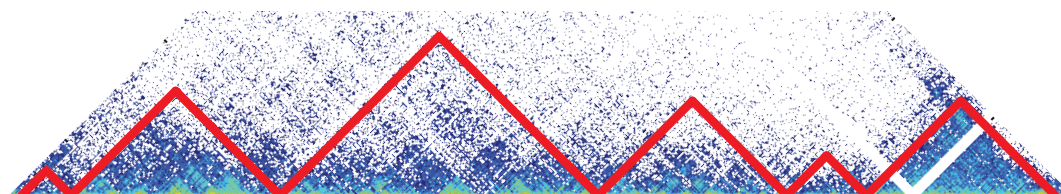
dRMSD (nm)





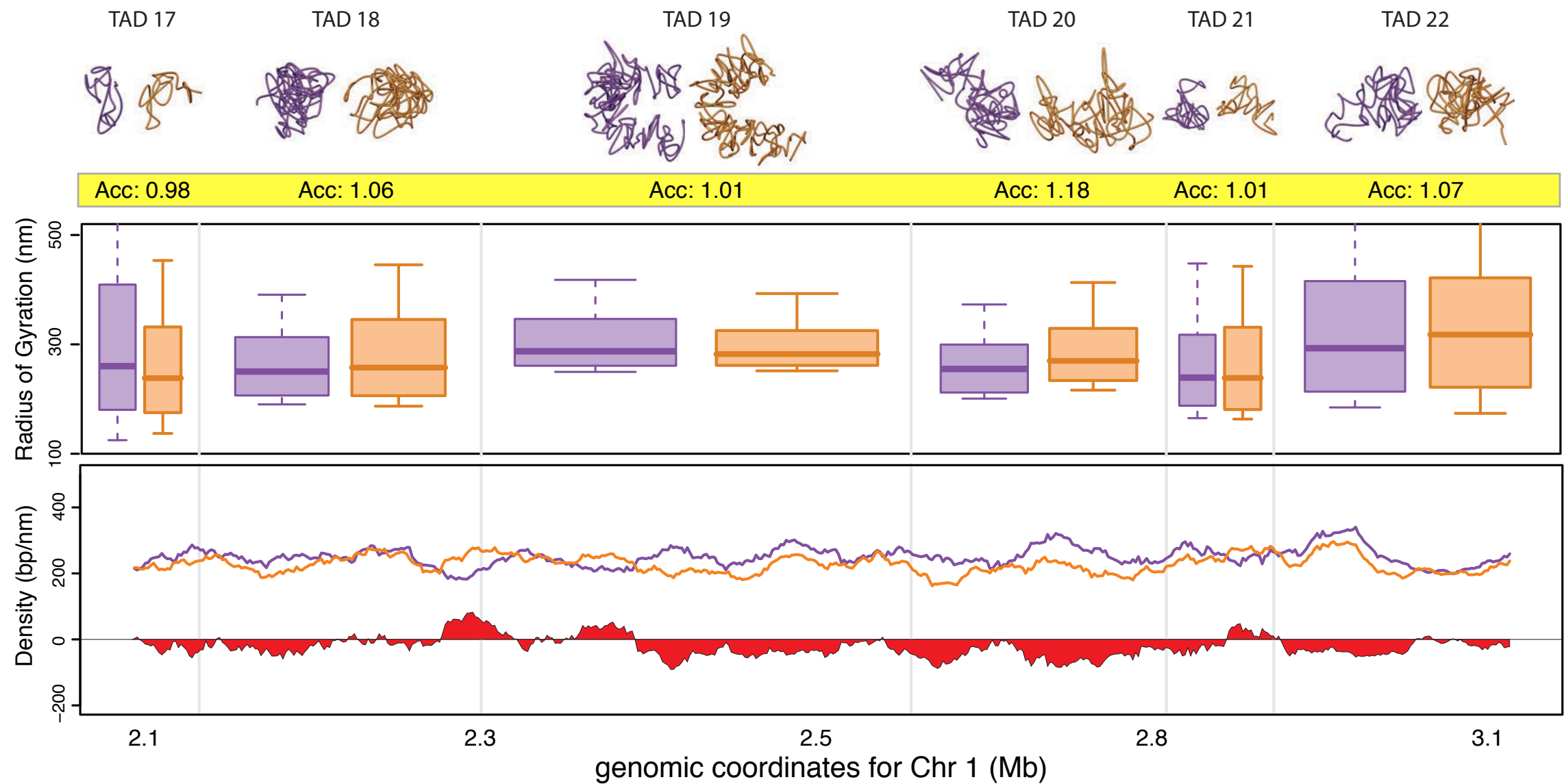
Model Accuracy

Chr1:21000000-31400000
6 TADs



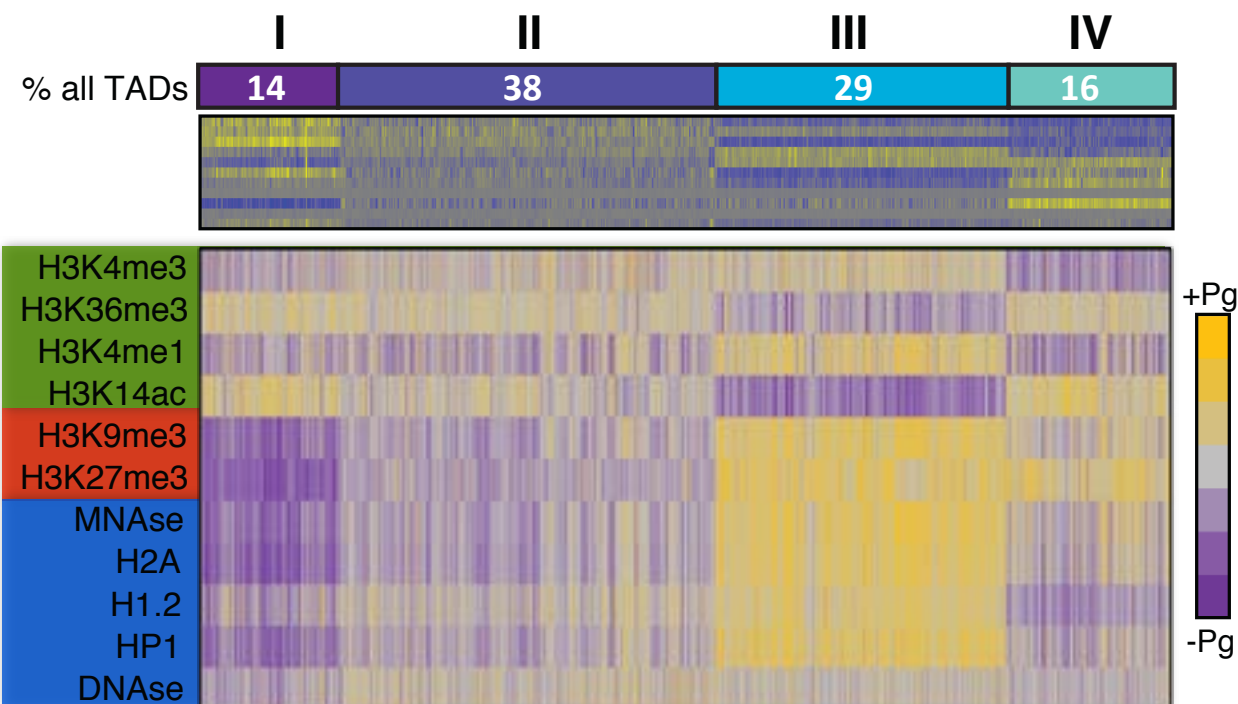
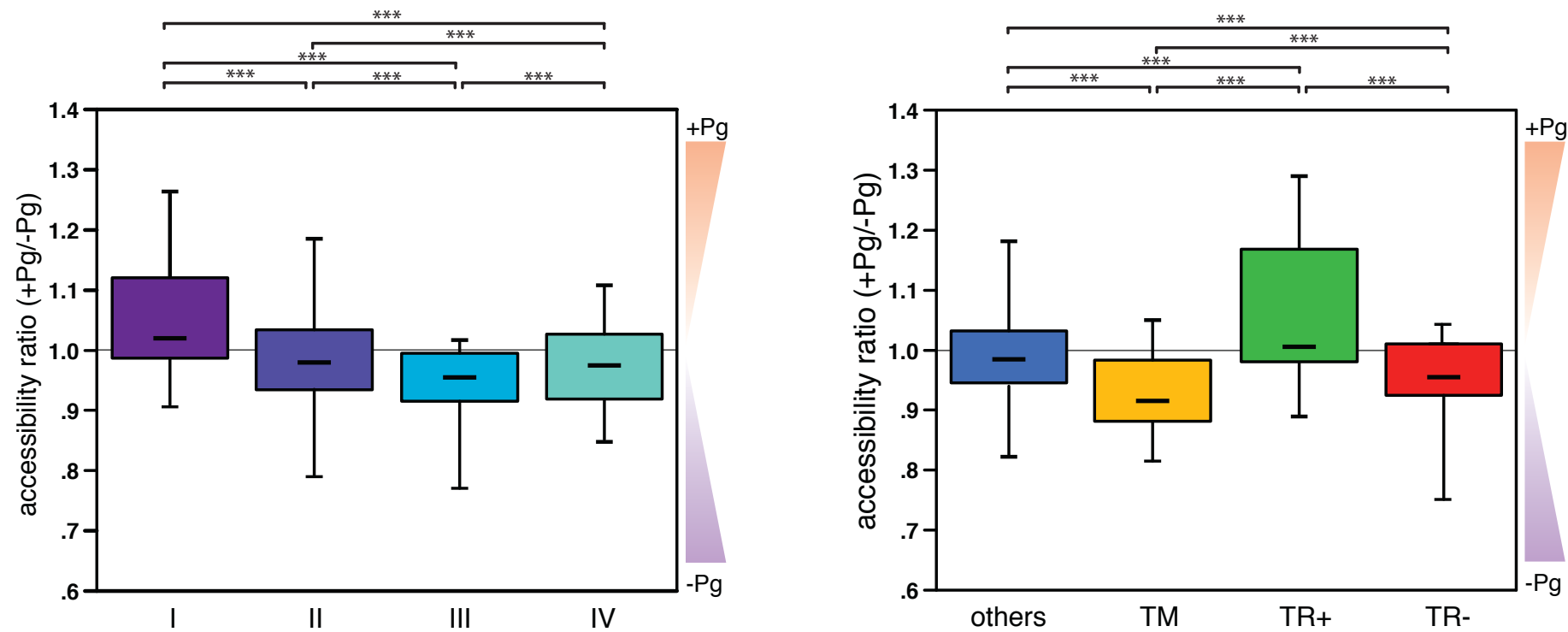
Accessibility changes of TADs

Chr1:21000000-31400000
6 TADs

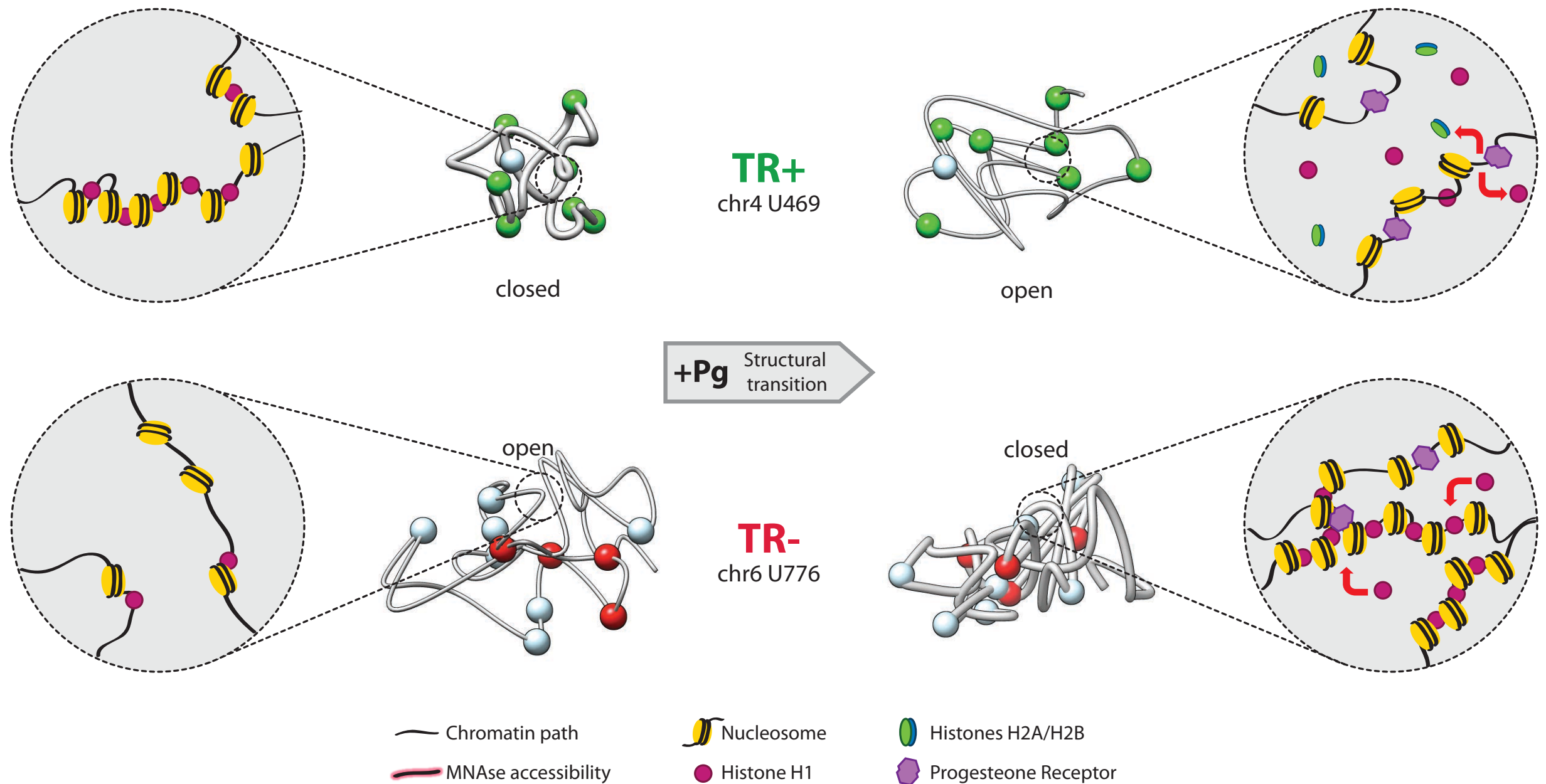


TADs respond differently

15 genomic regions with 105 TADs in total



Model for TAD regulation



Acknowledgments



Davide Baù

François le Dily

François Serra



Miguel Beato

Chromatin and Gene Expression Group (CRG)



Guillaume Filion

Genome Architecture Group (CRG)

<http://marciuslab.org>
<http://integrativemodeling.org>
<http://cnag.cat> · <http://crg.cat>

