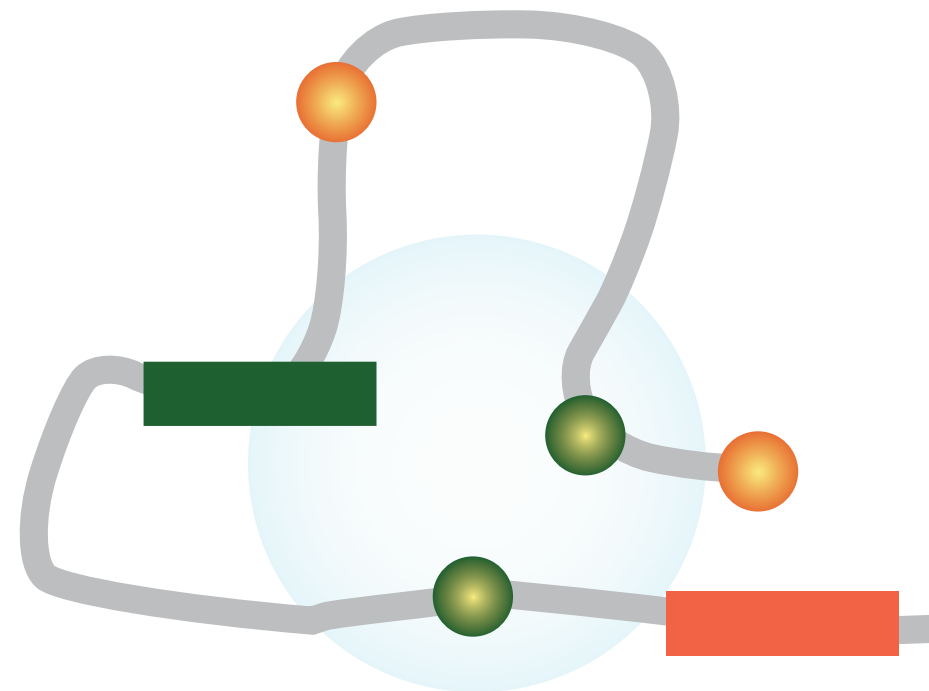
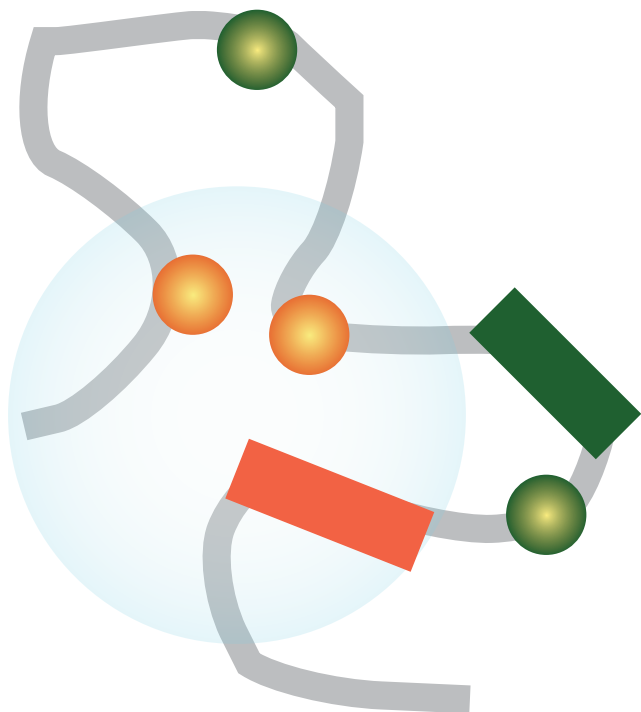


Modeling 3D genomes:
**Hormone induced structural
reorganization of TADs in the
breast cancer genome**

Marc A. Marti-Renom

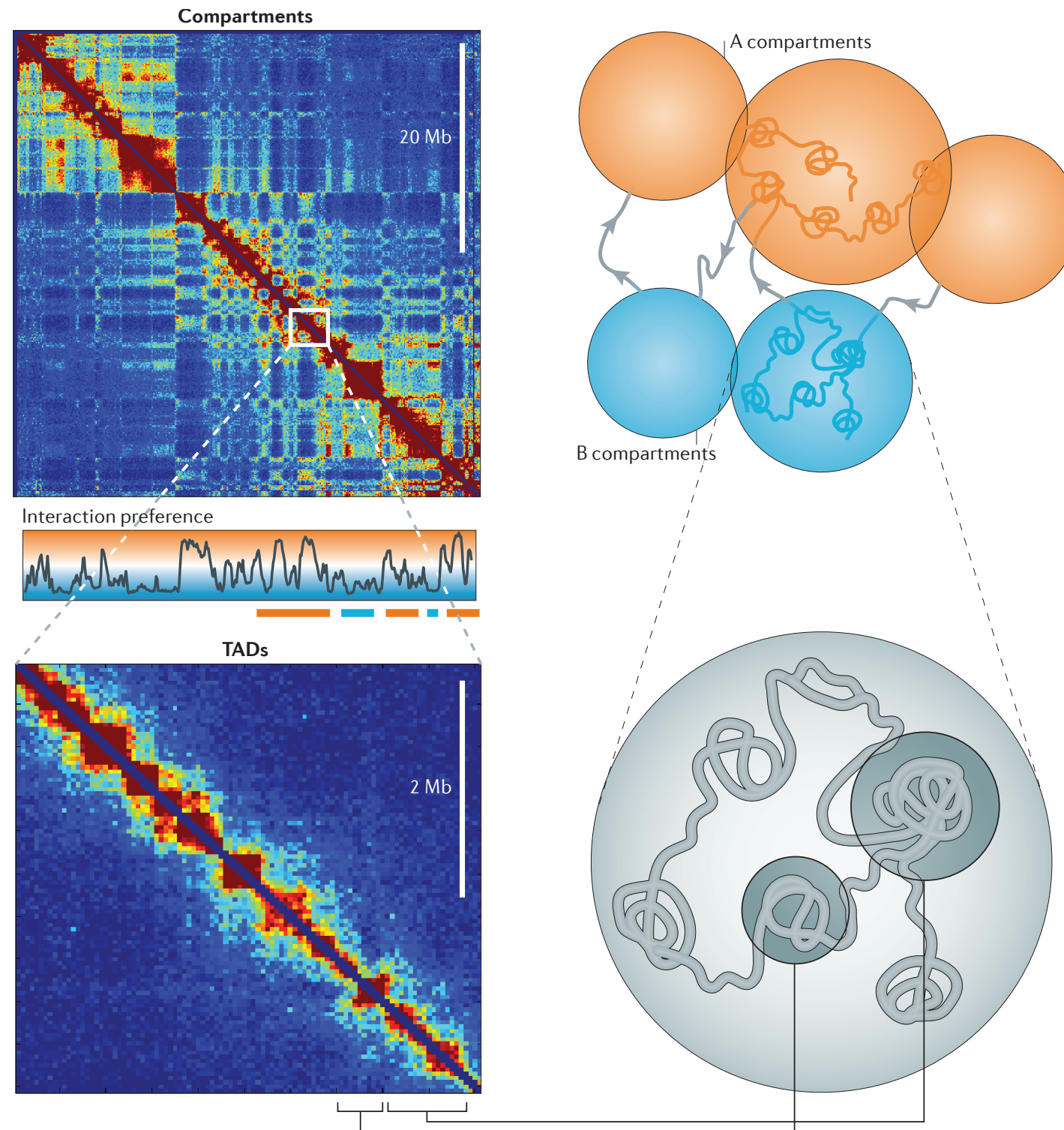
*Genome Biology Group (CNAG)
Structural Genomics Group (CRG)*

Complex genome organization



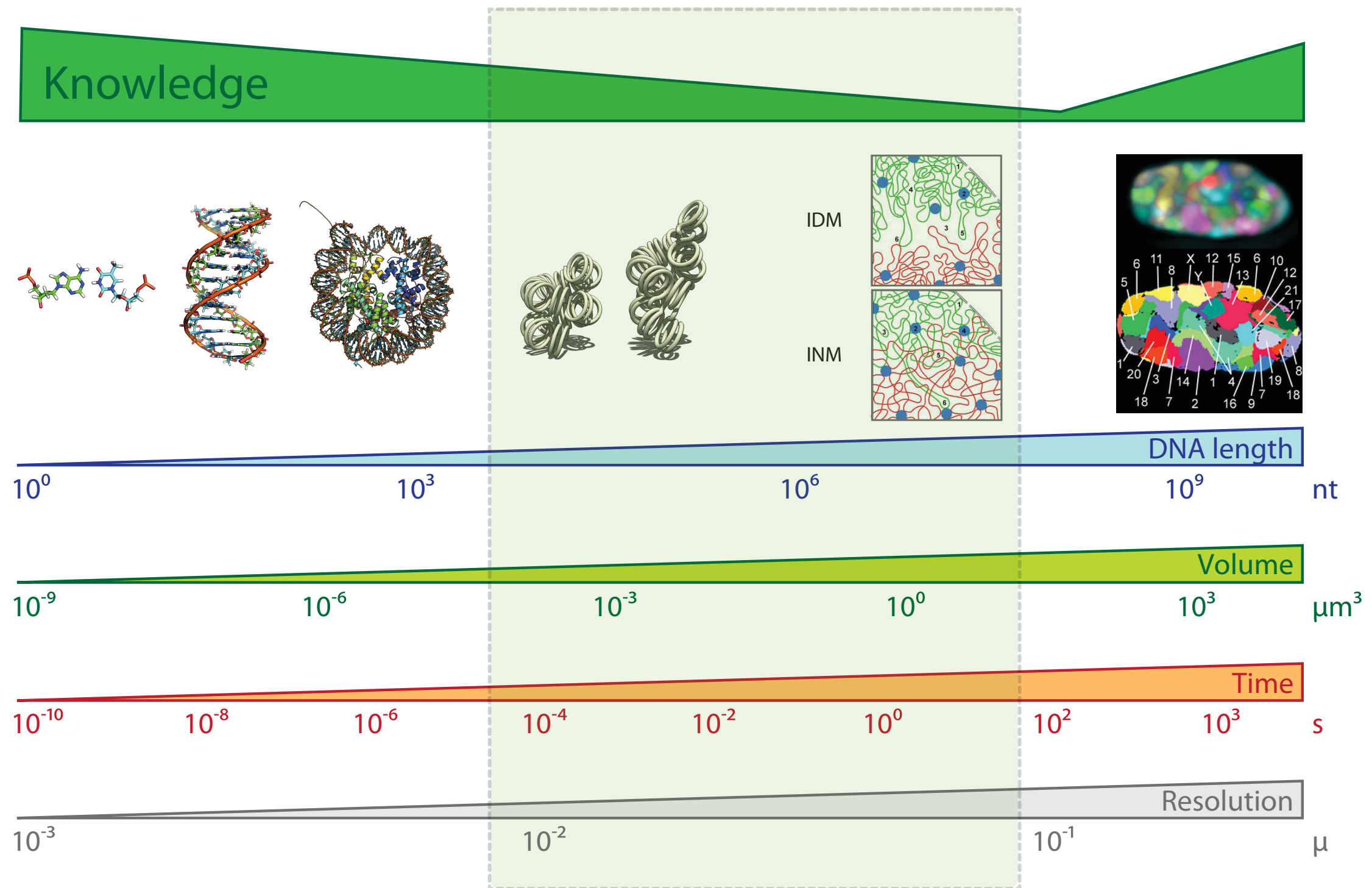
Genome Organization

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



Resolution Gap

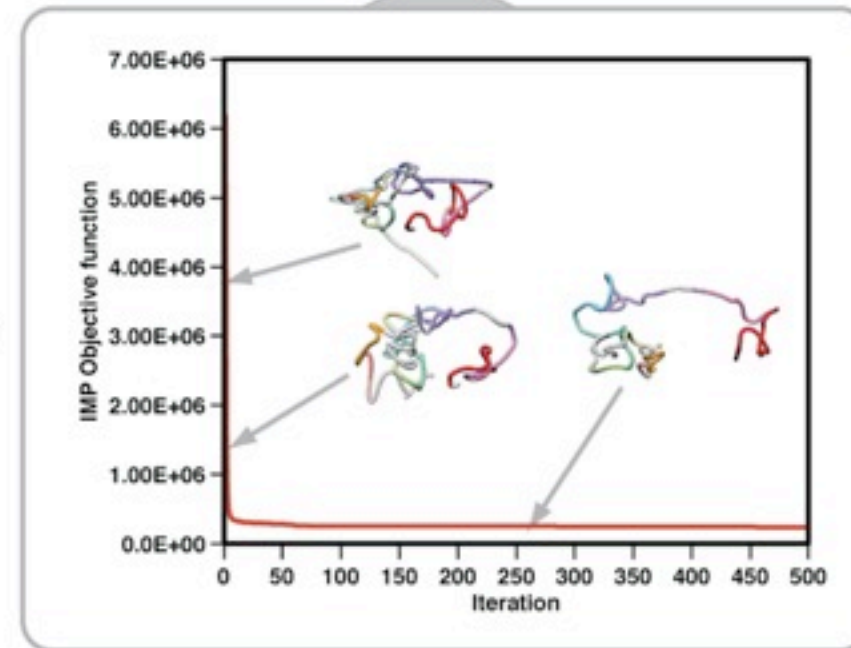
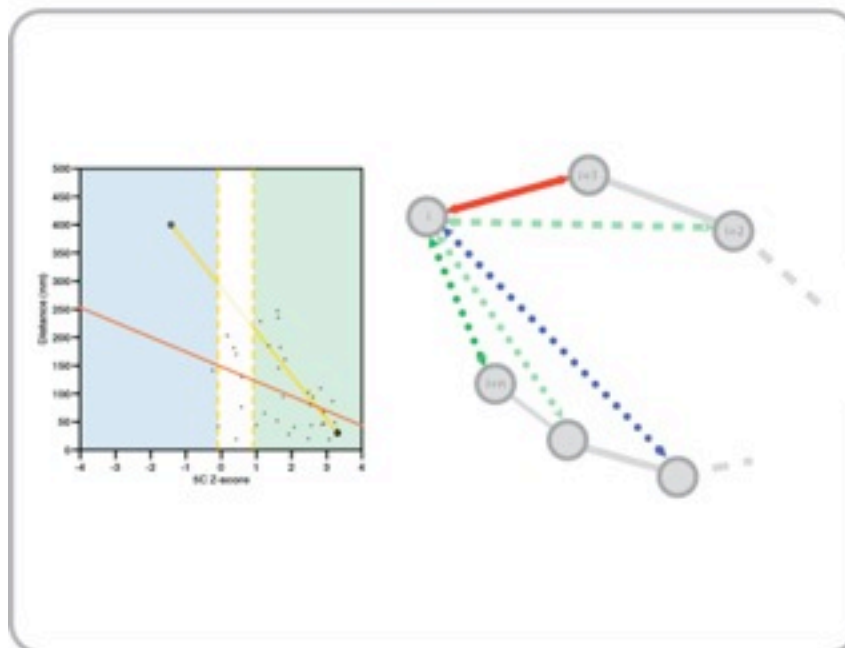
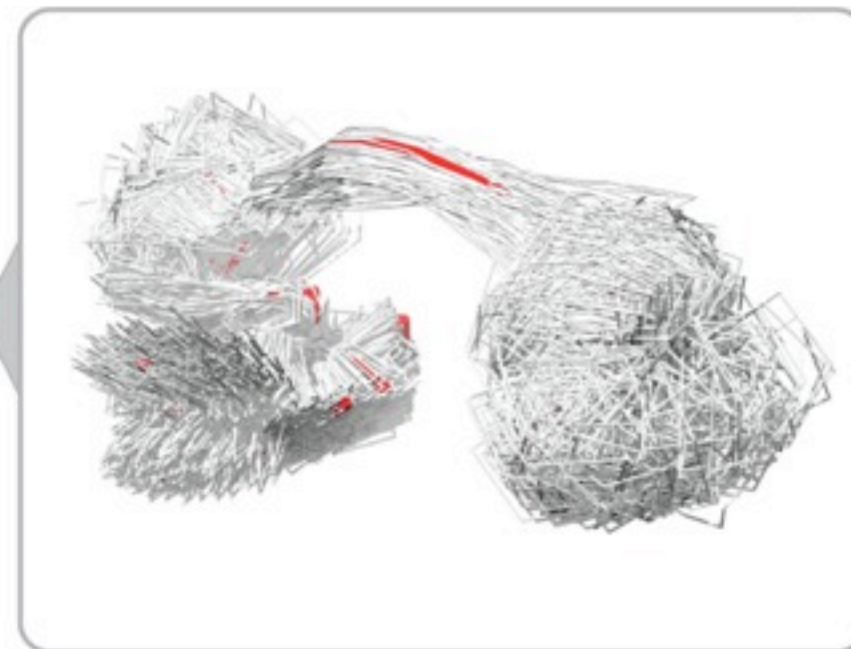
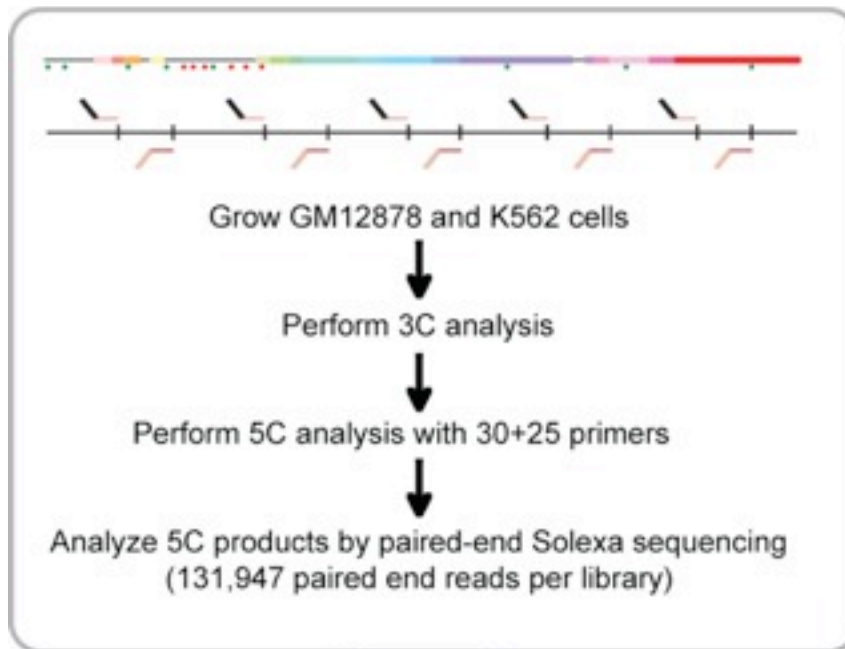
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)



Hybrid Method

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

Experiments

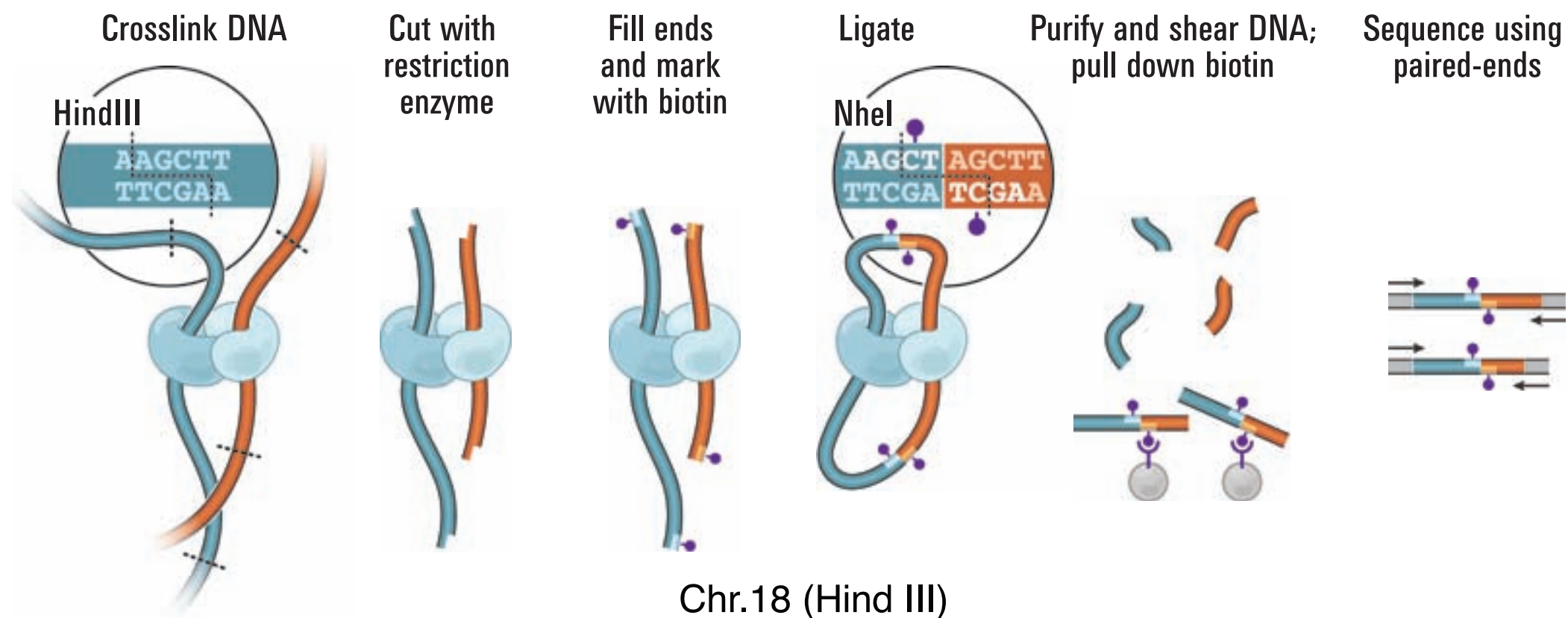


Computation

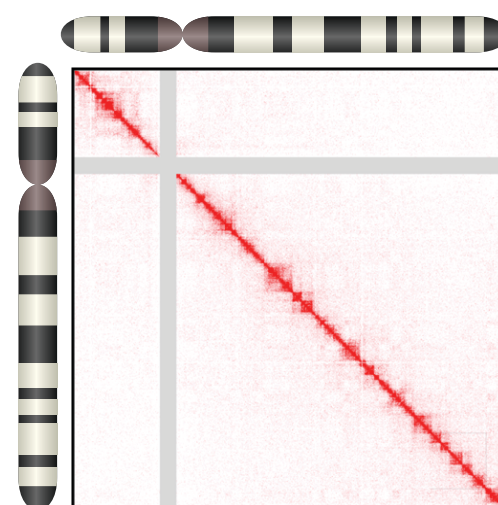
Hi-C technology

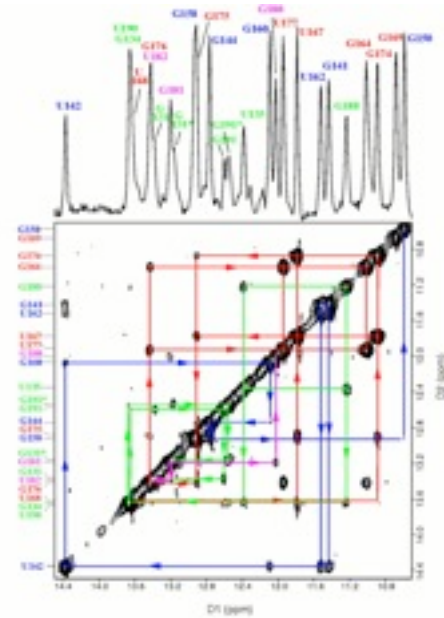
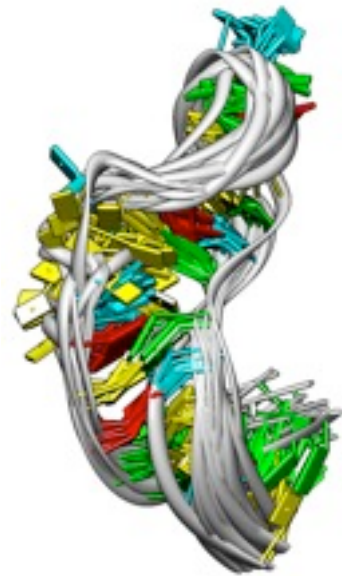
Lieberman-Aiden, E. et al. Science 326, 289–293 (2009).

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

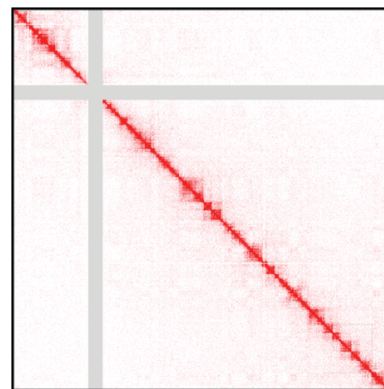
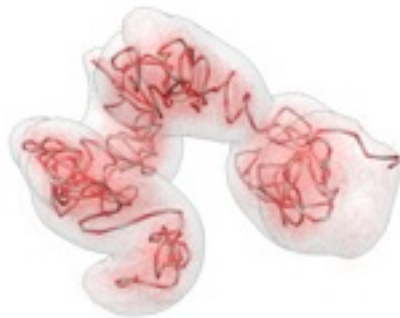


Chr.18 (Hind III)





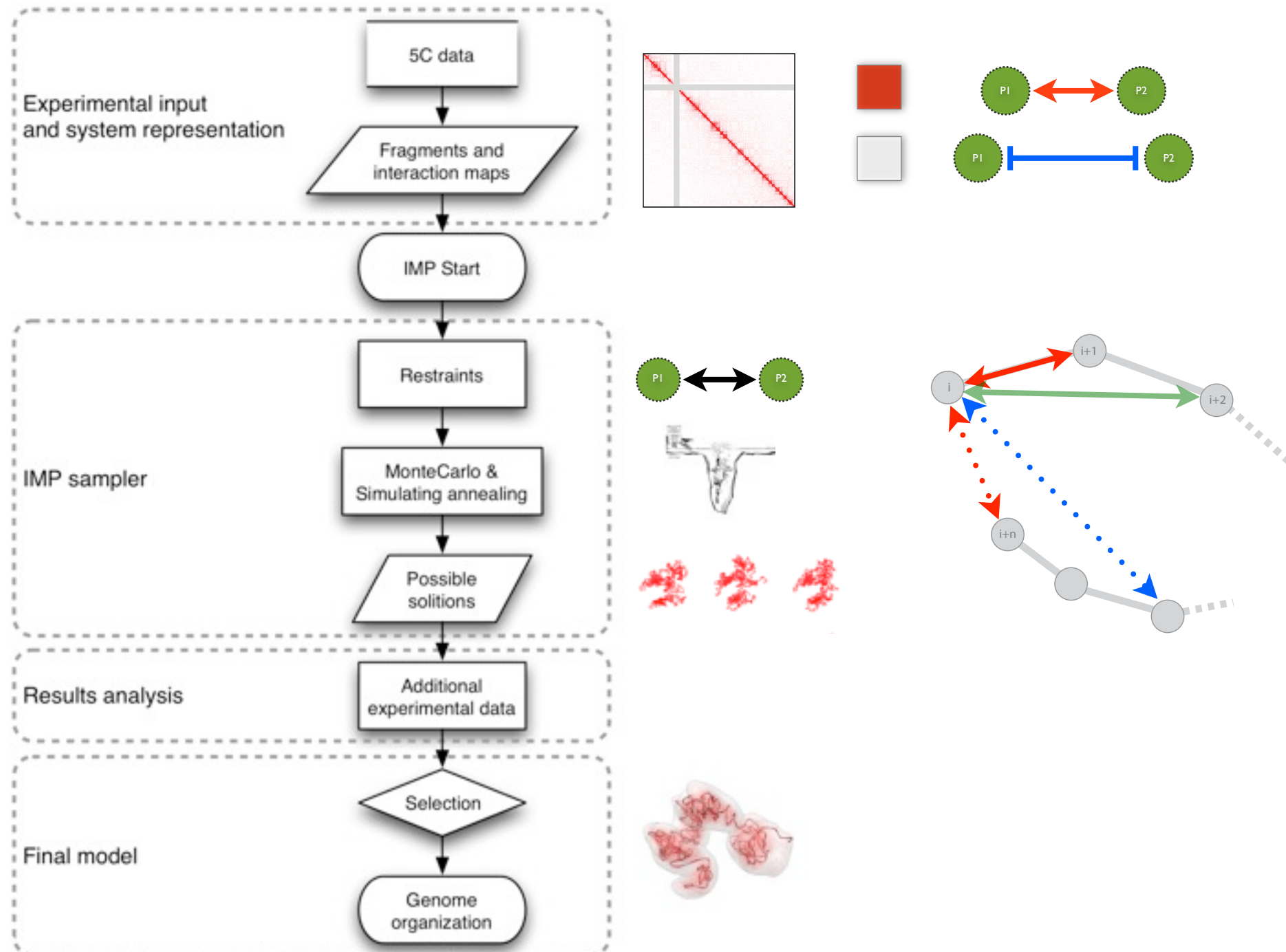
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data

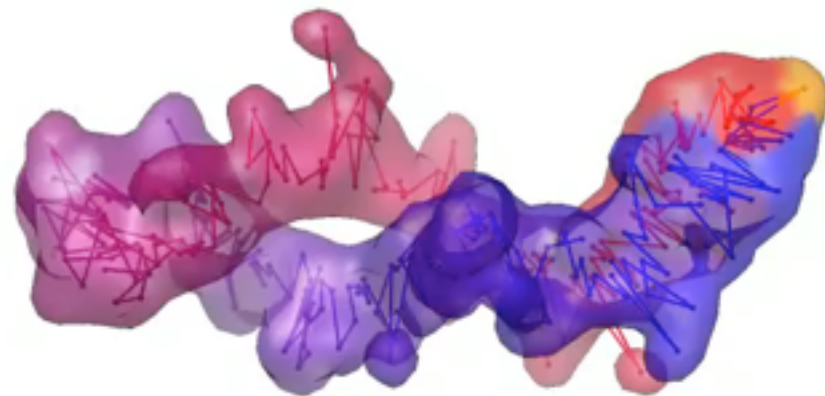
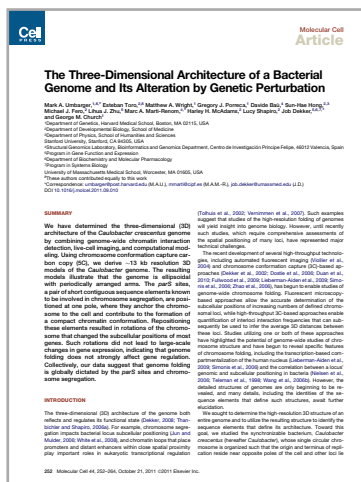
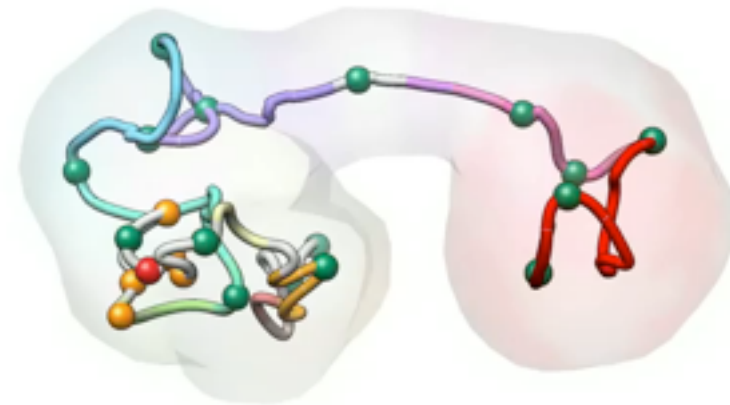
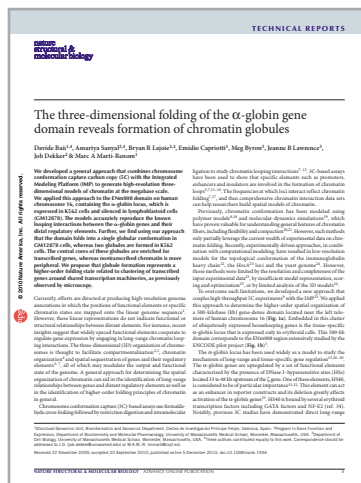
Integrative Modeling

<http://www.integrativemodeling.org>



Previous applications...

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



On TADs and hormones



Davide Baù



François le Dily



Miguel Beato

Chromatin and Gene Expression Group (CRG)

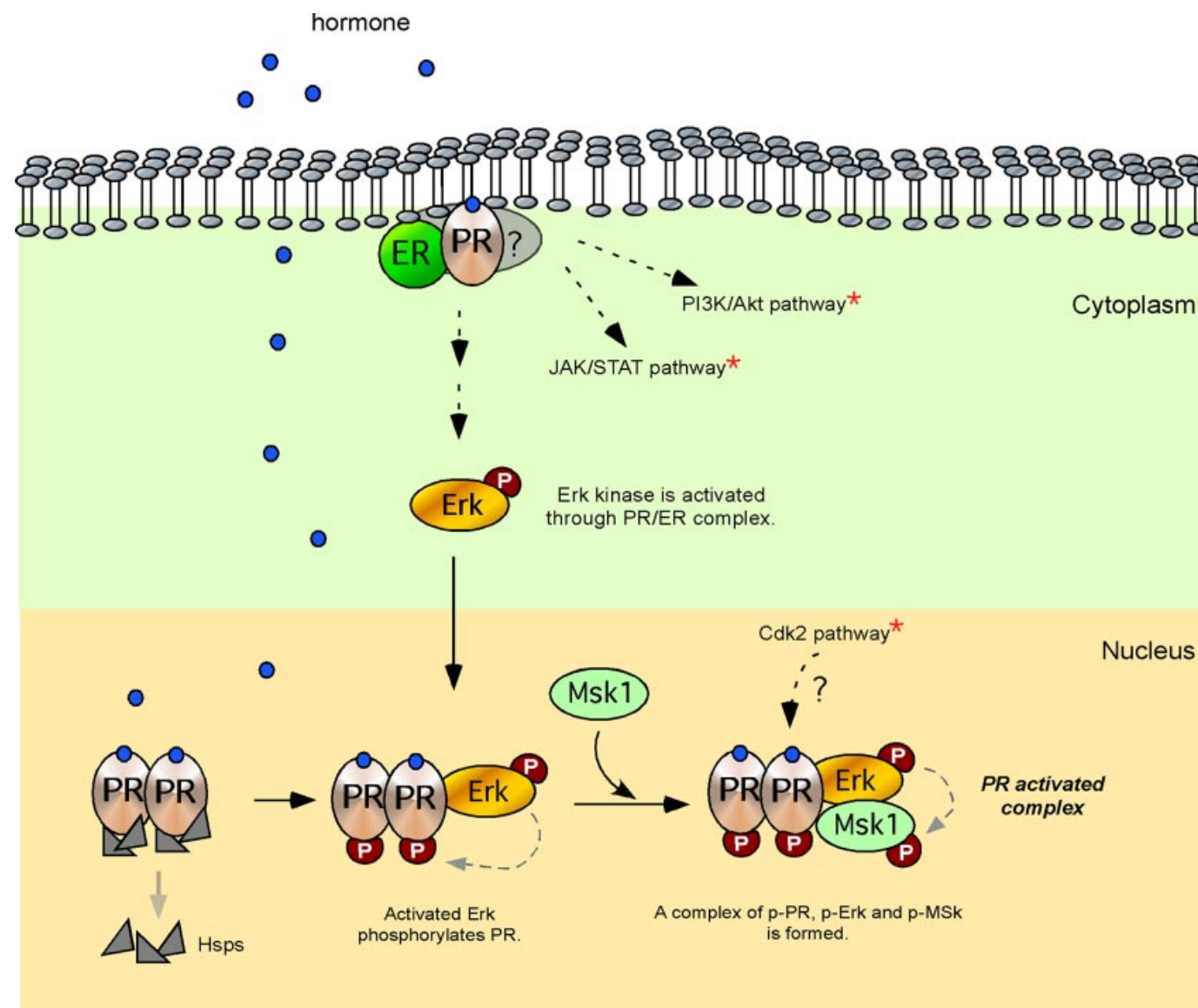


Guillaume Filion

Genome Architecture Group (CRG)



Progesterone-regulated transcription in breast cancer

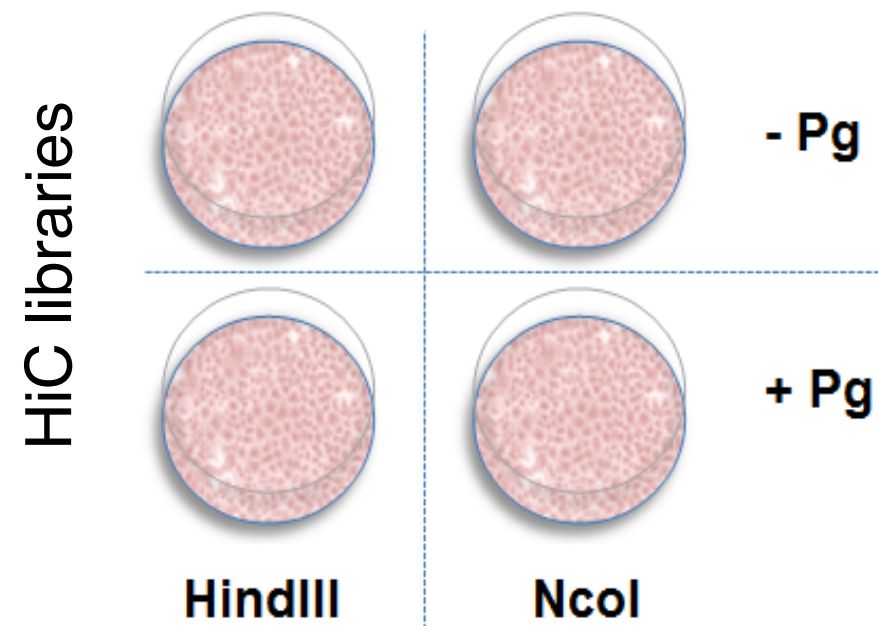


Vicent *et al* 2011, Wright *et al* 2012, Ballare *et al* 2012

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

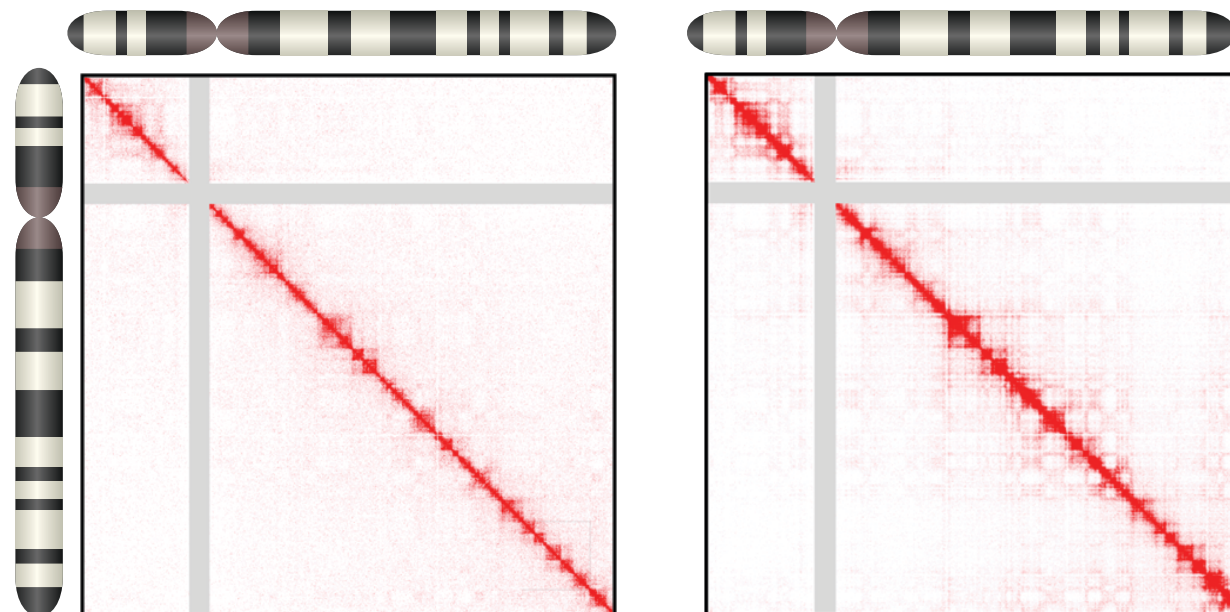
Regulation in 3D?

Experimental design



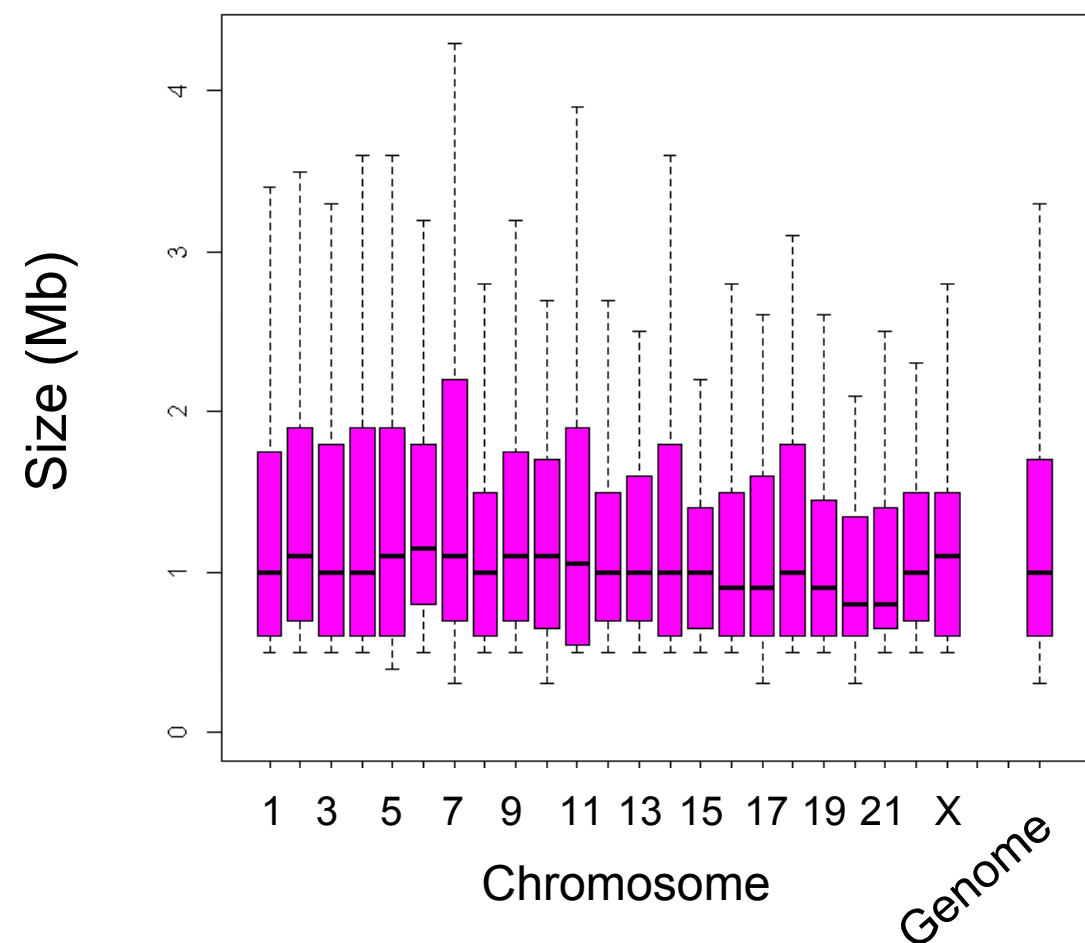
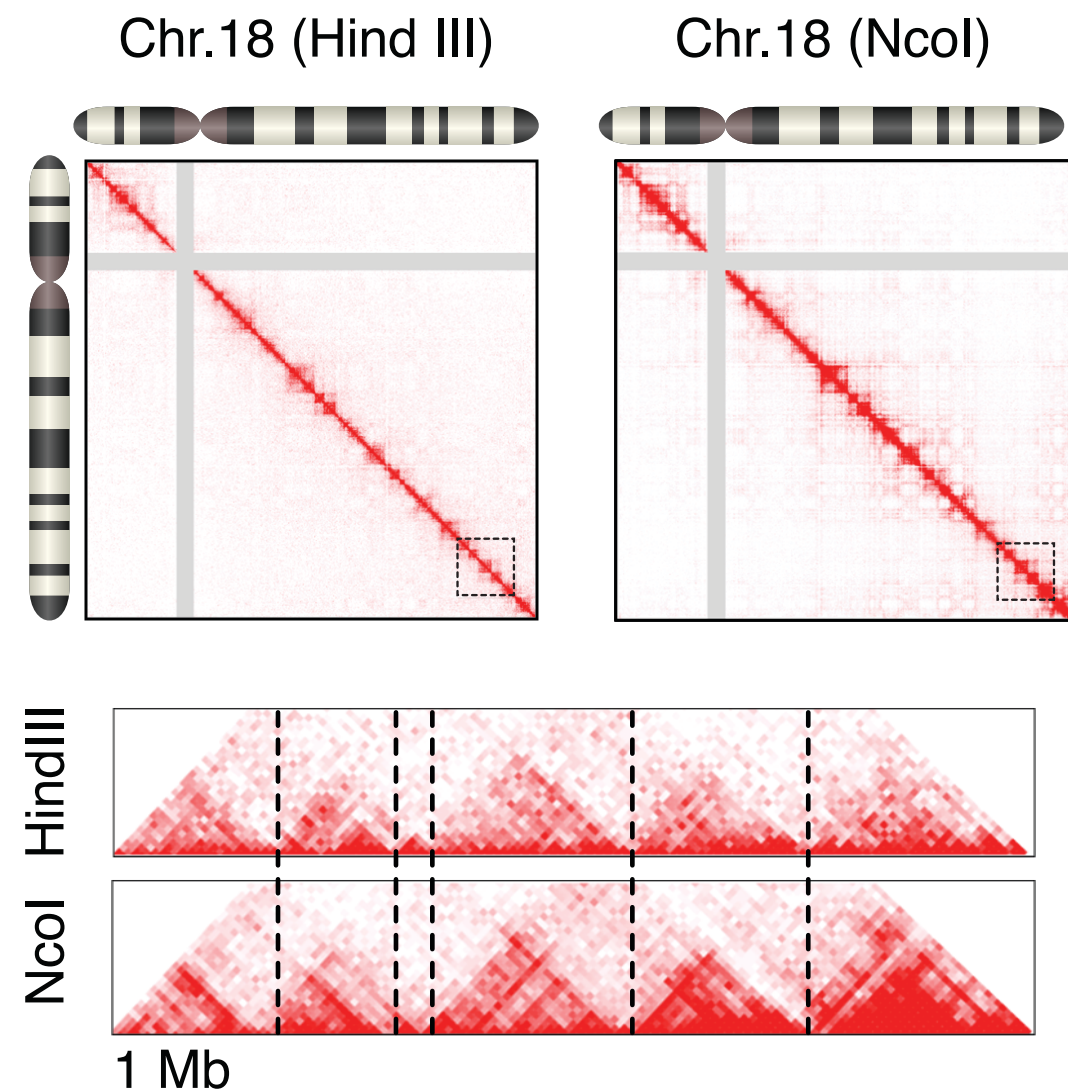
Chr.18 (Hind III)

Chr.18 (NcoI)



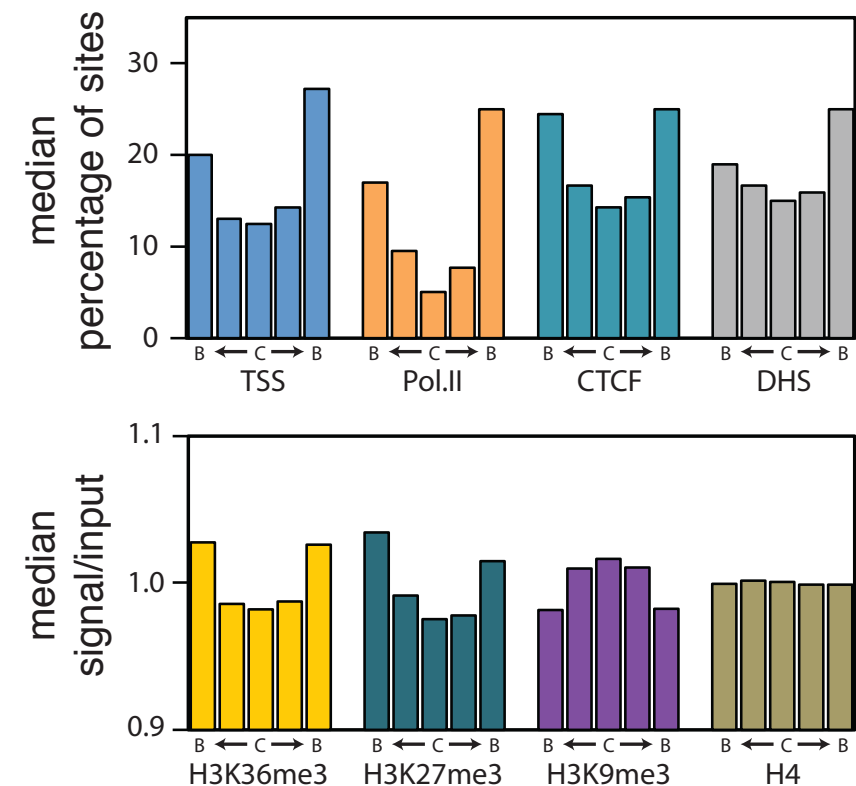
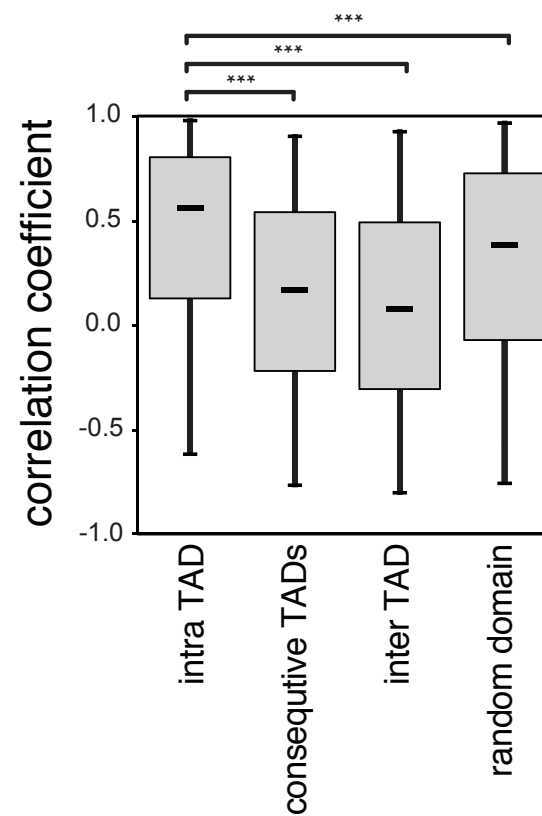
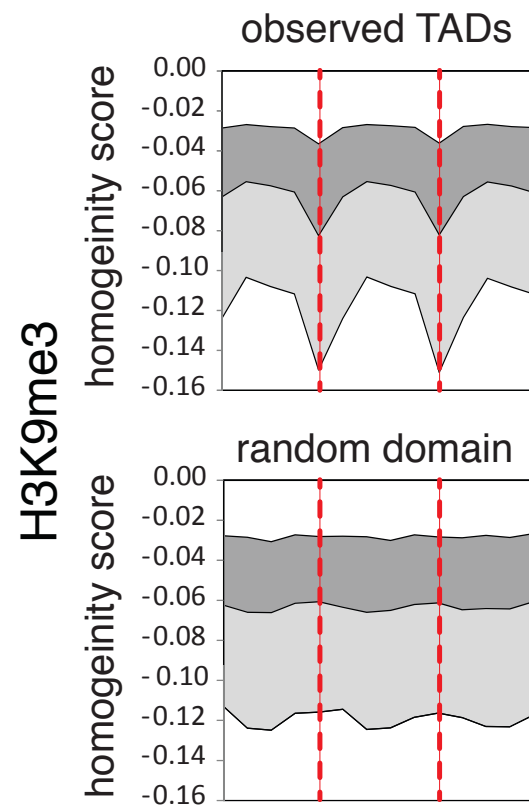
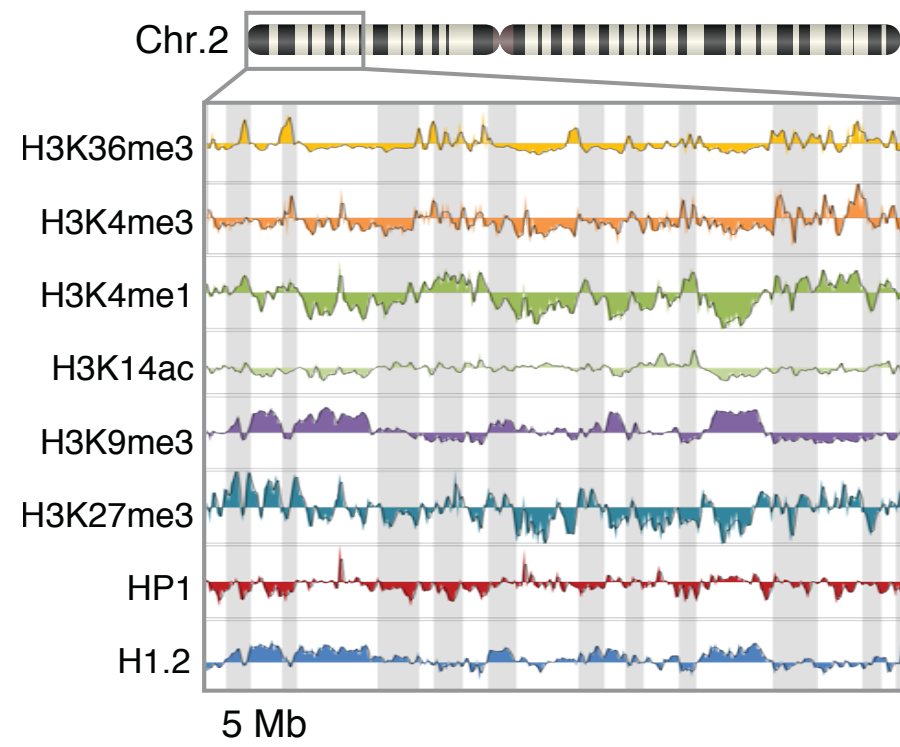


Chromosomes are organized into Topologically Associated Domains (TADs)

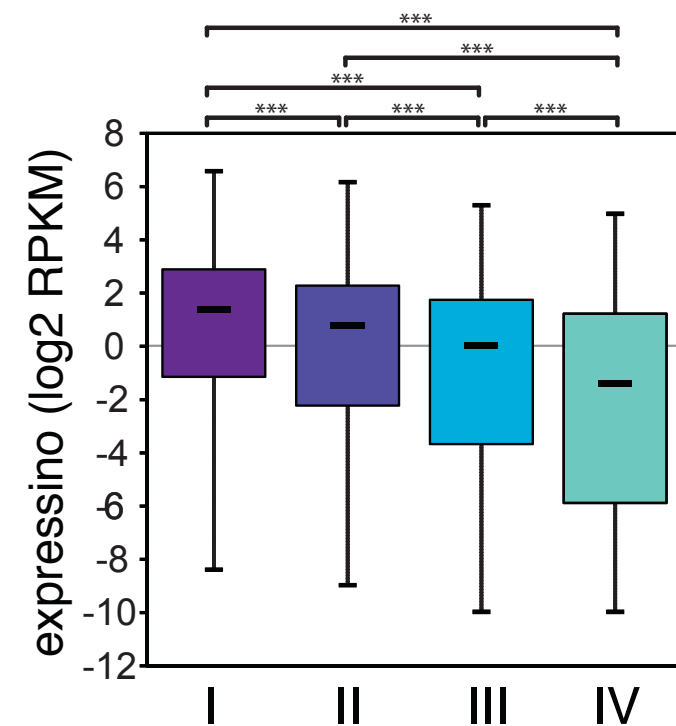
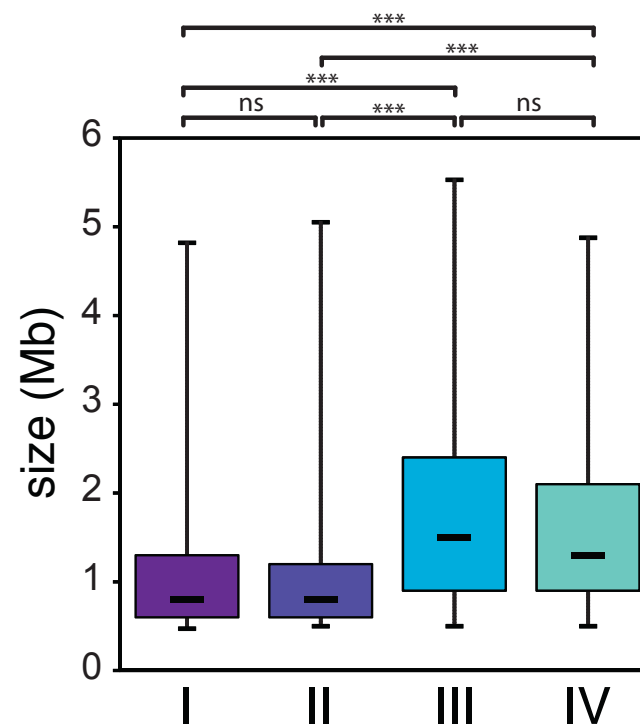
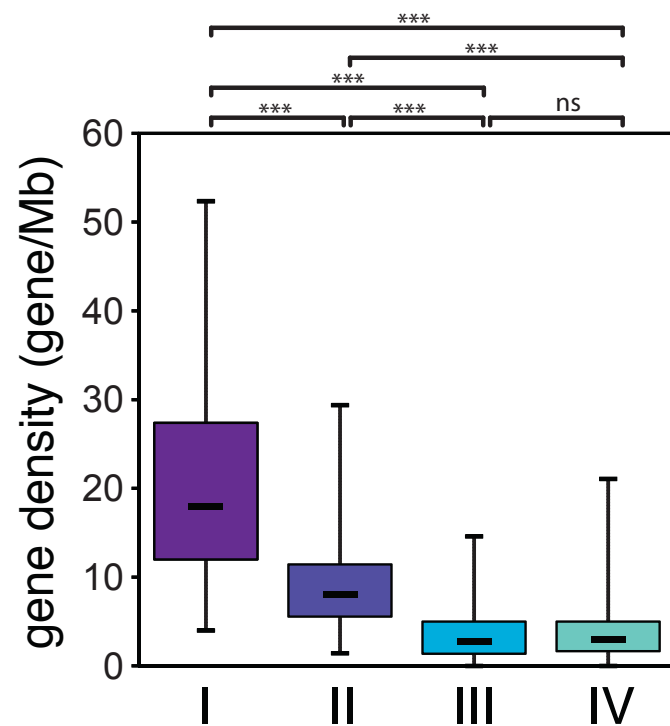
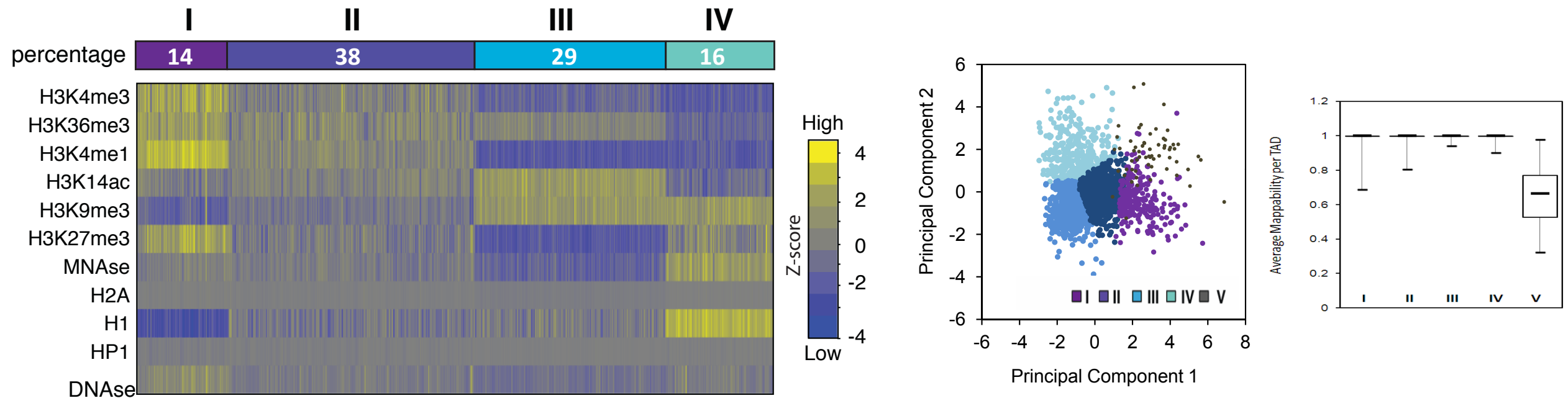




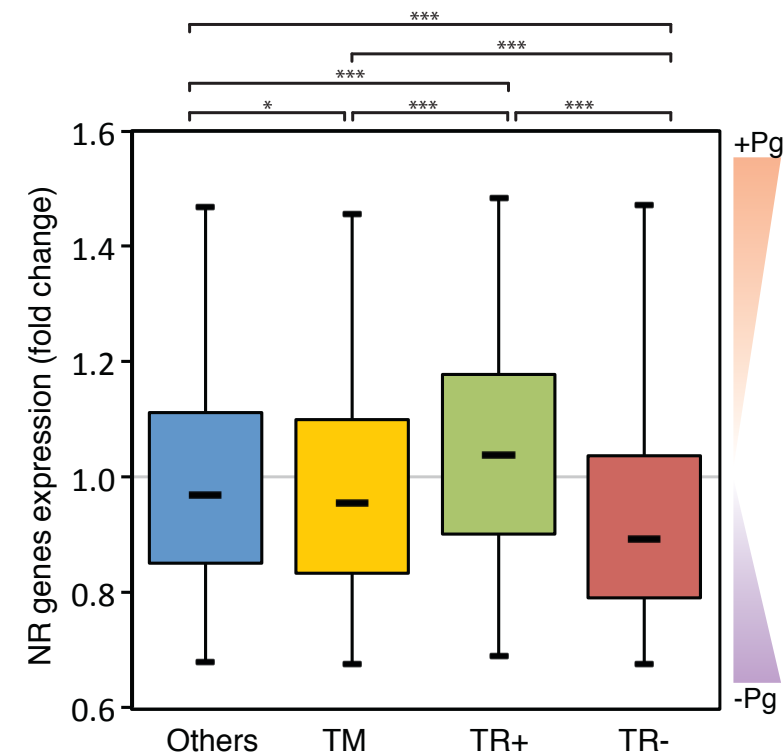
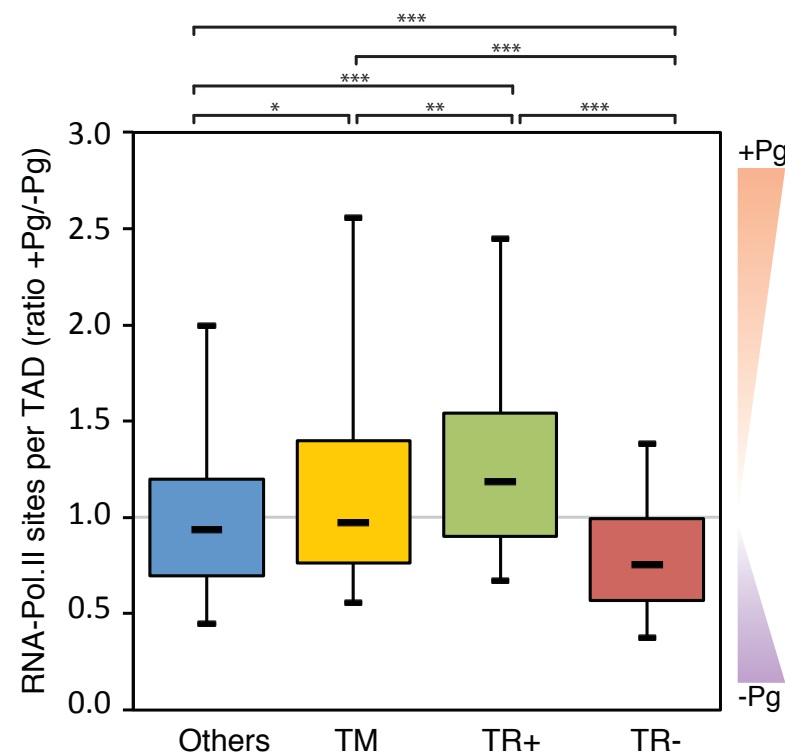
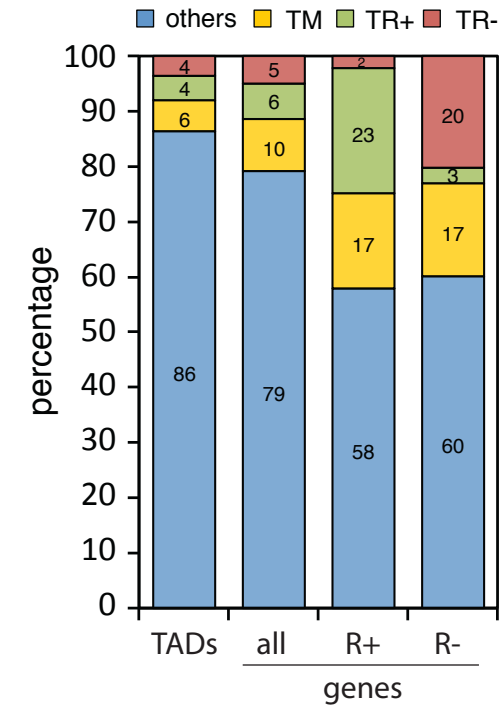
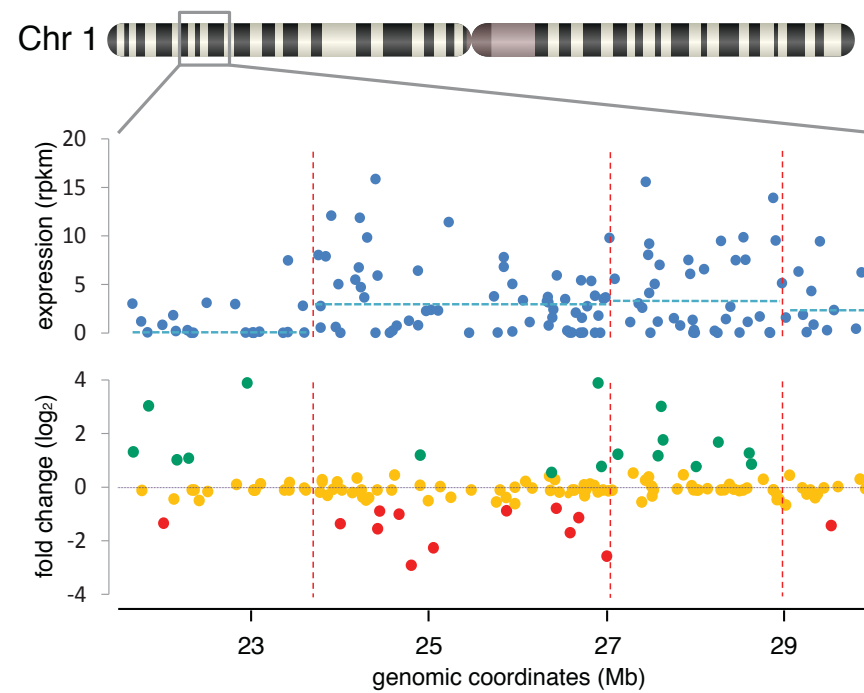
Are TADs homogeneous?



Functional Chromatin signatures of TADs



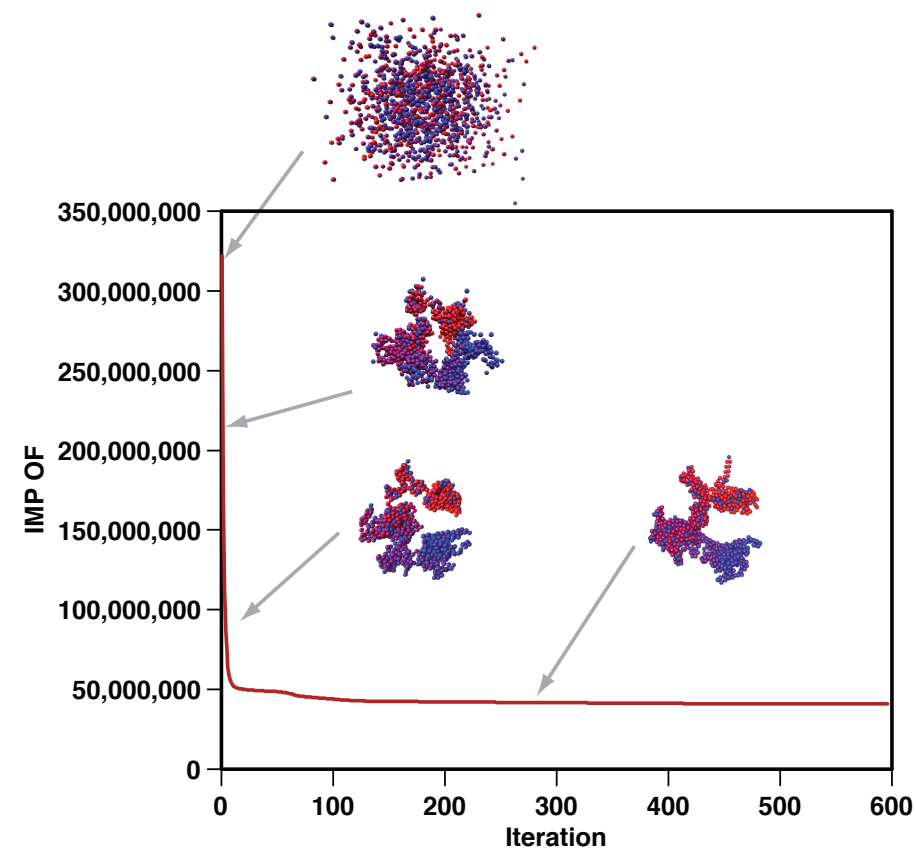
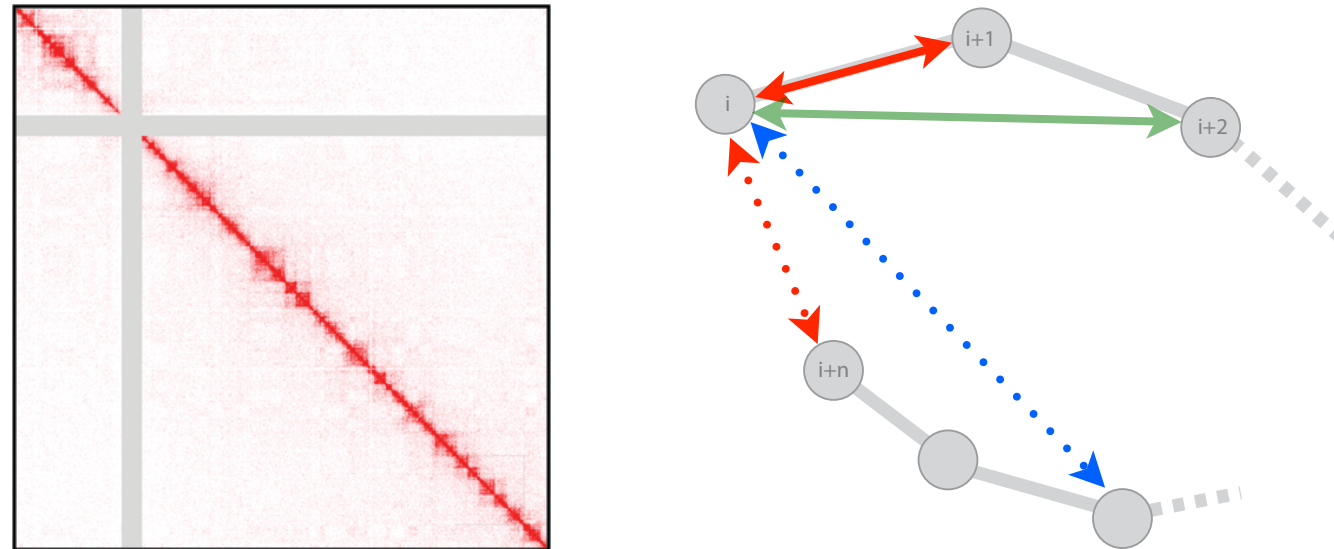
A role for TADs in Pg induced transcription changes



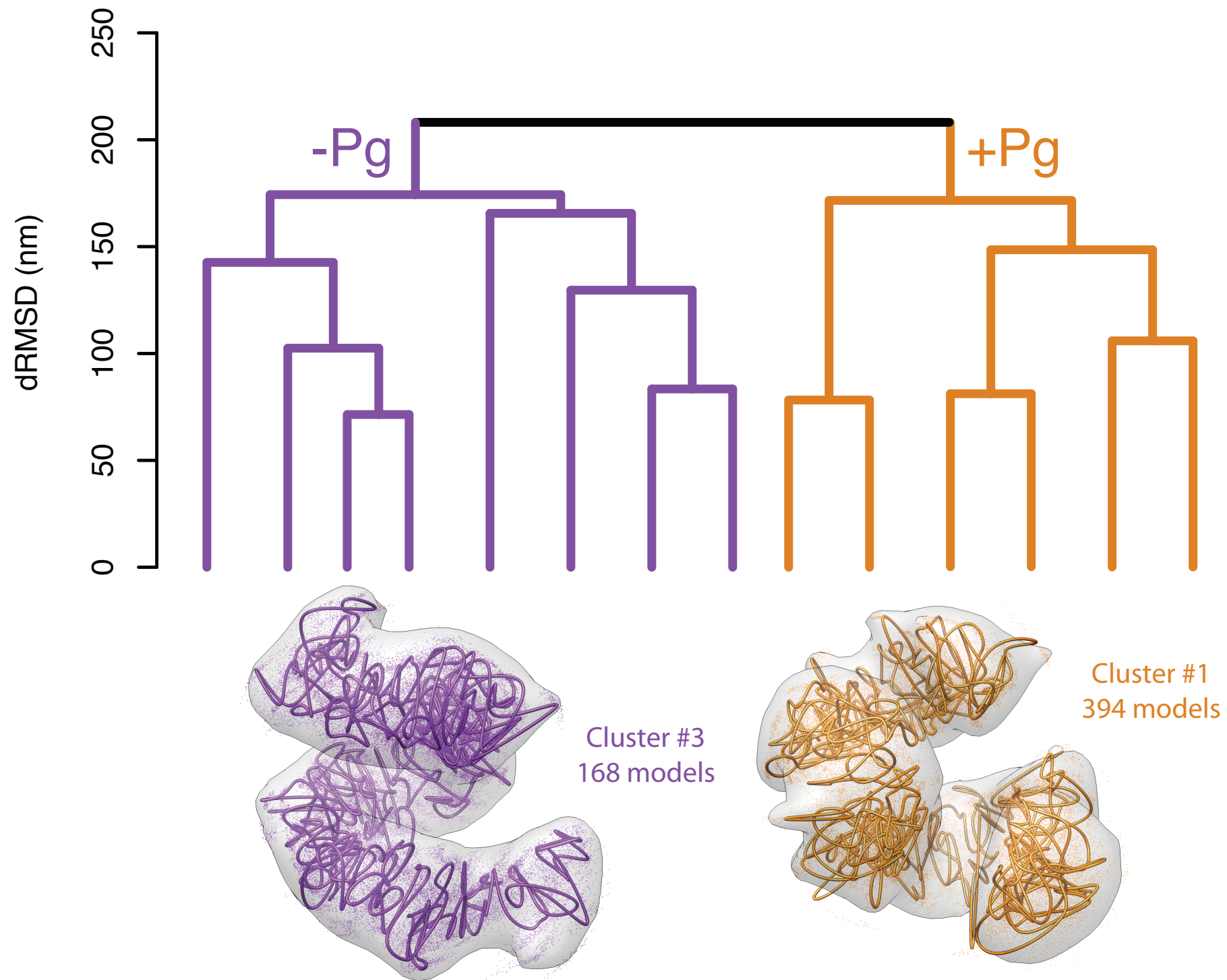


Modeling 3D TADs

11 genomic regions with 102 TADs in total



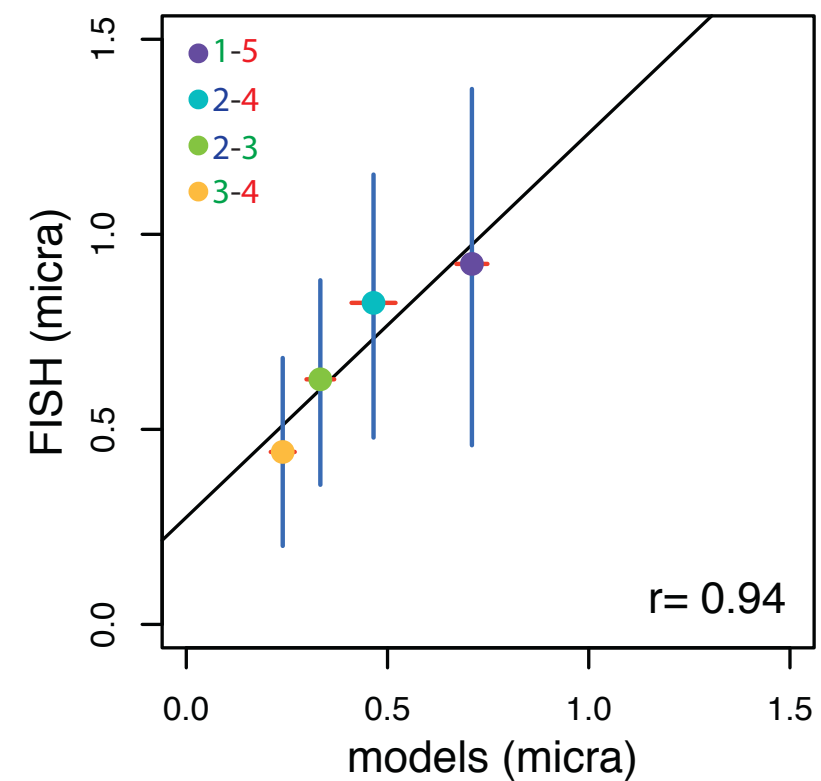
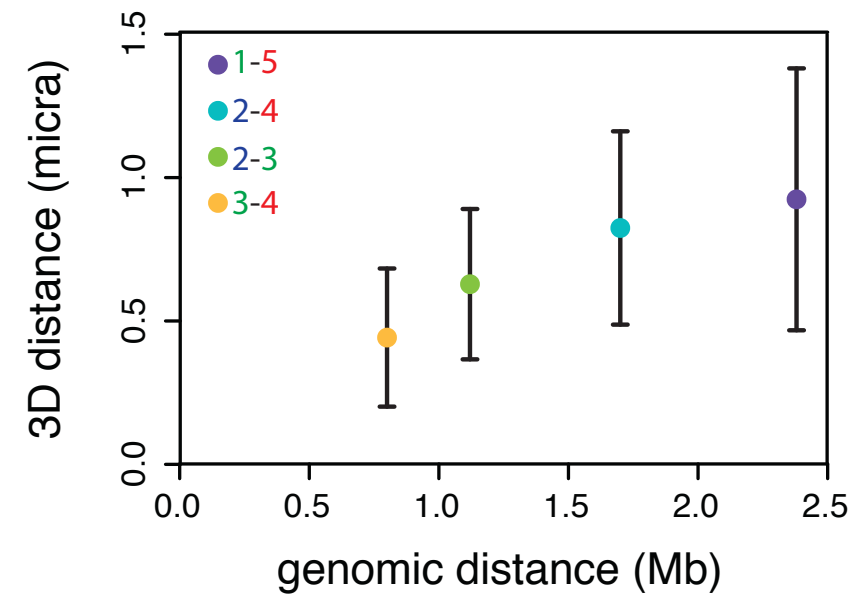
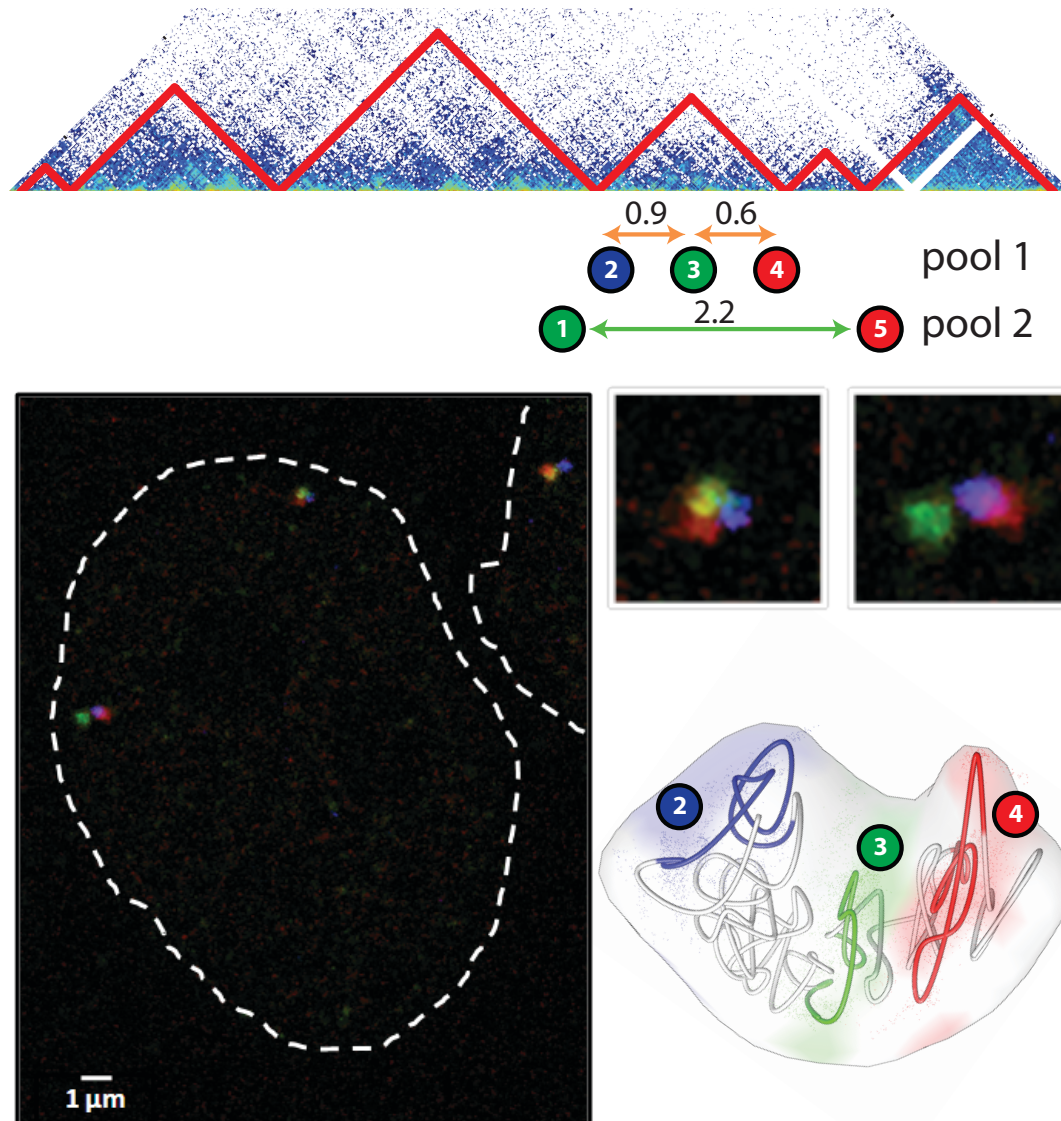
Clustering





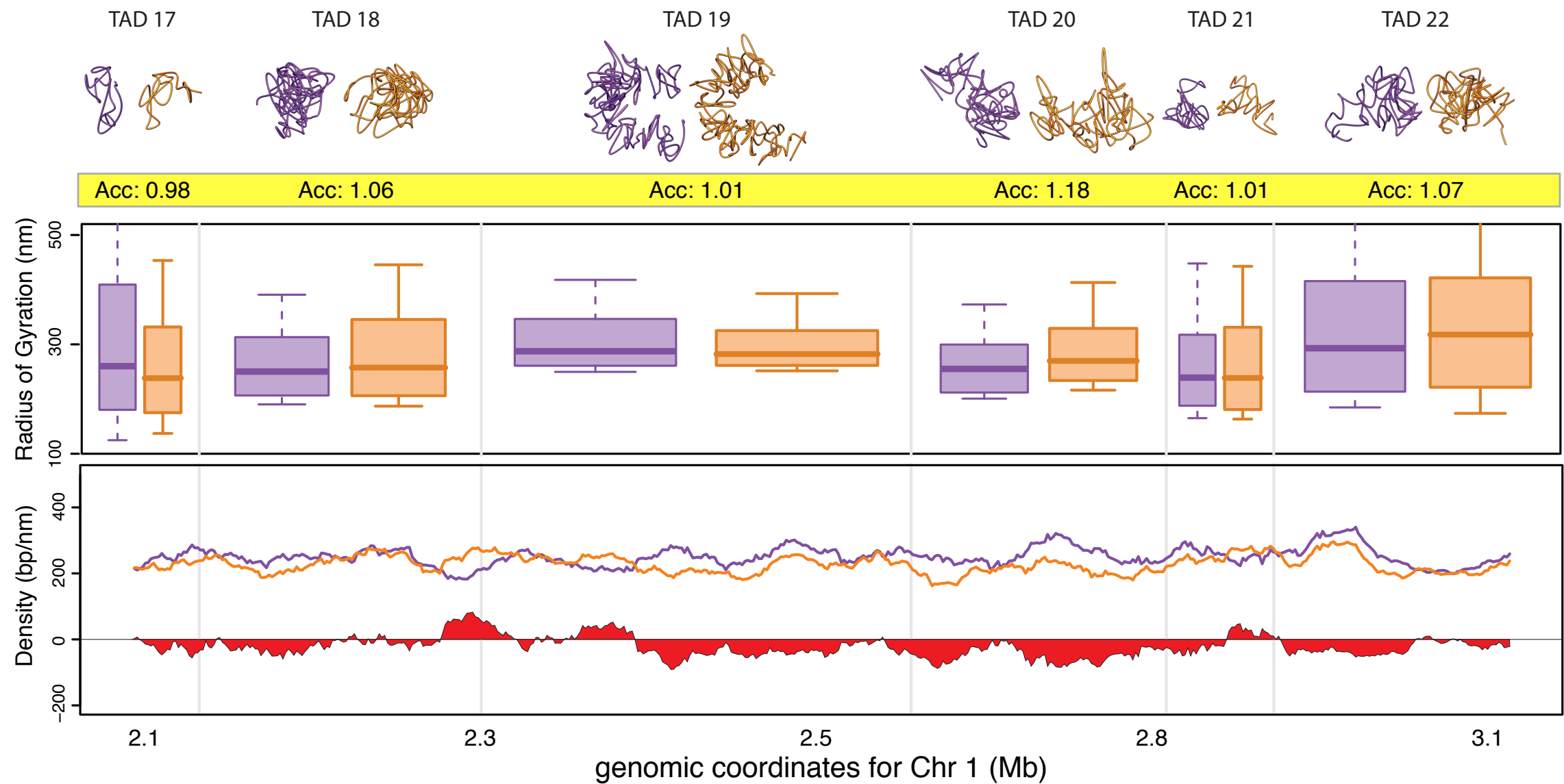
Model Accuracy

Chr1:21000000-31400000
6 TADs



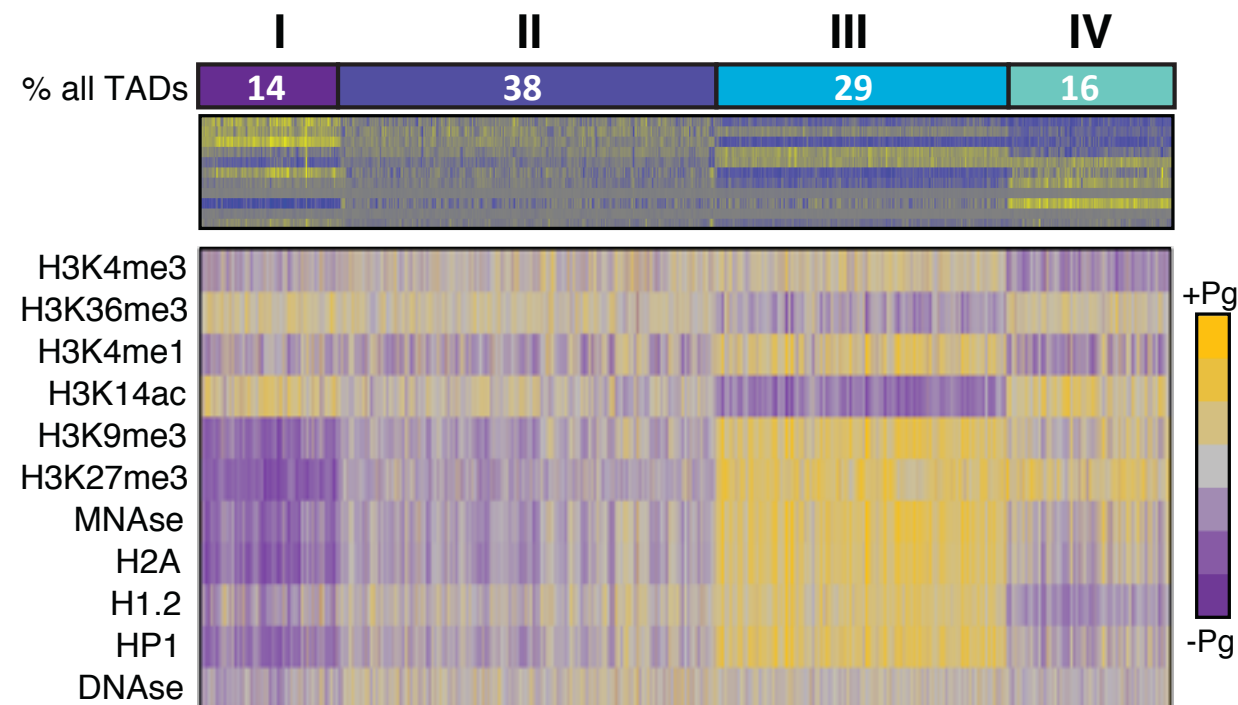
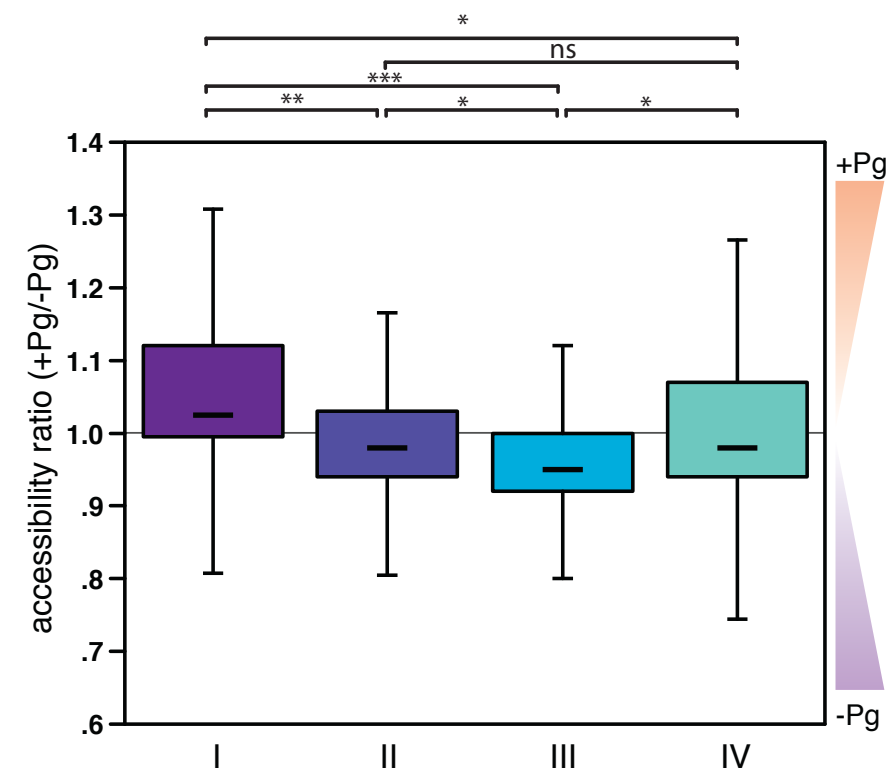
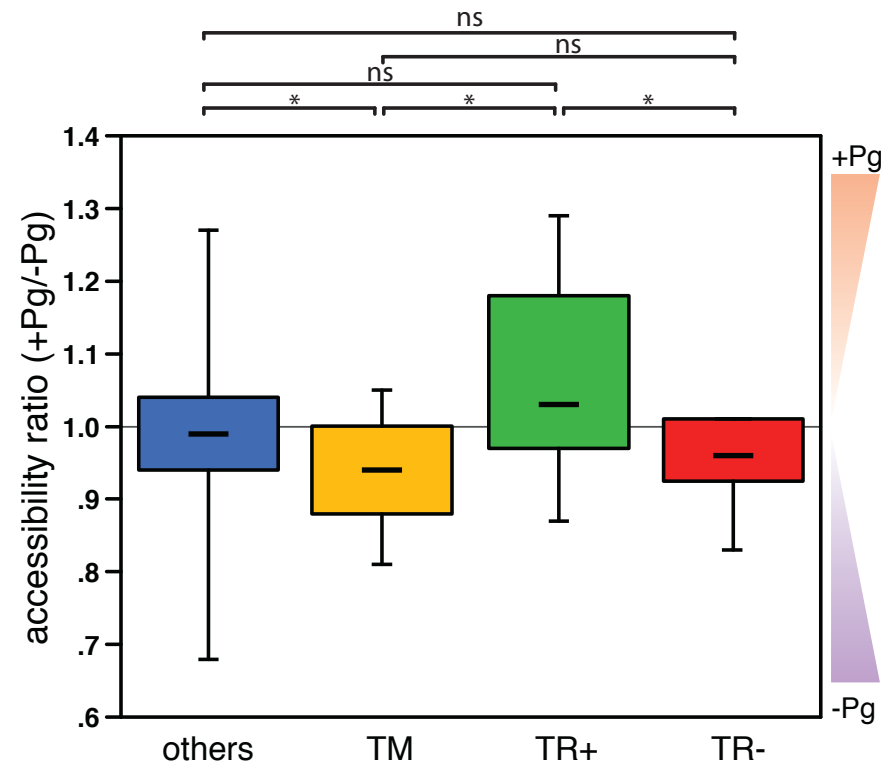
Accessibility changes of TADs

Chr1:21000000-31400000
6 TADs

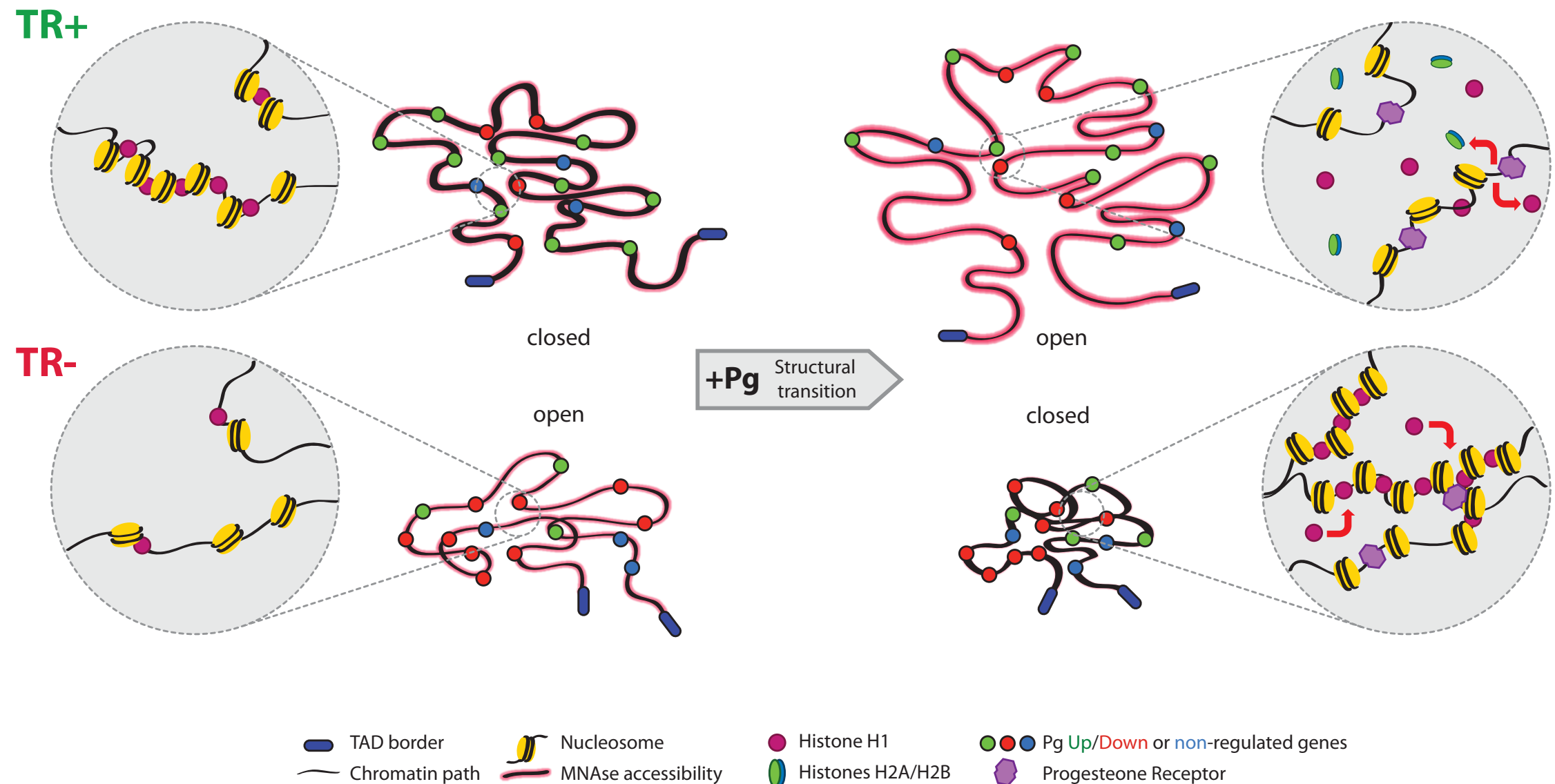


TADs respond differently

11 genomic regions with 102 TADs in total



Model for TAD regulation



Acknowledgments



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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>

