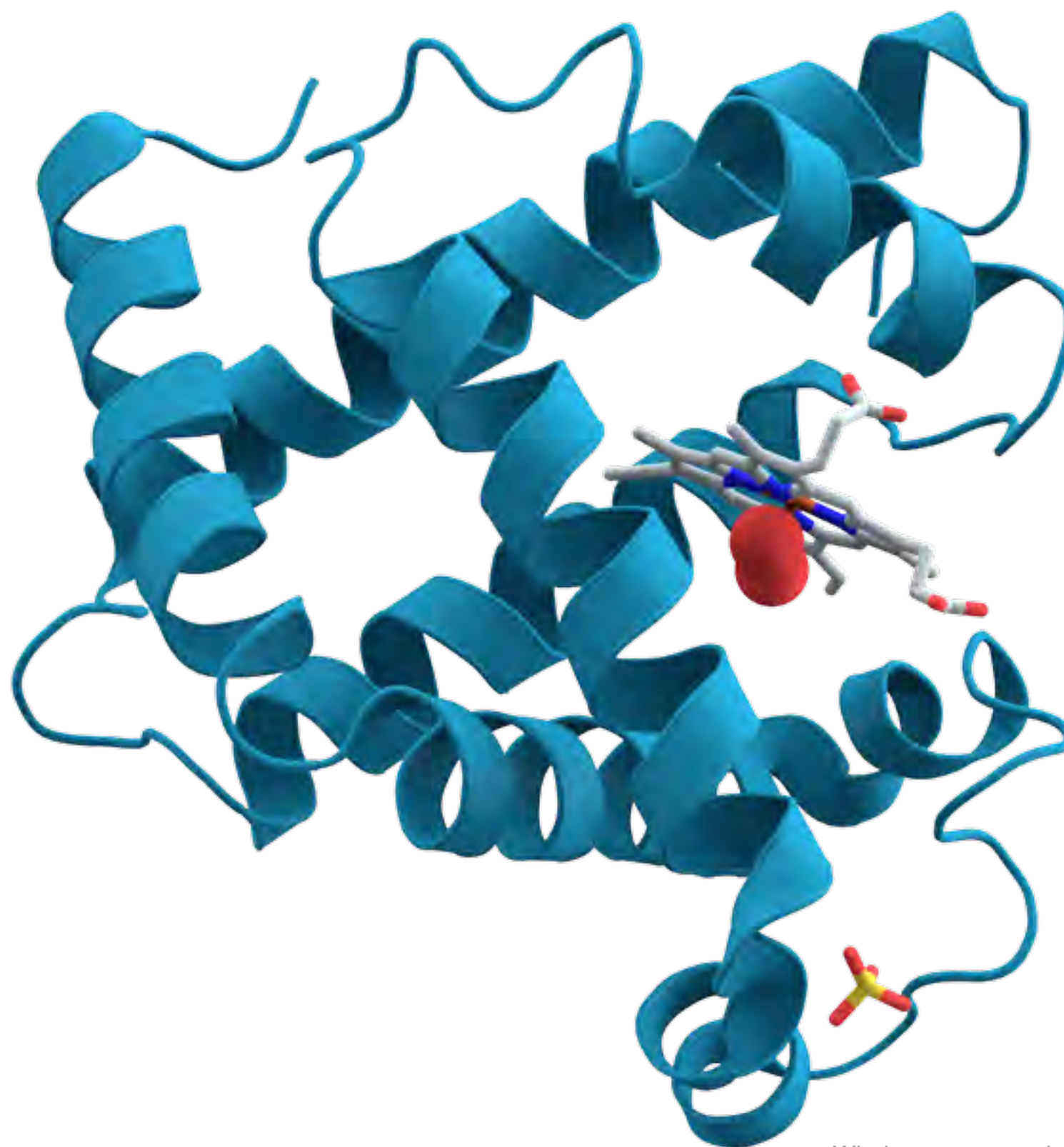


Determining the 3D structure of genomes and genomic domains.

Marc A. Marti-Renom

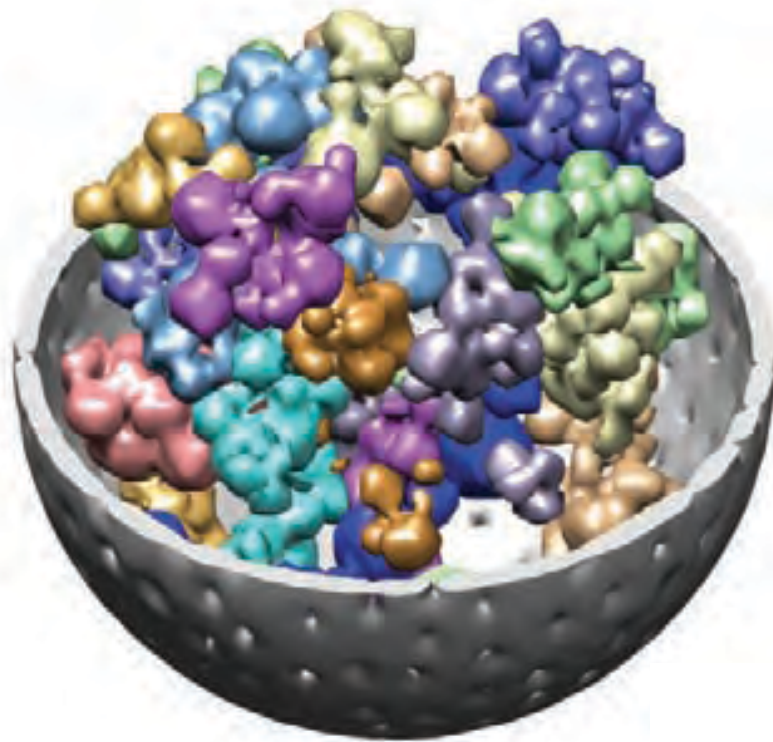
Genome Biology Group (CNAG)
Structural Genomics Group (CRG)

***iCrea**
INSTITUCIÓ CATALANA DE
RECERCA I ESTUDIS AVANÇATS

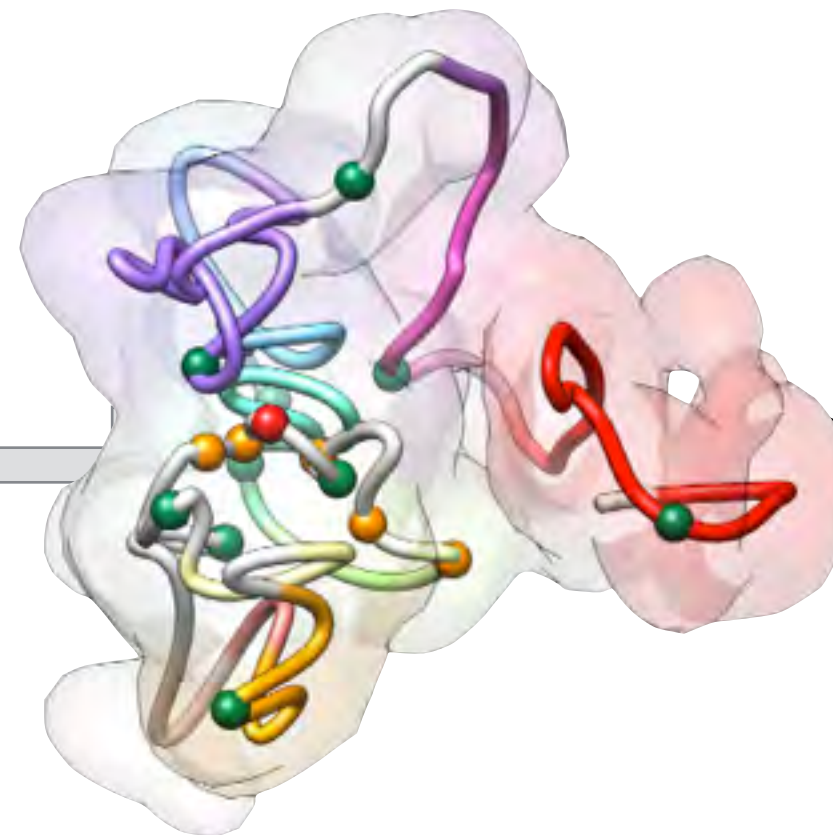
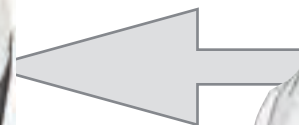


Whale sperm myoglobin structure (1960)

ST

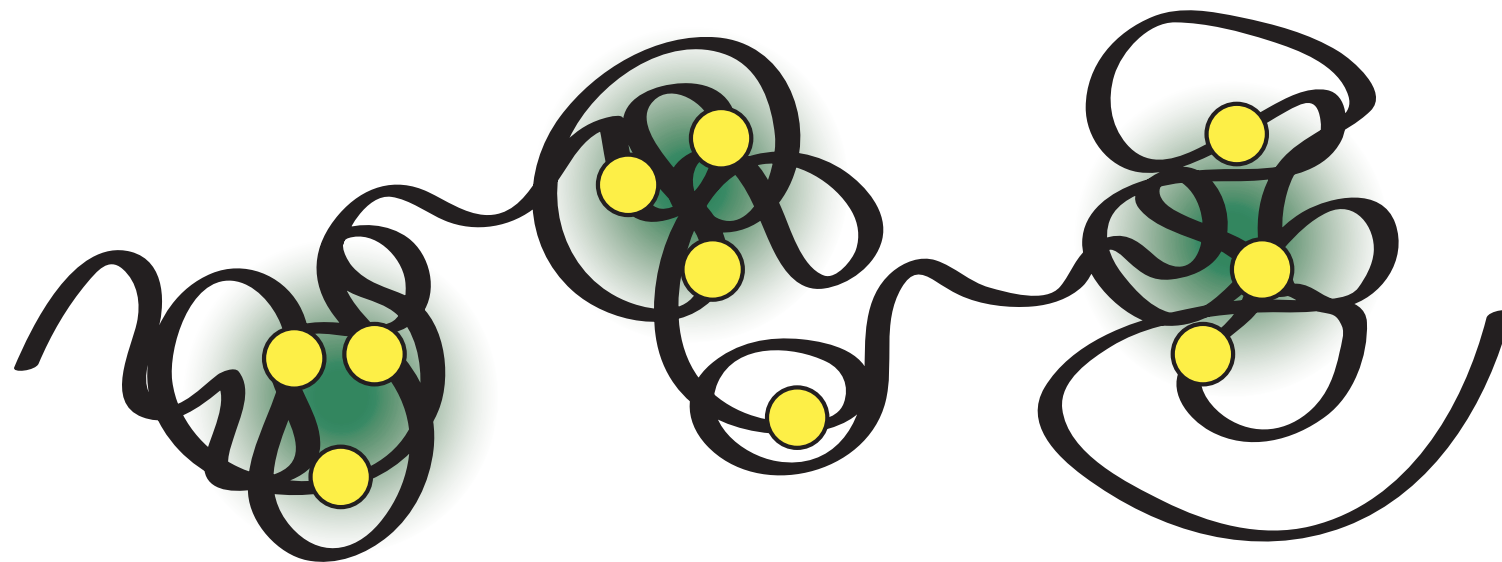
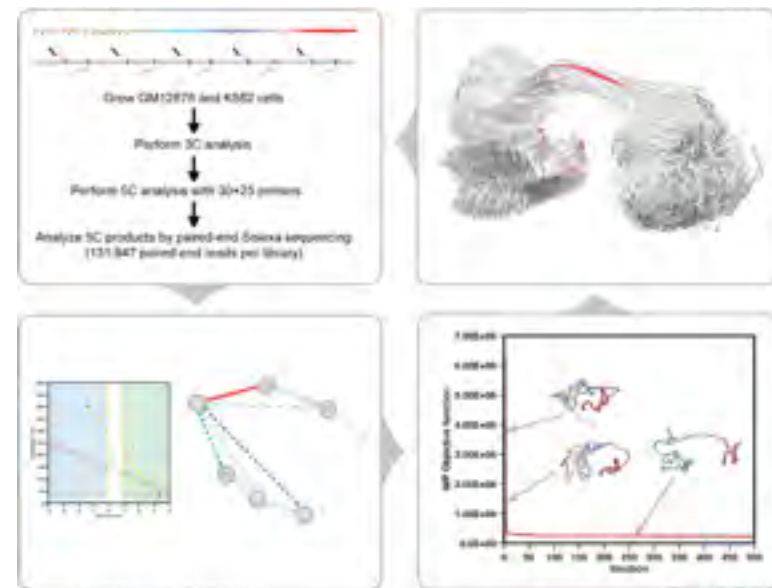


human genome (2011)



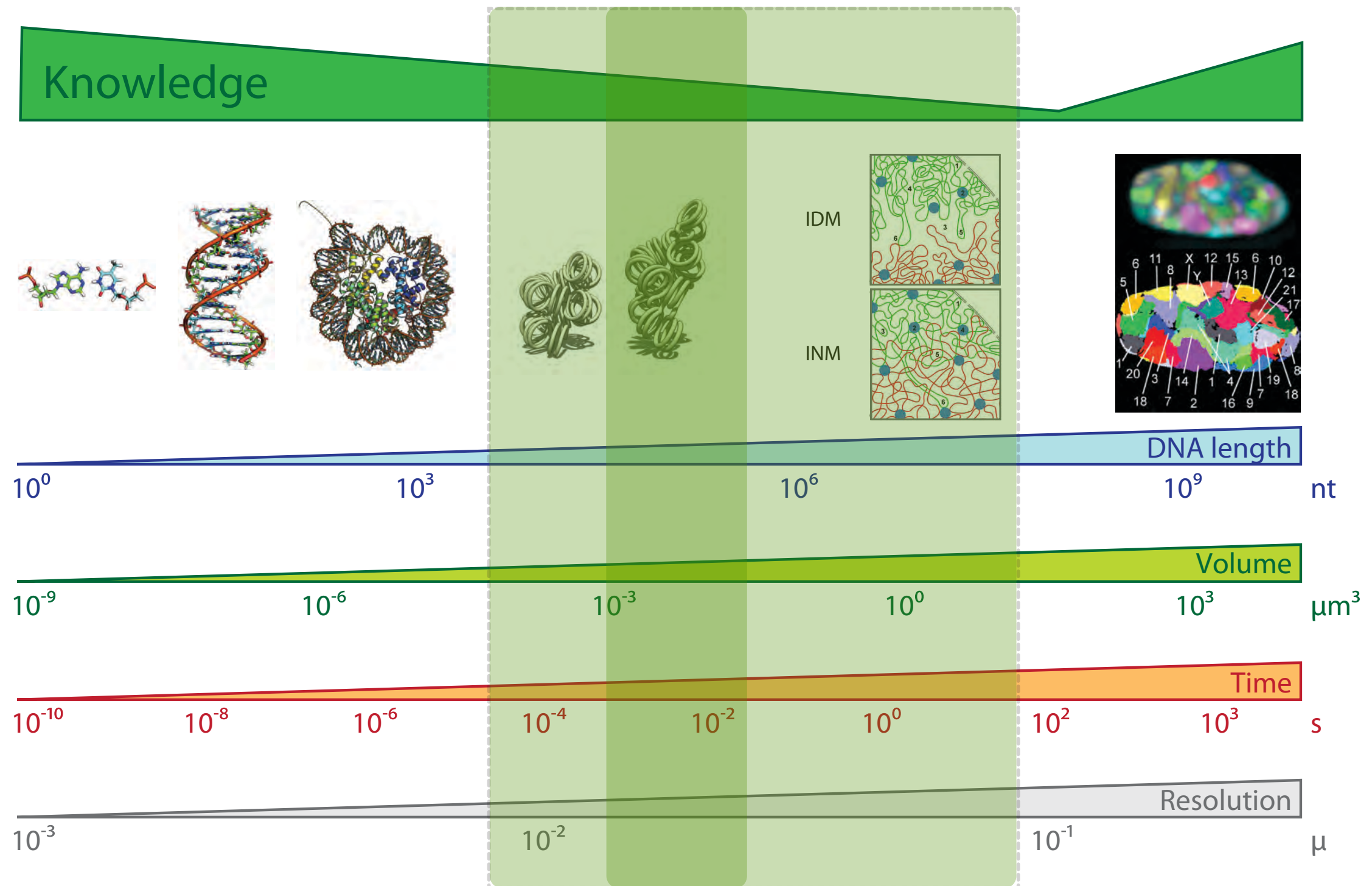
alpha-globin genomic domain structure (2011)

TION



Resolution Gap

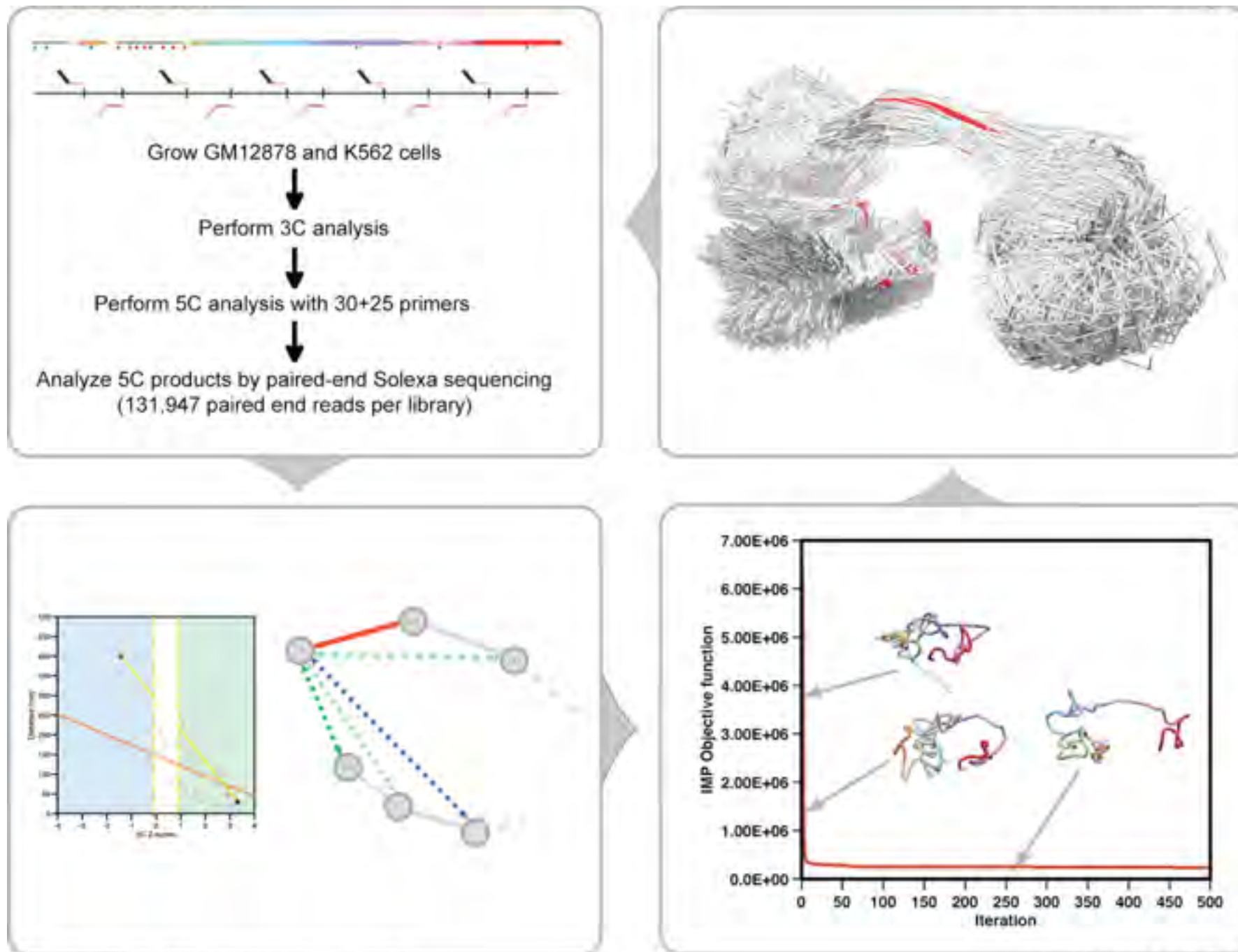
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)



Hybrid Method

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

Experiments

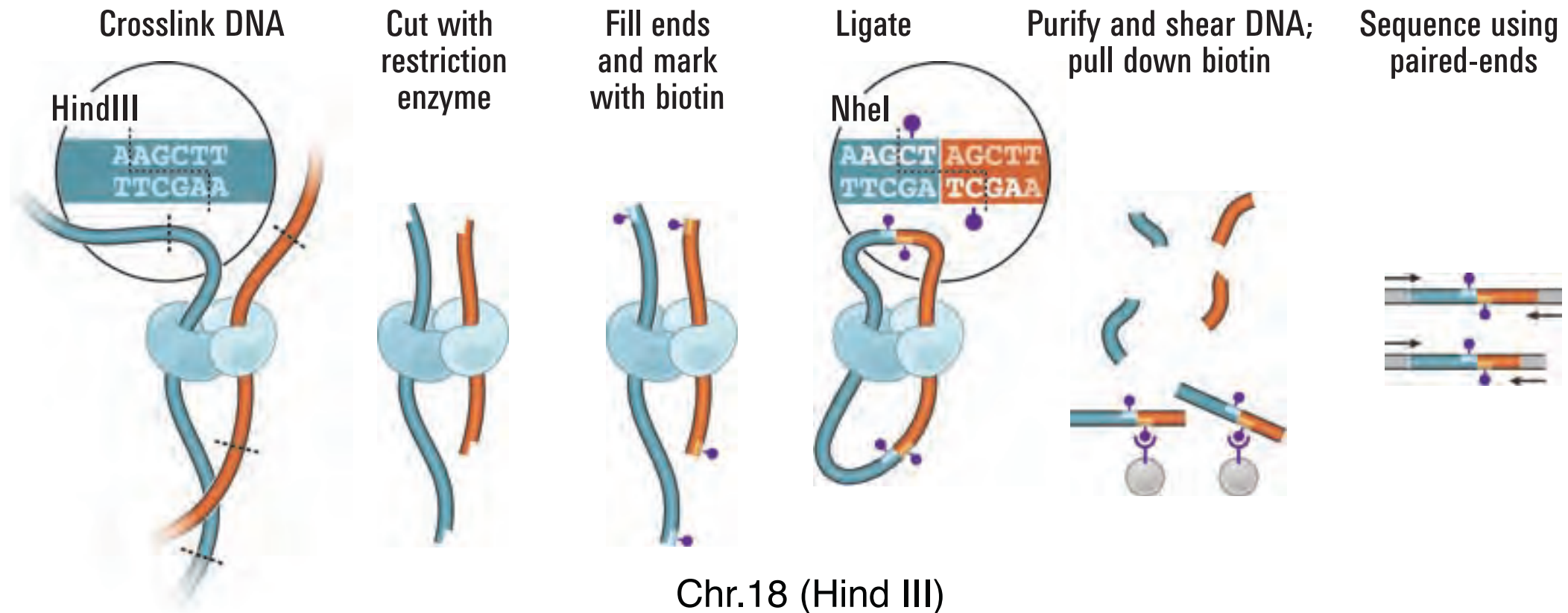


Computation

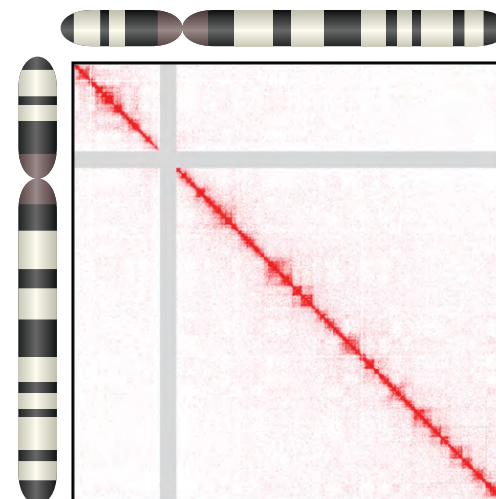
Hi-C technology

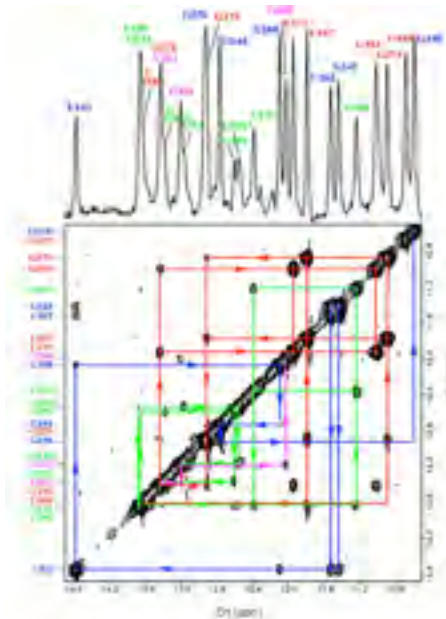
Lieberman-Aiden, E. et al. Science 326, 289–293 (2009).

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

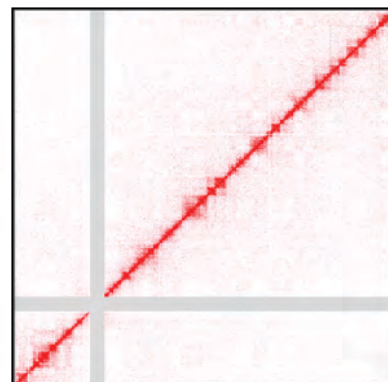
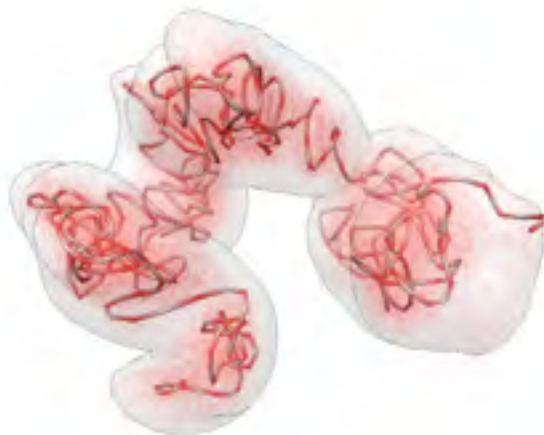


Chr.18 (Hind III)





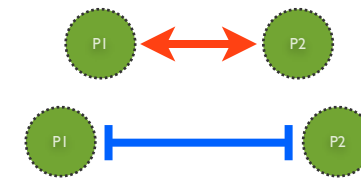
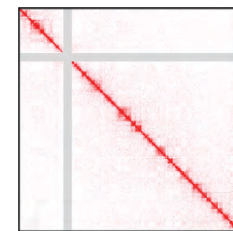
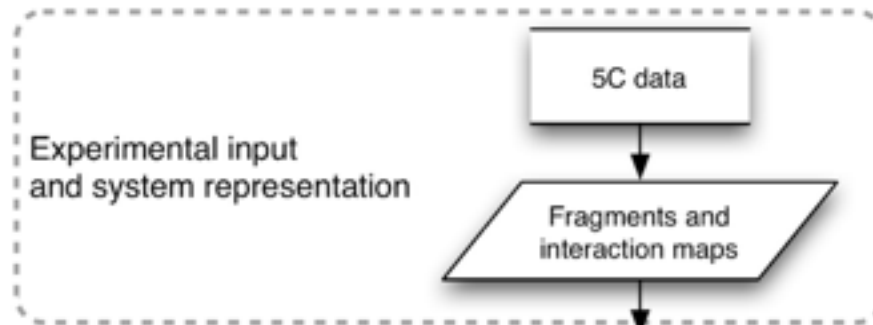
Biomolecular structure determination 2D-NOESY data



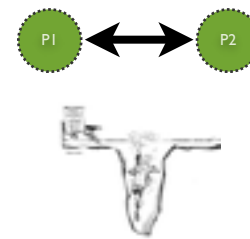
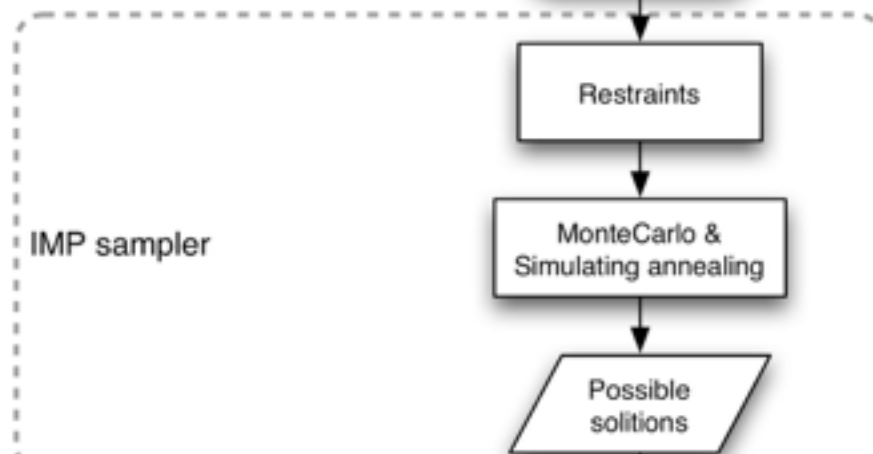
Chromosome structure determination 3C-based data

TADbit

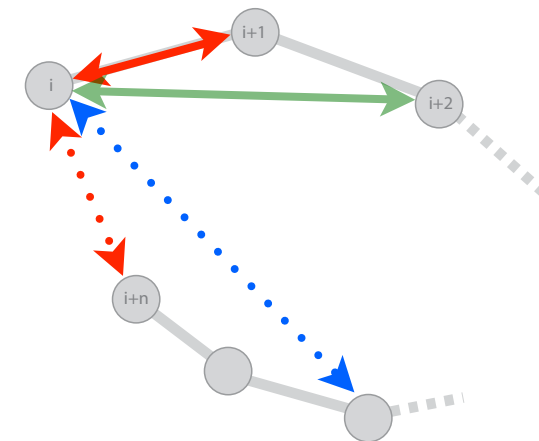
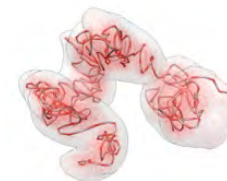
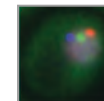
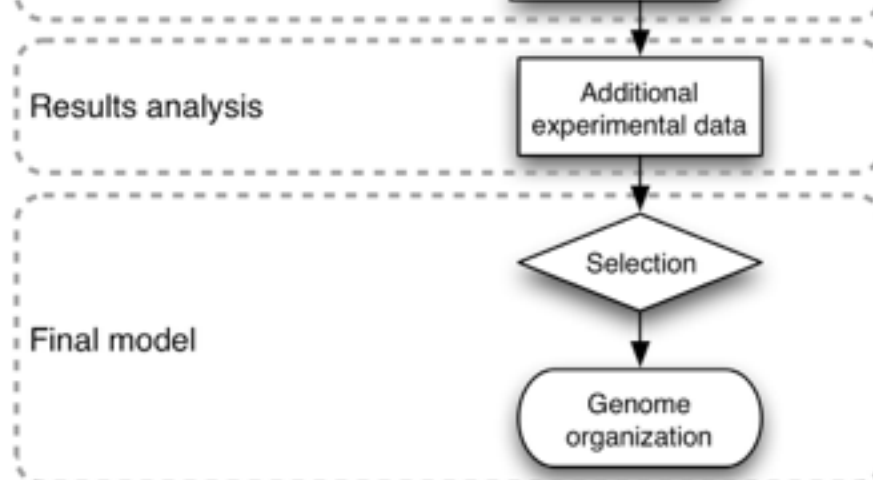
Normalization
TAD identification



3D Modeling

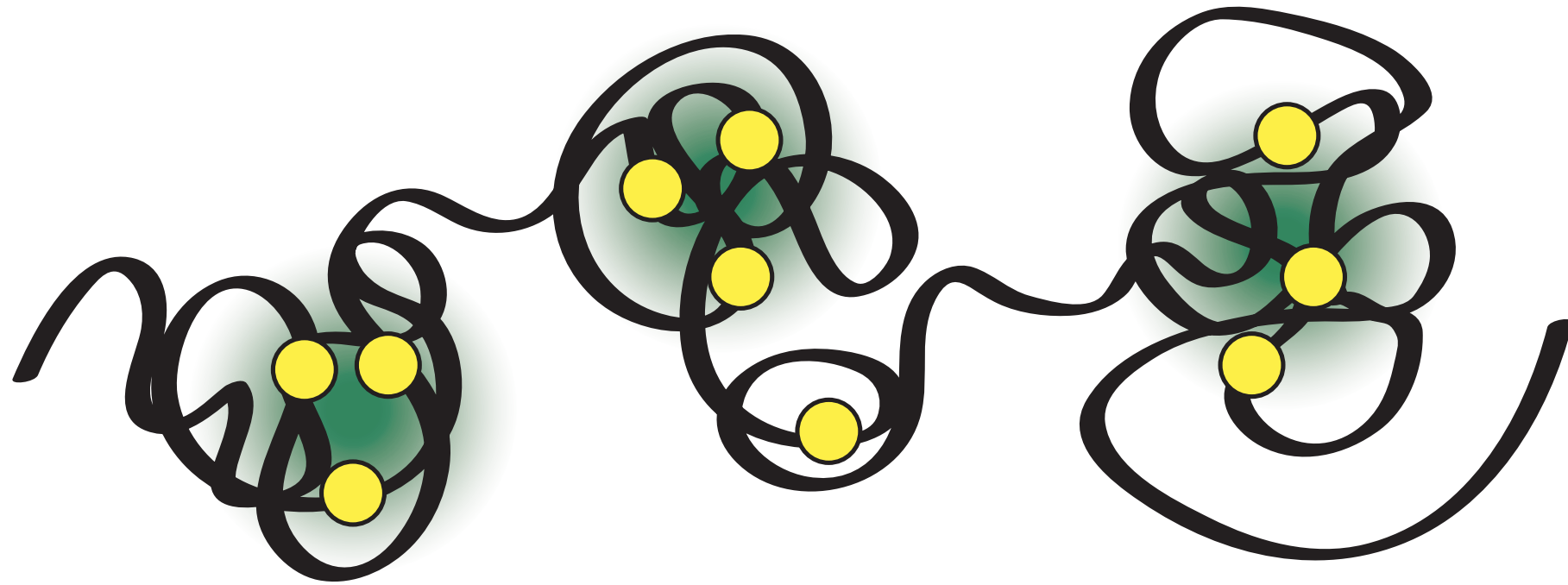


Extract structural properties





On TADs and hormones



François le Dily



Davide Baù



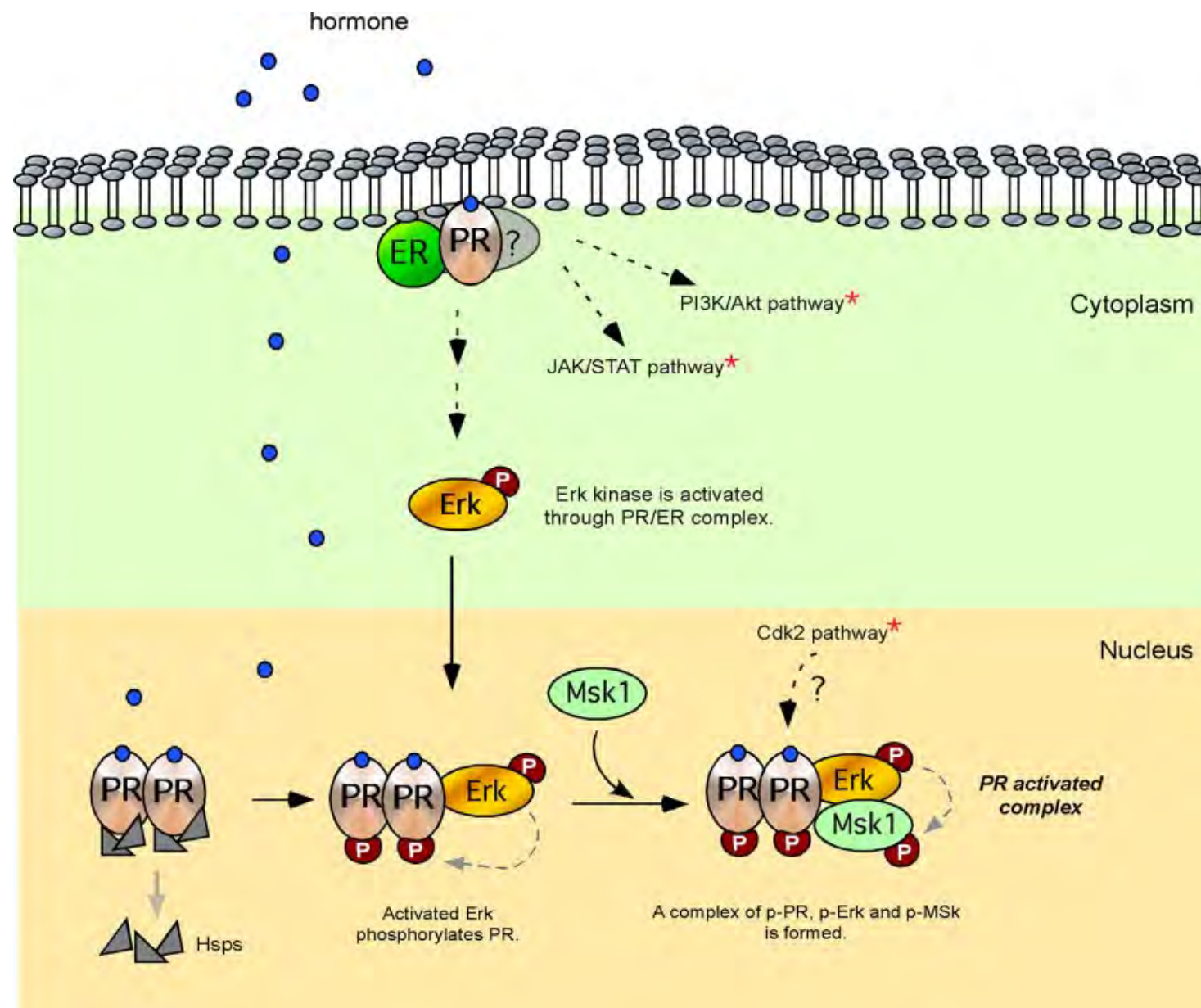
François Serra



Miguel Beato & Guillaume Filion

Gene Regulation, Stem Cells and Cancer
Centre de Regulació Genòmica
Barcelona, Spain

Progesterone-regulated transcription in breast cancer

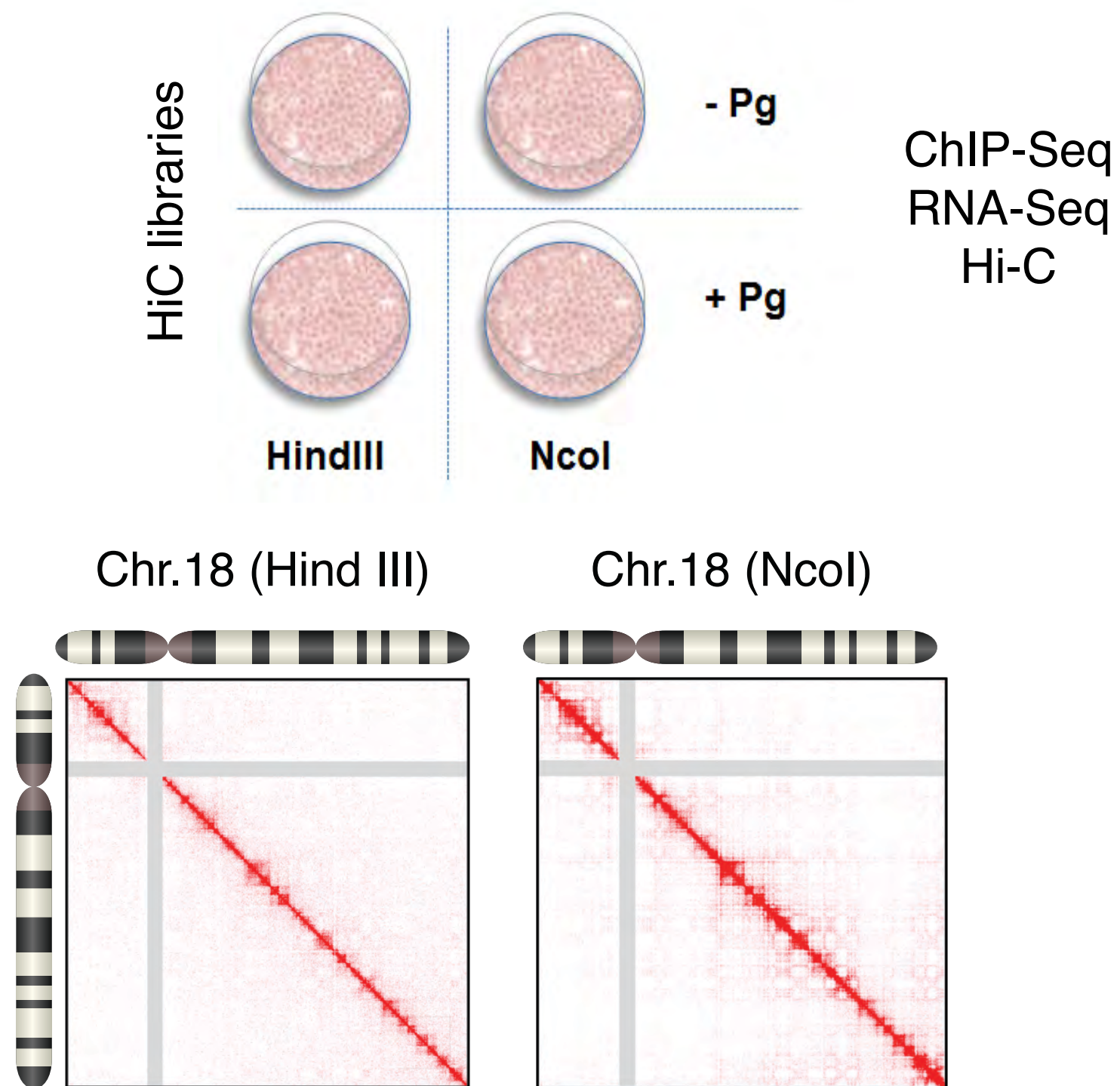


> 2,000 genes **Up**-regulated
> 2,000 genes **Down**-regulated

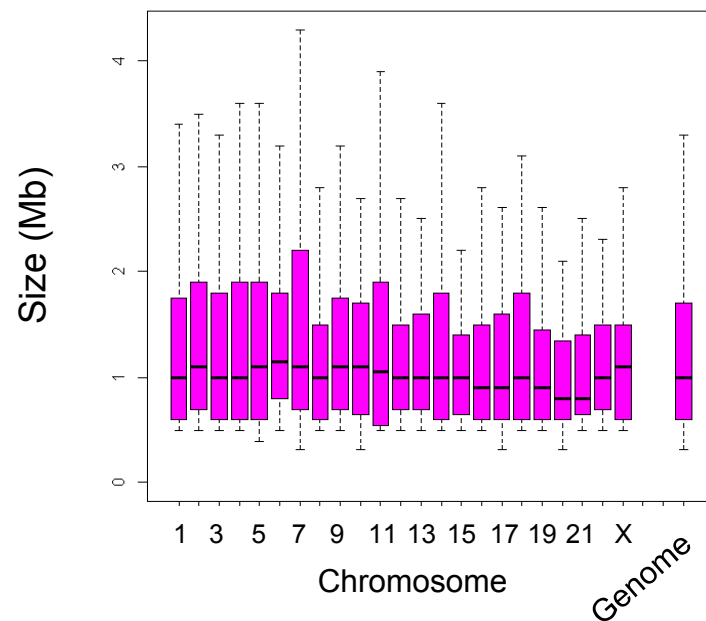
Regulation in 3D?

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

Experimental design

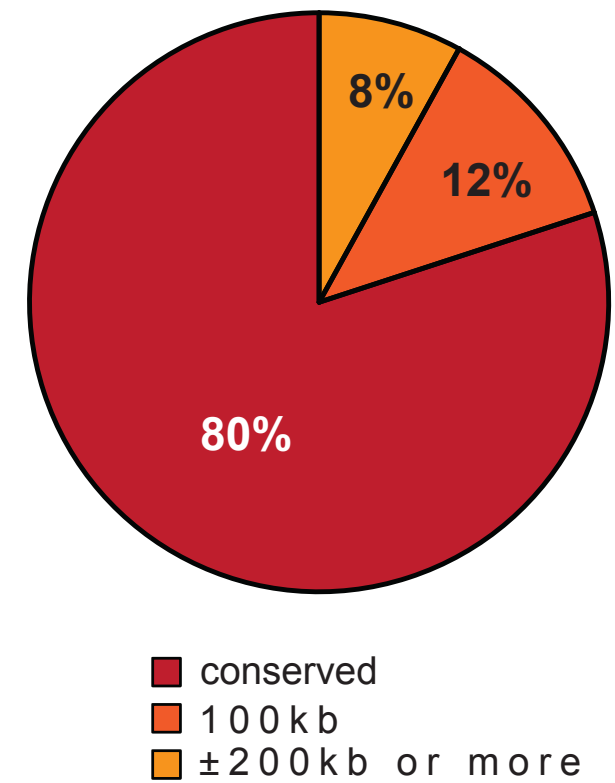
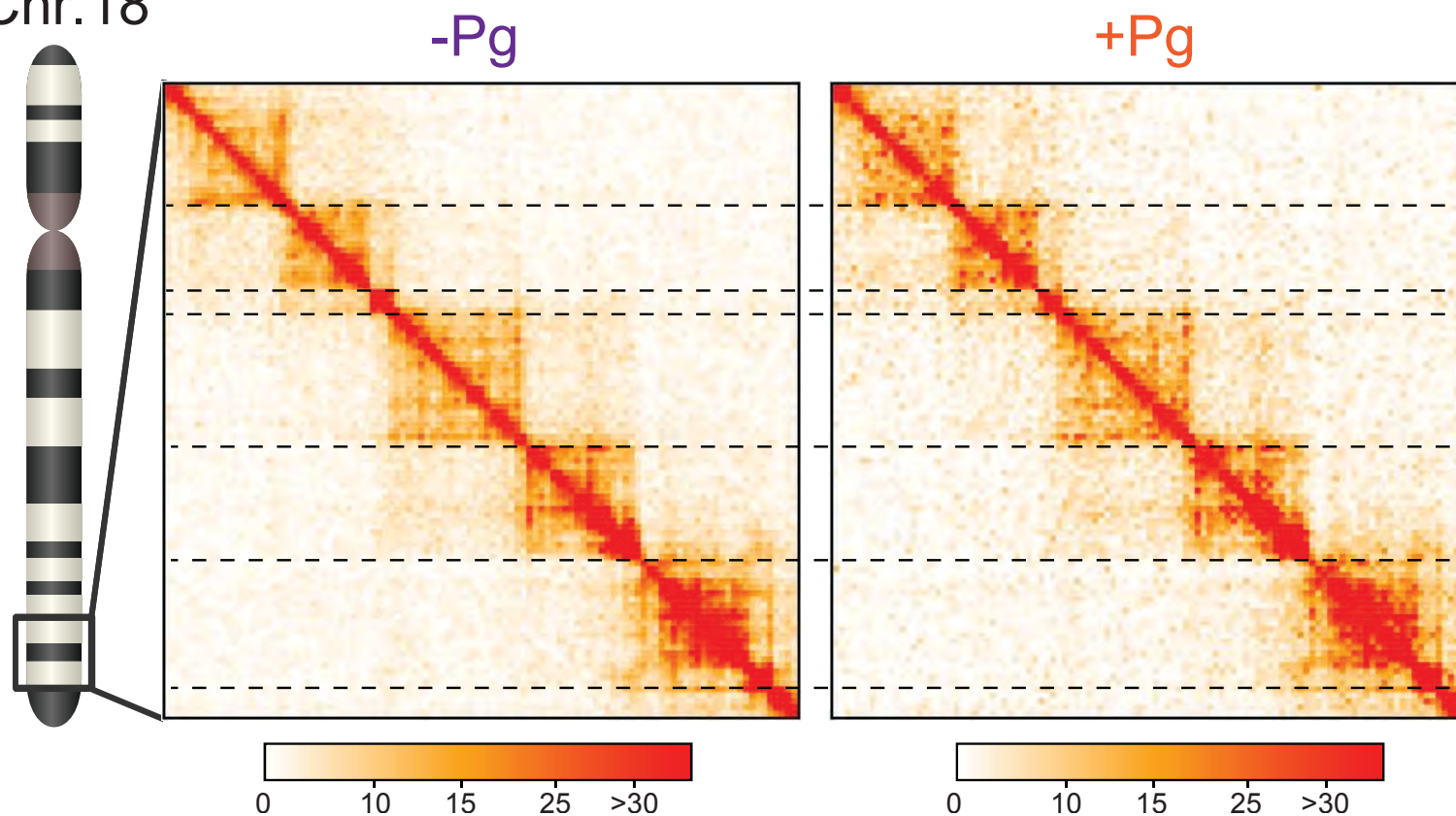


Are there TADs? how robust?

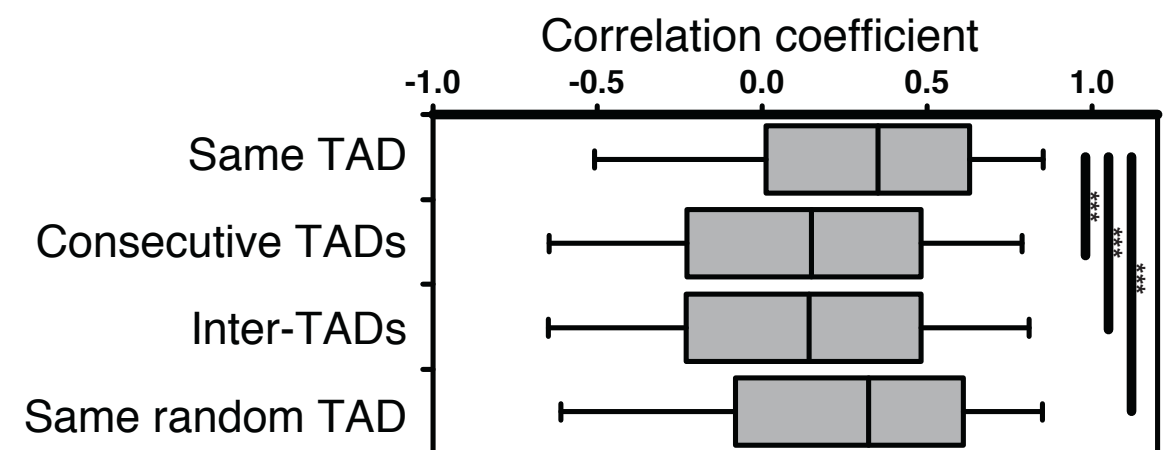
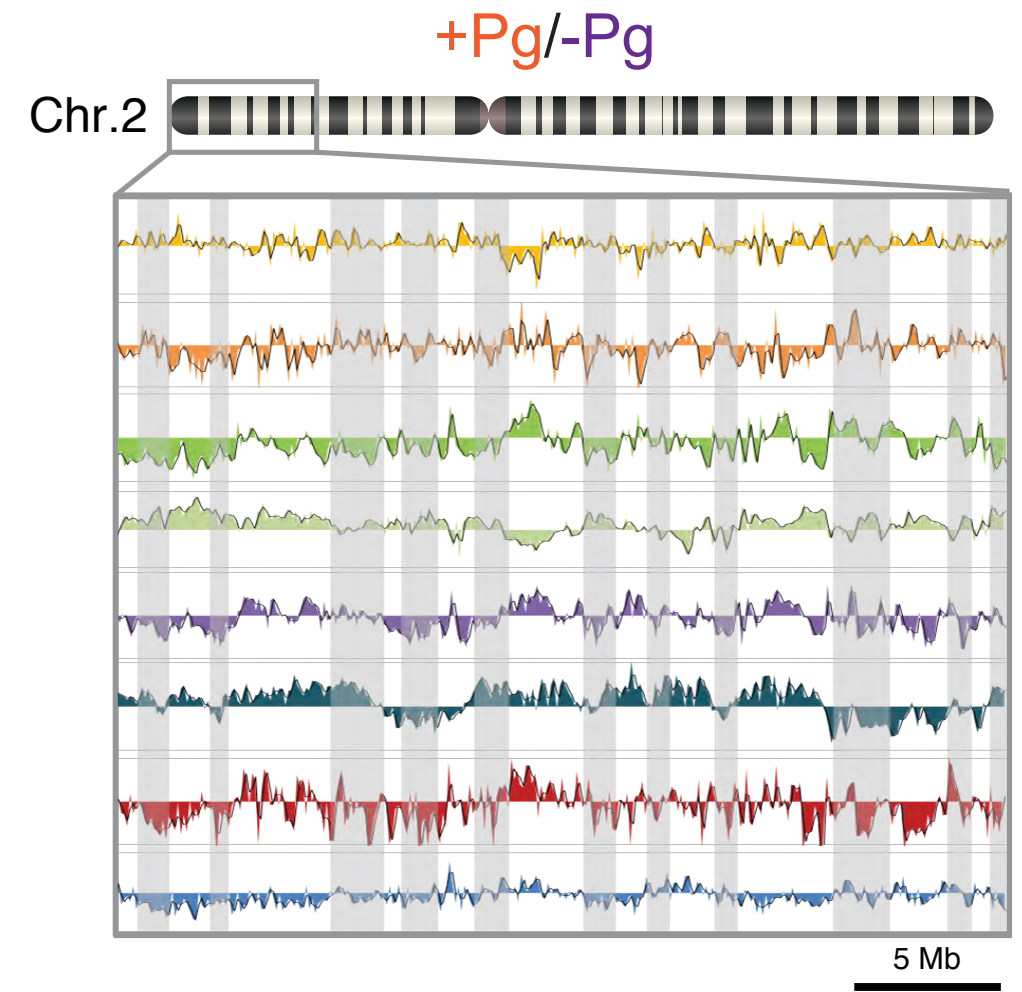
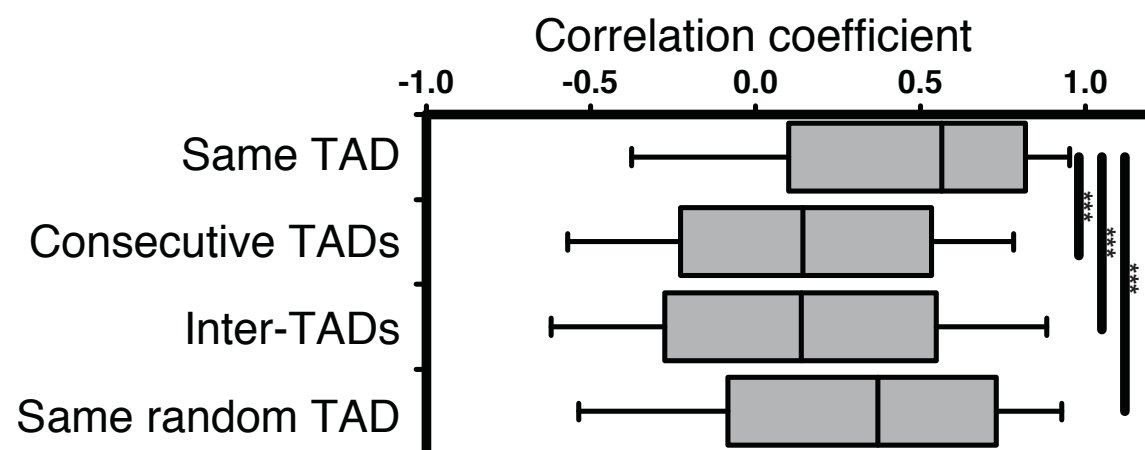
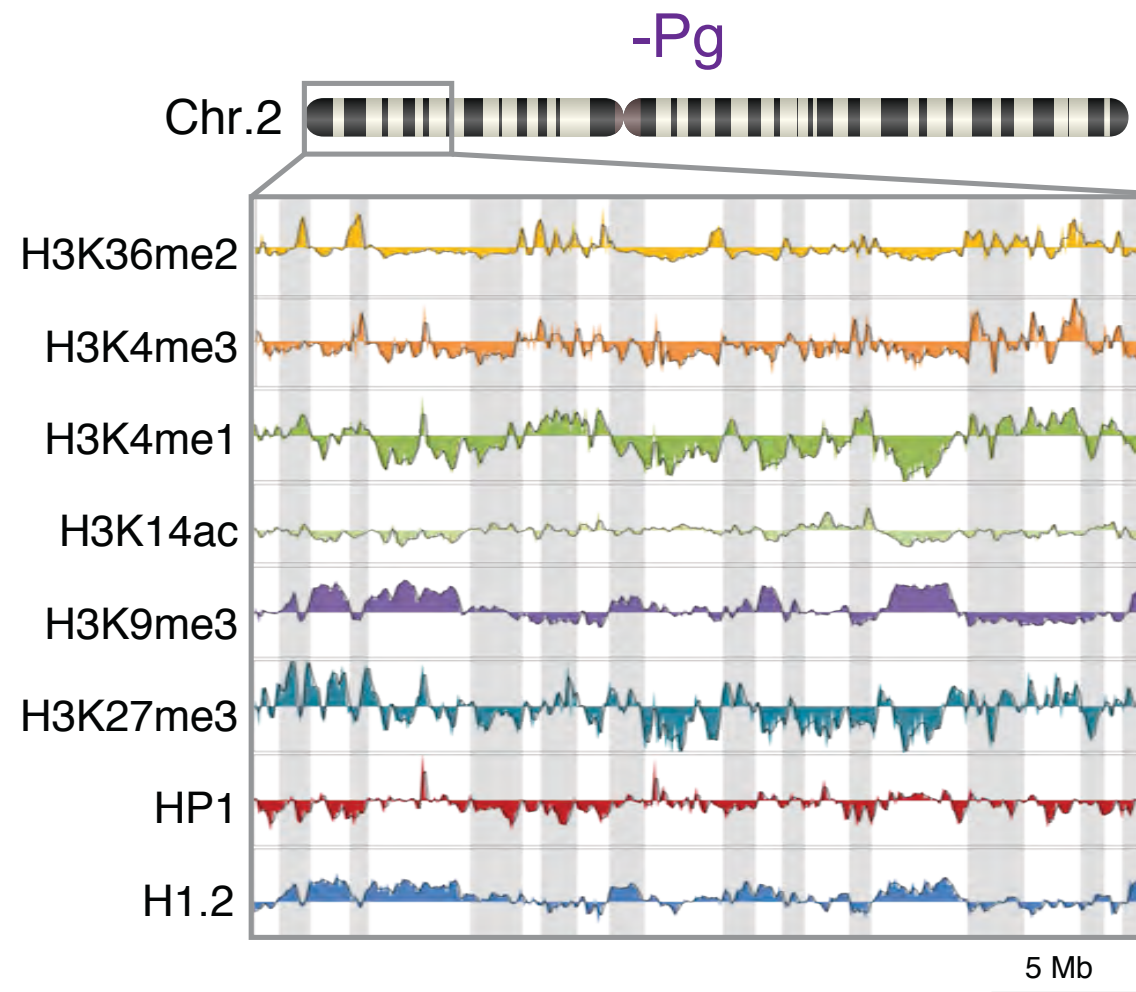


>2,000 detected TADs

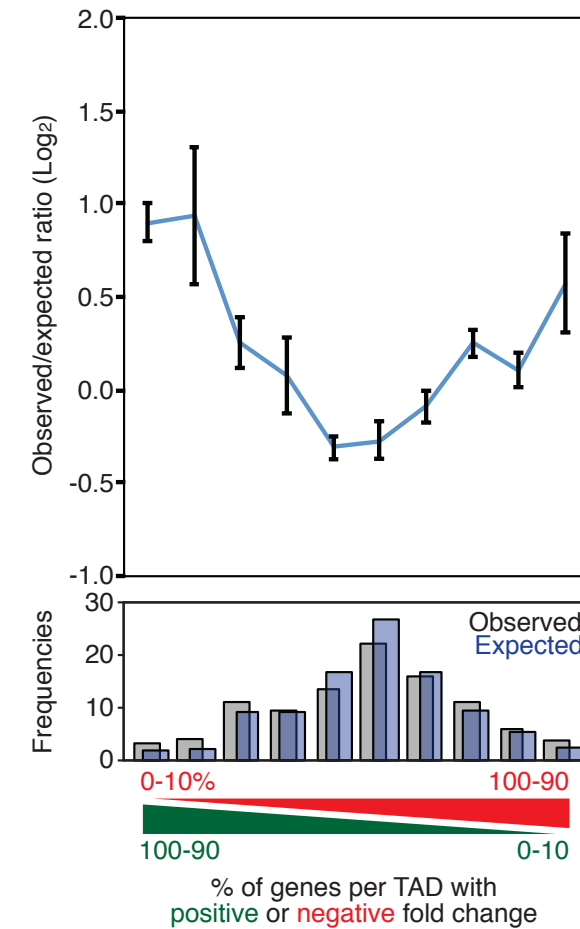
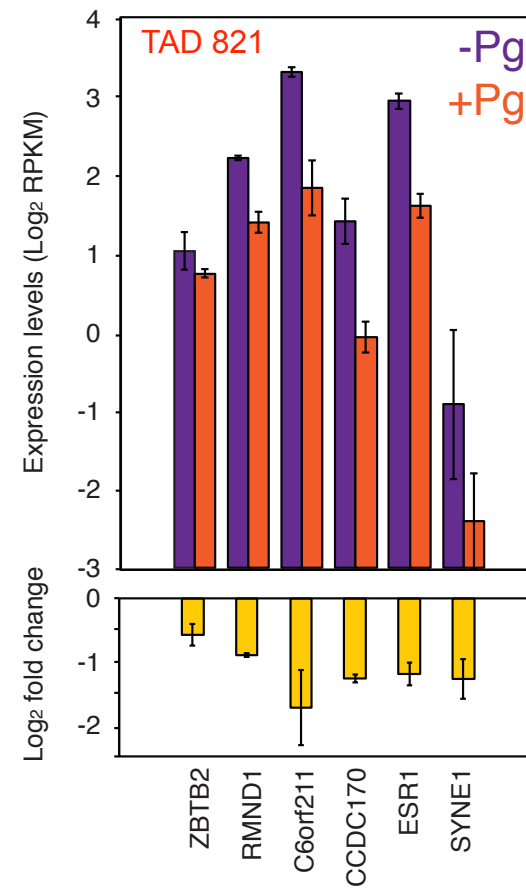
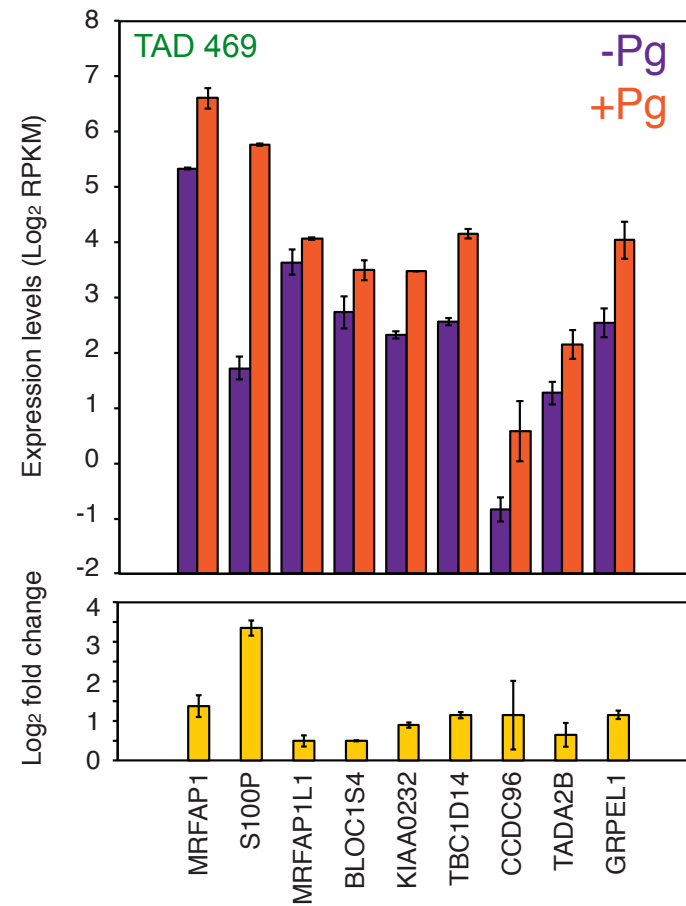
Chr.18



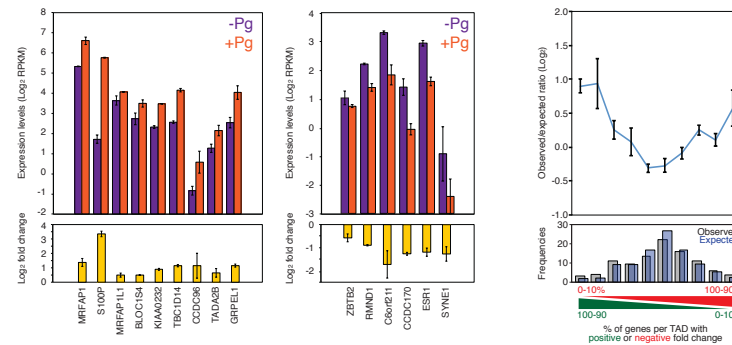
Are TADs homogeneous?



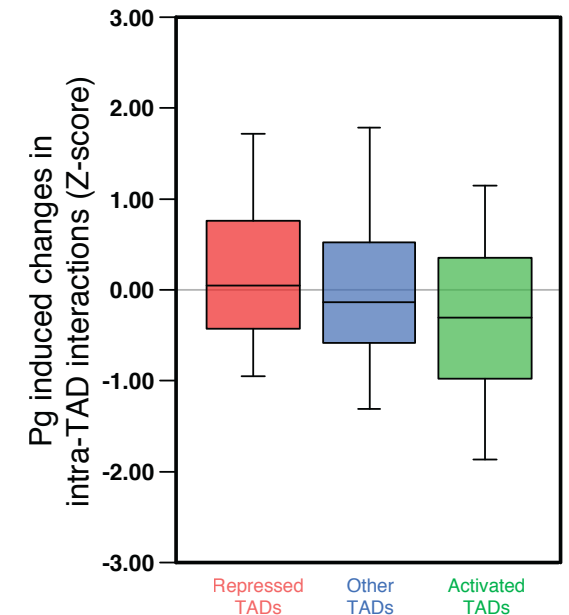
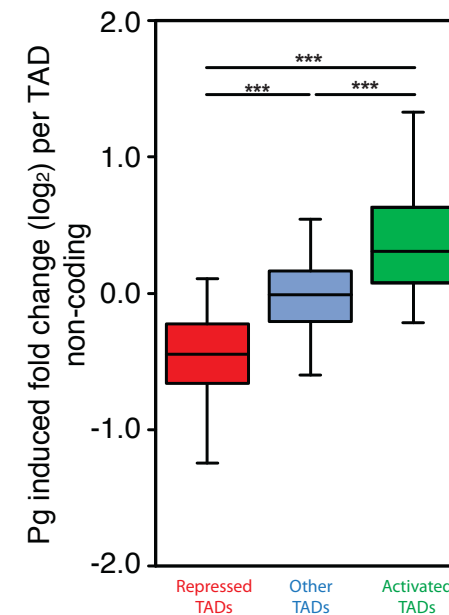
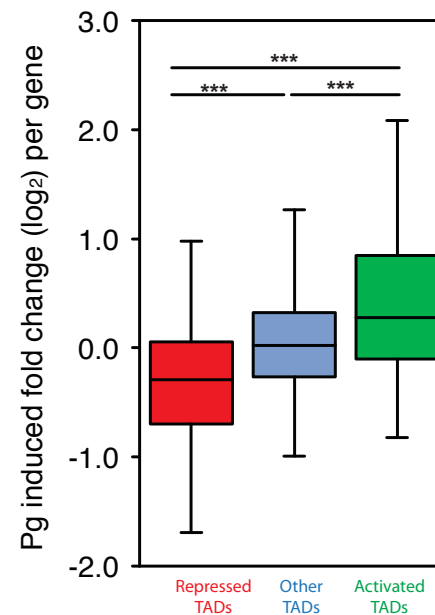
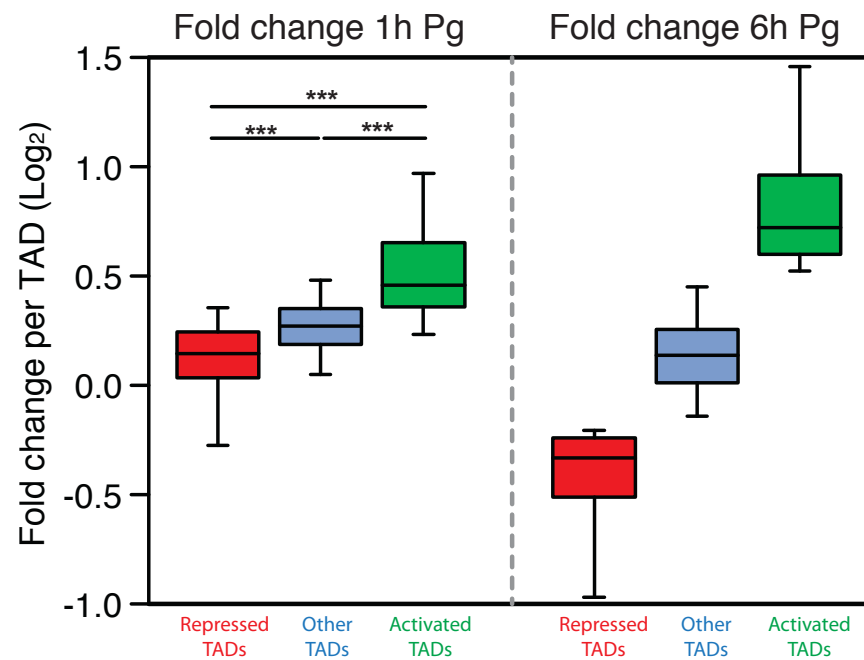
Do TADs respond differently to Pg treatment?



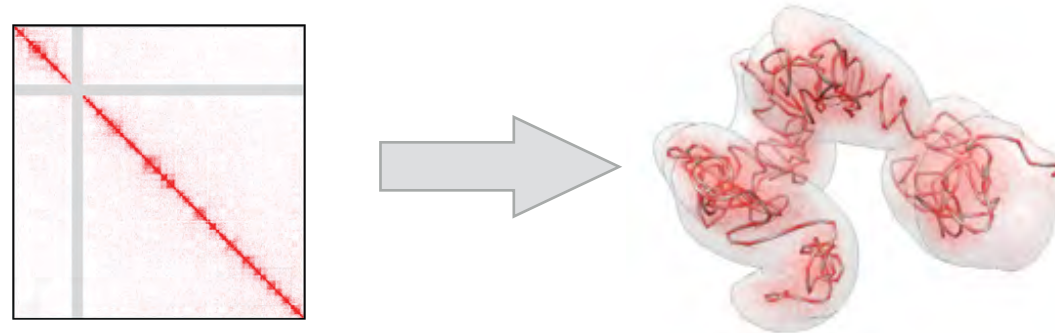
Do TADs respond differently to Pg treatment?



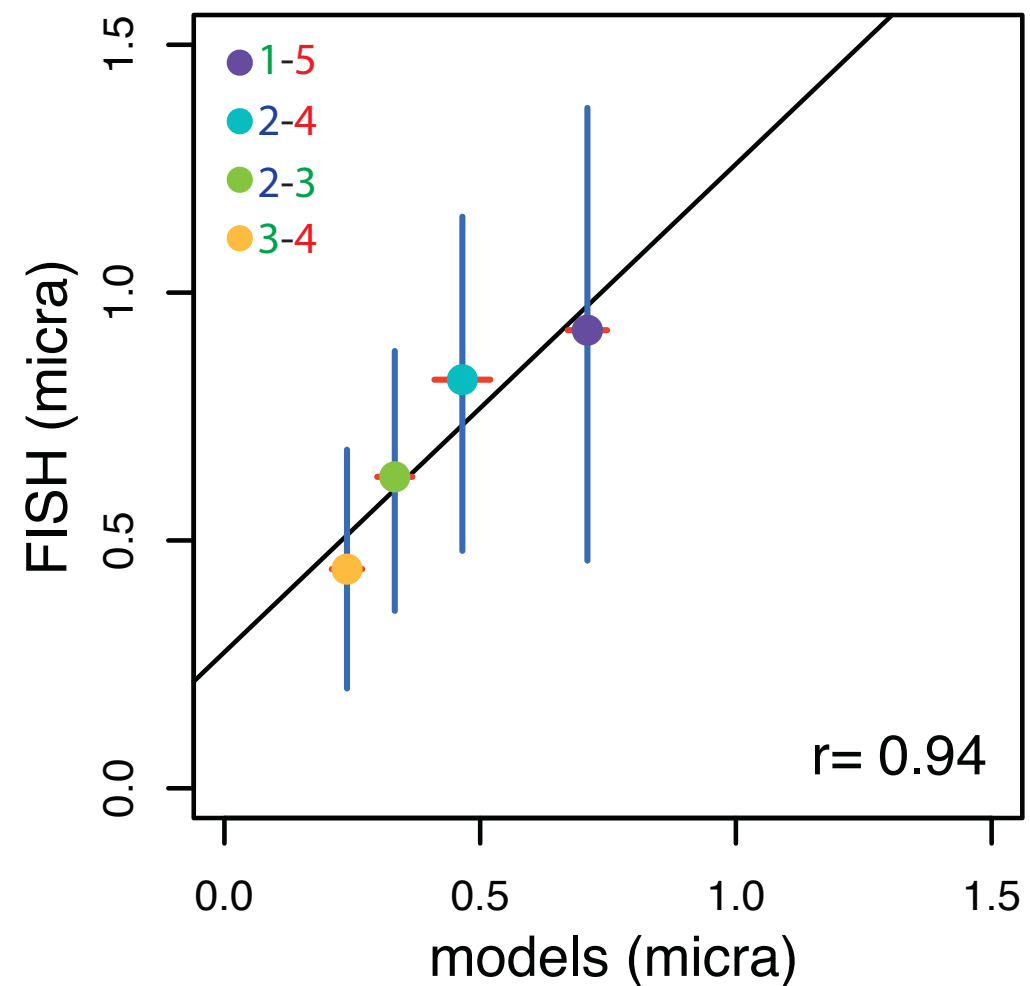
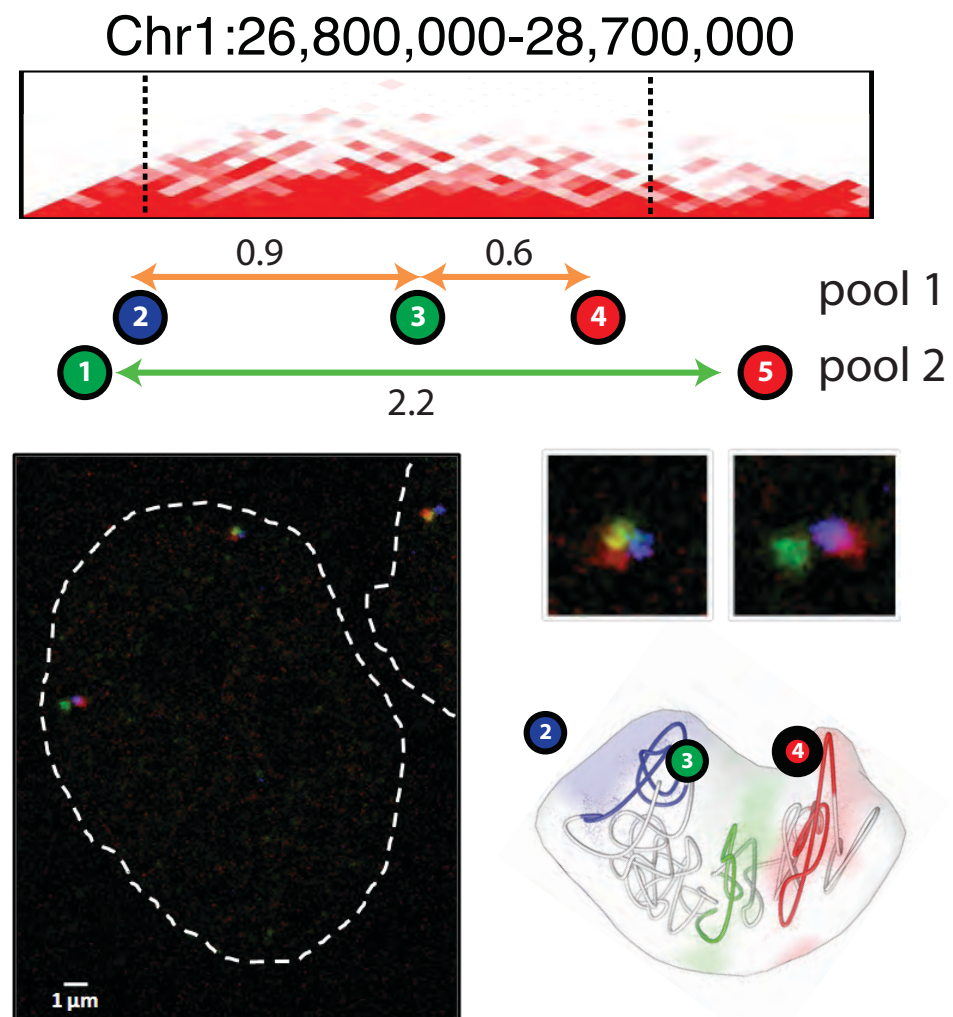
Pg induced fold change per TAD (6h)



Modeling 3D TADs

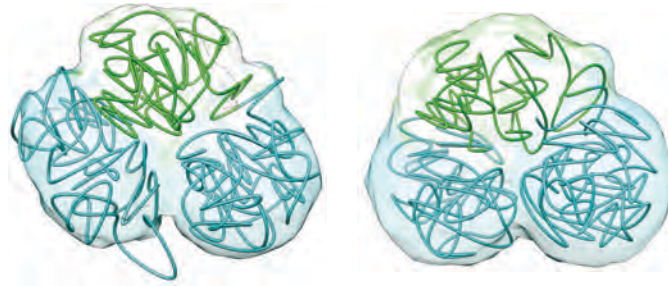


61 genomic regions containing 209 TADs covering 267Mb

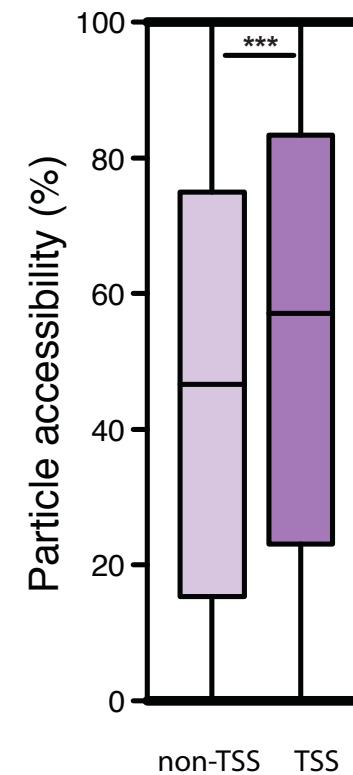
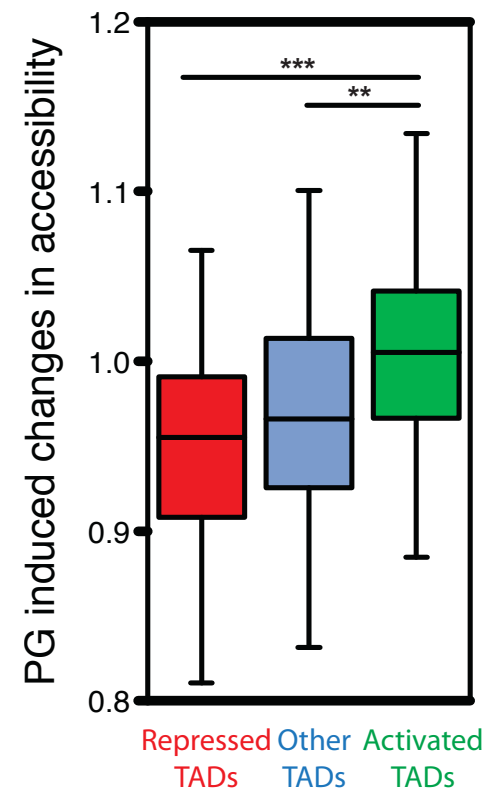
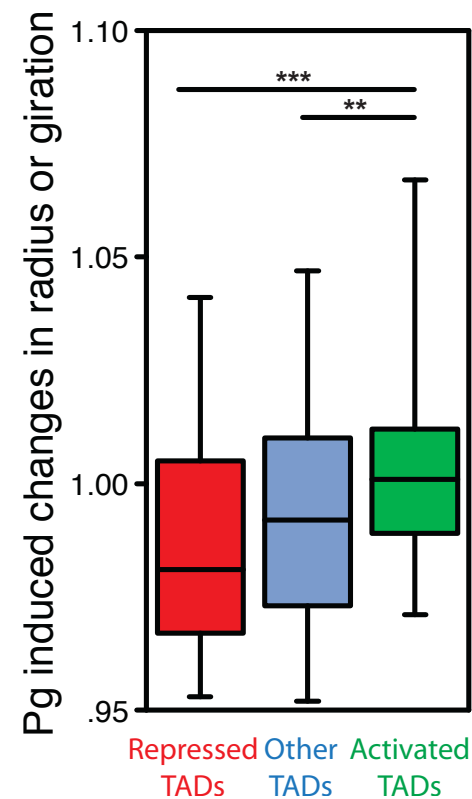
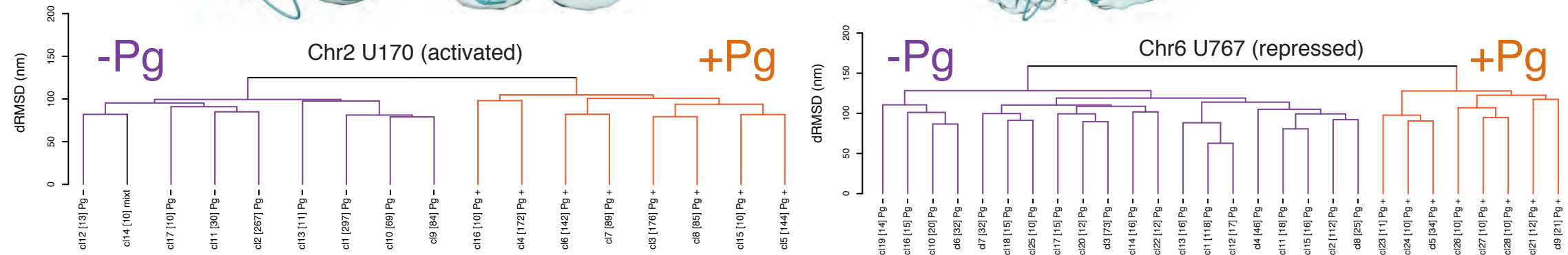
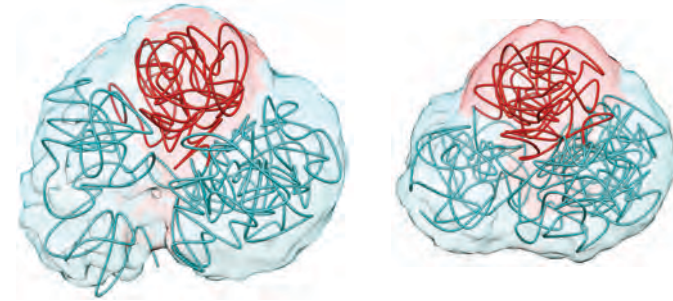


How TADs respond structurally to Pg?

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



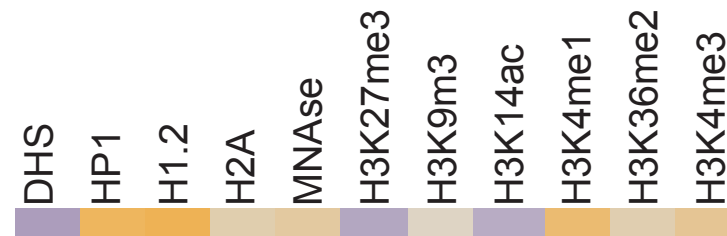
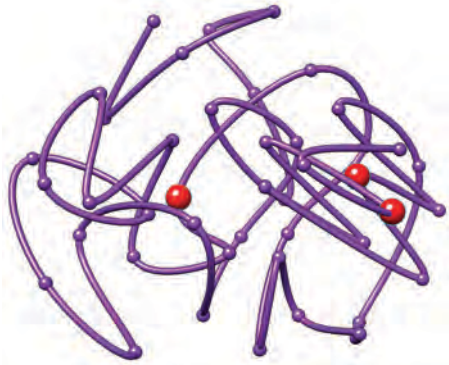
Chr6:71,800,000-76,500,000



Model for TAD regulation

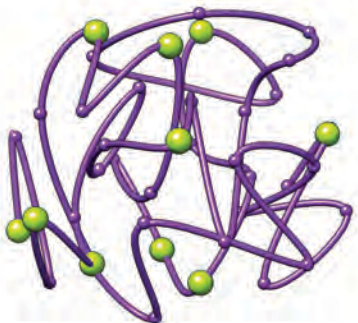
Repressed TAD

chr1 U41

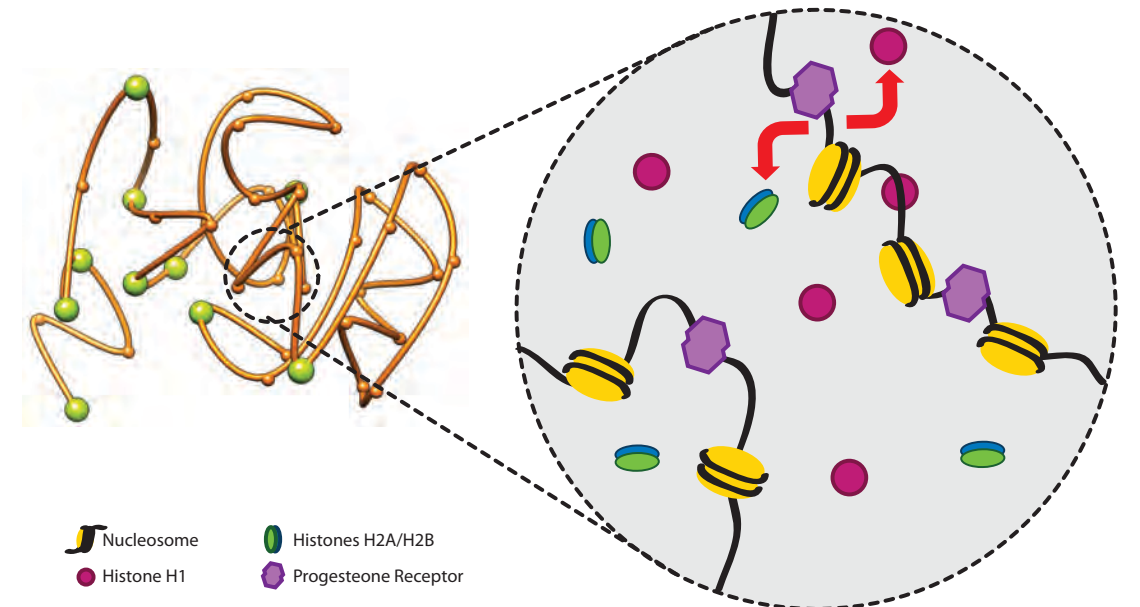
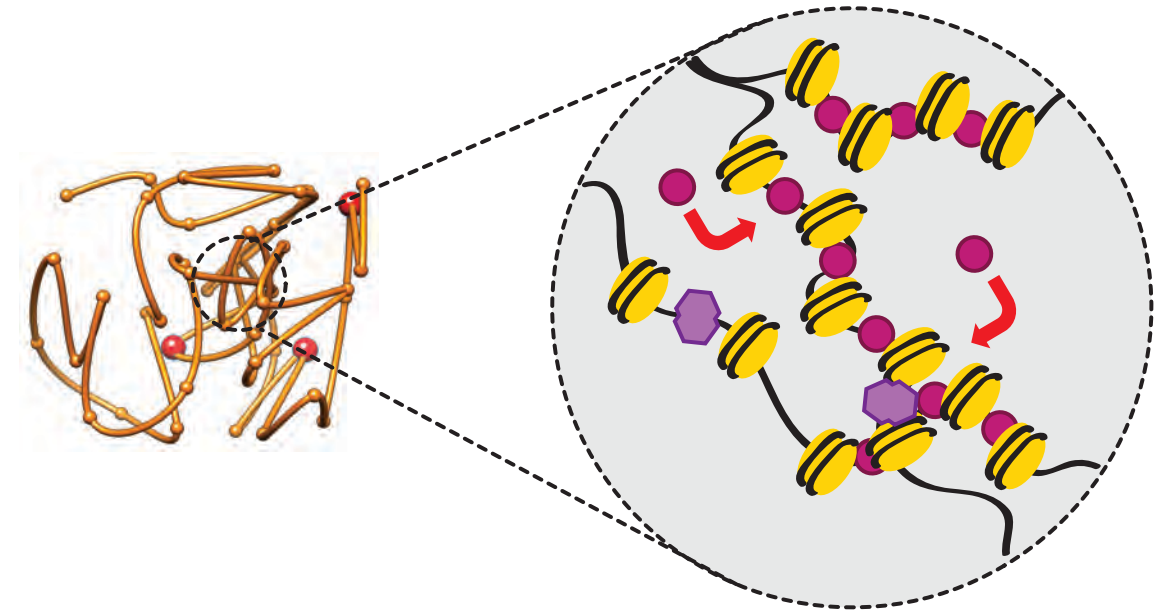


Activated TAD

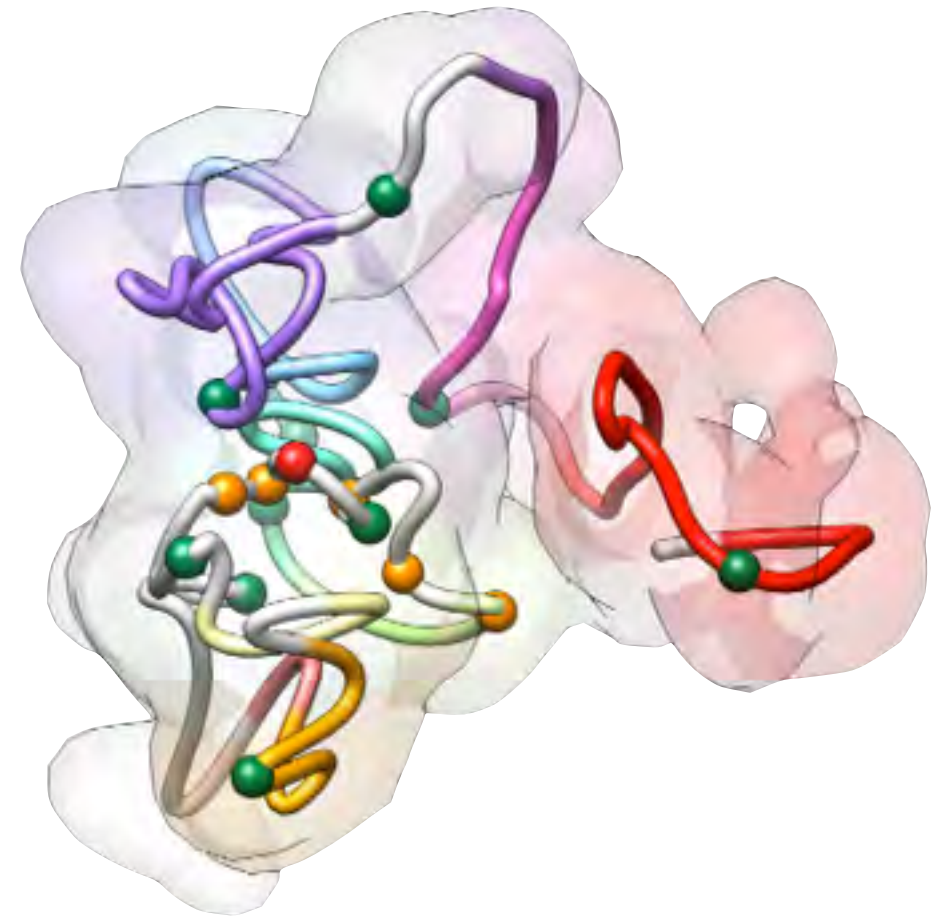
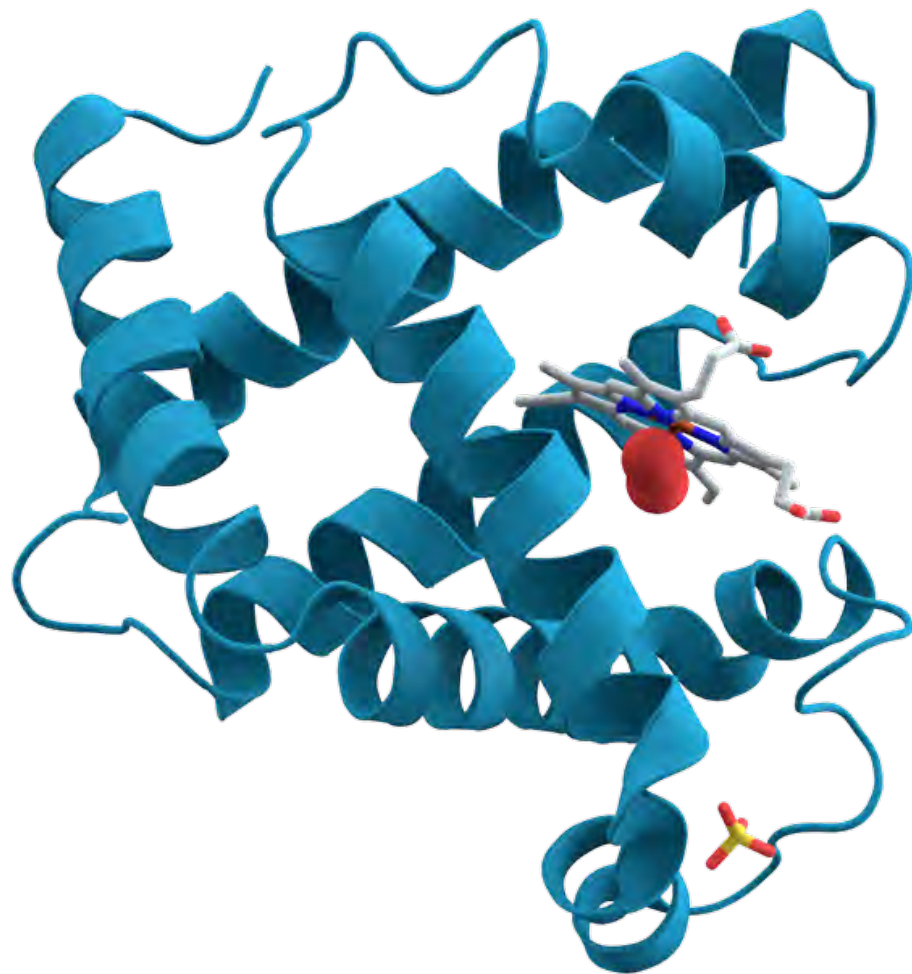
chr2 U207



Structural transition
+Pg

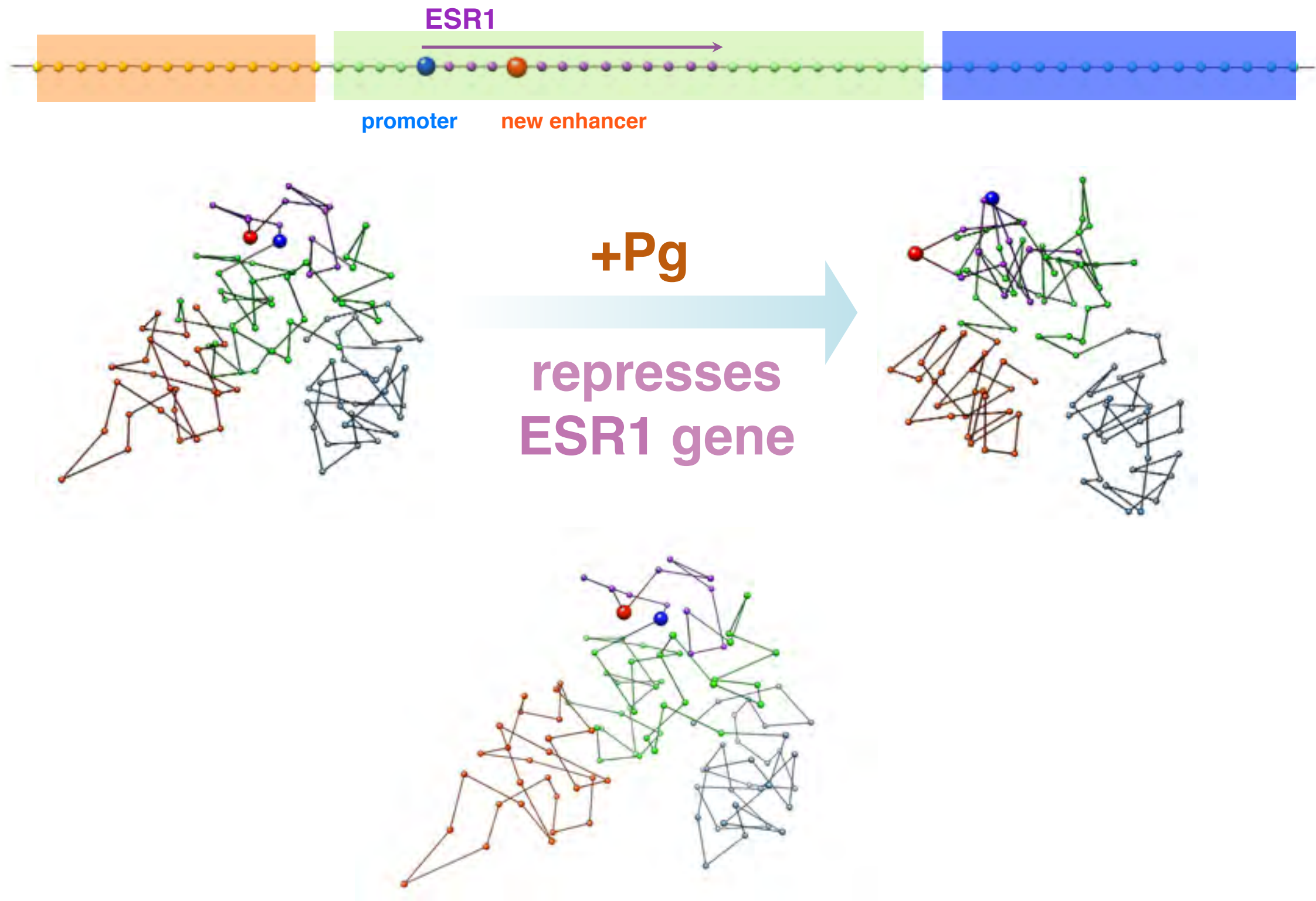


 Nucleosome
 Histone H1
 Histones H2A/H2B
 Progesterone Receptor



STRUCTURE  **FUNCTION**

Structure >> Function!



Acknowledgments



Davide Baù
François le Dily
François Serra

David Dufour
Mike Goodstadt
Gireesh Bogu
Francisco Martínez-Jiménez



Job Dekker

Program in Systems Biology
Department of Biochemistry and Molecular Pharmacology
University of Massachusetts Medical School
Worcester, MA, USA



Kerstin Bystricky

Chromatin and gene expression
Laboratoire de Biologie Moléculaire Eucaryote - CNRS
Toulouse, France



Miguel Beato & Guillaume Filion

Gene Regulation, Stem Cells and Cancer
Centre de Regulació Genòmica
Barcelona, Spain

<http://marciuslab.org>
<http://3DGenomes.org>
<http://cnag.cat> · <http://crg.cat>

