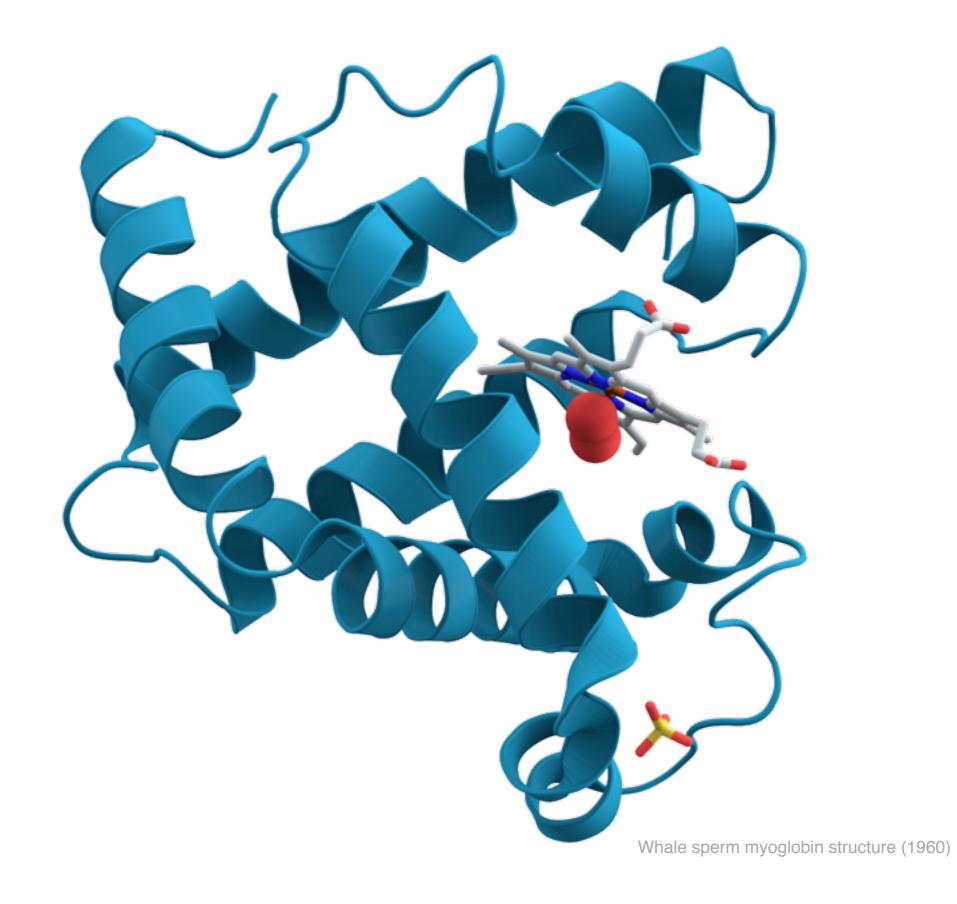
Structure determination of genomes and genomic domains by satisfaction of spatial restraints

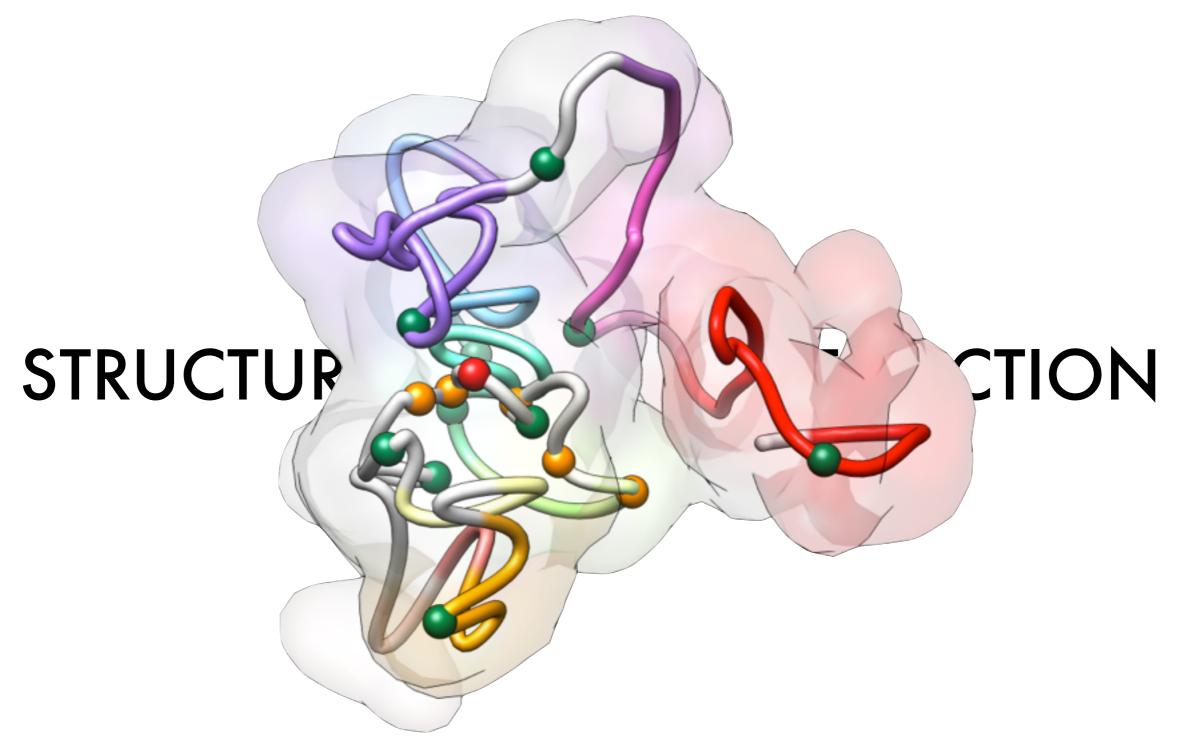
Marc A. Marti-Renom Genome Biology Group (CNAG) Structural Genomics Group (CRG)





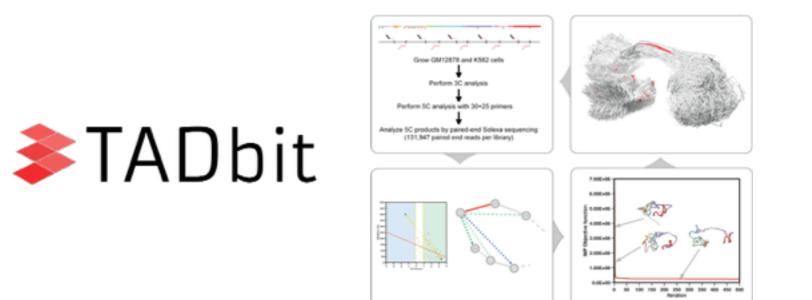






alpha-globin genomic domain structure (2011)



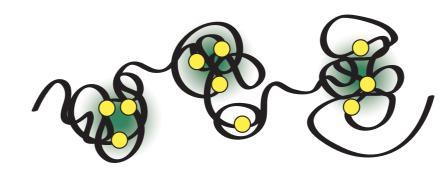








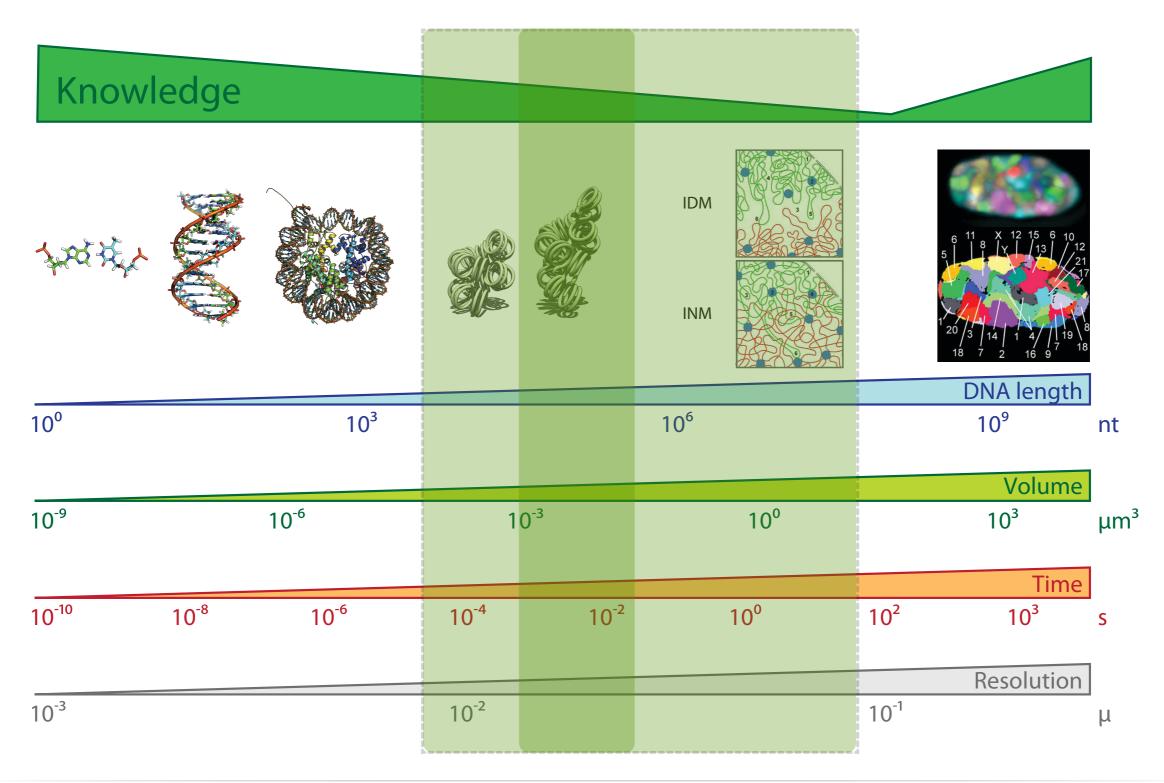






Resolution Gap

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

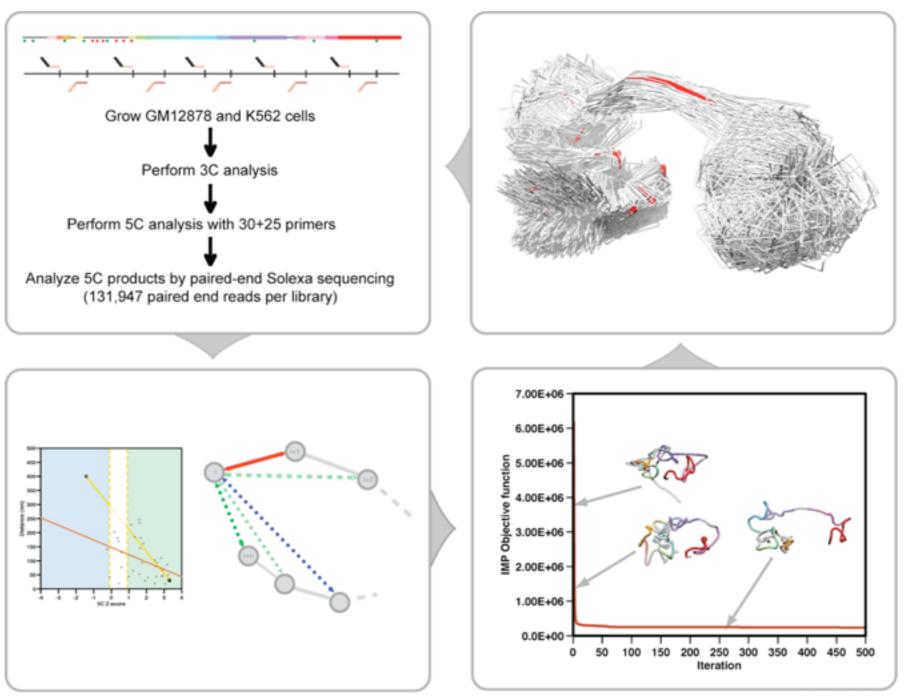




Hybrid Method

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

Experiments



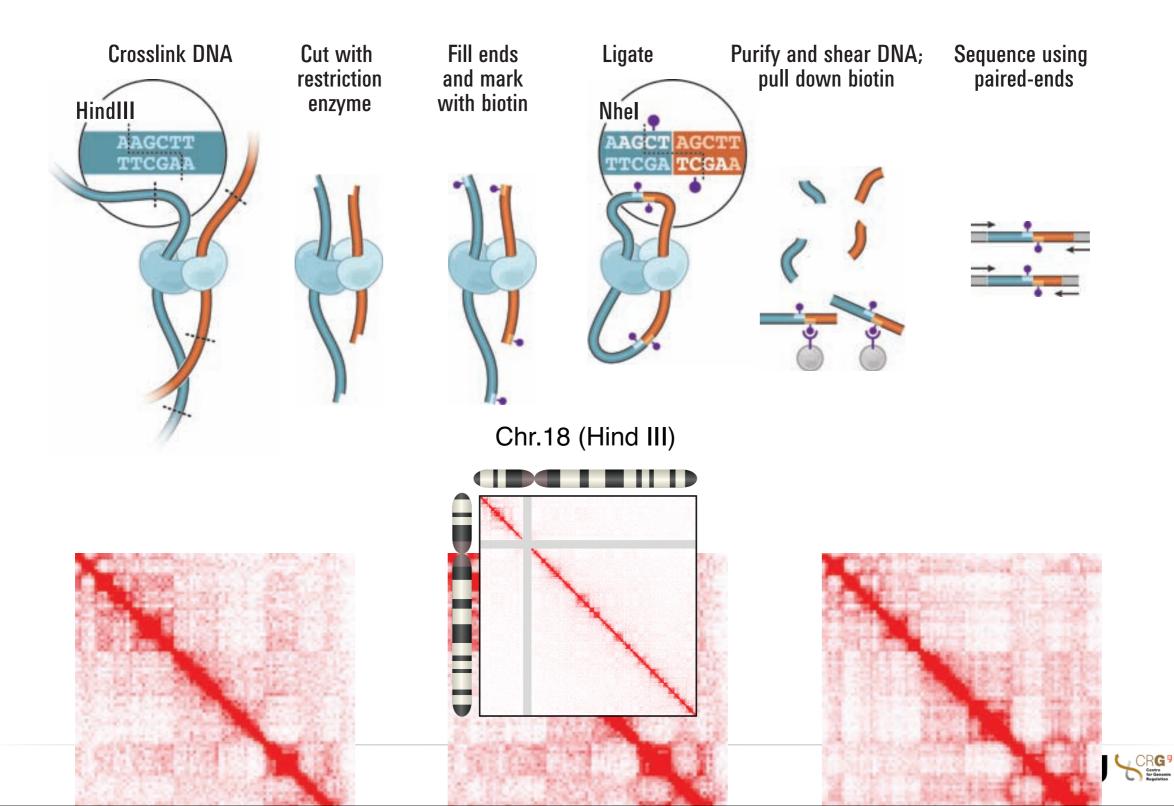
Computation

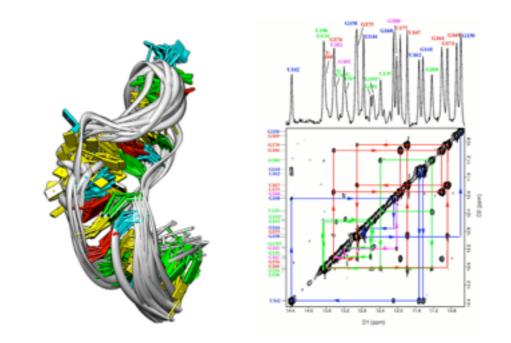




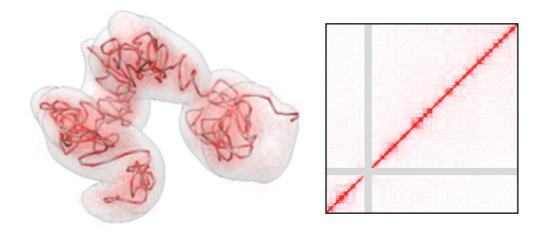
Hi-C technology

Lieberman-Aiden, E. et al. Science 326, 289-293 (2009). http://3dg.umassmed.edu





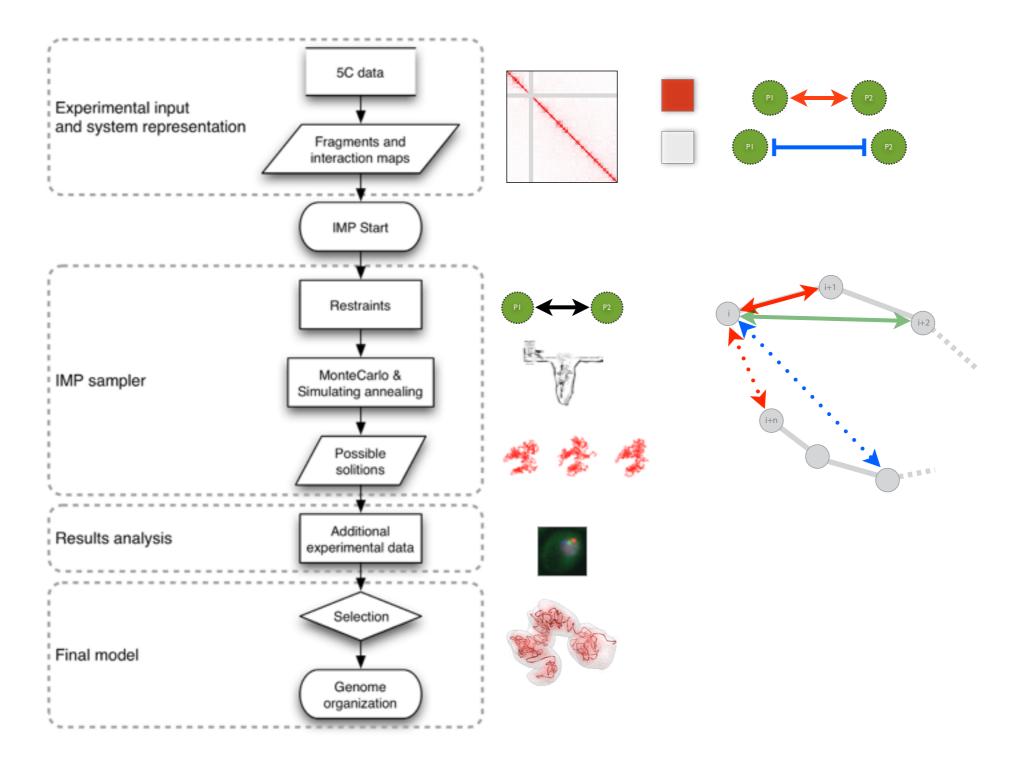
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data



TADbit



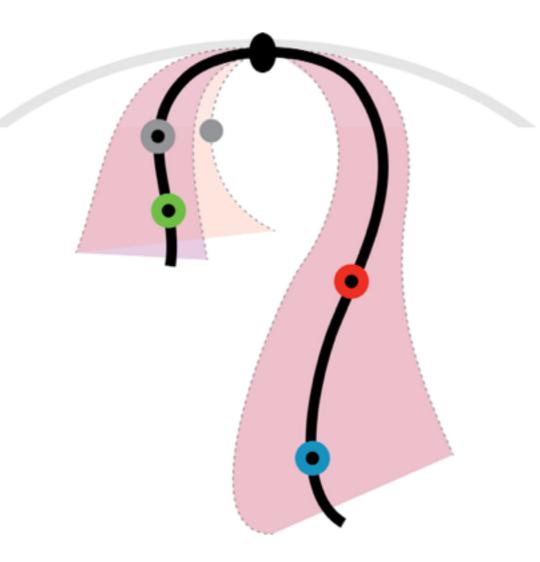








Mating-specific structure for yeast chrlll?





Jon-Matthew Belton UMASS



Davide Baù CNAG/CRG

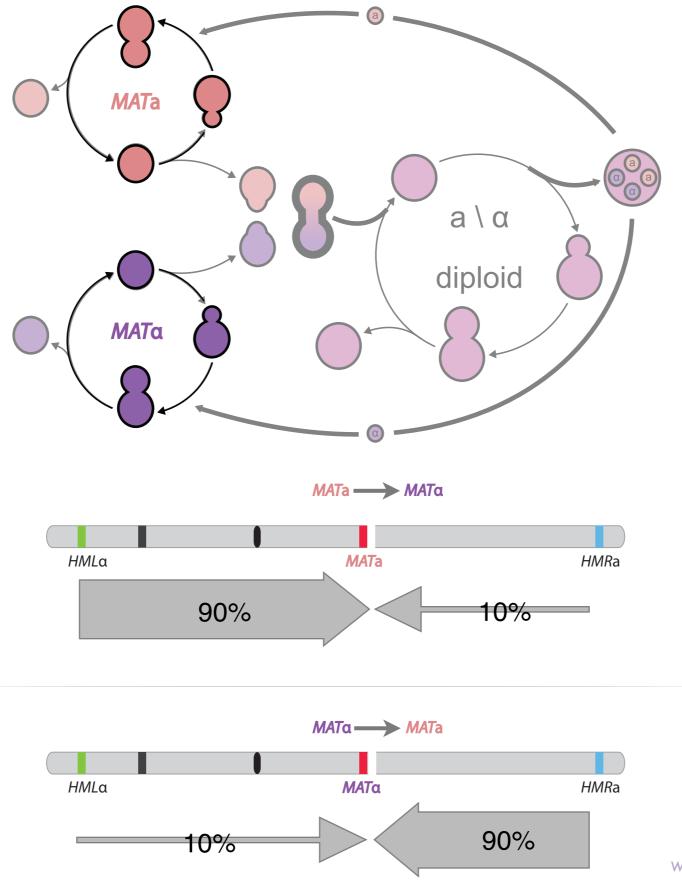


Program in Systems Biology Department of Biochemistry and Molecular Pharmacology University of Massachusetts Medical School Worcester, MA, USA



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

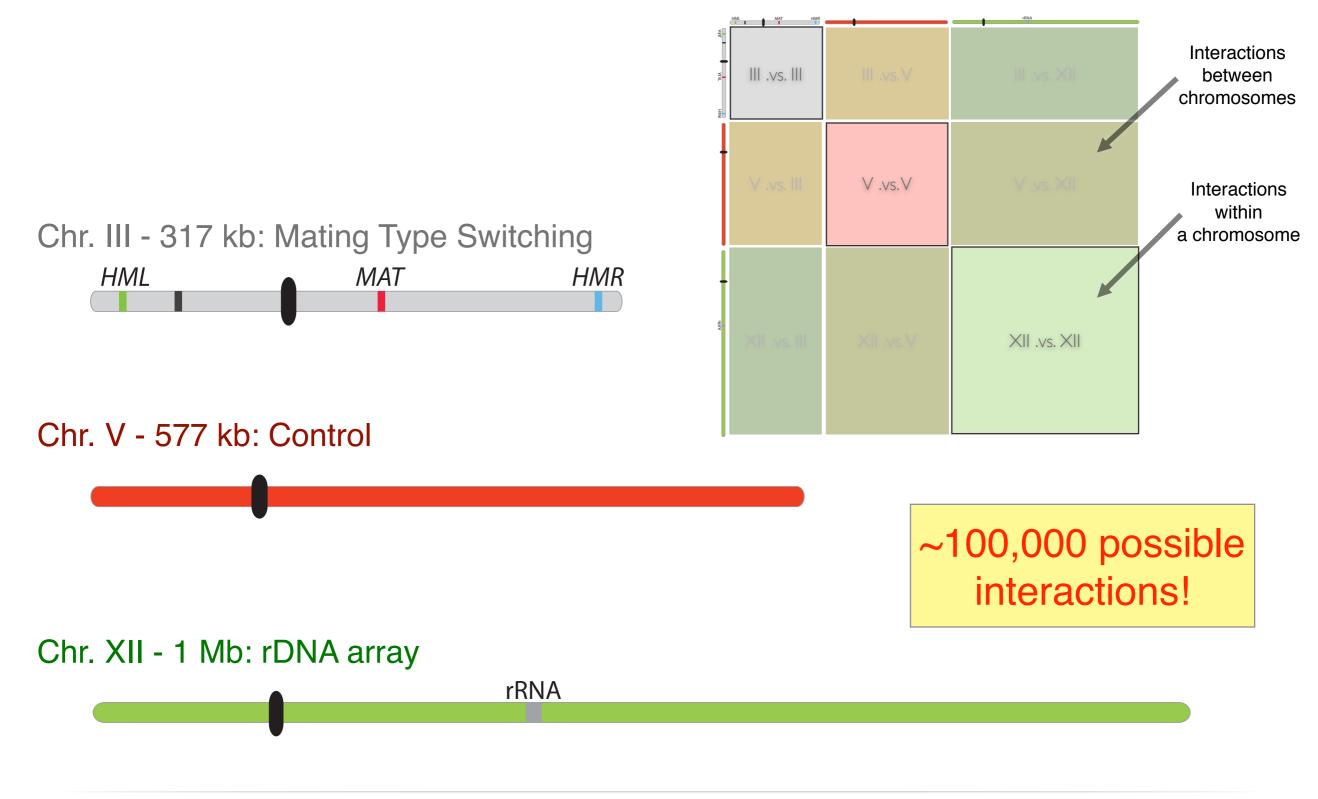




Wu, X. H., C. Wu, et al. Genetics (1997).



5C chromosome conformation

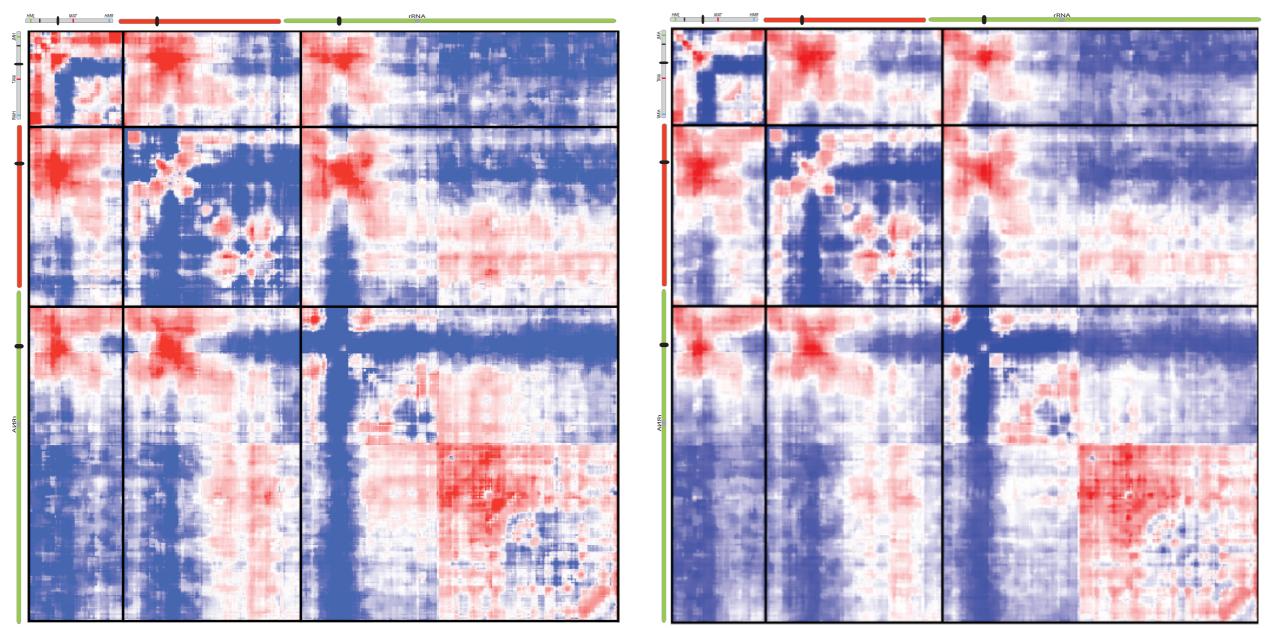




Global structure is similar between mating types

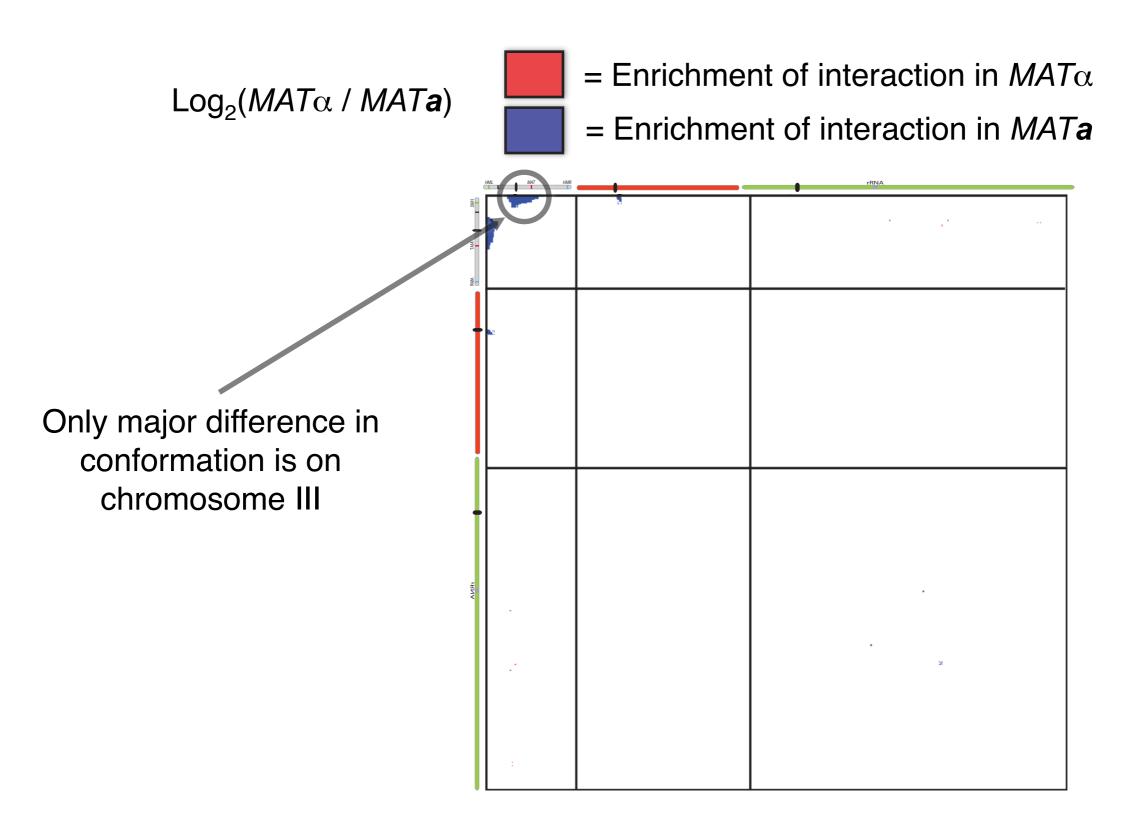
MATa

ΜΑΤα





Difference in chromosome conformation



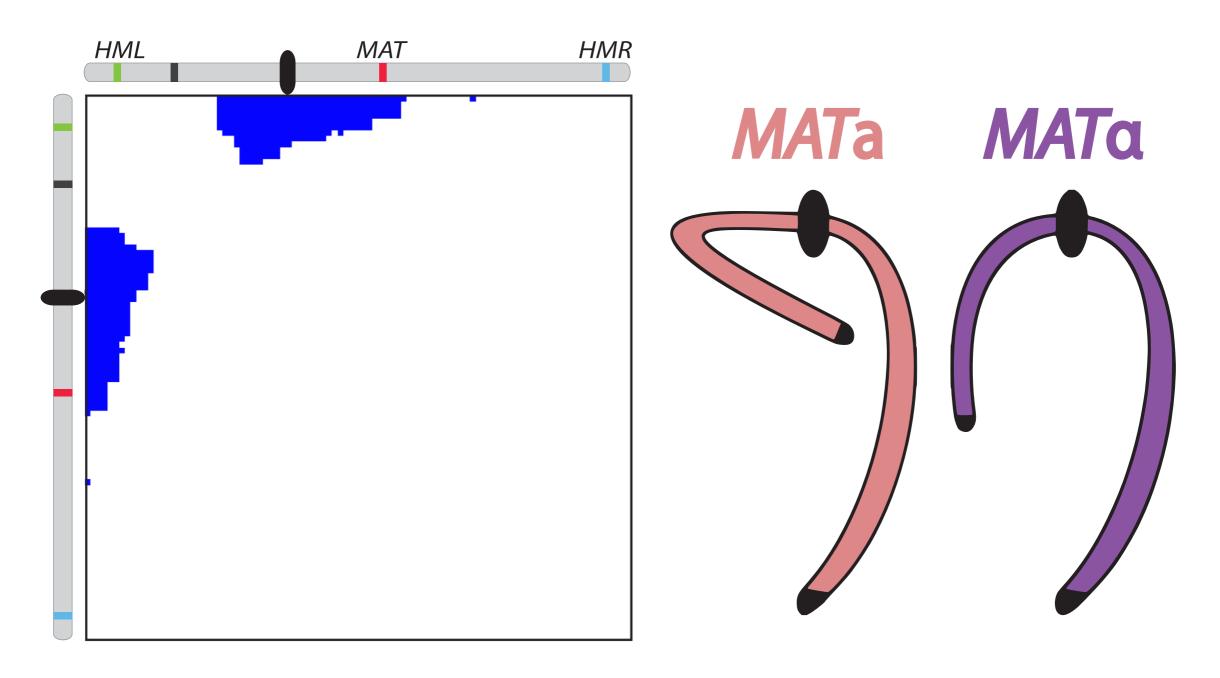


Difference in conformation of the left arm of chromosome III

 $Log_2(MAT\alpha / MATa)$

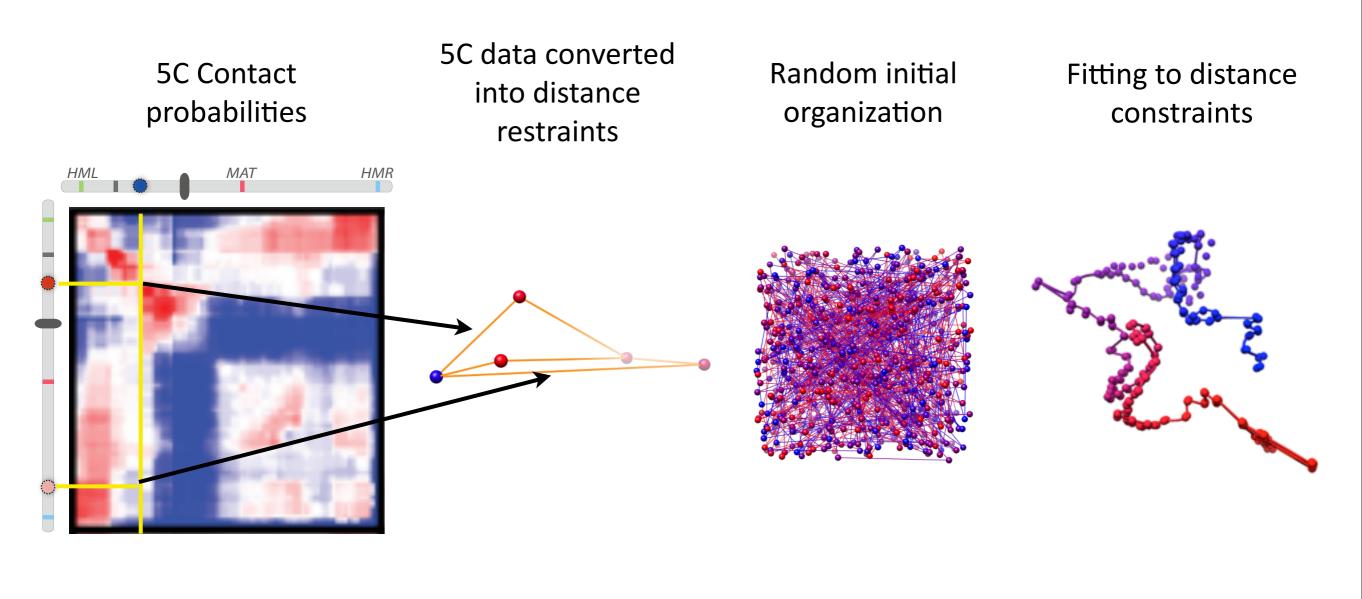


- = Enrichment of interaction in $MAT\alpha$
- = Enrichment of interaction in MATa





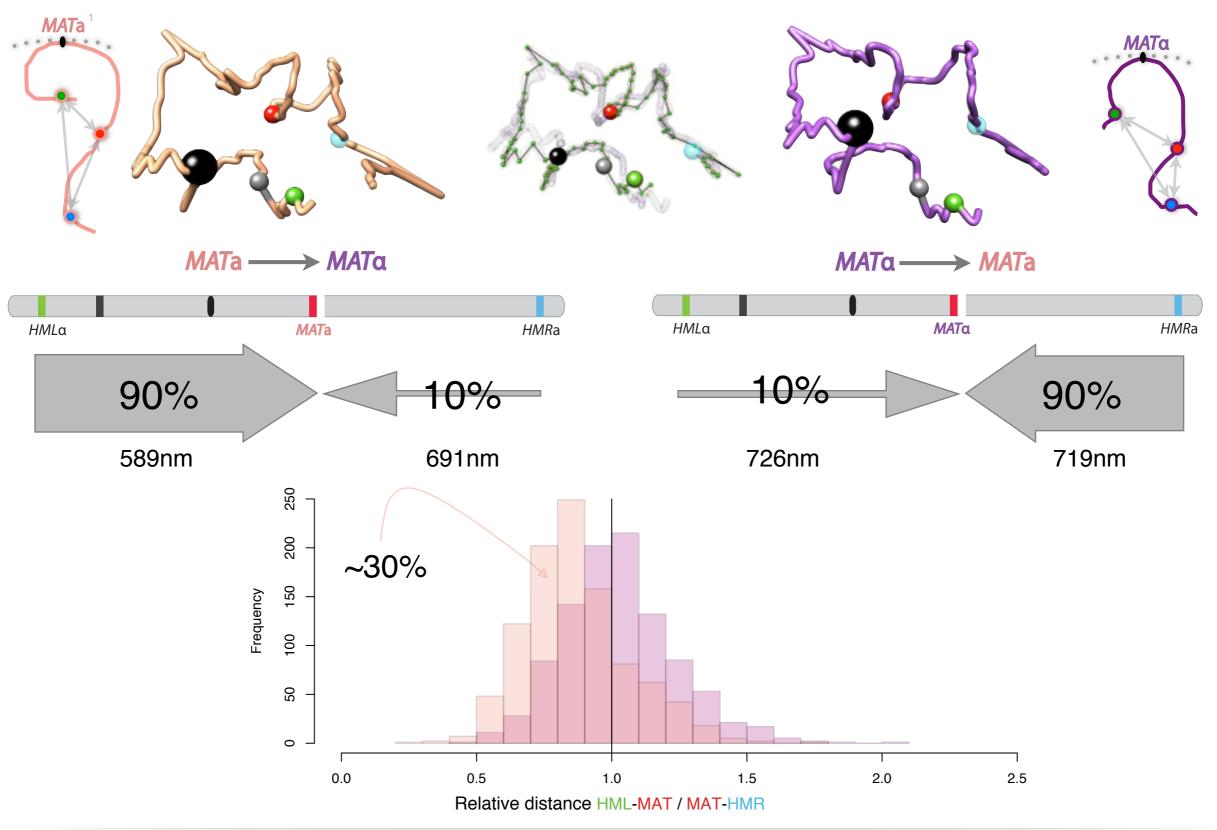
Average 3D models of ChrIII using IMP



| MATa | 5,000 models | MATa |
|------|----------------|------|
| | 1,000 selected | MAIU |



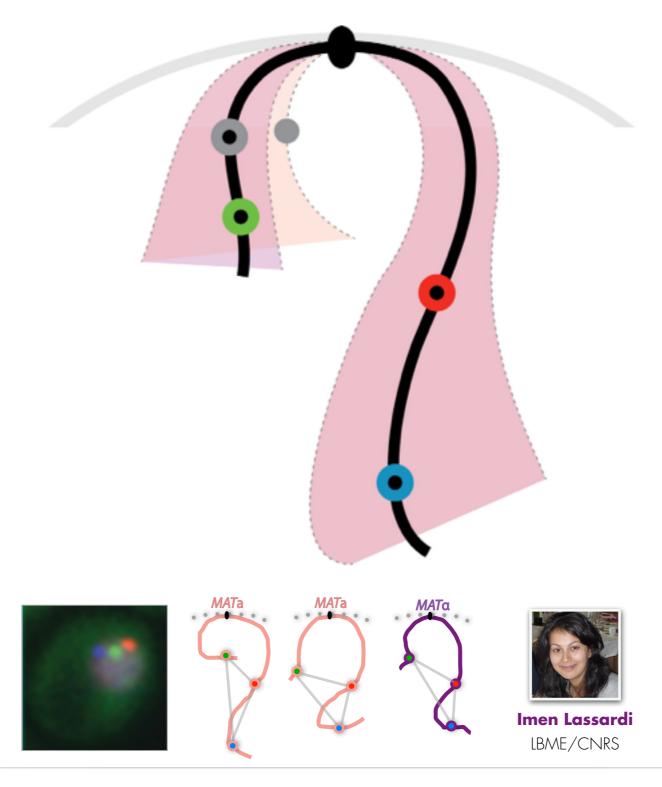
Mating type-specific conformation of chromosome III





3D chrlll for mating in yeast

Sub-population in MATa responsible of mating-type recombination





Structuring the COLORs of chromatin

M



Davide Baù



François Serra



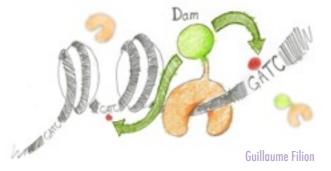
Guillaume Filion Gene Regulation, Stem Cells and Cancer Centre de Regulació Genòmica Barcelona, Spain

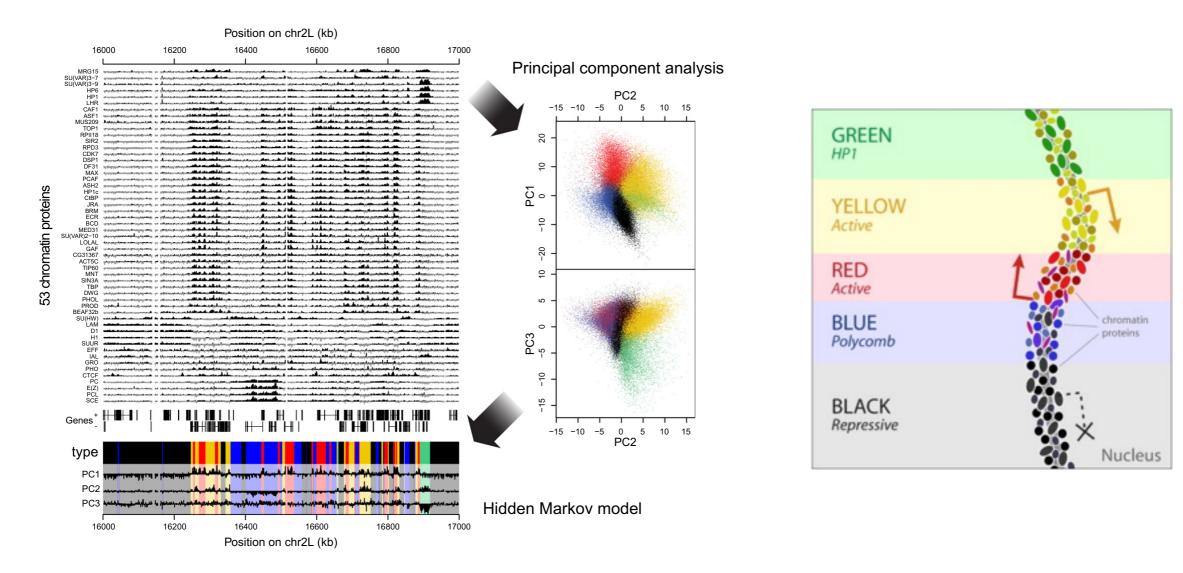


The COLORs

Filion et al. (2010). Cell, 143(2), 212–224.



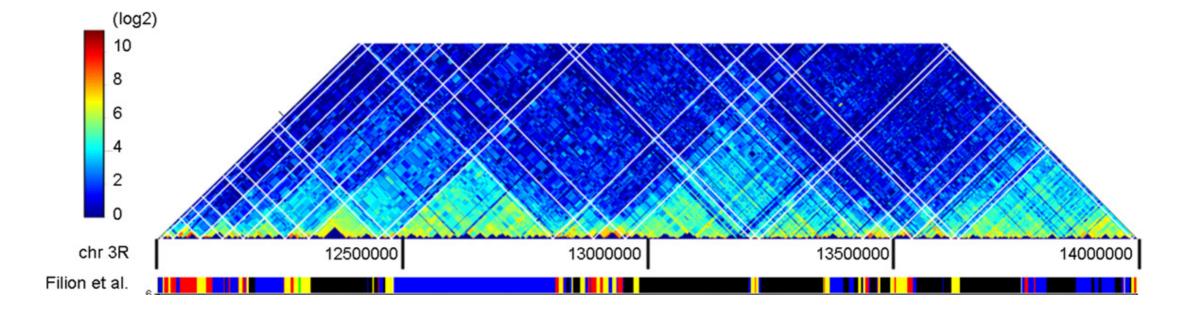


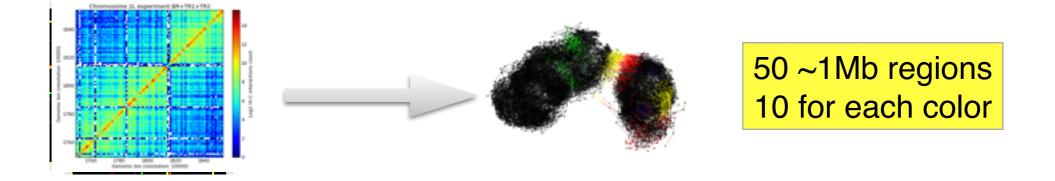




Functional COLORs

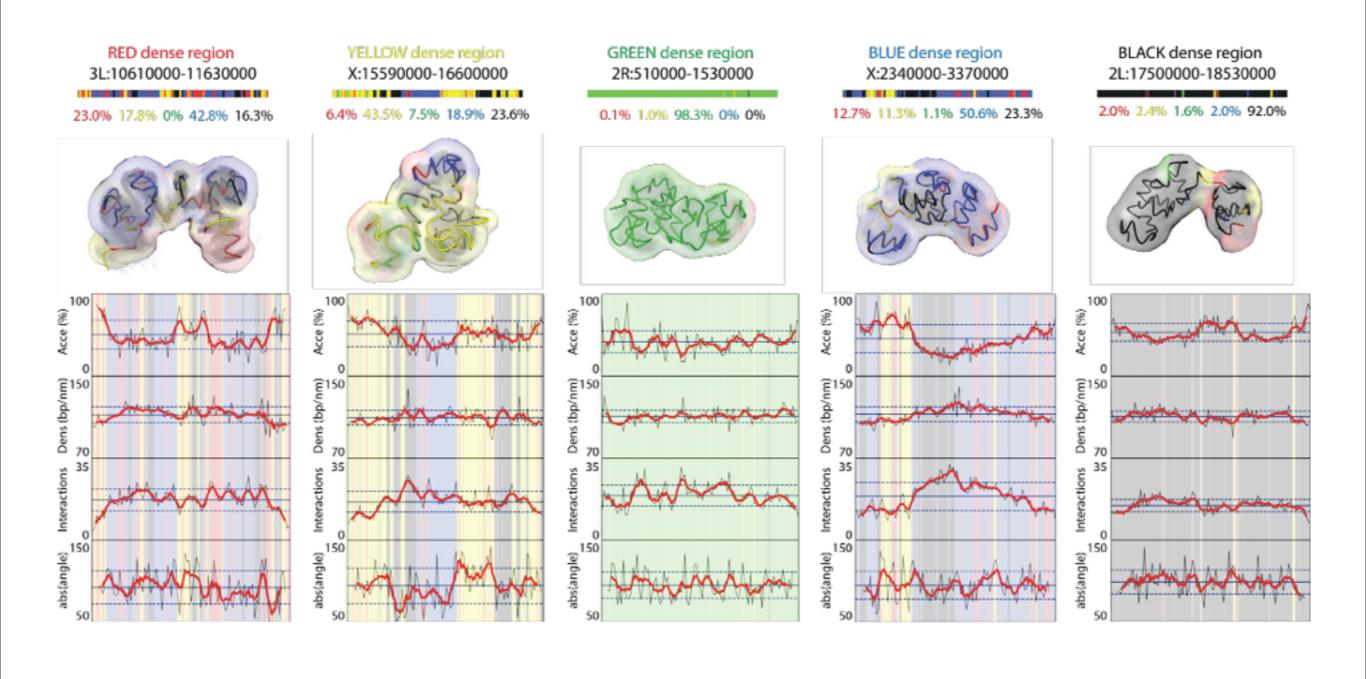
Hou et al. (2012). Molecular Cell, 48(3), 471–484.





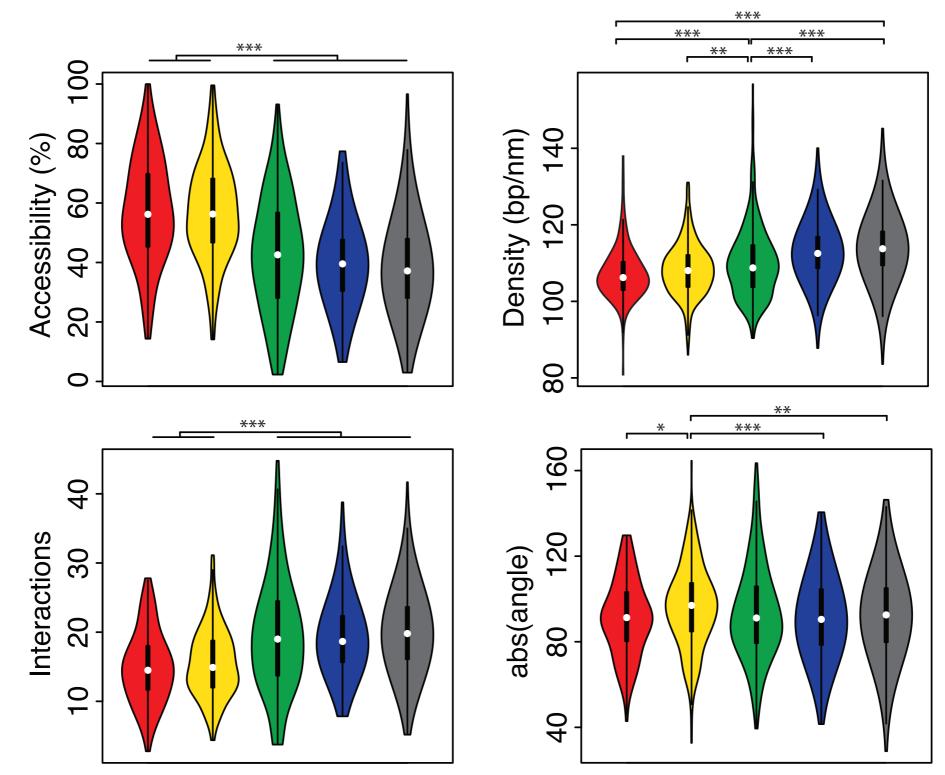


Structural COLORs



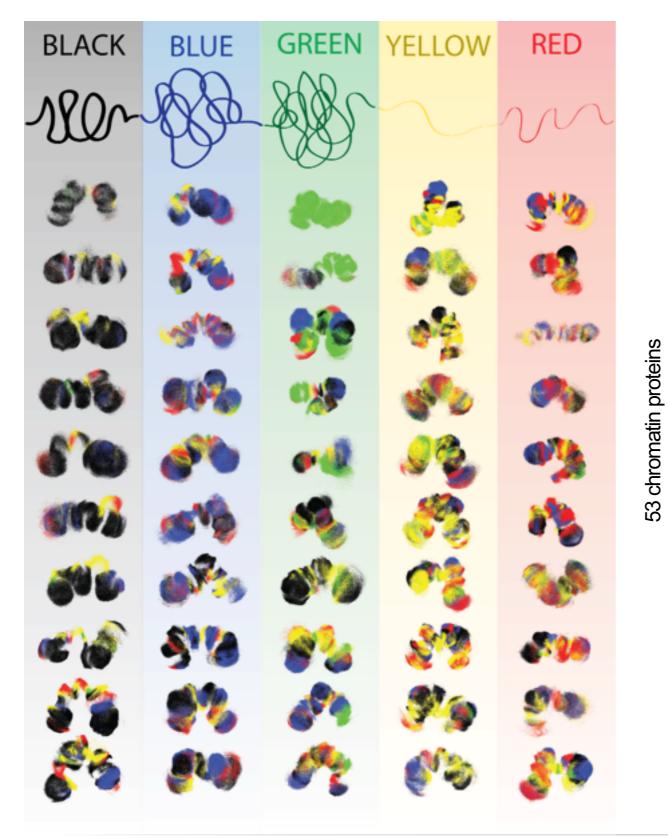


Structural COLORs





Structural COLORs

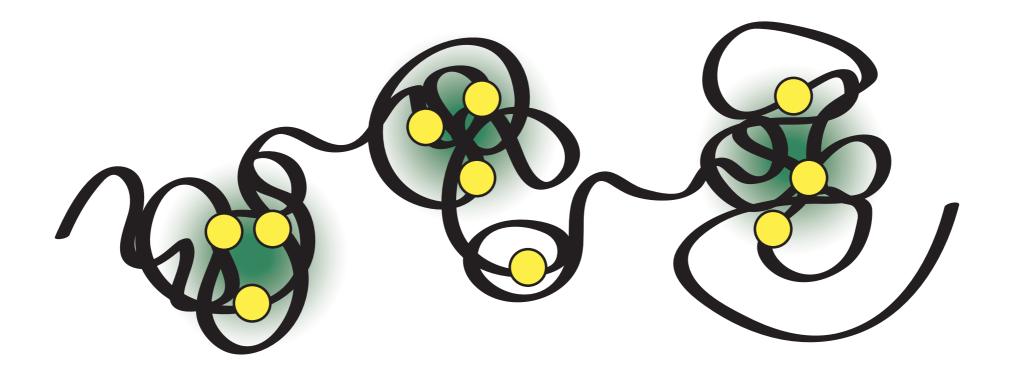


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On TADs and hormones



François Serra



Davide Baù



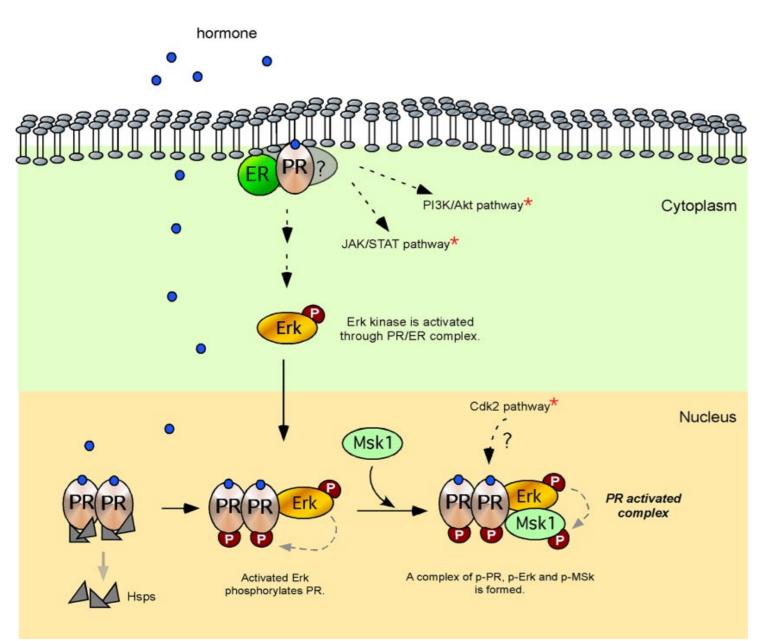
François le Dily



Miguel Beato & Guillaume Filion Gene Regulation, Stem Cells and Cancer Centre de Regulació Genòmica Barcelona, Spain



Progesterone-regulated transcription in breast cancer



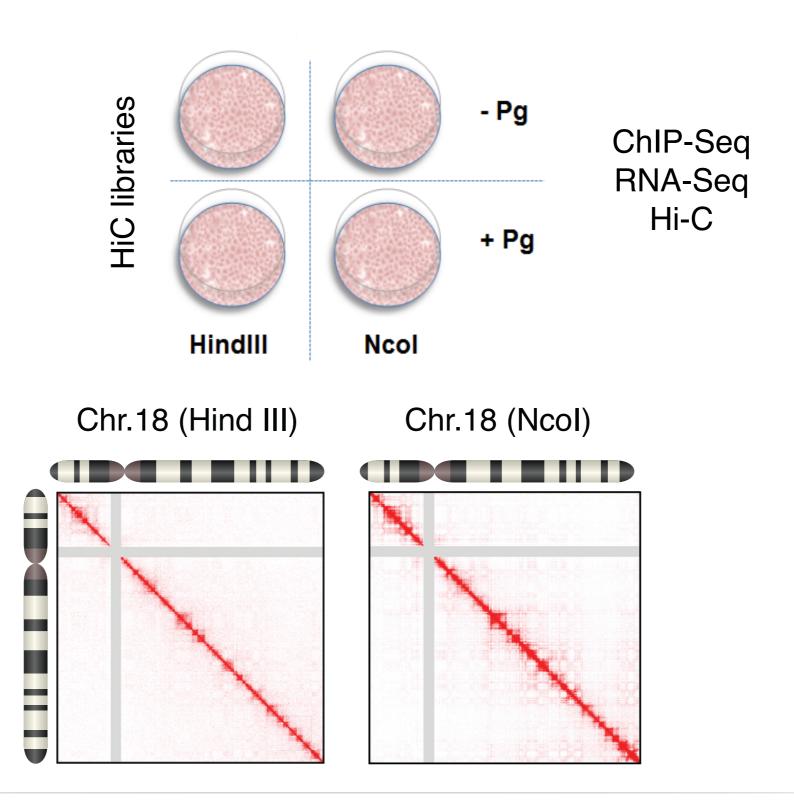
Vicent et al 2011, Wright et al 2012, Ballare et al 2012

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

Regulation in 3D?

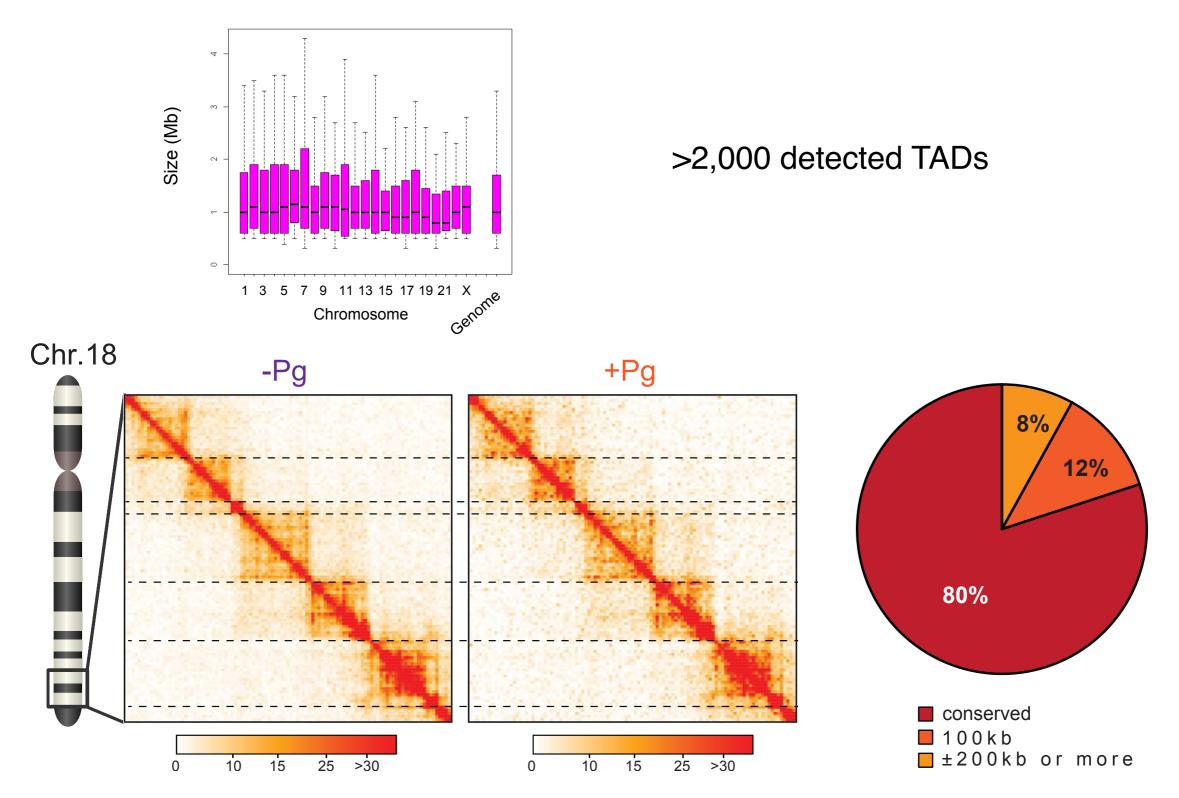


Experimental design



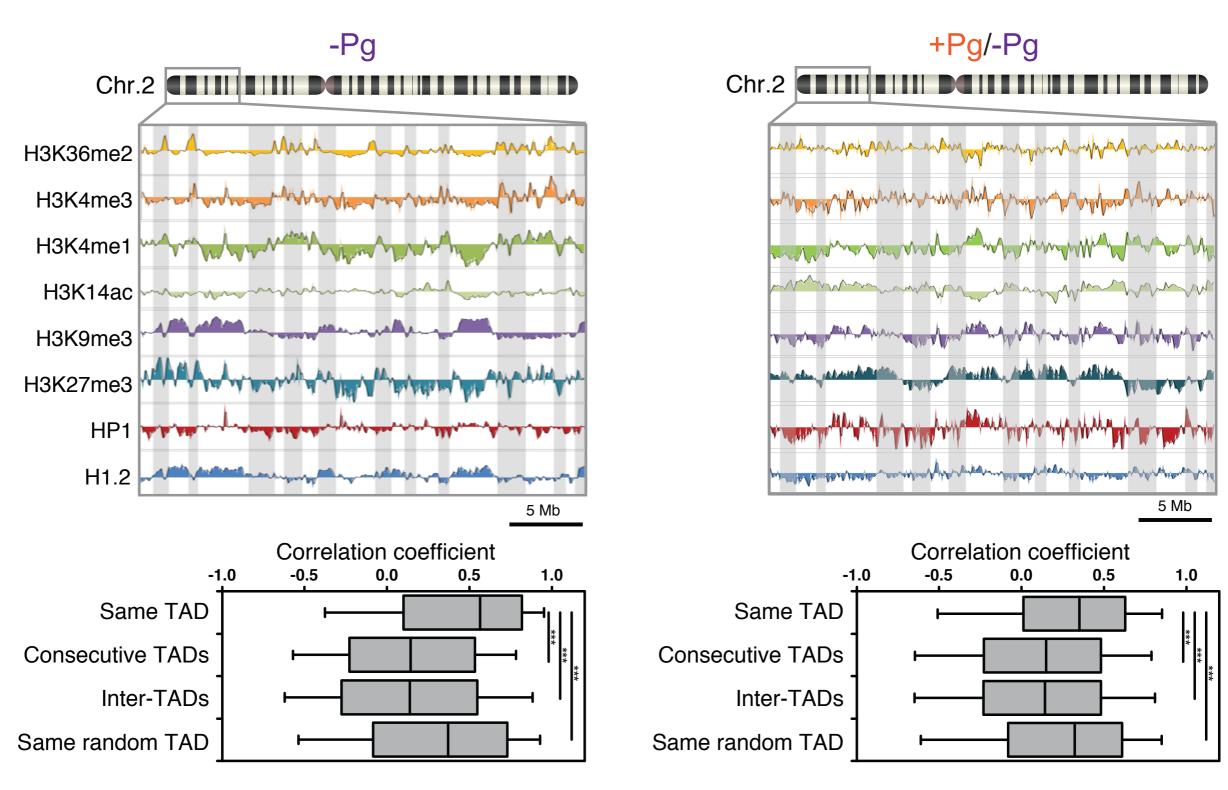


Are there TADs? how robust?



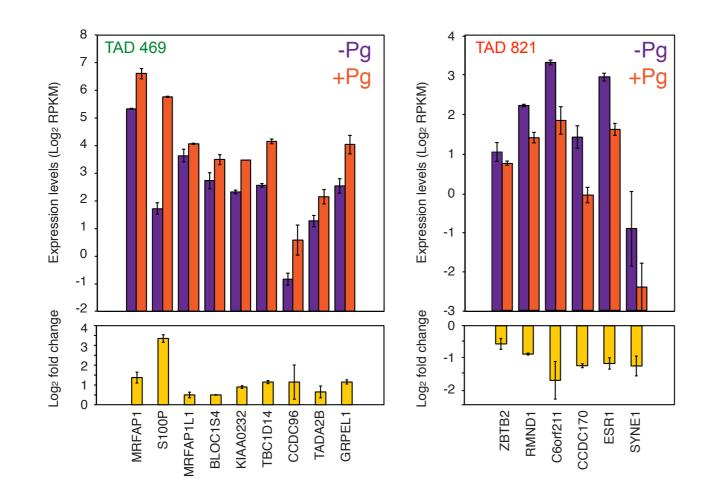


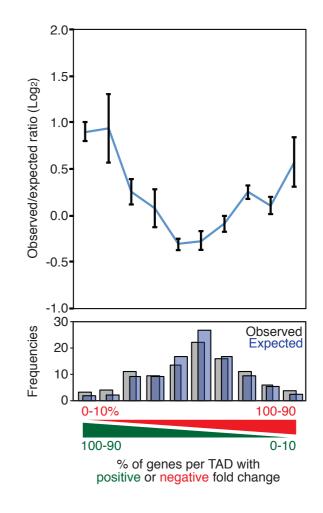
Are TADs homogeneous?





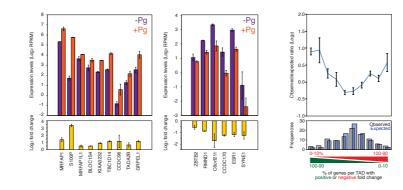
Do TADs respond differently to Pg treatment?



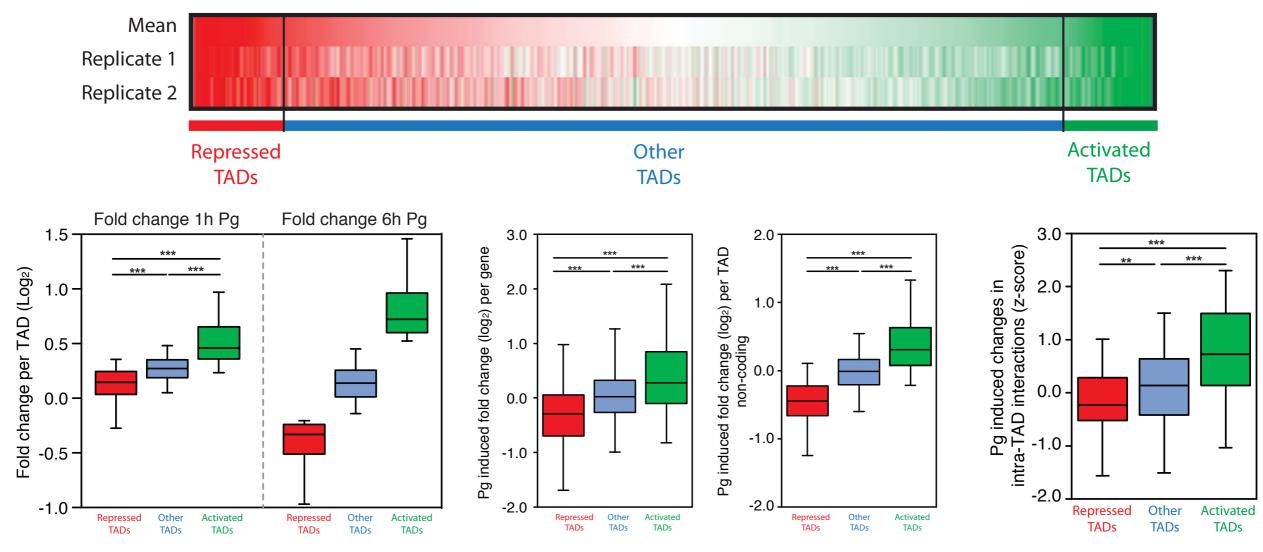




Do TADs respond differently to Pg treatment?

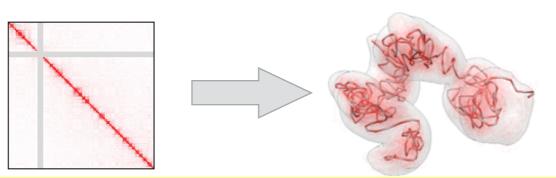


Pg induced fold change per TAD (6h)

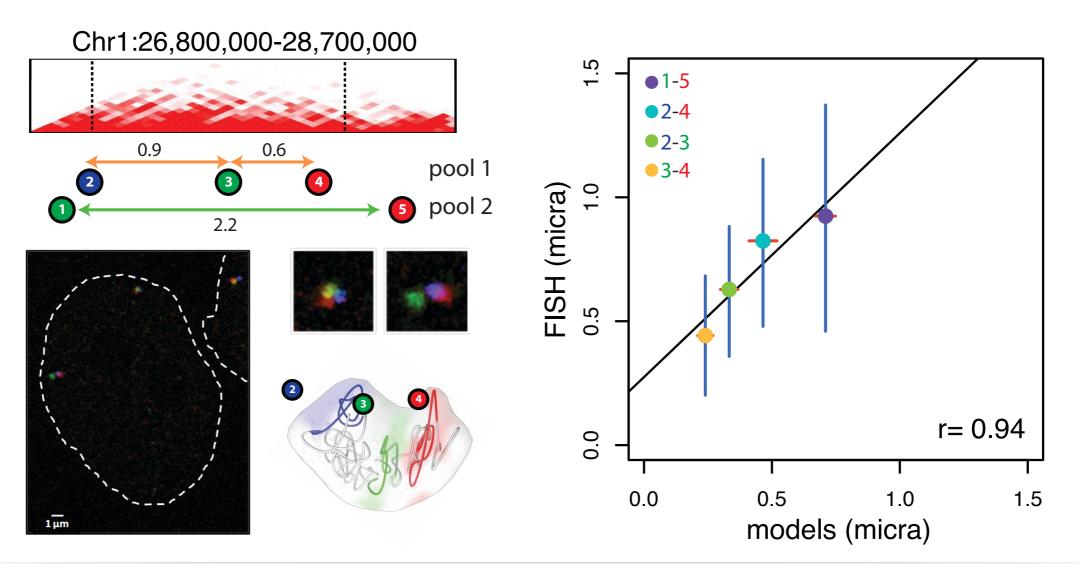




Modeling 3D TADs

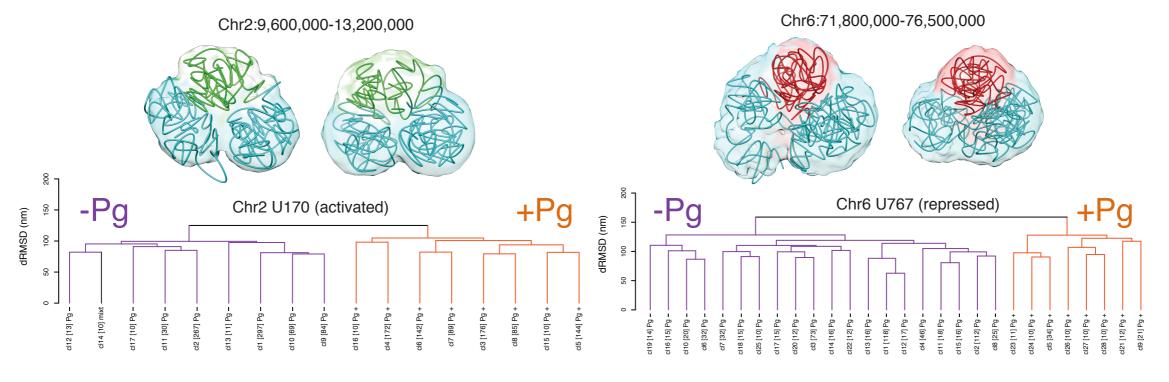


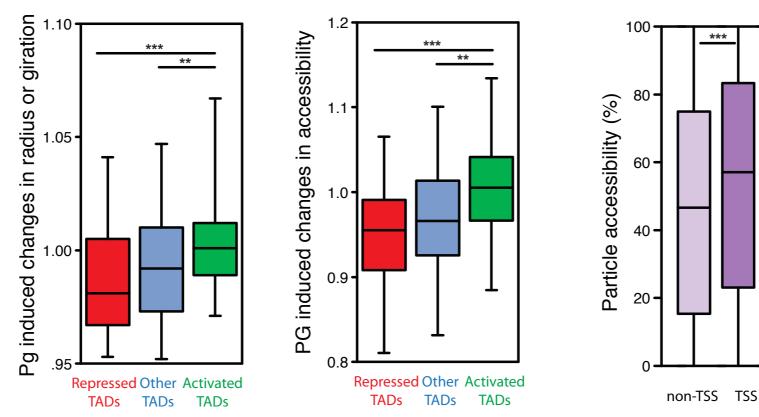
61 genomic regions containing 209 TADs covering 267Mb





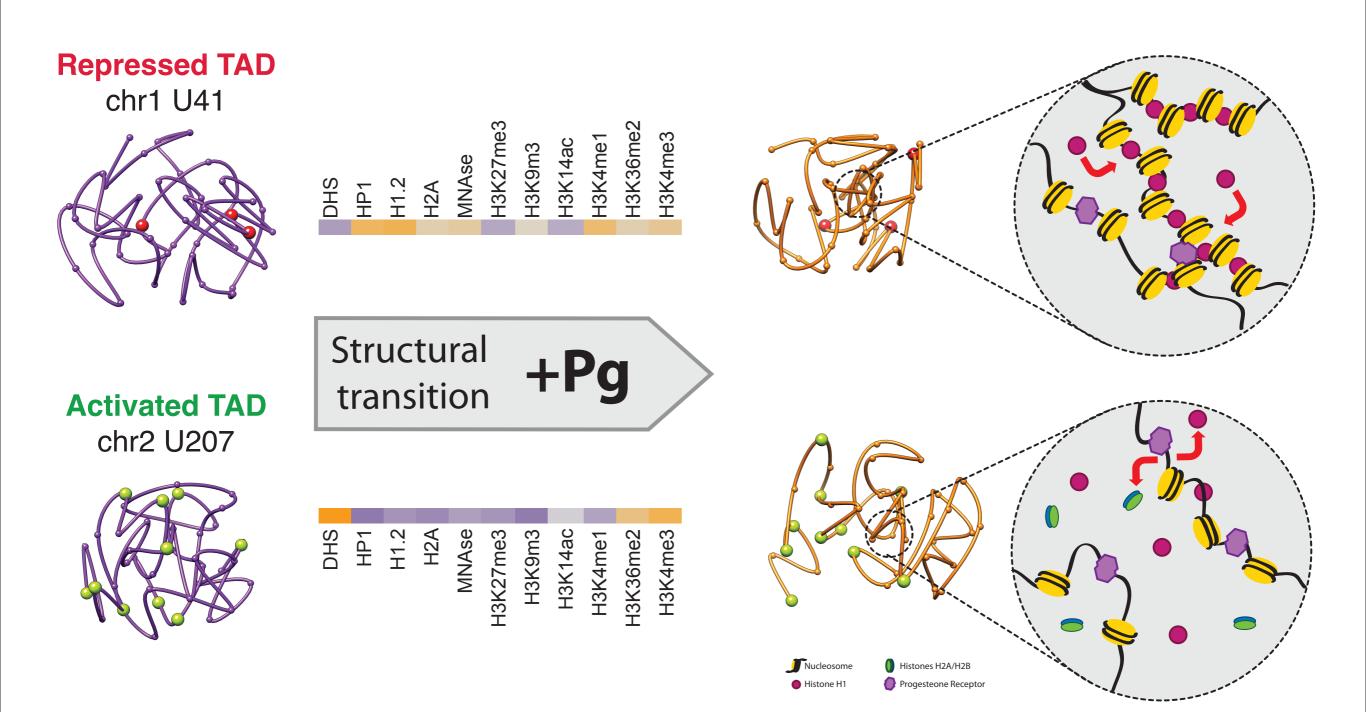
How TADs respond structurally to Pg?



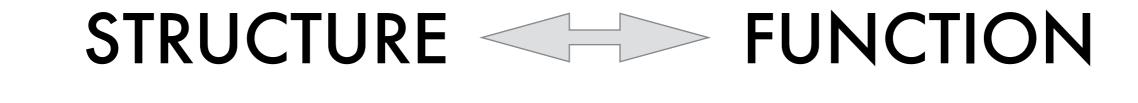


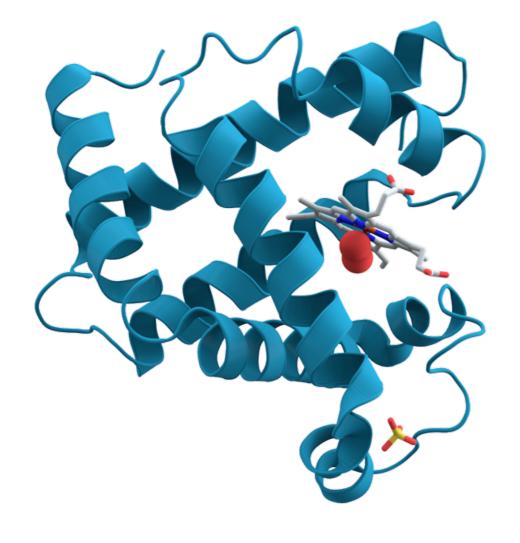


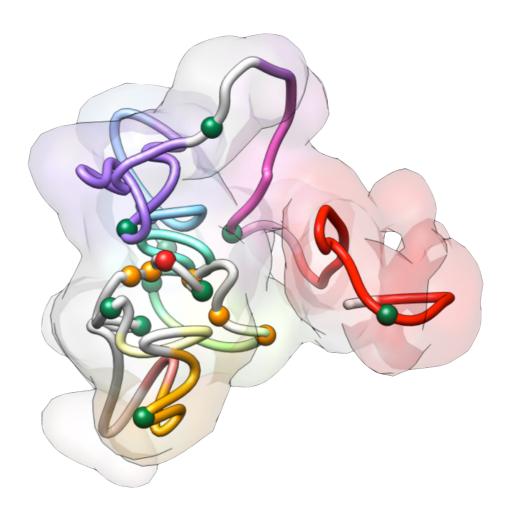
Model for TAD regulation





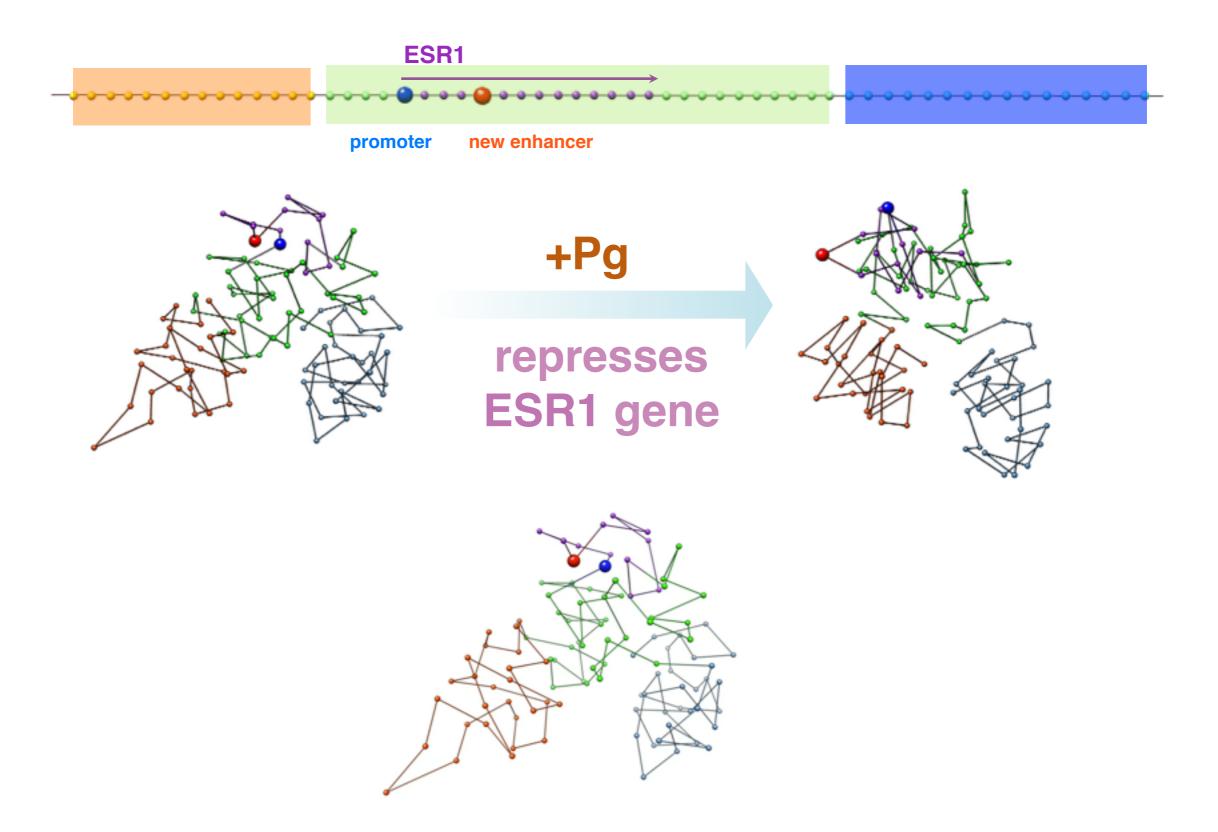








Structure >> Function!



Acknowledgments



Davide Baù François le Dily François Serra

David Dufour Mike Goodstadt Gireesh Bogu Francisco Martínez-Jiménez



erc

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

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