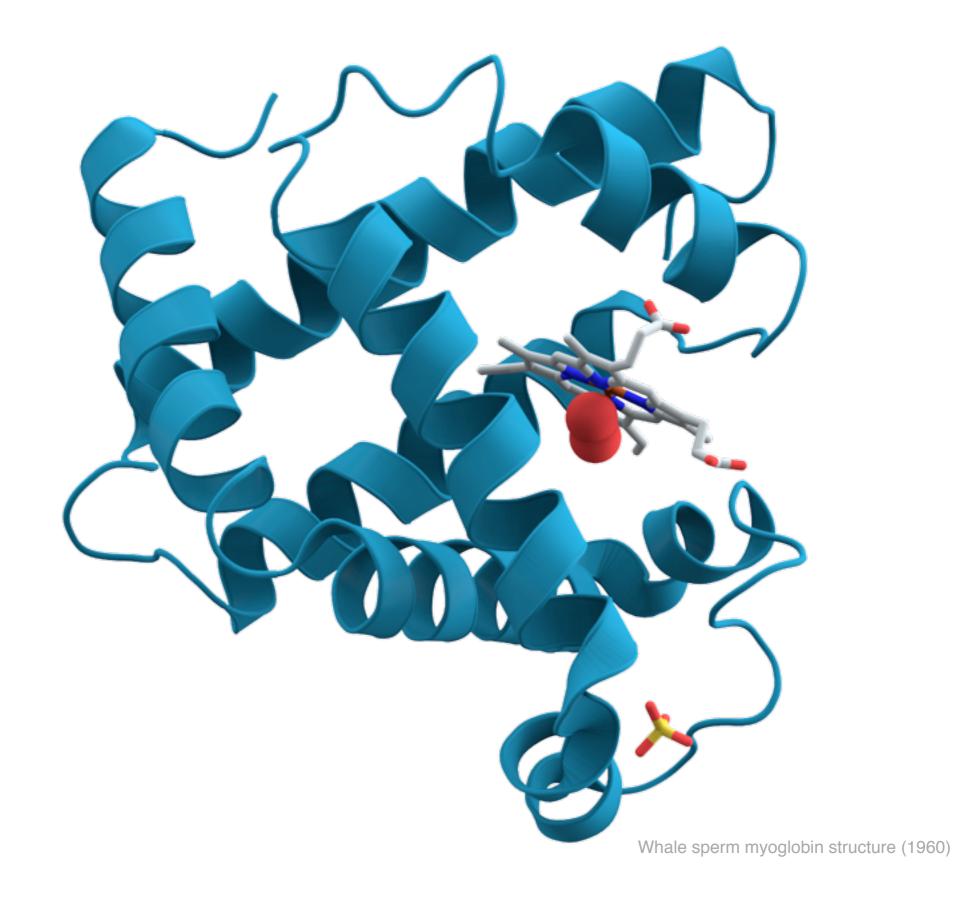
Structure determination of genomes and genomic domains by satisfaction of spatial restraints

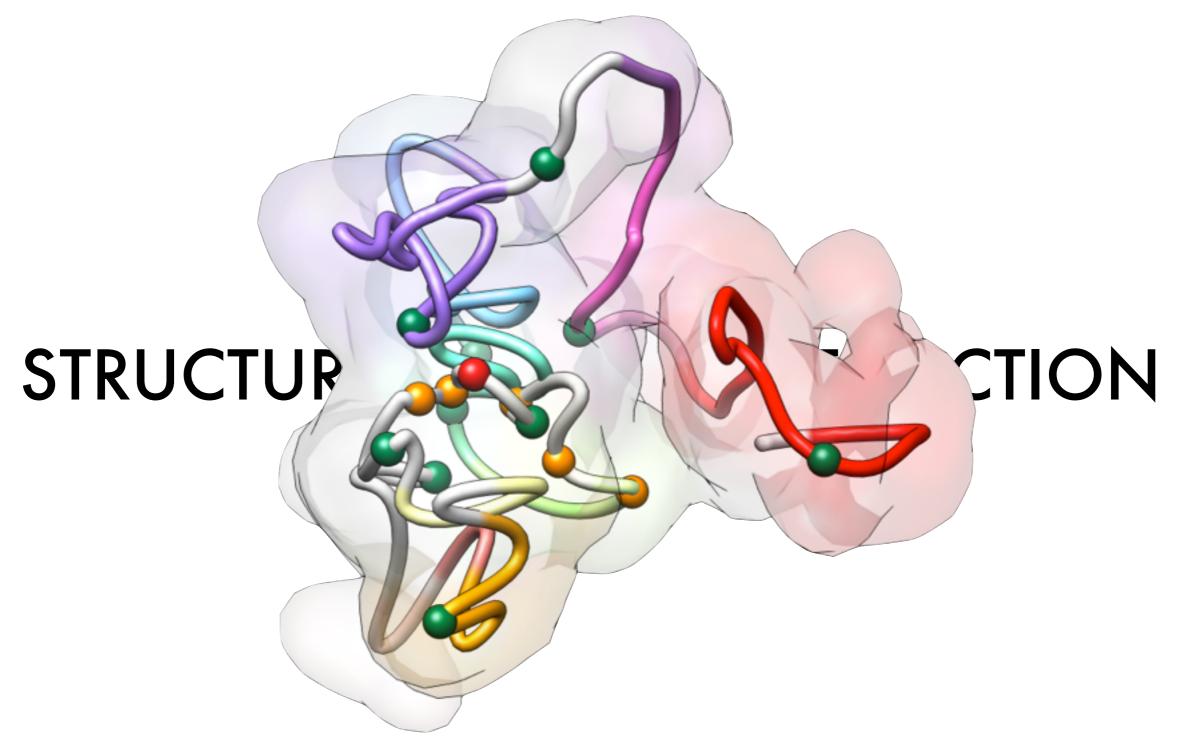
Marc A. Marti-Renom Genome Biology Group (CNAG) Structural Genomics Group (CRG)





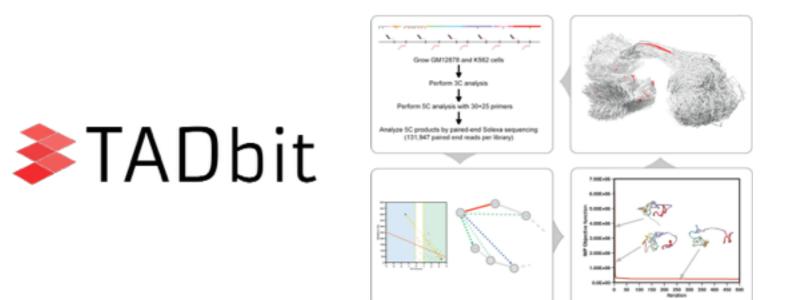


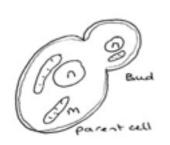




alpha-globin genomic domain structure (2011)



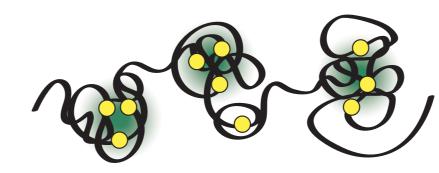








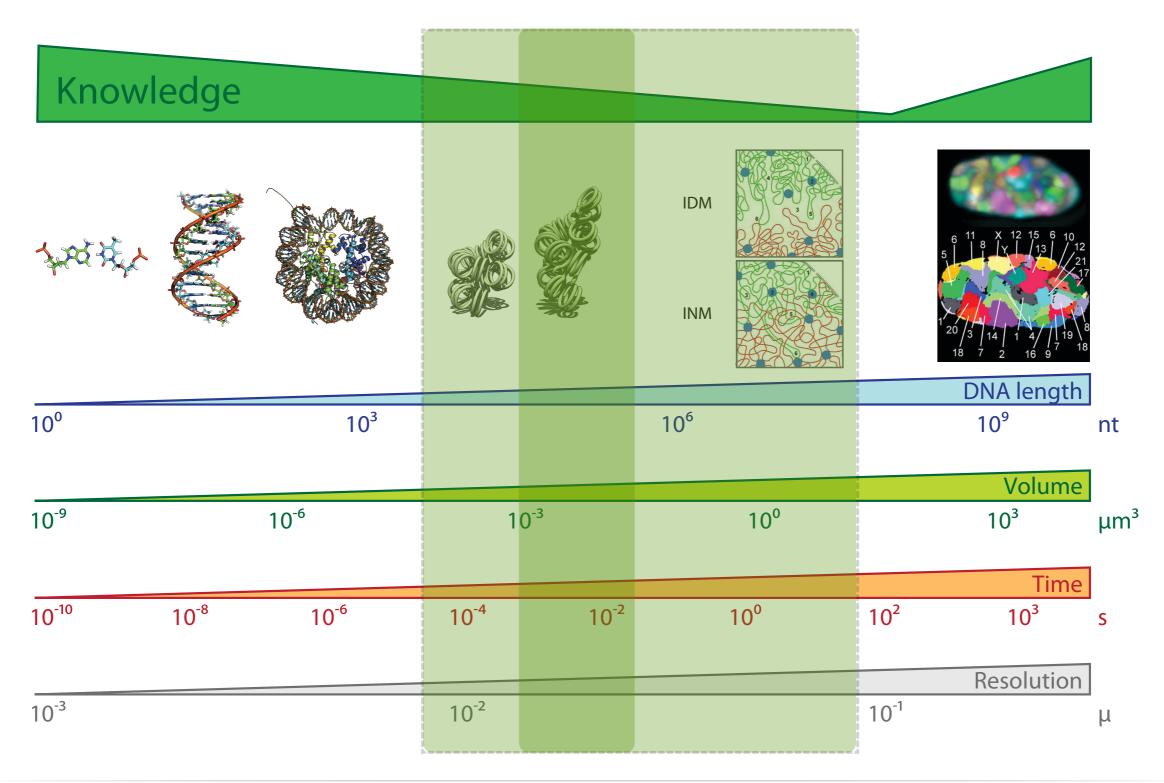






Resolution Gap

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

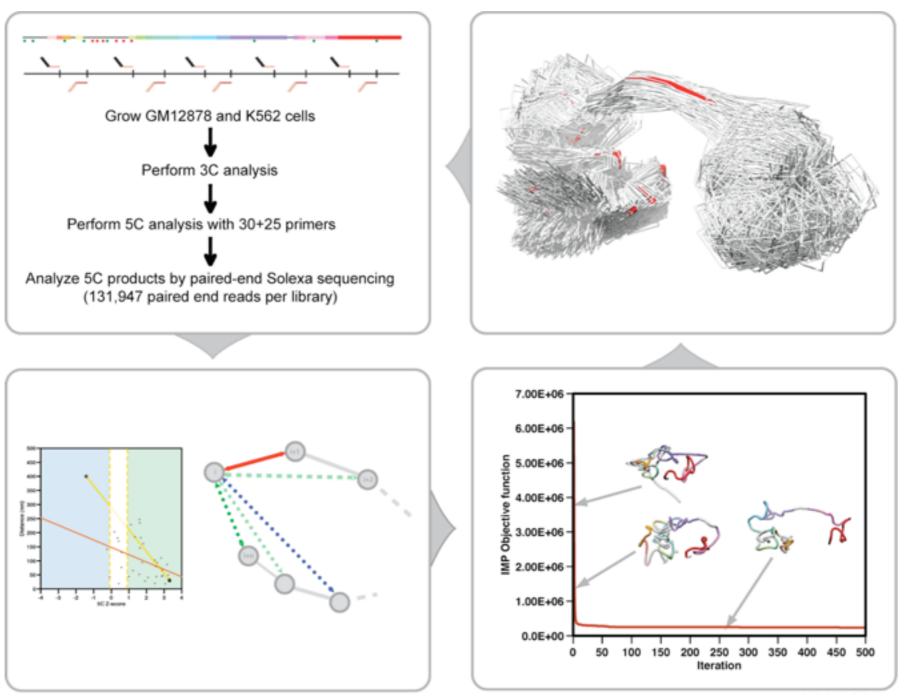




Hybrid Method

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

Experiments



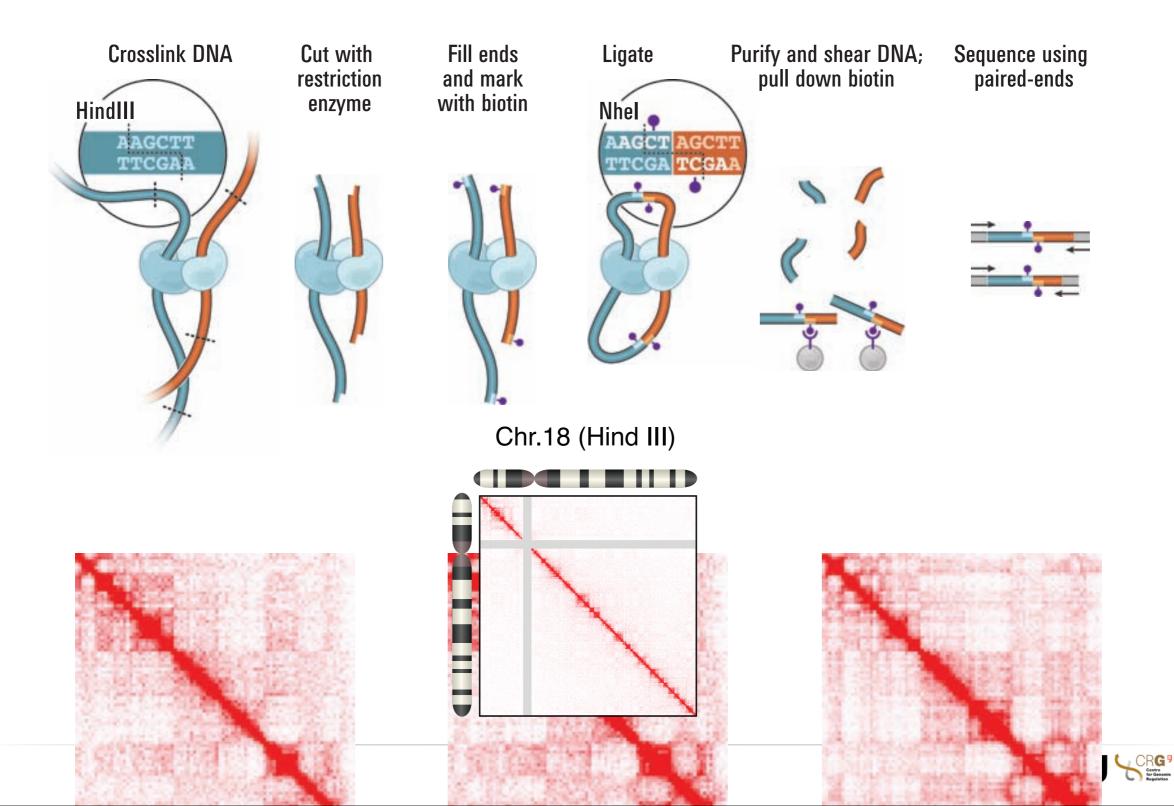
Computation

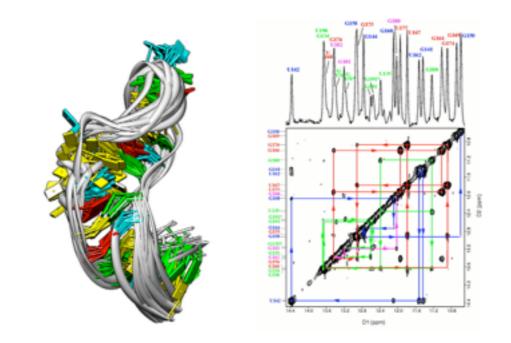




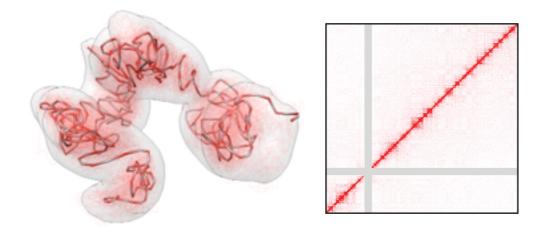
Hi-C technology

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





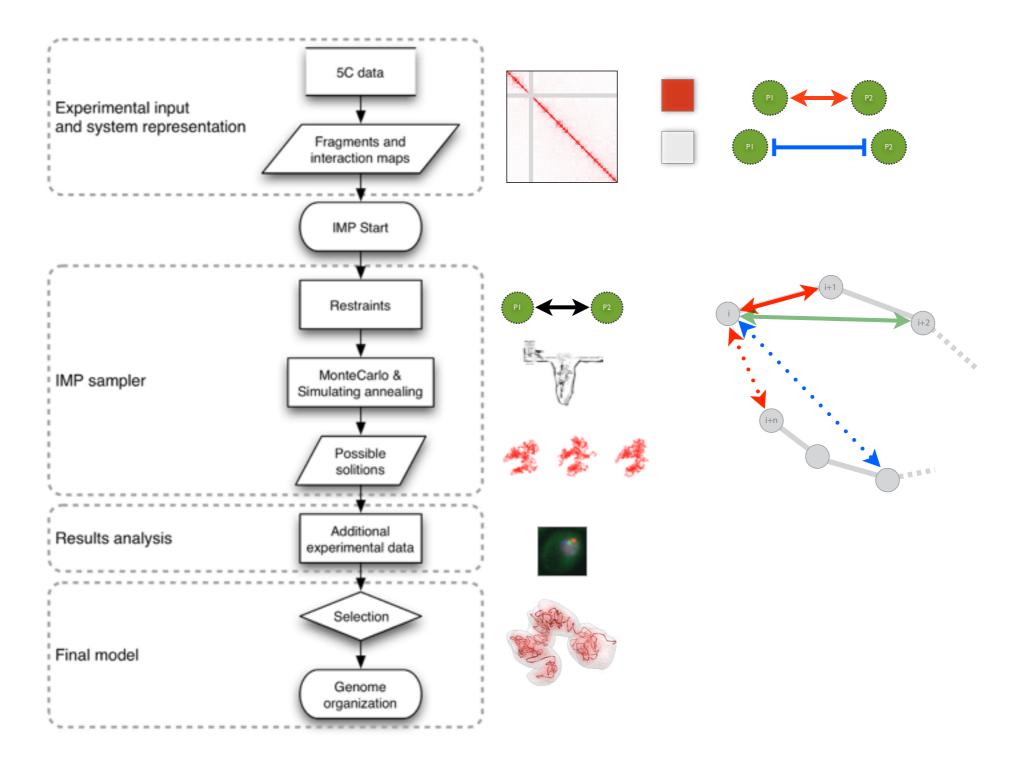
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data



TADbit



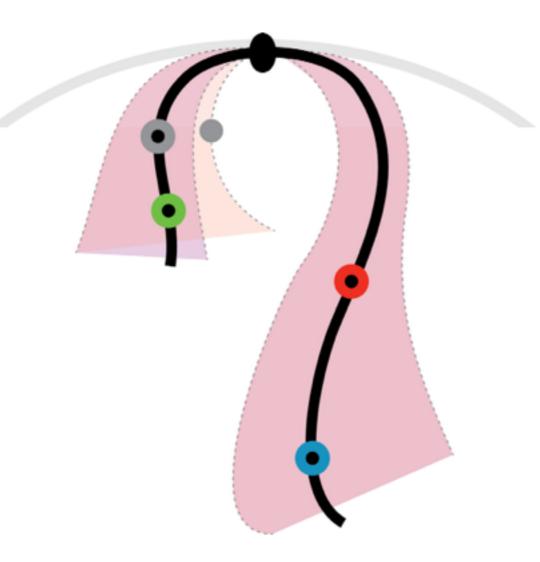








Mating-specific structure for yeast chrlll?





Jon-Matthew Belton UMASS



Davide Baù CNAG/CRG

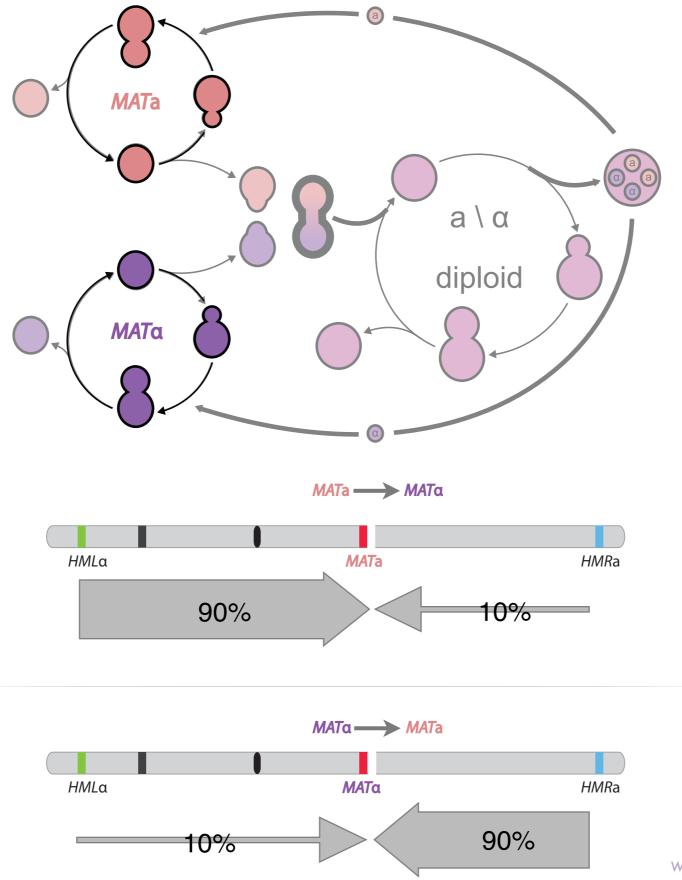


Program in Systems Biology Department of Biochemistry and Molecular Pharmacology University of Massachusetts Medical School Worcester, MA, USA



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

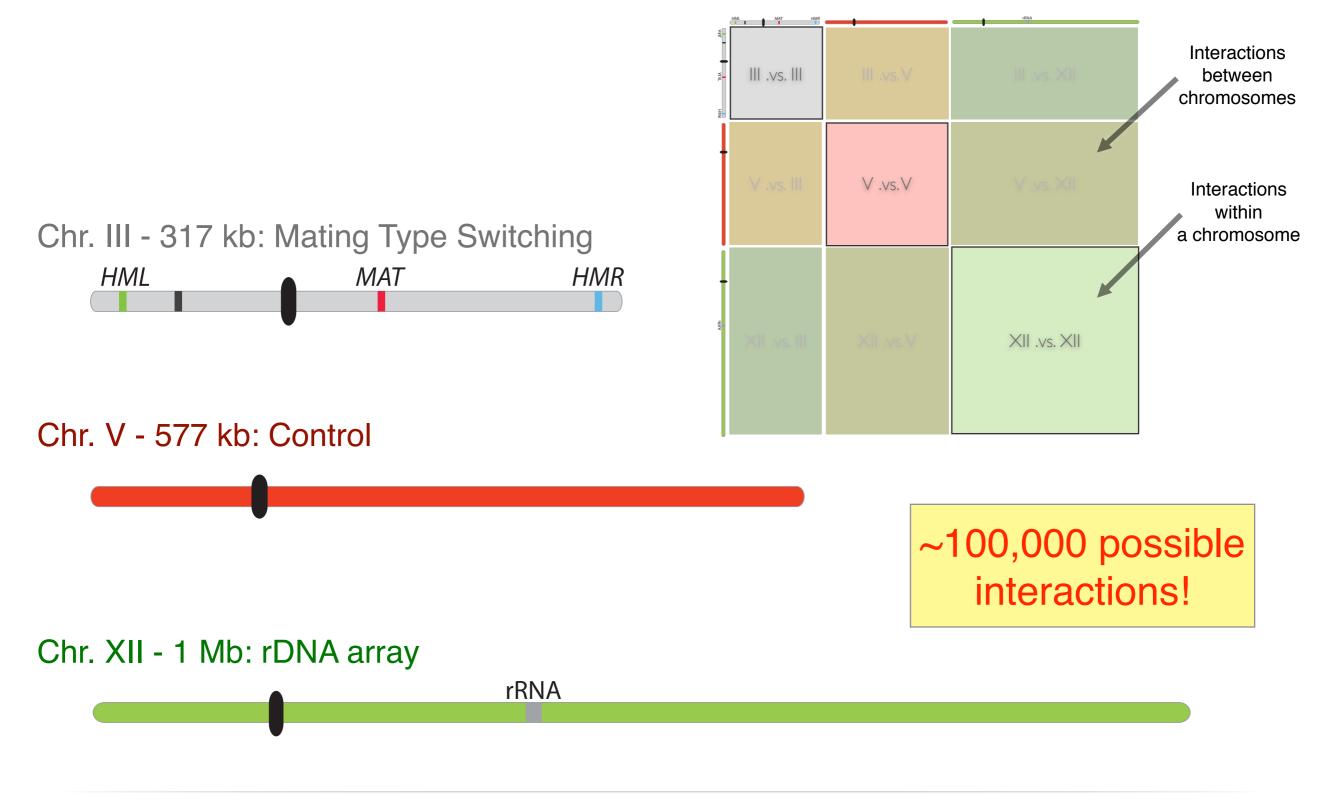




Wu, X. H., C. Wu, et al. Genetics (1997).



5C chromosome conformation

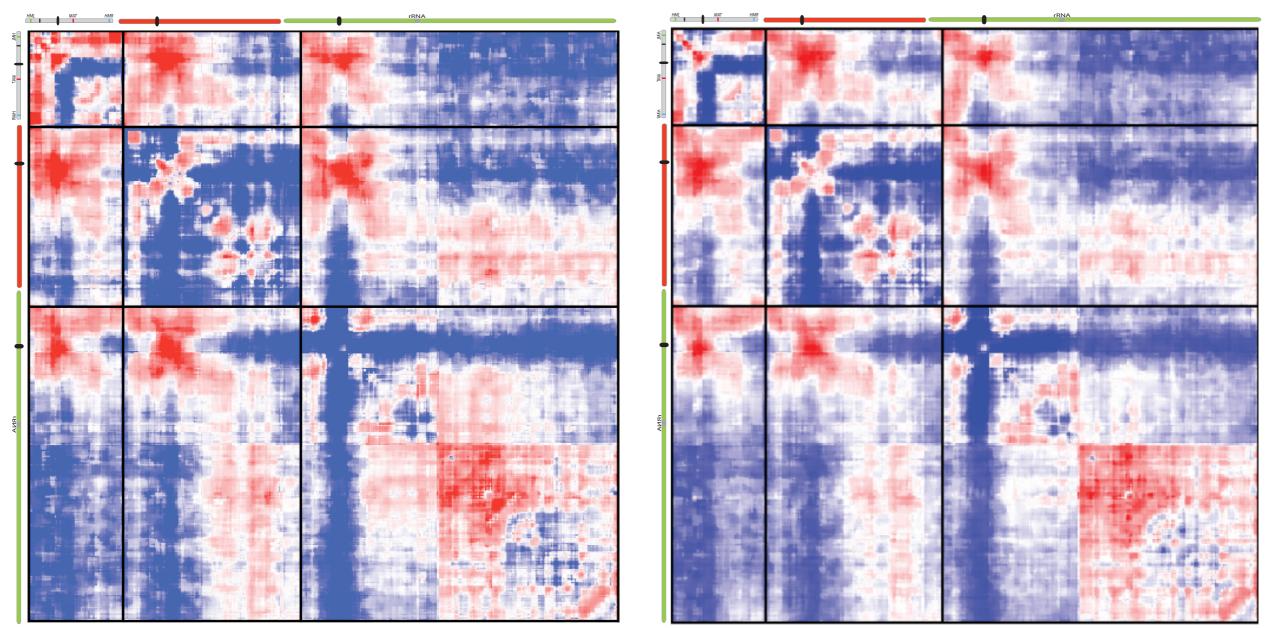




Global structure is similar between mating types

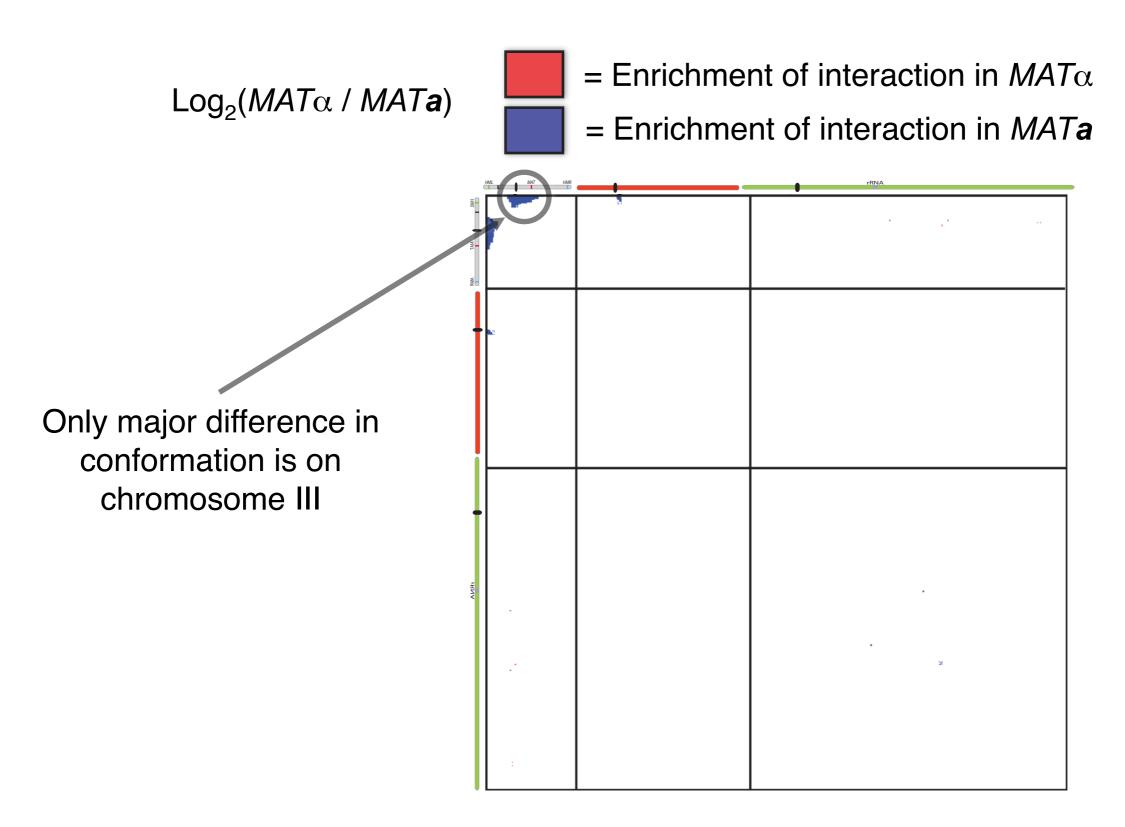
MATa

ΜΑΤα





Difference in chromosome conformation



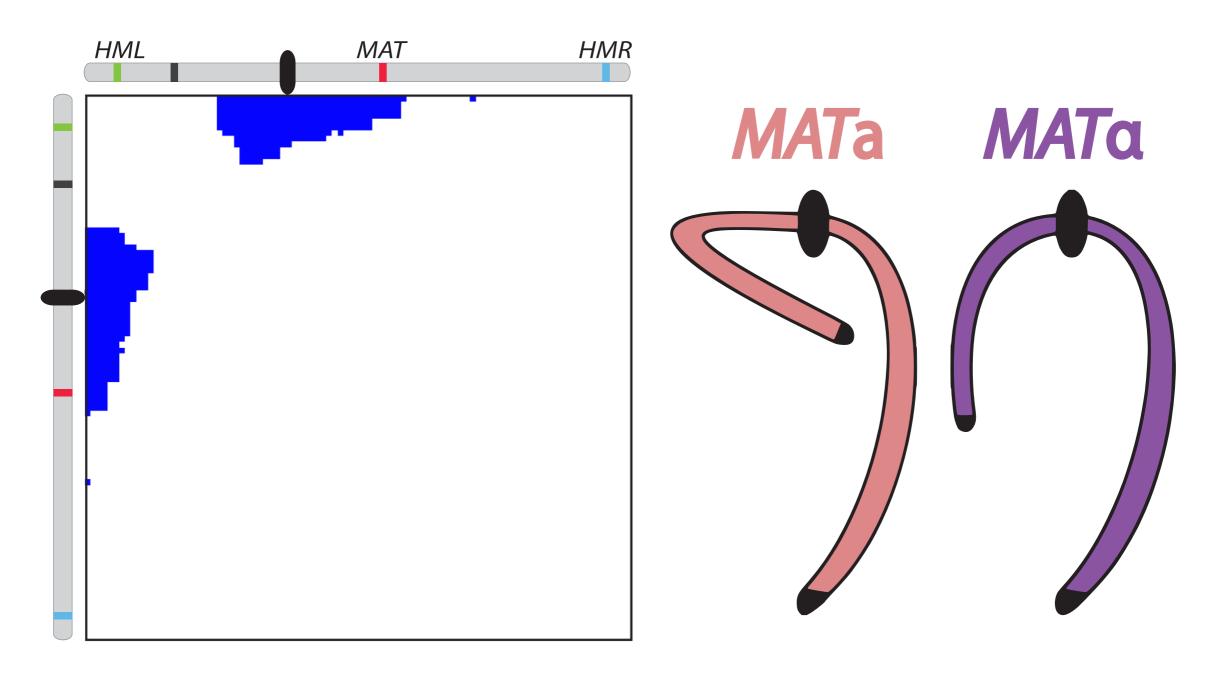


Difference in conformation of the left arm of chromosome III

 $Log_2(MAT\alpha / MATa)$

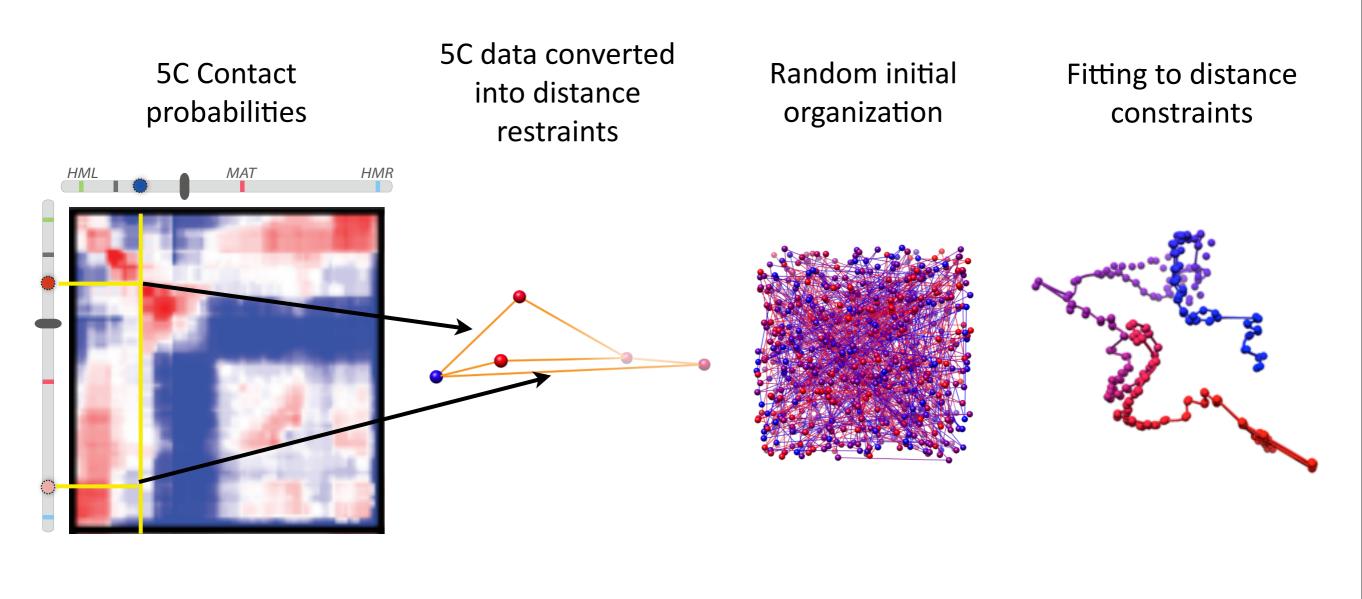


- = Enrichment of interaction in $MAT\alpha$
- = Enrichment of interaction in MATa





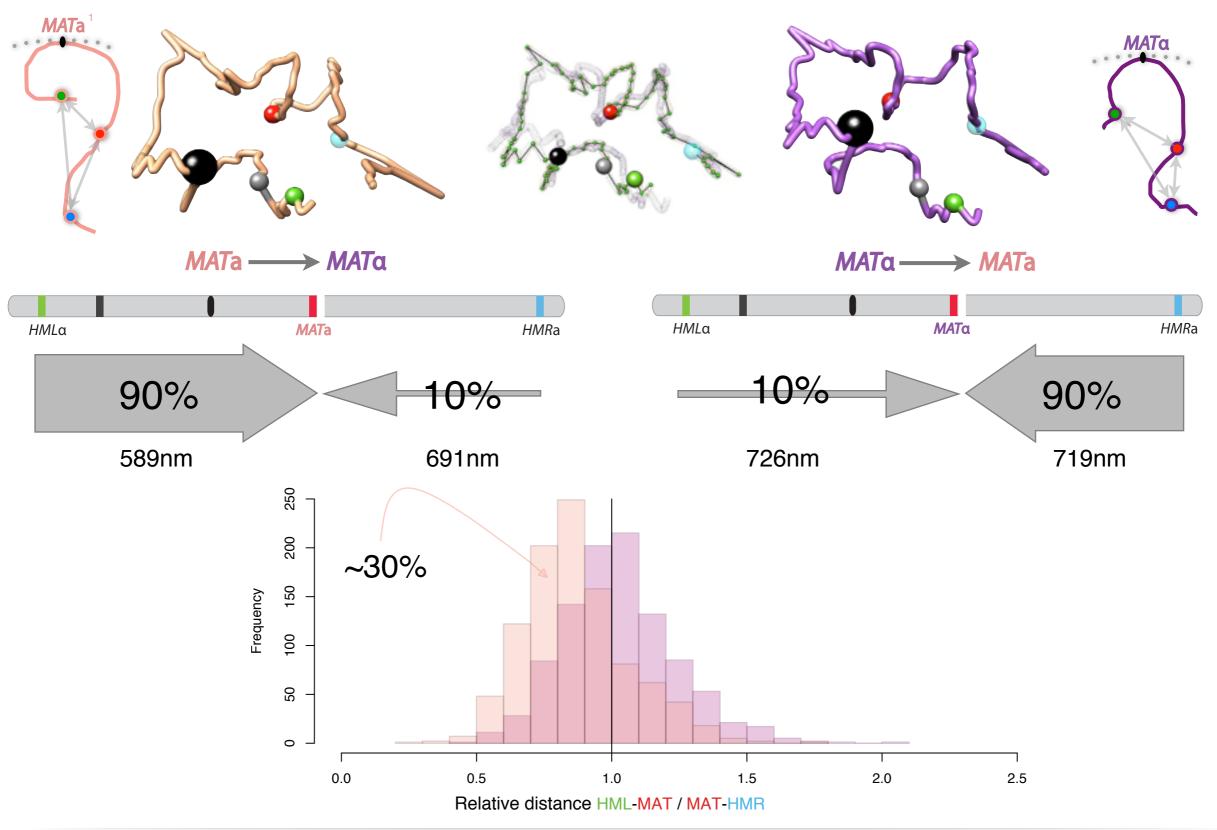
Average 3D models of ChrIII using IMP



MATa	5,000 models	MATa
	1,000 selected	MAIU



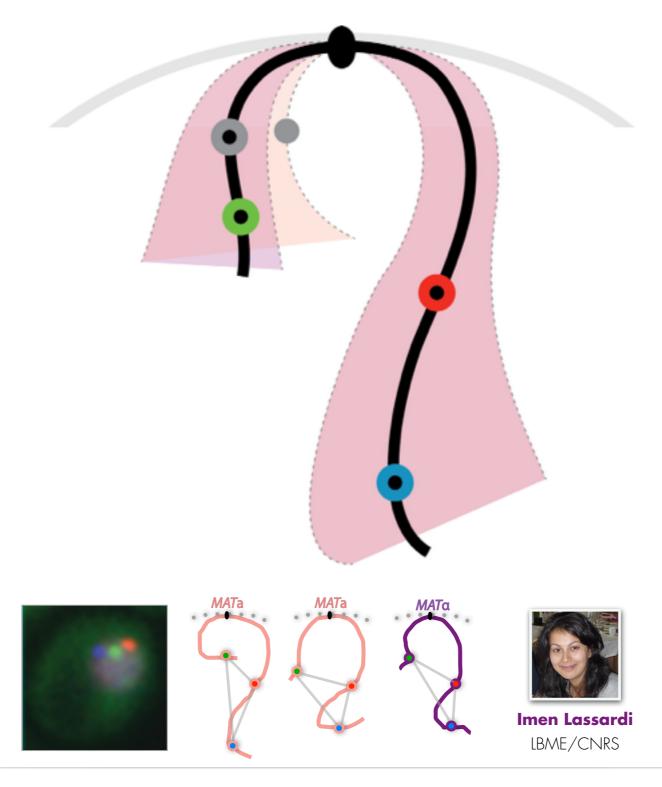
Mating type-specific conformation of chromosome III





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



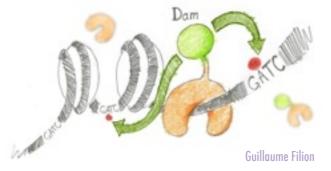
Guillaume Filion Gene Regulation, Stem Cells and Cancer Centre de Regulació Genòmica Barcelona, Spain

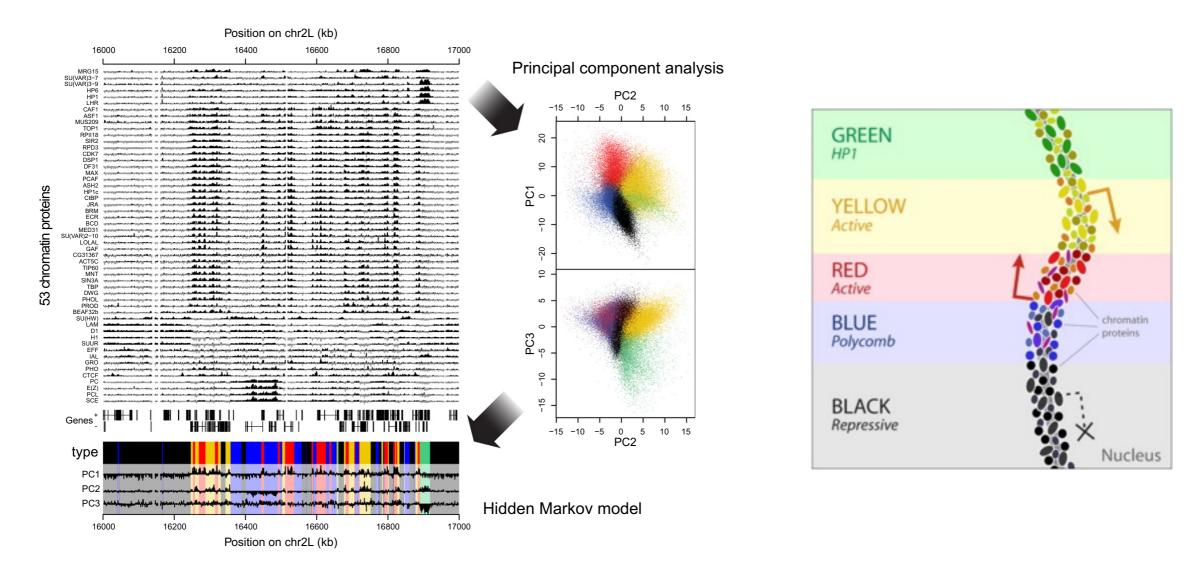


The COLORs

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



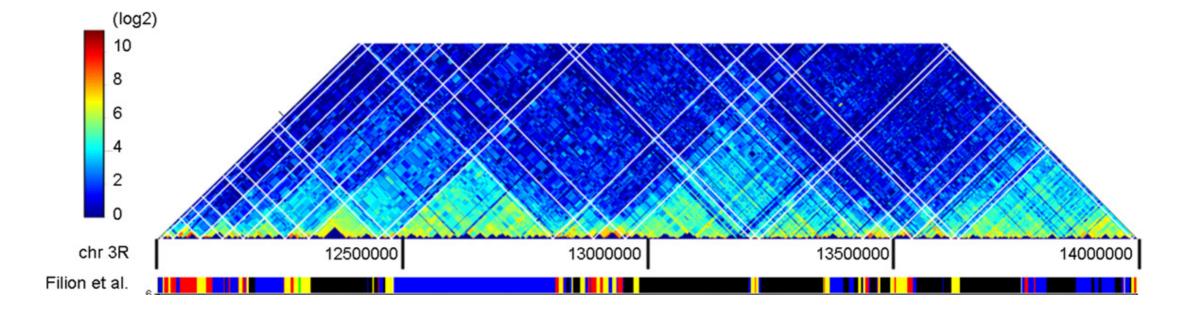


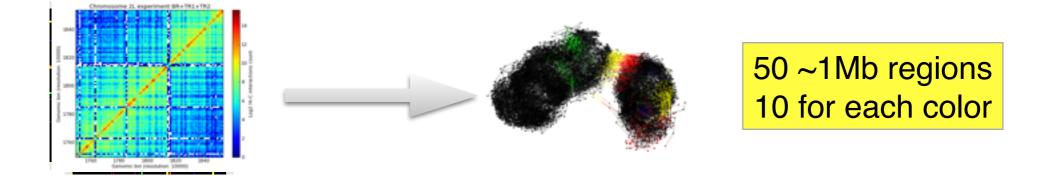




Functional COLORs

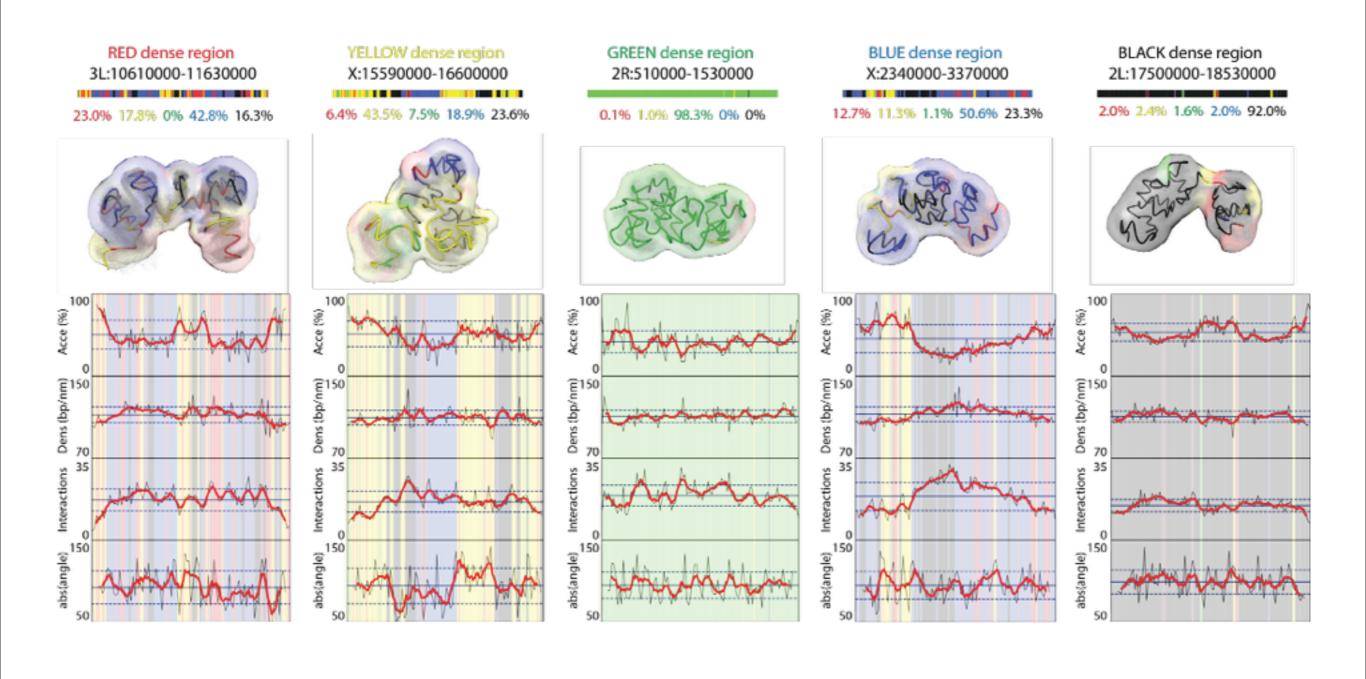
Hou et al. (2012). Molecular Cell, 48(3), 471–484.





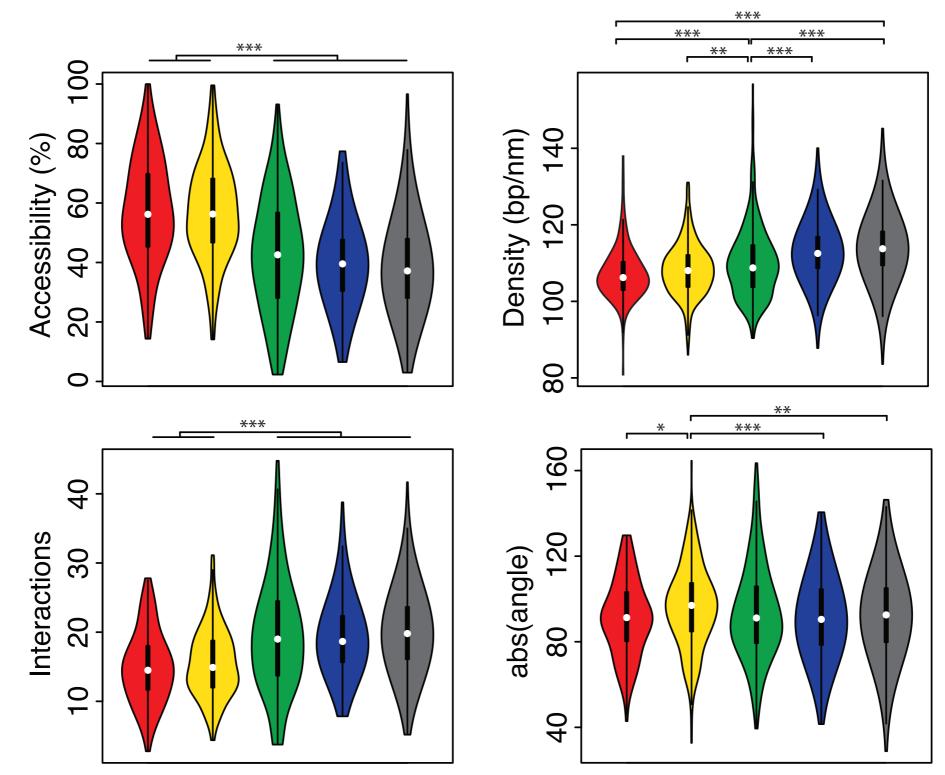


Structural COLORs



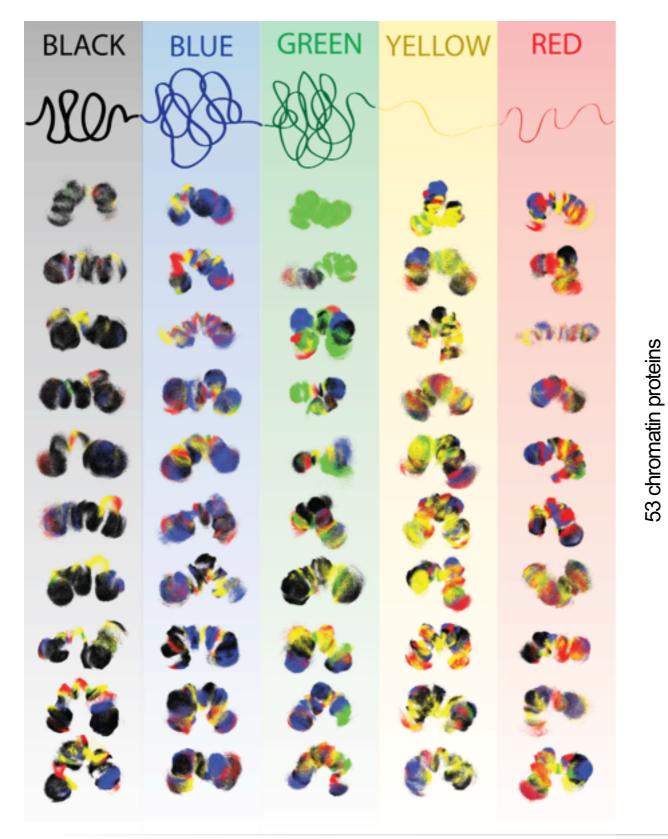


Structural COLORs





Structural COLORs

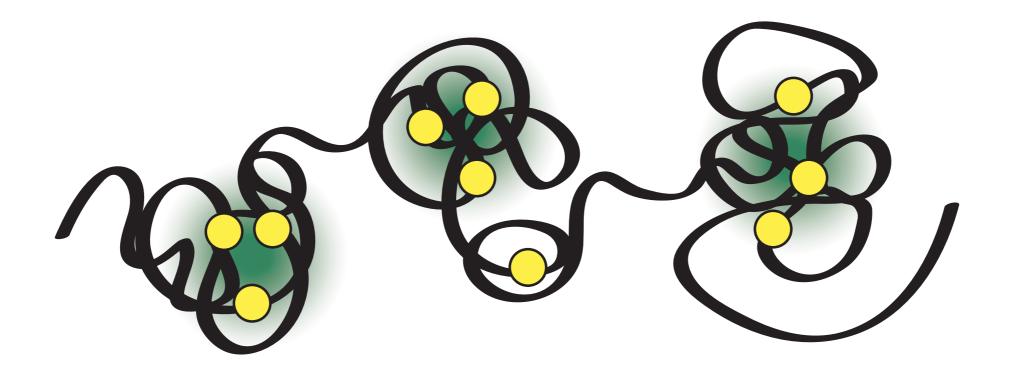


			Position on	CHIZE (KD)		
160	000	16200	16400	16600	16800	170
			1			
MRG15			and and a surger of the surger	A stranger was to a support		
SU(VAR)3-7	Annal a bring when we		and the construction of the second second	A have a second state of the second state of t	and the second state of the second states of the se	
SU(VAR)3-9 HP6		- description and the second		an and an and an and an and an and		
HP0	And the second second second second	- destantioned		a stra de suran and and	and south a state of the second	Autoro aluntos
LHR		a pharman and a second			and the second	
CAF1				a and a second sec		
ASF1		to stationers and him helles	All and a state of the state of	d interest a shall be at a state of the	a sector and a sector of the s	
MUS209 TOP1		to please the second design of the second	and a set of the set o	and the second se		and a second second
RPII18			hallow and an an a second statement of	a block and a state of the state of the		Advantant and and
SIR2		- statut towned	and a state of the	at the same a second party of a second secon	and the second state a state of the second sta	and the second second
RPD3	wheels at least state of the second		and any other states and a supporter that	a billion of the state of the s		A date of lattices
CDK7			and the second s	of hits and a shift is shown with a	And a state of the second s	the state of the state
DSP1 DF31		to change and the second secon	and the second sec			
MAX	April 10	an aller and an all all all all all all all all all	attended on the second second	d be		and and a support
PCAF	and the second design and the	pr patricipation and the day	Address of the second states of the		and the second share and a second second	Contraction of the local of
ASH2	the state of the s	an and the property of the line of the	and a second sec	of hits and a second		and the state of the state of the
HP1c		to pressure and the first	ales a constant of the second	d Manager and State States and the	an and the survey and my days and a share	
CtBP		In Aparetterinter	Adding the same of some of the same of the	d bild a sea and stilling from any dates	and the second	strated and address
JRA BRM	Administration and the set	In Specific Address		Ind. Allanda		
ECR	And the second share	a den an en de des.	addena and a second	d ble on monday de auder	the second de the second with	Contraction of the second s
BCD	1.4		Alexandren and Armen.	- I billion and a state of the	and a second state of the second s	
MED31	Antiburners and a set		A BARRIER STATE ST	- Barry Ath Barry	and and the state of the second state of the	Municipal grades
U(VAR)2-10	laterial a second and a first of the second	the Person and Supply Supply	and a second	al billion any any hope from the state of the second state	and the second s	
LOLAL GAF	and the second s	or otherspectuated and	All and a state of the state of	Jth		Managements and and and
CG31367	10.00.000.000.000.000.000.000.000.000.0	an samt a dest at traible them.	and have an a surrow at a sure be	of the second state and the	and an an an and the state of t	the day the day
ACT5C	Selling and a strategy of the second		a debuge a second second	al adaman and a subday of the same	and a reason the all was a shown	
TIP60	A children in a start of the st	an parameter de de Malana	Alland	at between your descent and the open states	and the second and the second s	
MNT		In particular states and	and a second sec	a hanne production and the	and the second state of th	Alatic States and a second second
SIN3A TBP	Address of the second s	In Speechanteling	All all and a second seco	d bits or a statistic statistic statistics		and the second s
DWG	Address of the second sec	In Legenderschlung	all days of the second second second			And a state of the second s
PHOL	territe bara when any of the		and a second a second a second	at hits and an advantation of the state	make Ad- batenes here -	and and an an an and an
PROD	upter denne and some	a parangeneticatester	And and a state of the state of	a manager a season of the	as an and the second second	
BEAF32b			Make According to a state	a the subscription of the state	al and shared a state of the second	April 4 100 100 100 100 100 100
SU(HW)	and a stand of the second state	to be and an other second	and the second s	d. adda and data and a face of the second	and the second sec	
LAM D1	and the Rest of Street Street Street	to all and a state of the state		and the second se		
H1		-	the sector data balance as a sector of			
SUUR		- have some		a provide designed and and pro-	and the second s	
EFF	to an example of the second second			and the second se	and and the second s	man and the second second
IAL	12.000000000000000000000000000000000000	a hereiterstation			and the second	
GRO PHO	and a second data and the	In States-benefitigited instates	and the second state of a second state	of the second states of the se	and the design of the second sec	Weighter the second
CTCF	Shere building a childrage	an and a state of the state of the	and the	A second a self of a second second	a ball a surger that a stress of	Sector of the sector
PC	Construction of the second		and the second s			and the second second
E(Z)	approximation and a second		A designed and a state of the s	-	الار و الدين معد التي والمراف العظام المراجع العالي	
PCL	d-4.5.5		and the second s		والإيساد مدادي ومحاد الحصدي ويهم هام	Harrison queros
SCE	opposite the second sec	-	And a state of the same state of the state of the same		and a second and a s	providence developed





On TADs and hormones



François Serra



Davide Baù



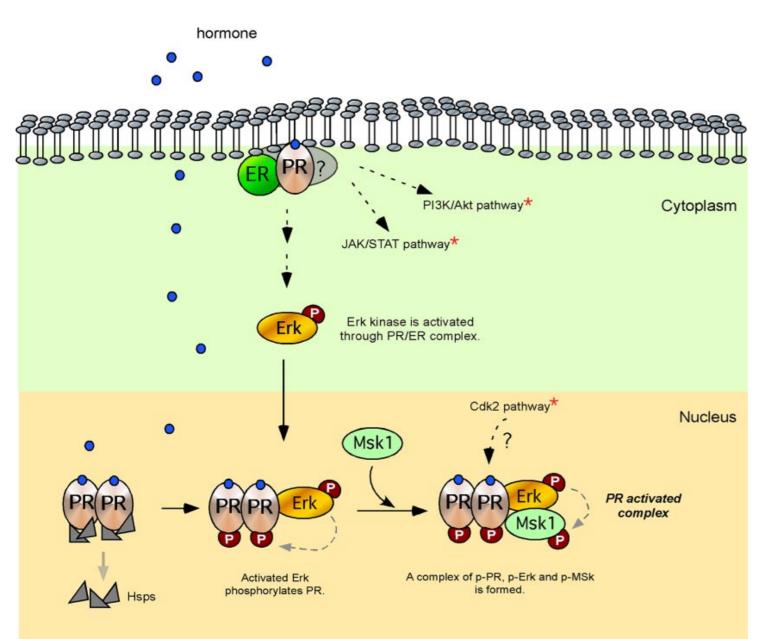
François le Dily



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



Progesterone-regulated transcription in breast cancer



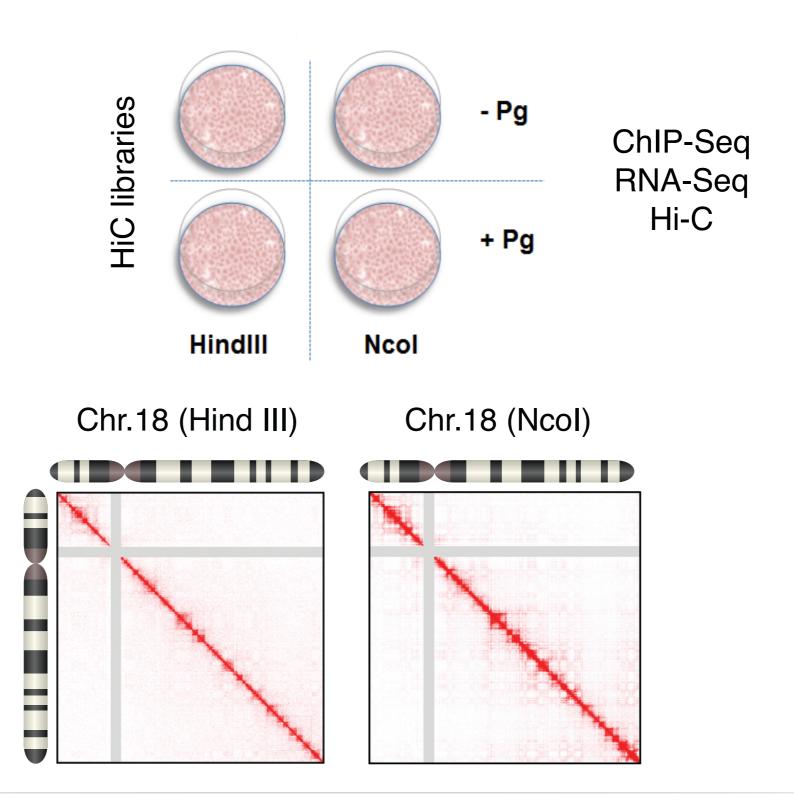
Vicent et al 2011, Wright et al 2012, Ballare et al 2012

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

Regulation in 3D?

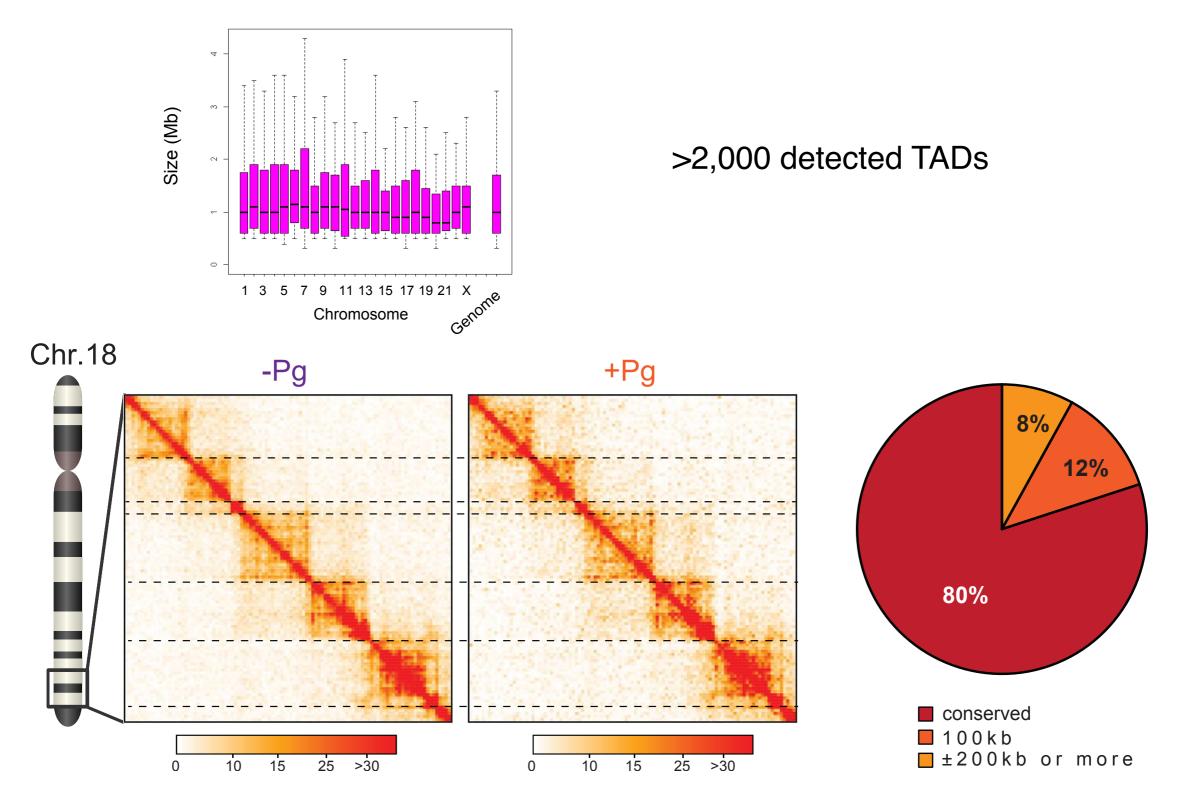


Experimental design



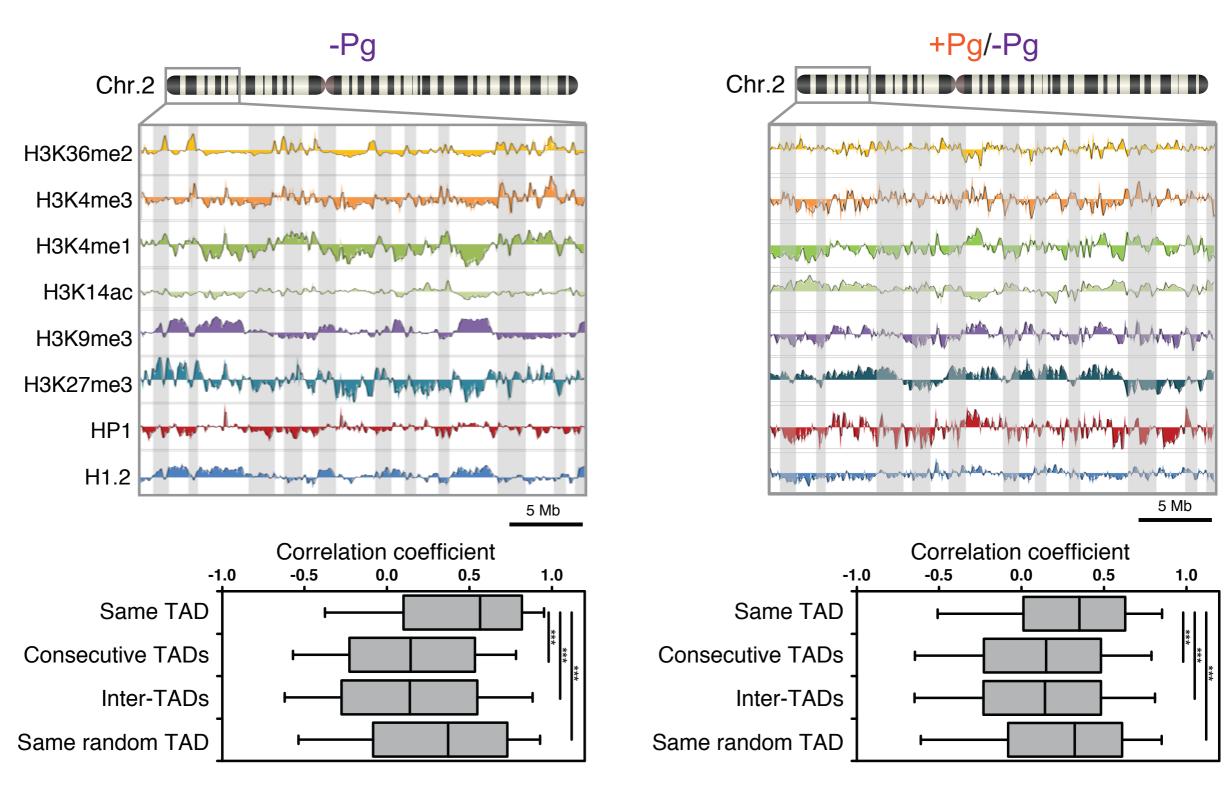


Are there TADs? how robust?



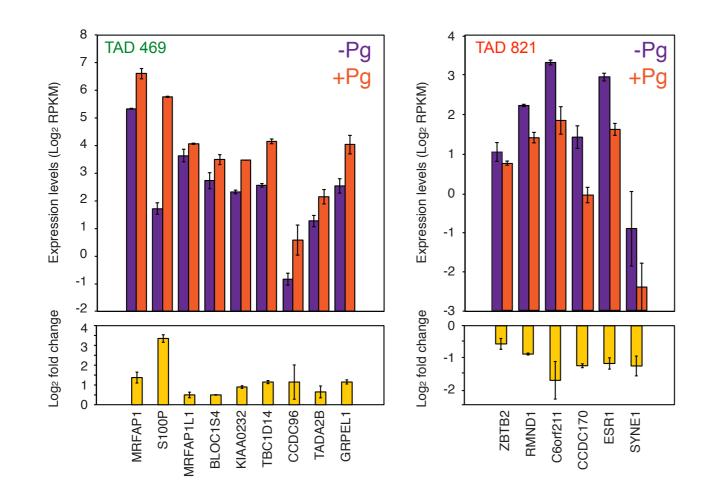


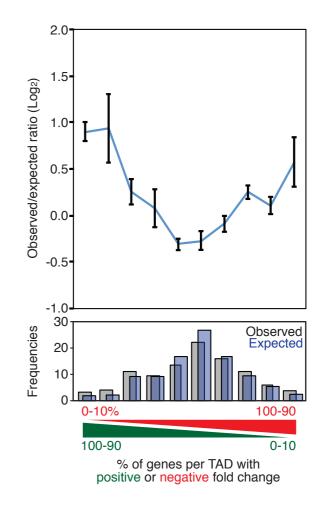
Are TADs homogeneous?





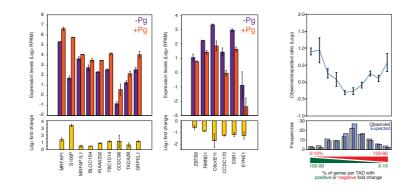
Do TADs respond differently to Pg treatment?



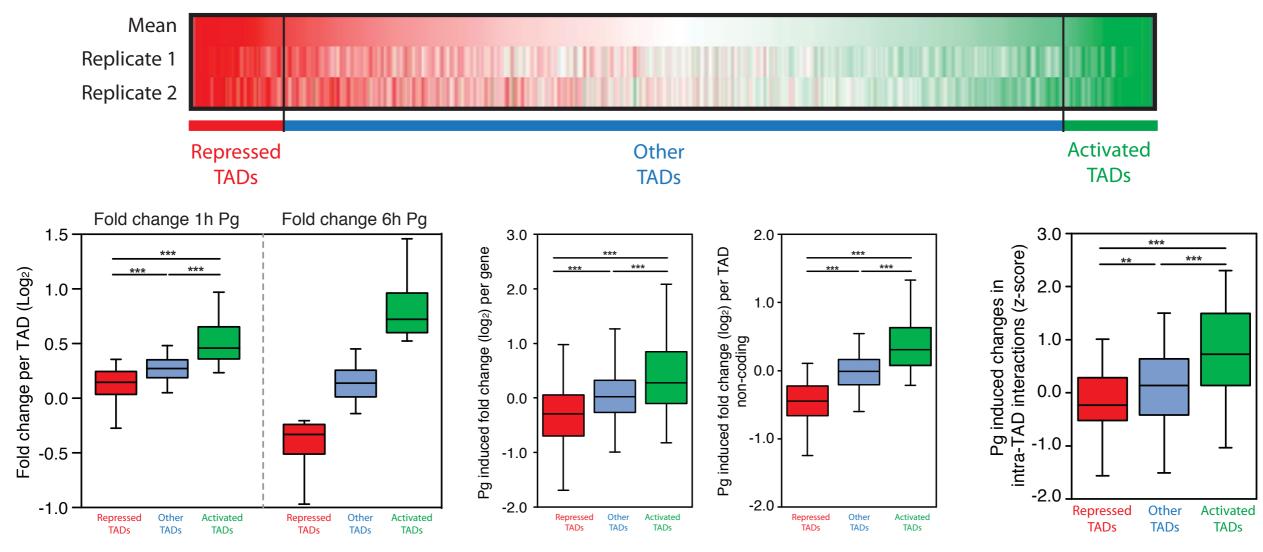




Do TADs respond differently to Pg treatment?

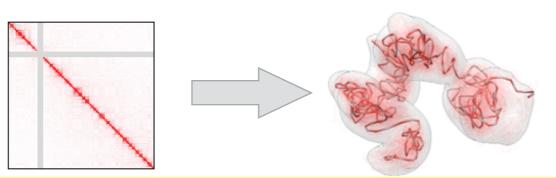


Pg induced fold change per TAD (6h)

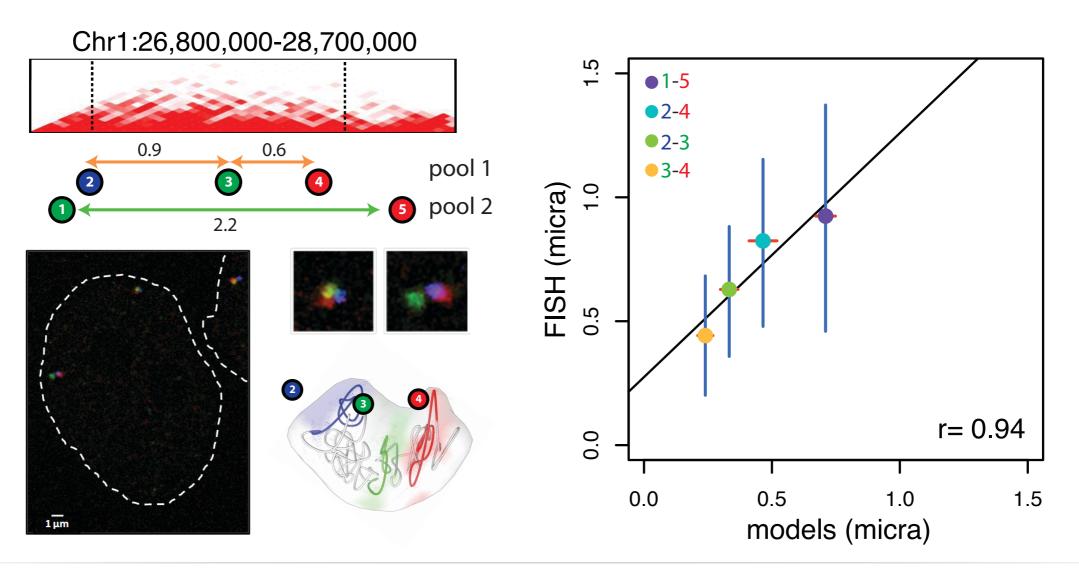




Modeling 3D TADs

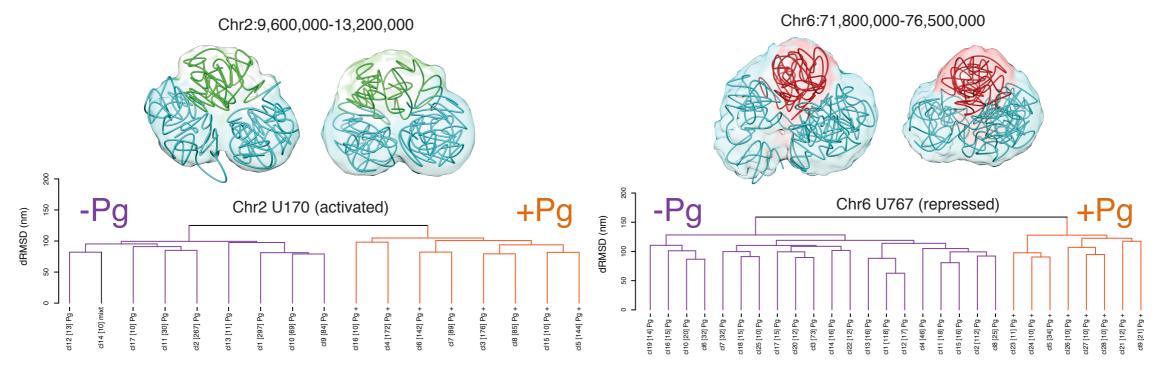


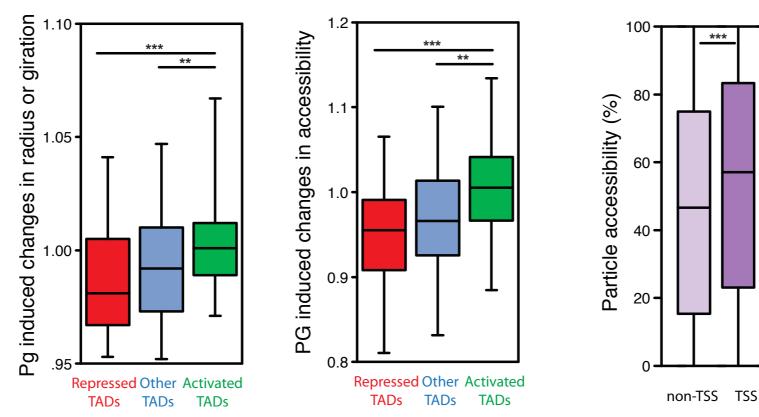
61 genomic regions containing 209 TADs covering 267Mb





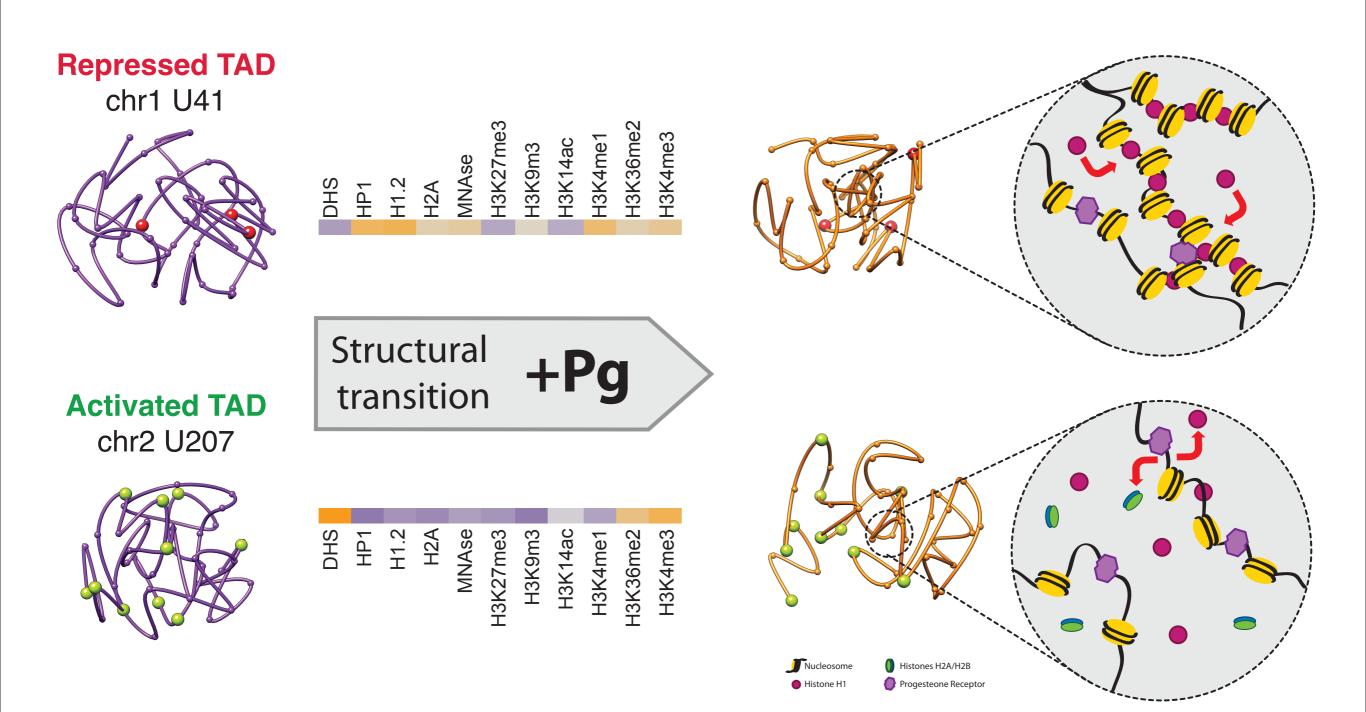
How TADs respond structurally to Pg?



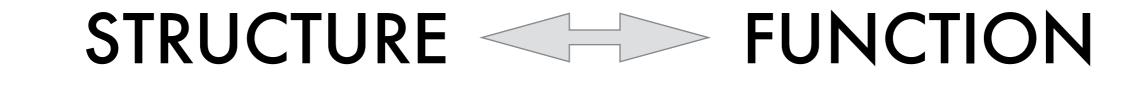




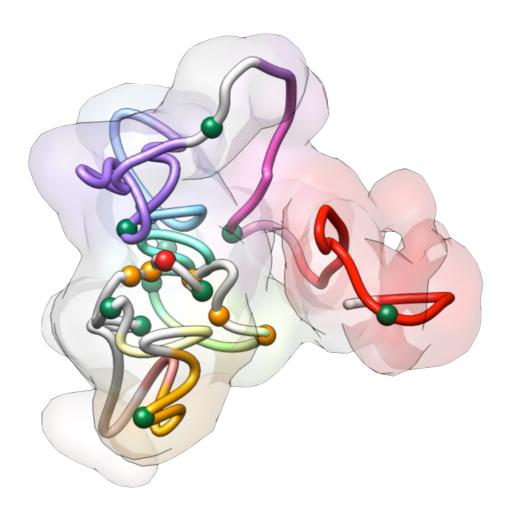
Model for TAD regulation





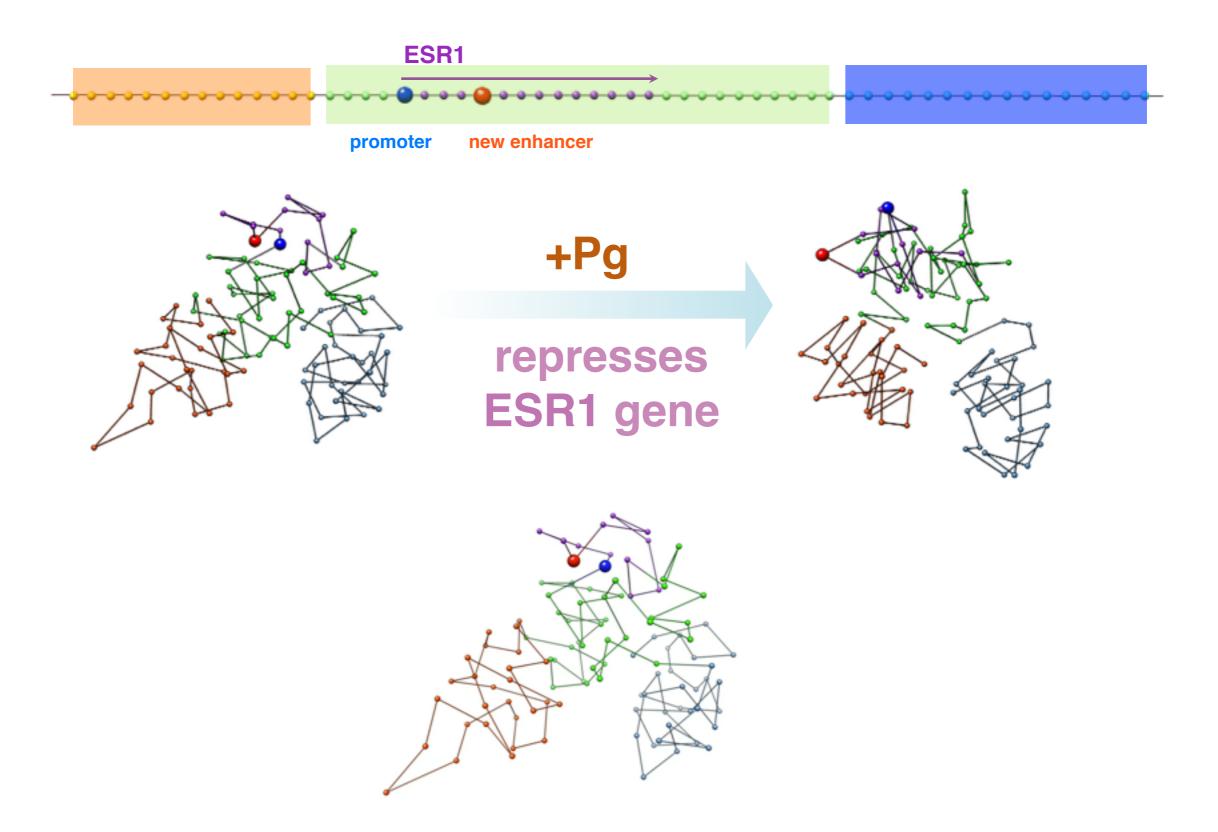








Structure >> Function!



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

http://marciuslab.org http://cnag.cat · http://crg.cat









NSTITUCIÓ CATALANA DE ECERCA | ESTUDIS AVANCATS