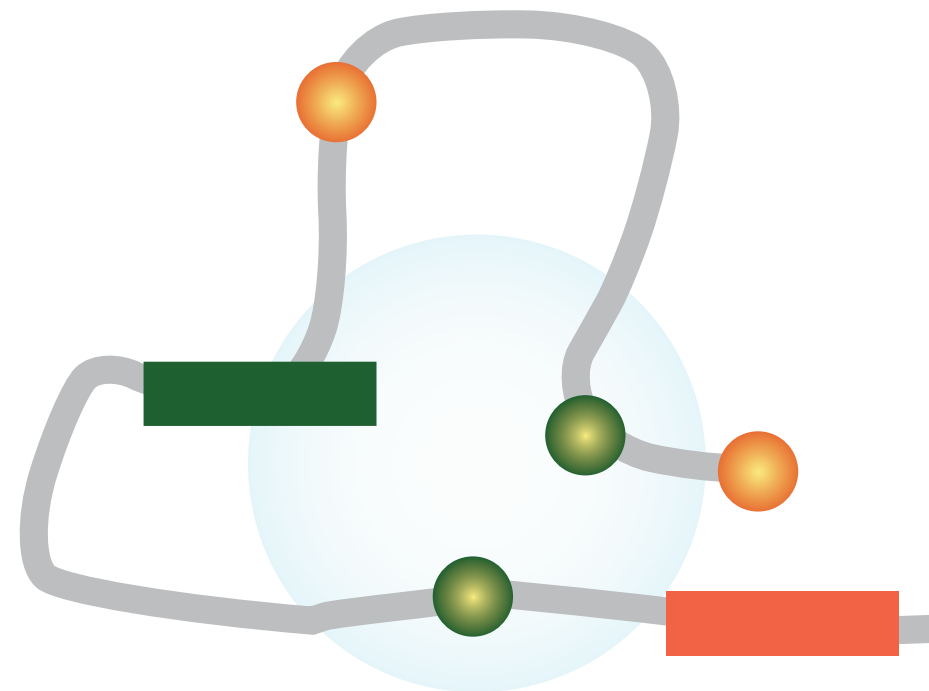
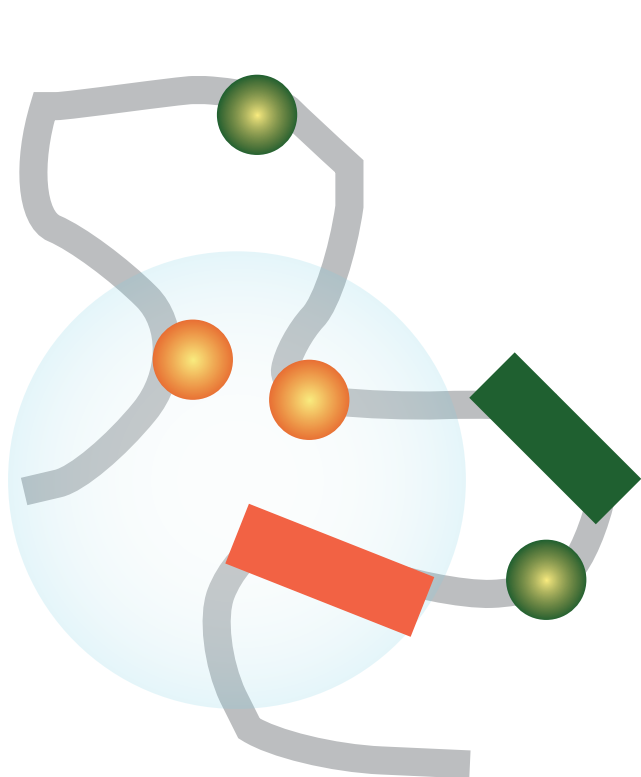


Modeling 3D genomes:
**Determination of hormone
induced structural changes
in TADs**

Marc A. Marti-Renom

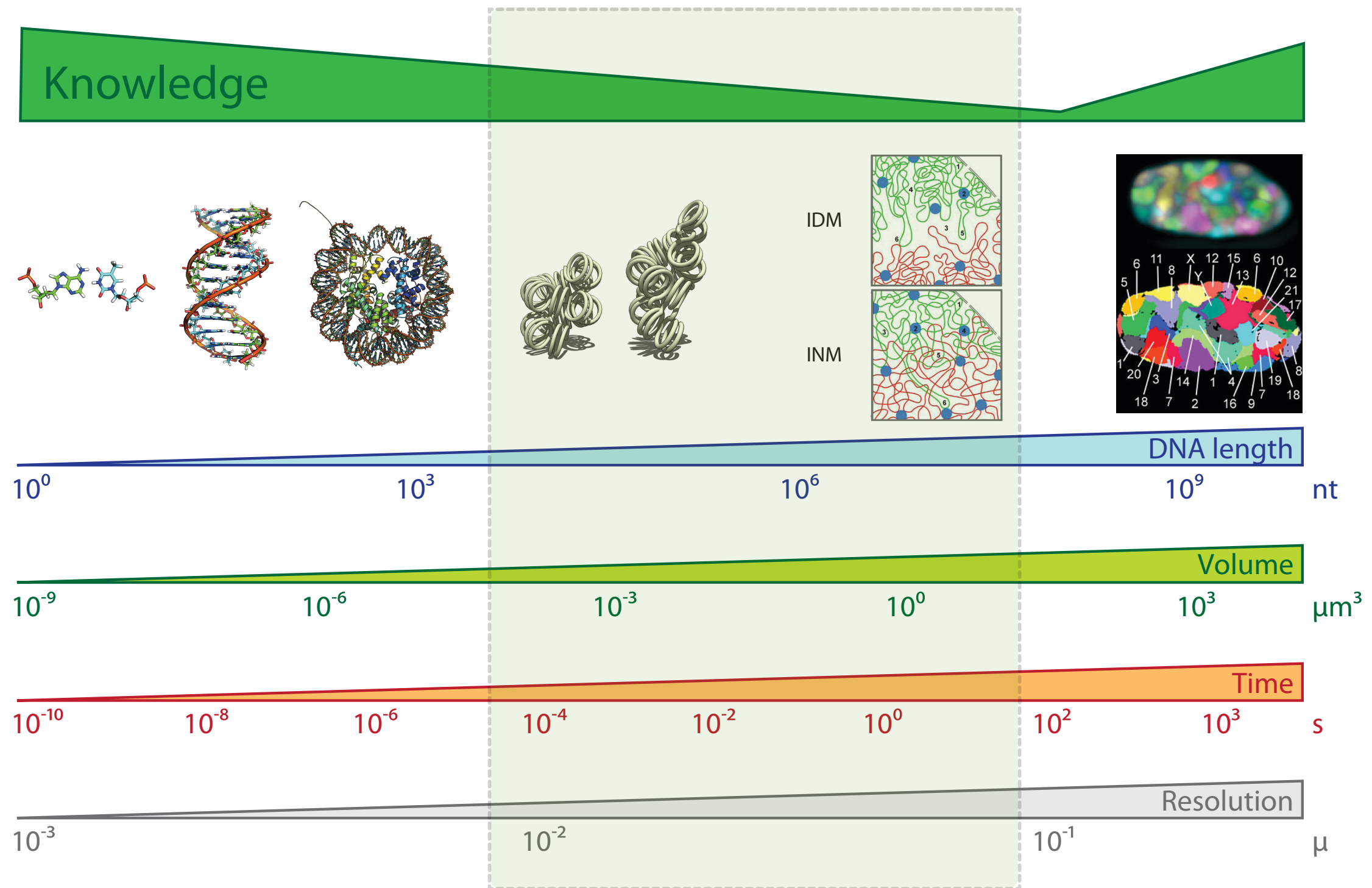
*Genome Biology Group (CNAG)
Structural Genomics Group (CRG)*

Complex genome organization



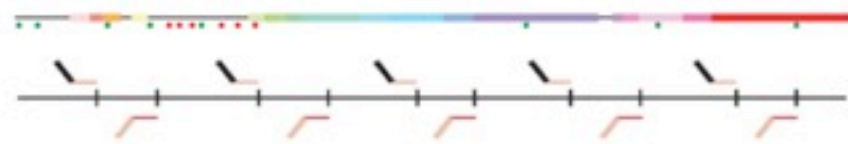
Resolution Gap

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





Experiments

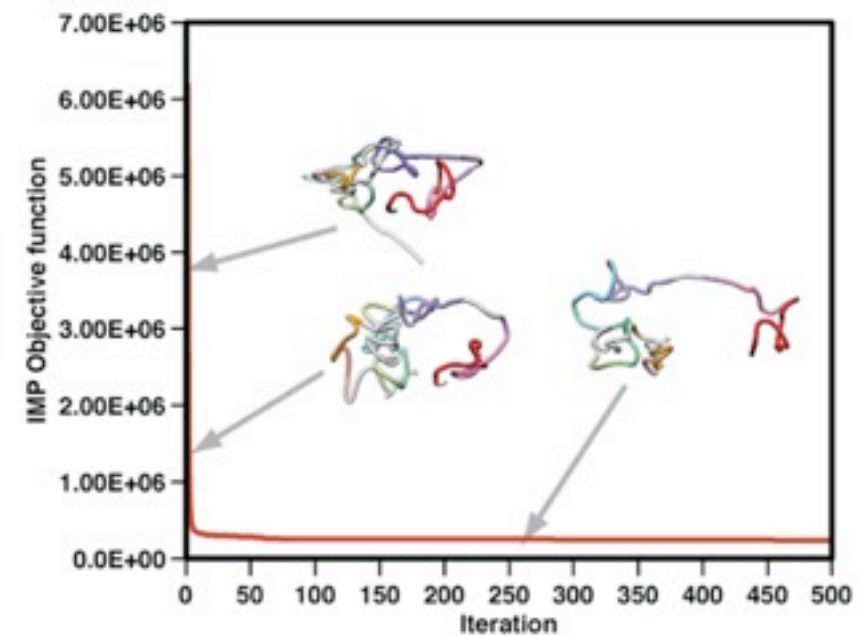
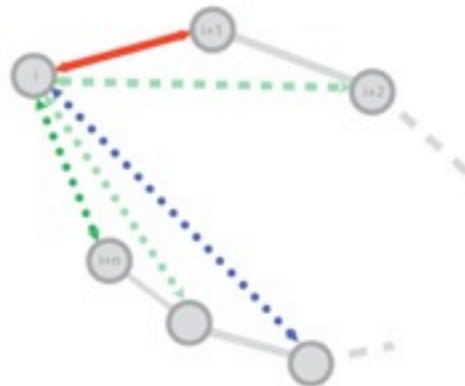
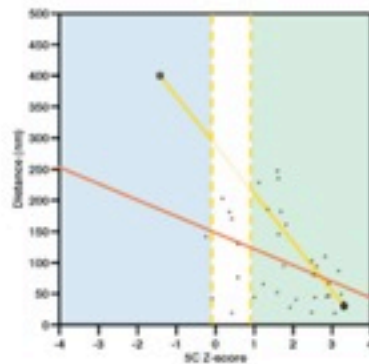
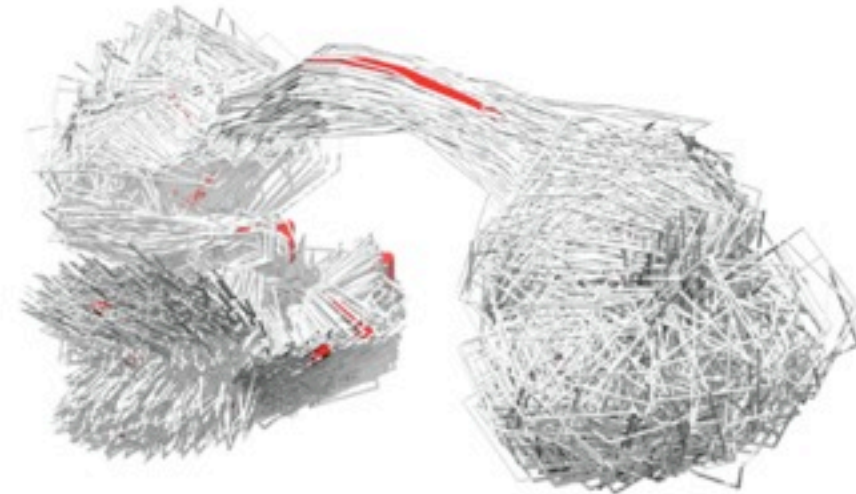


Grow GM12878 and K562 cells

Perform 3C analysis

Perform 5C analysis with 30+25 primers

Analyze 5C products by paired-end Solexa sequencing
(131,947 paired end reads per library)



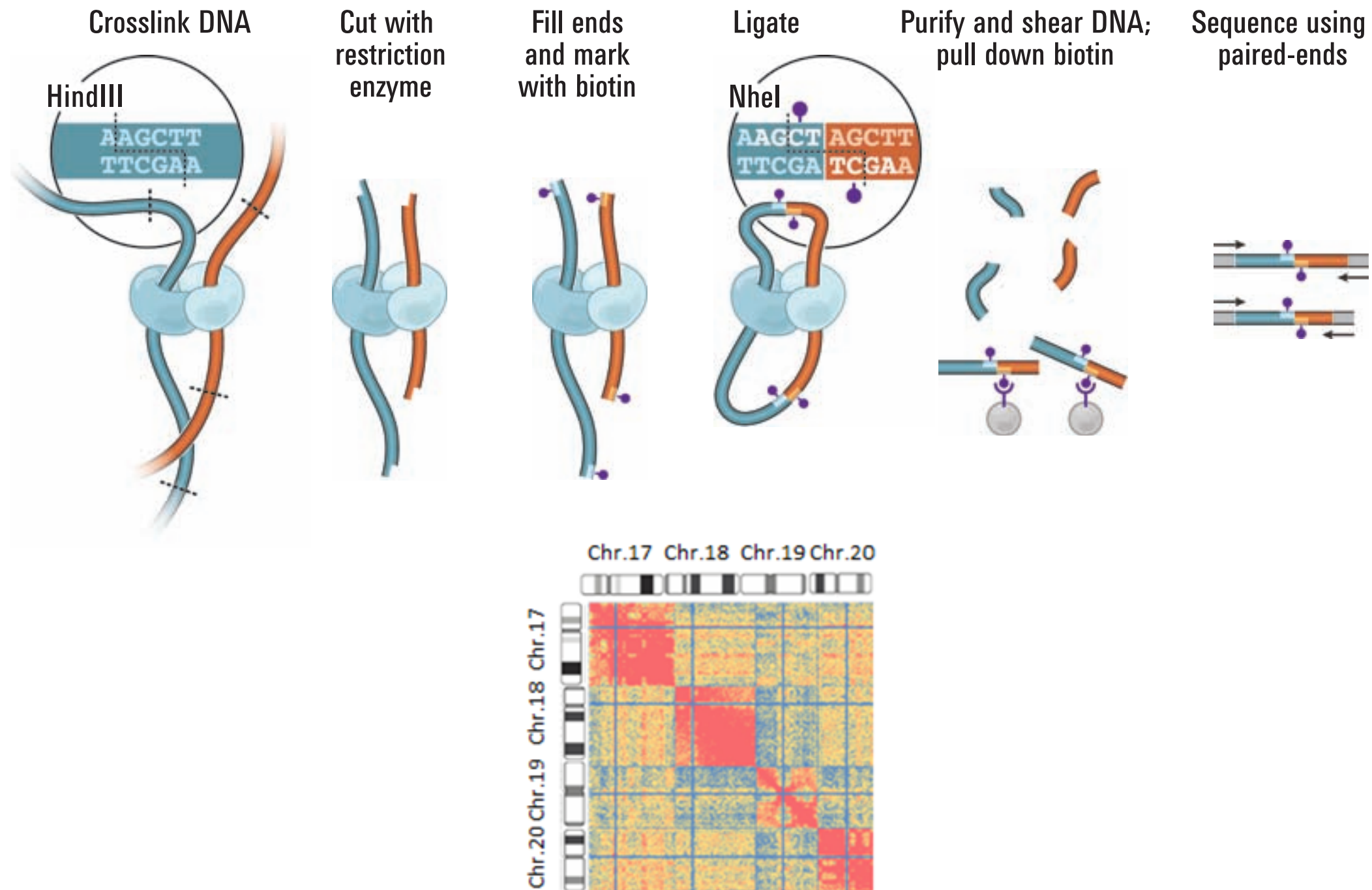
Computation

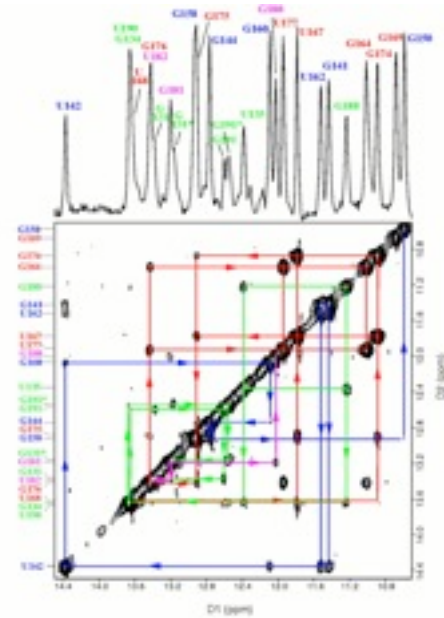
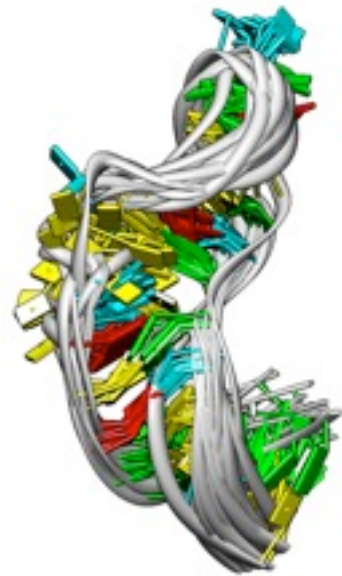


Hi technology

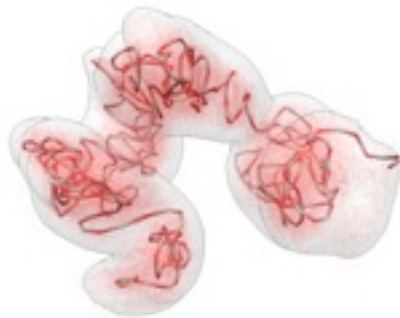
Lieberman-Aiden, E. et al. Science 326, 289–293 (2009).

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





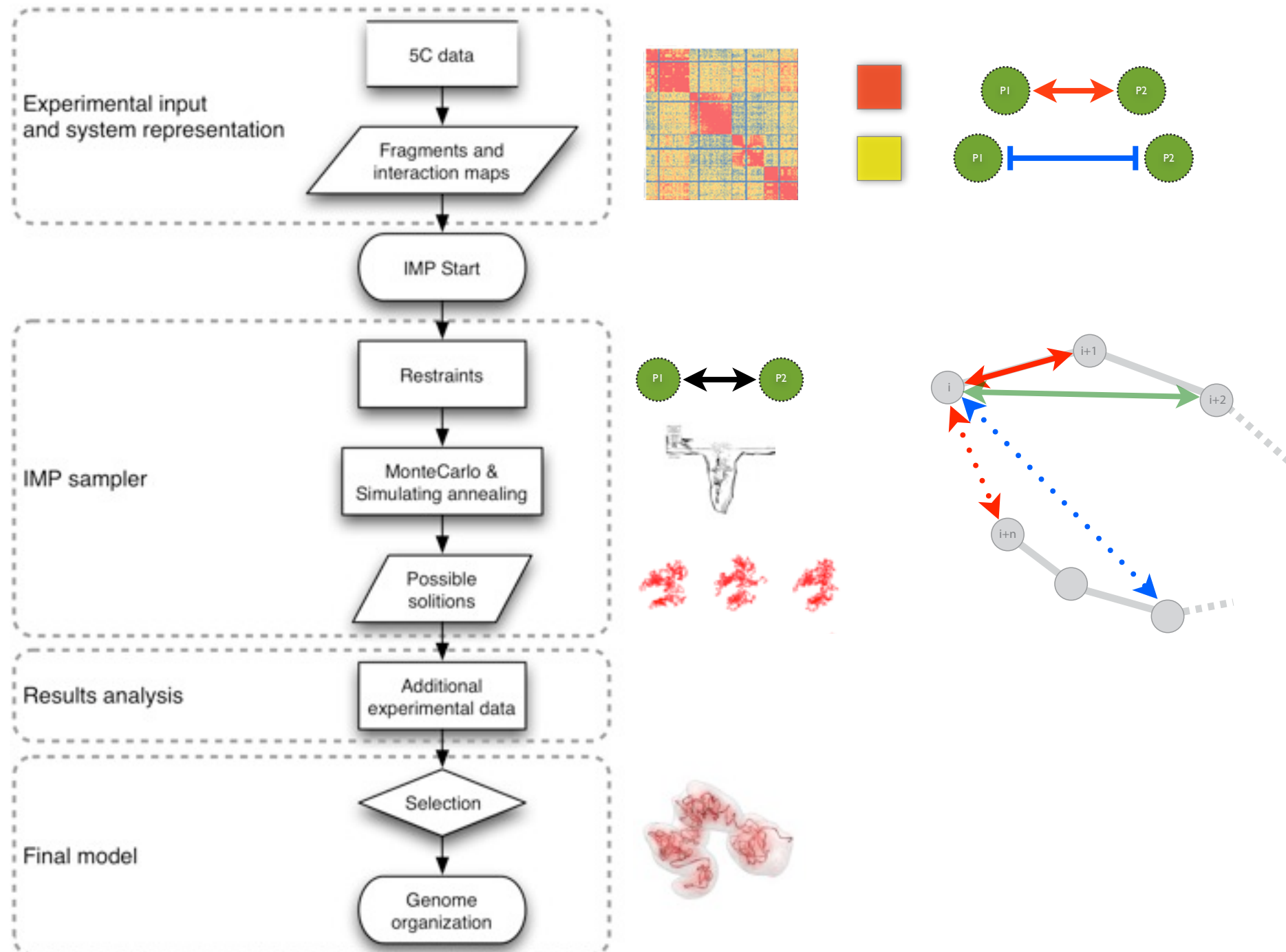
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data

Integrative Modeling

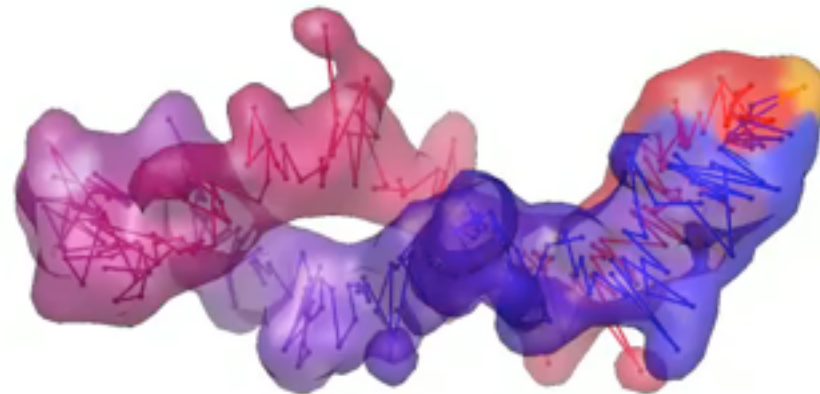
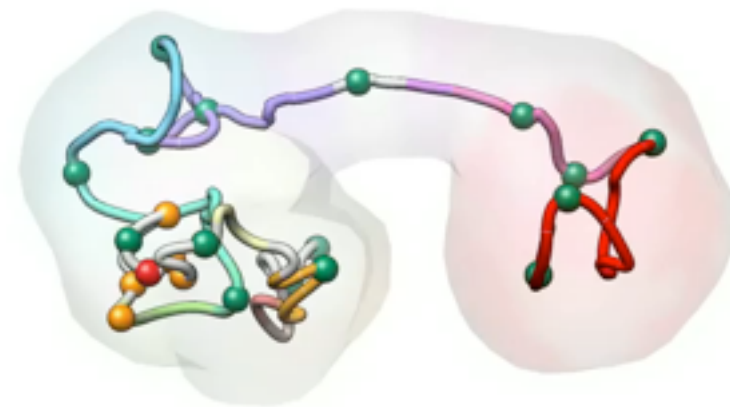
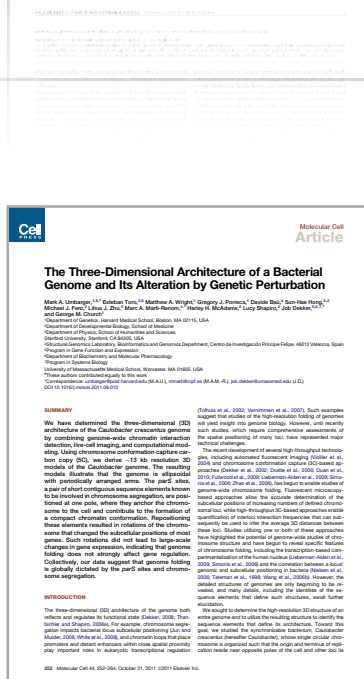
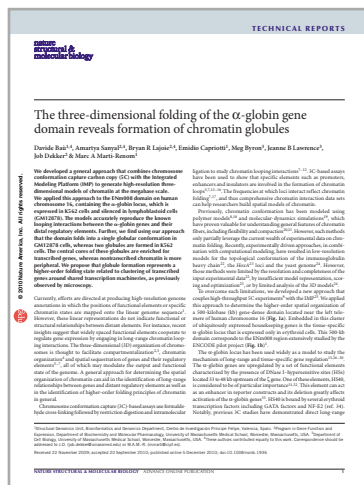
<http://www.integrativemodeling.org>



Previous applications...

Baù, D. et al. Nat Struct Mol Biol (2011).

Umbarger, M. A. et al. Mol Cell (2011).



3D TAD response to hormone



Davide Baù



François le Dily



Miguel Beato

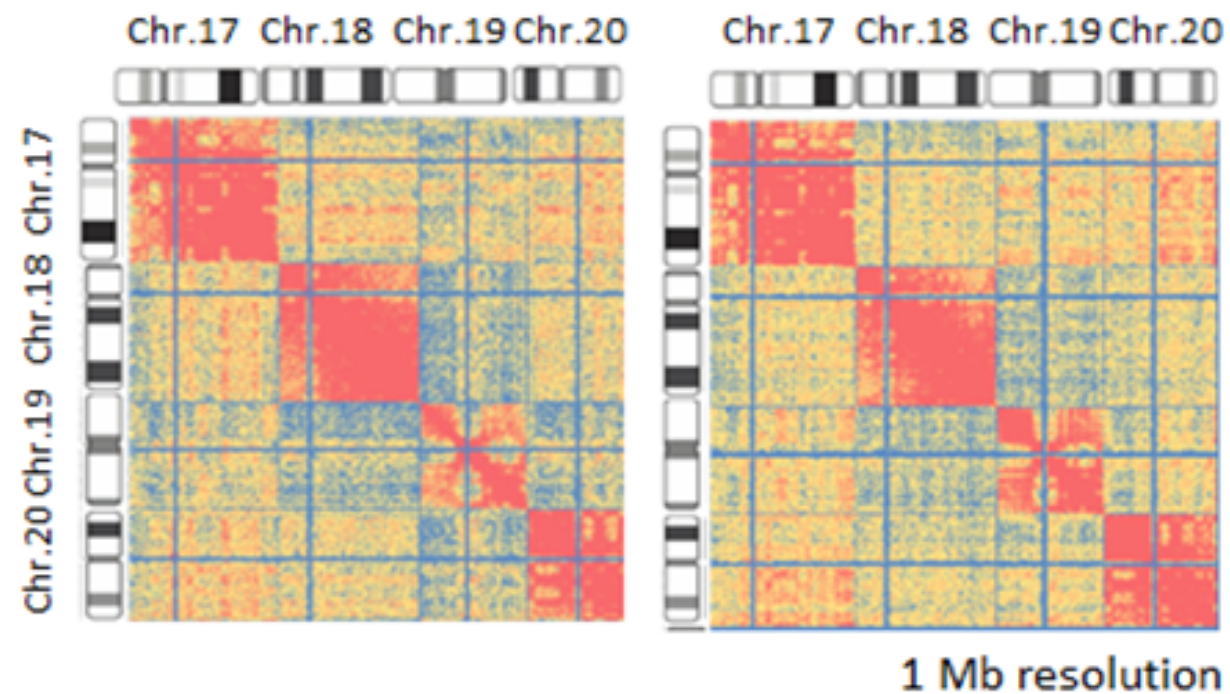
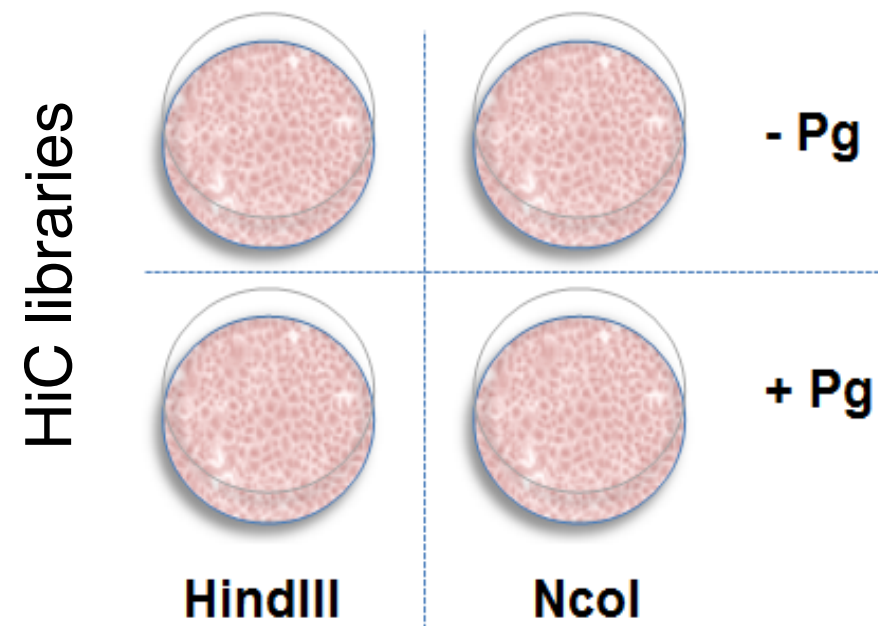
Chromatin and Gene Expression Group (CRG)



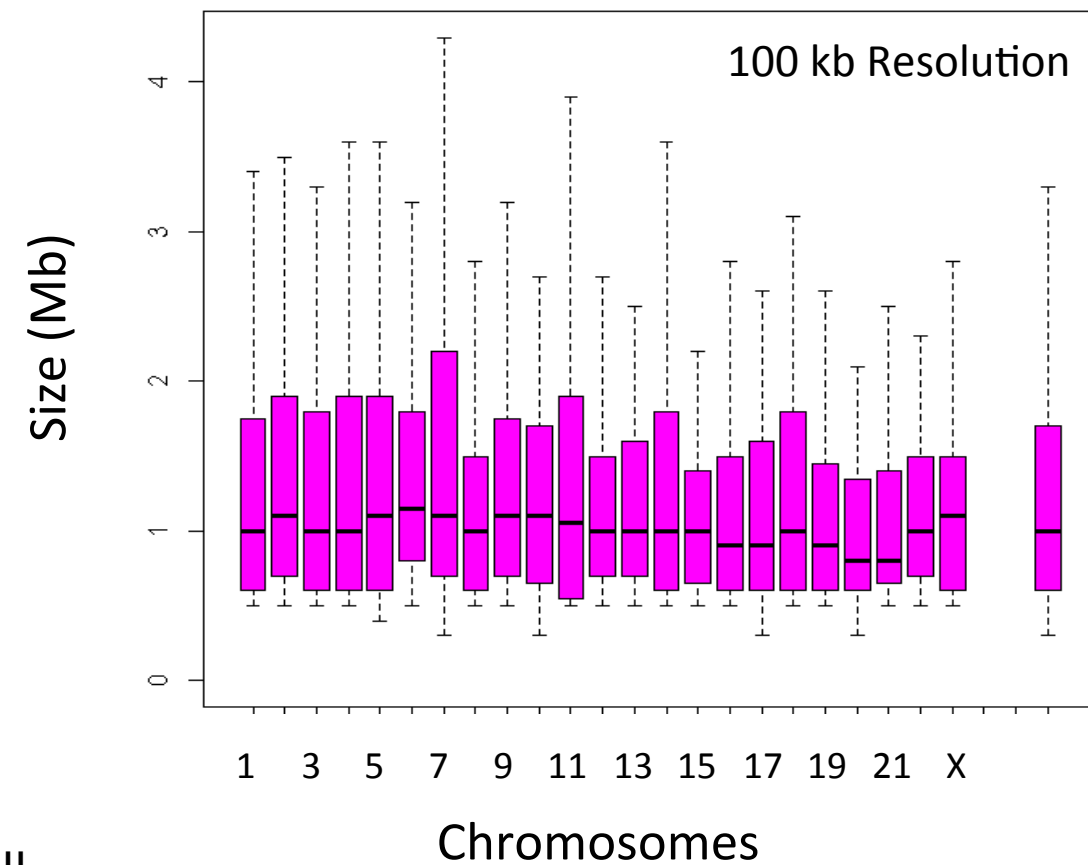
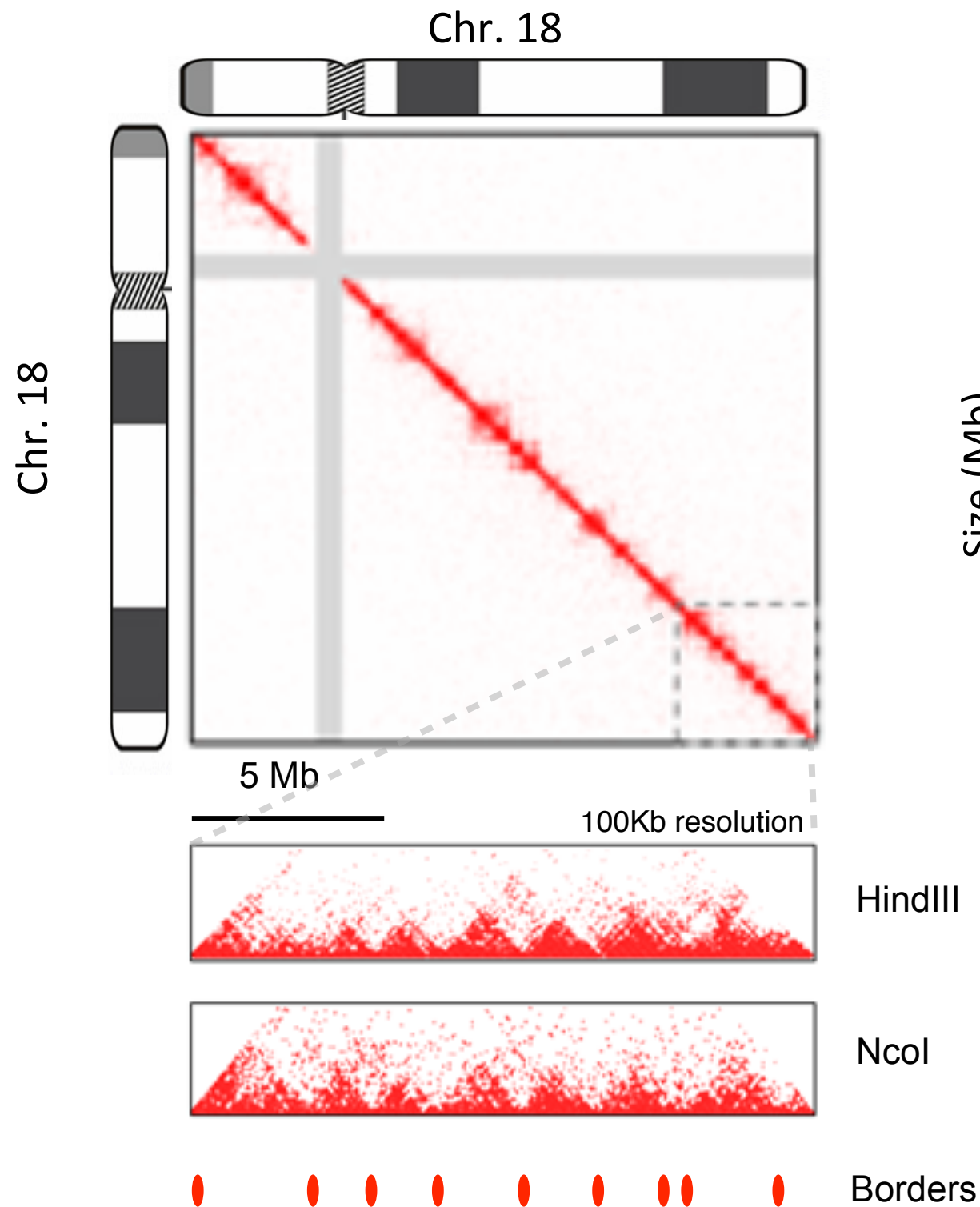
Guillaume Filion

Genome Architecture Group (CRG)

Experimental design

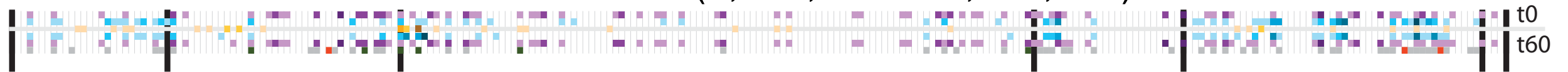


Topologically Associated Domains (TADs)

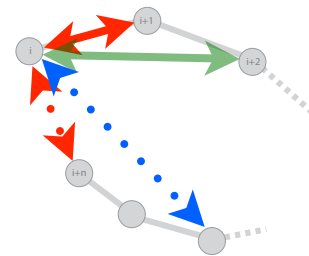


Modeling TADs

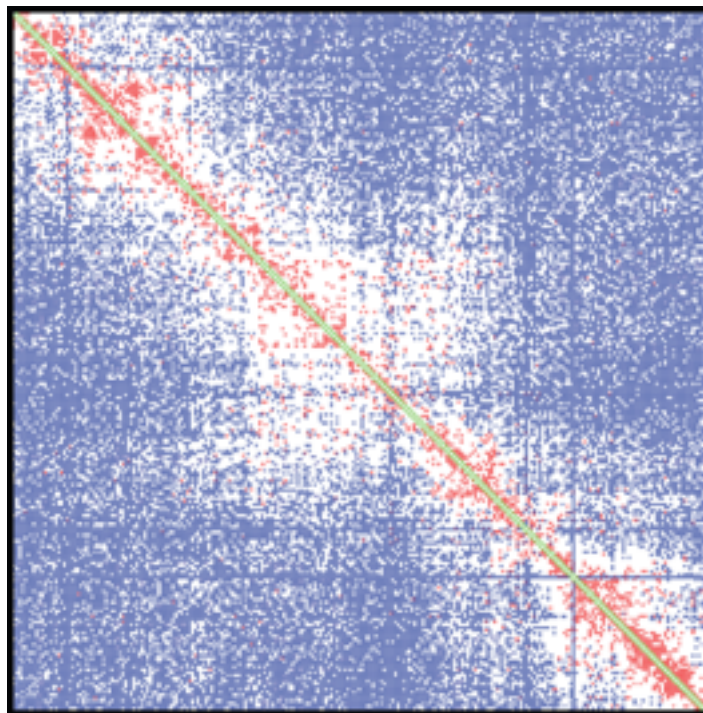
Human Chr2 (8,480,000 - 13,460,000)



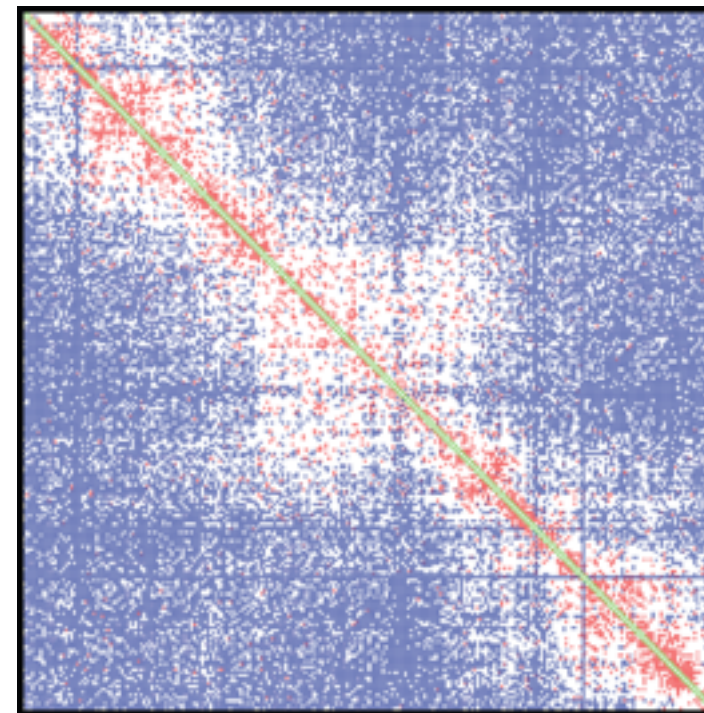
Harmonic · Harmonic Lower Bound · Harmonic Upper Bound



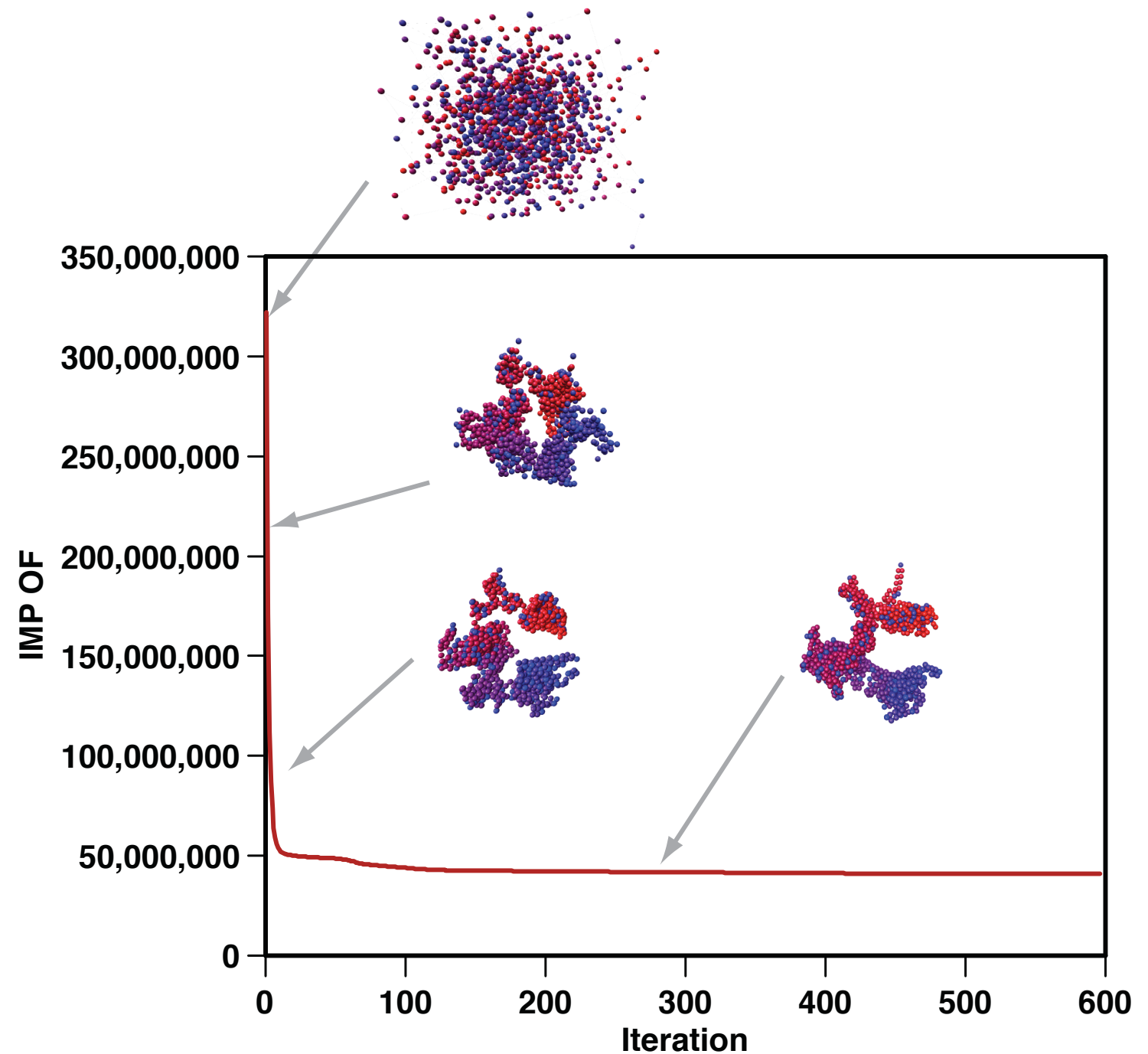
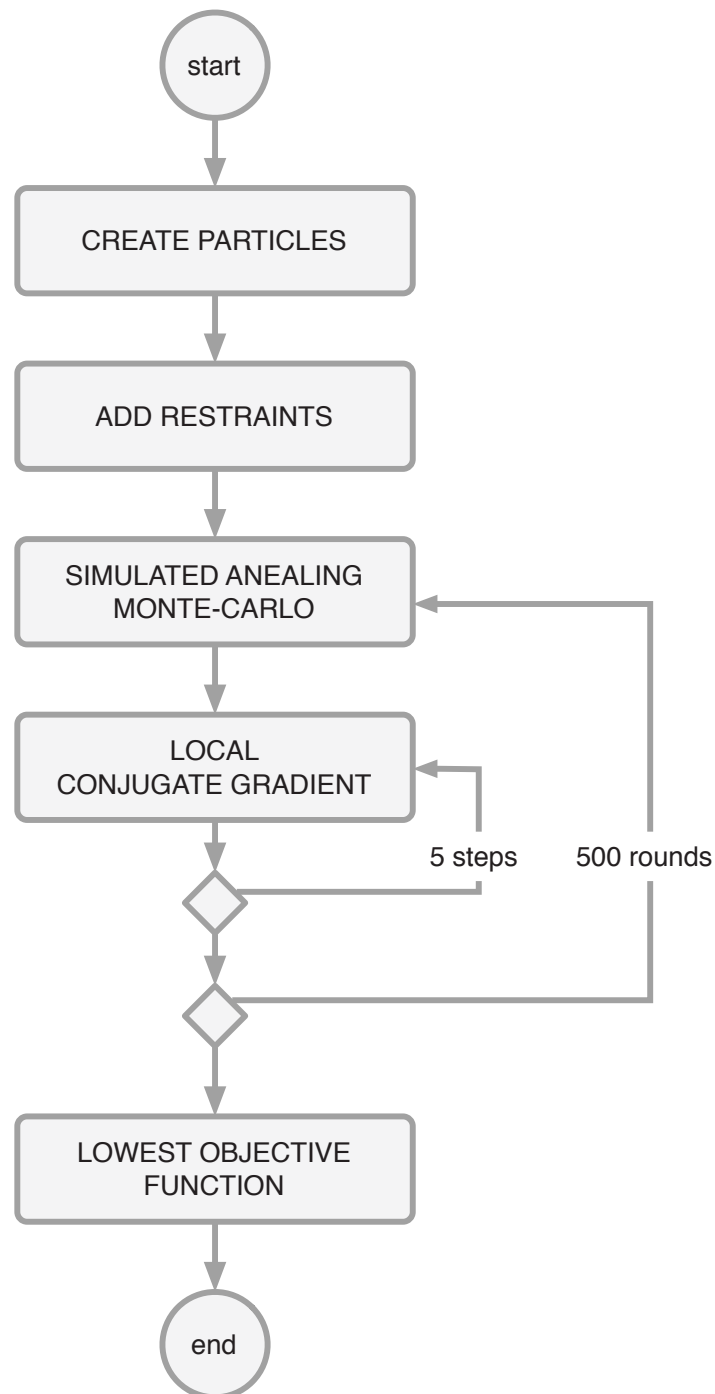
T0



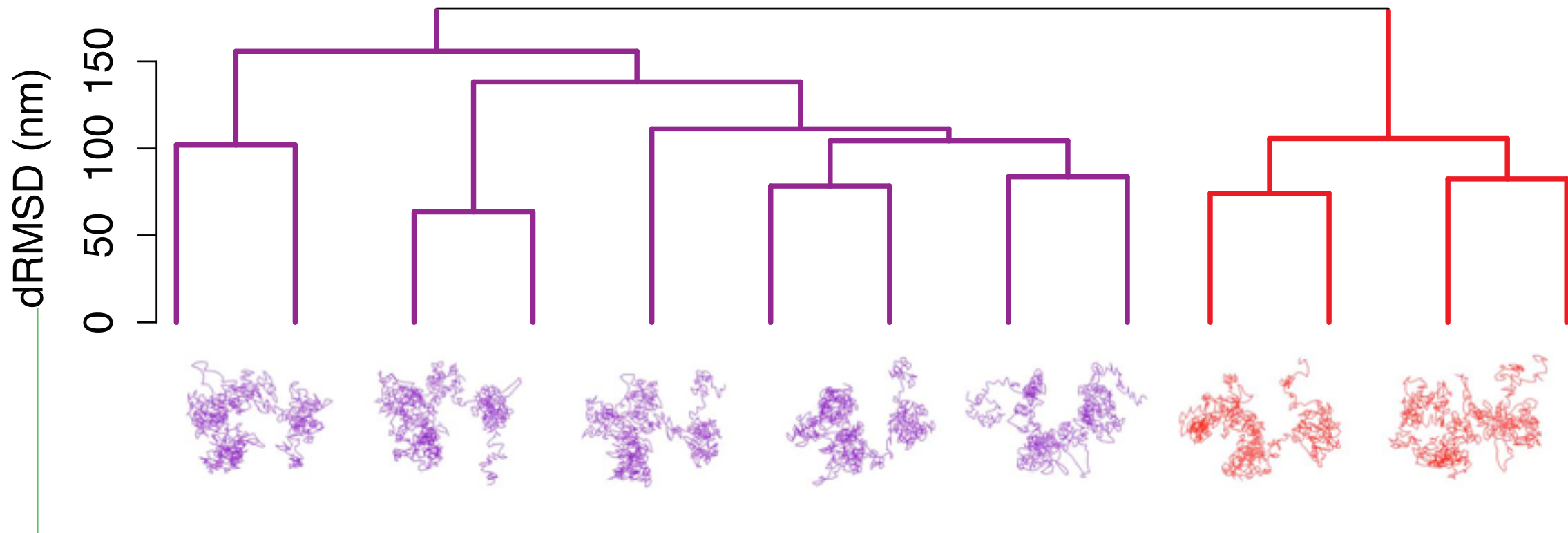
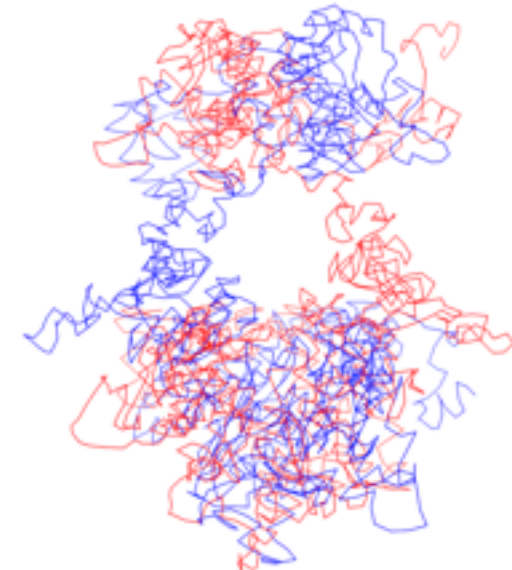
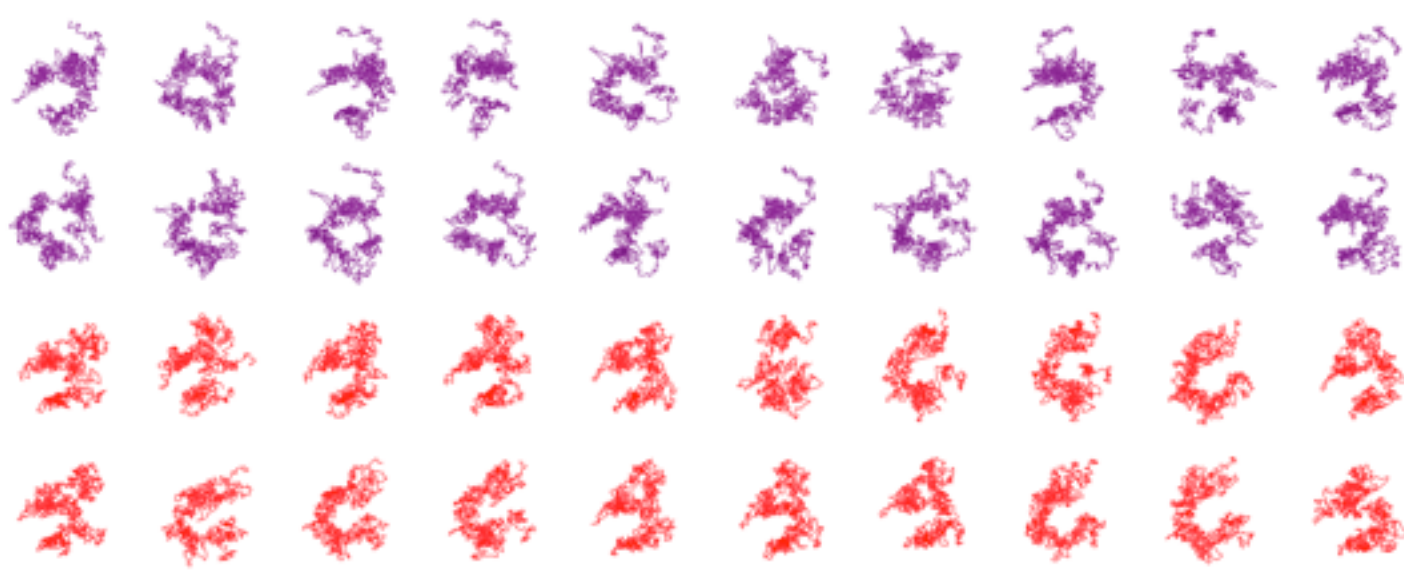
T60



Optimization of the scoring function

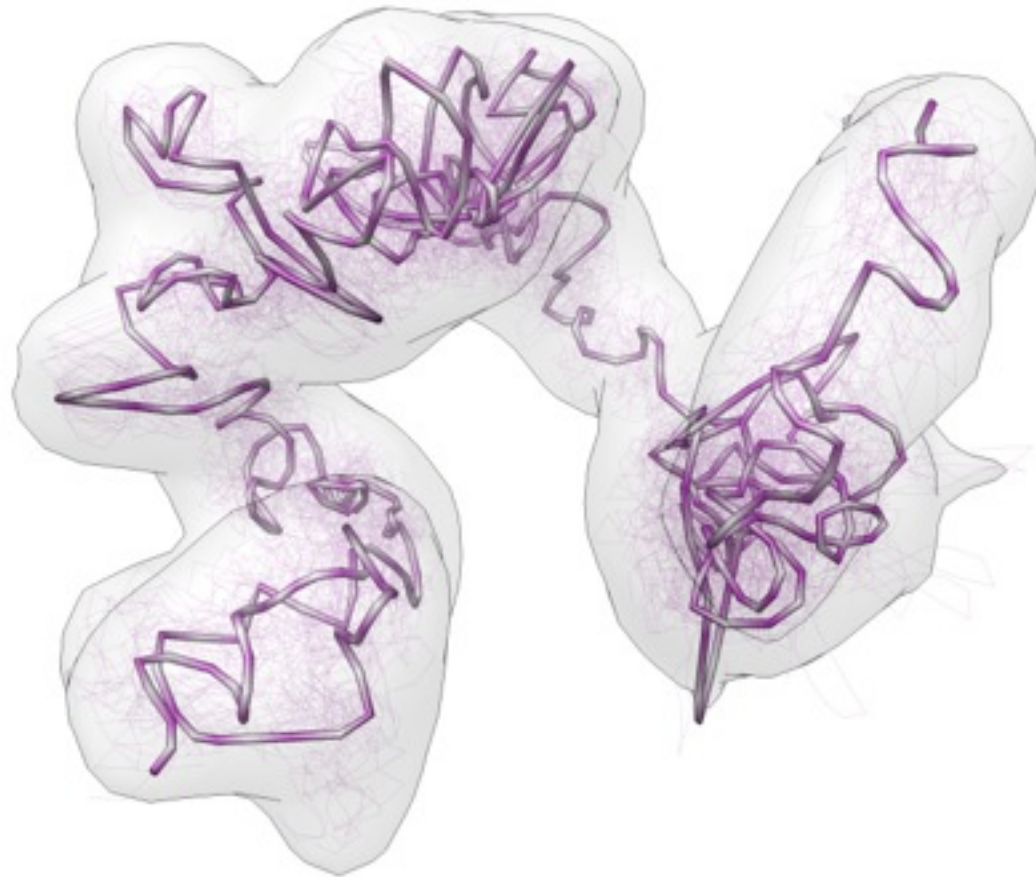


Clustering

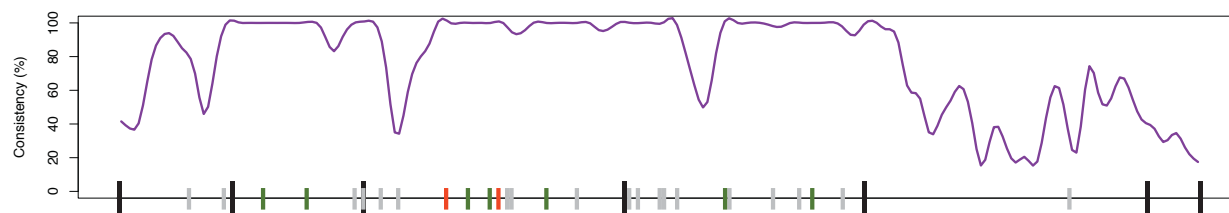


Clustering

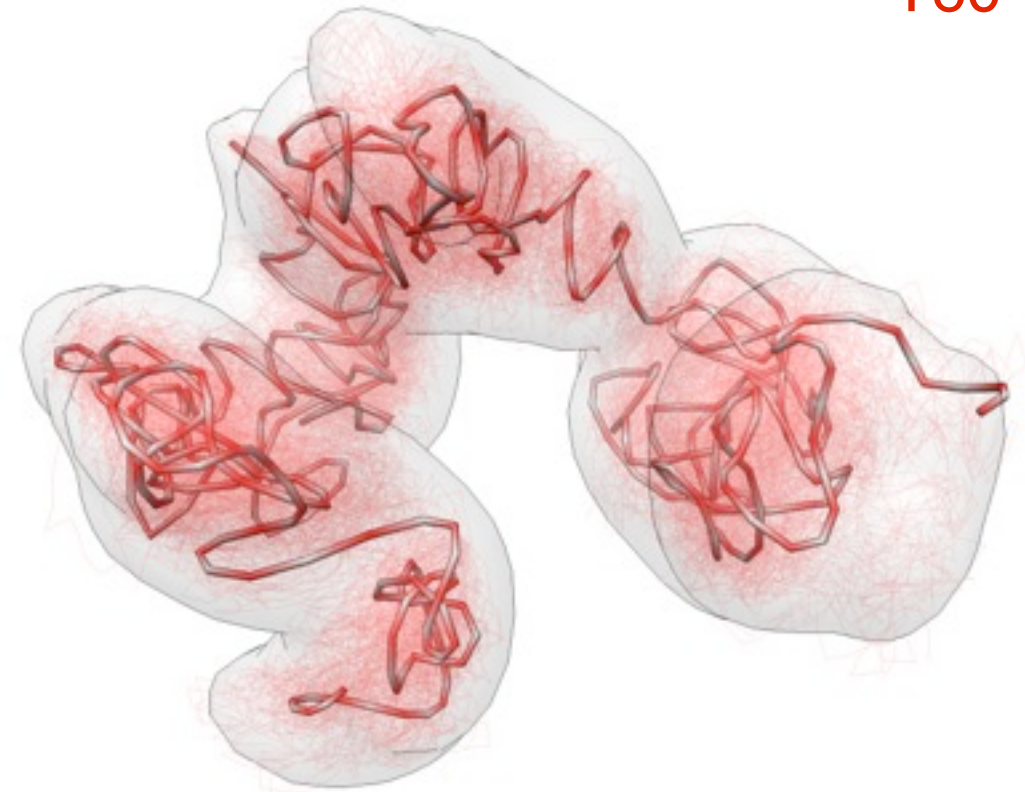
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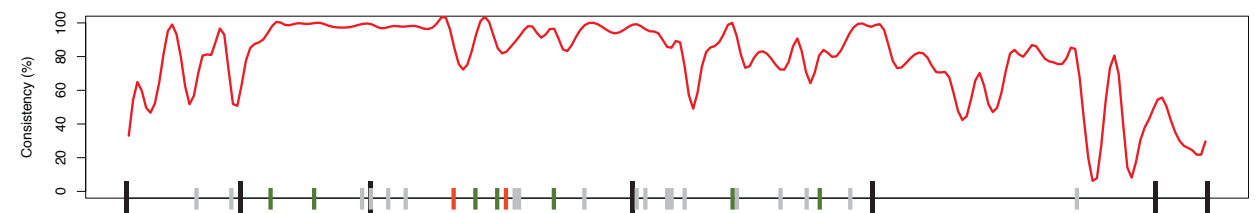
Cluster #3
13 models
MaxDist: ~1400nm



T60

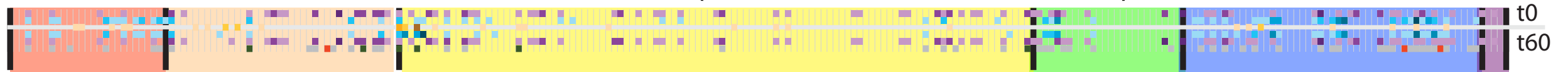


Cluster #1
42 models
MaxDist: ~1400nm

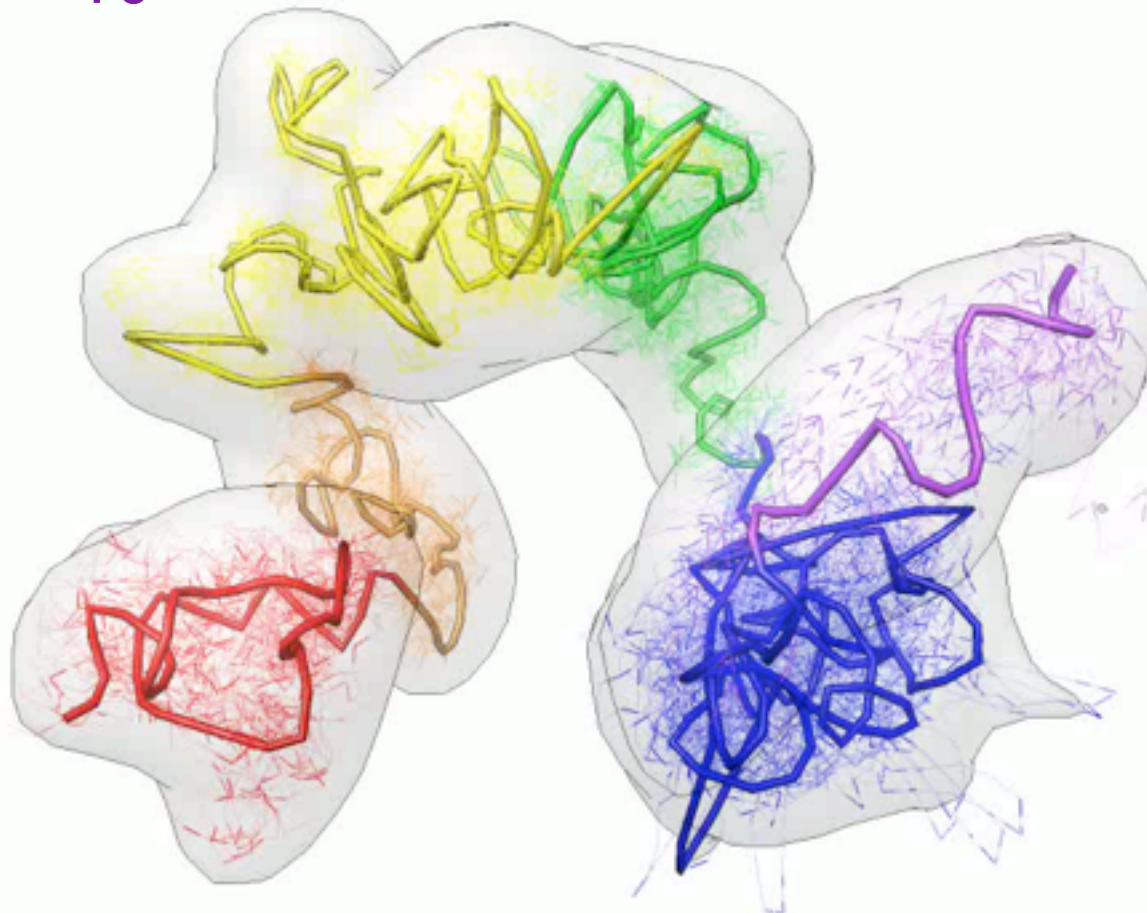


Structural TADs

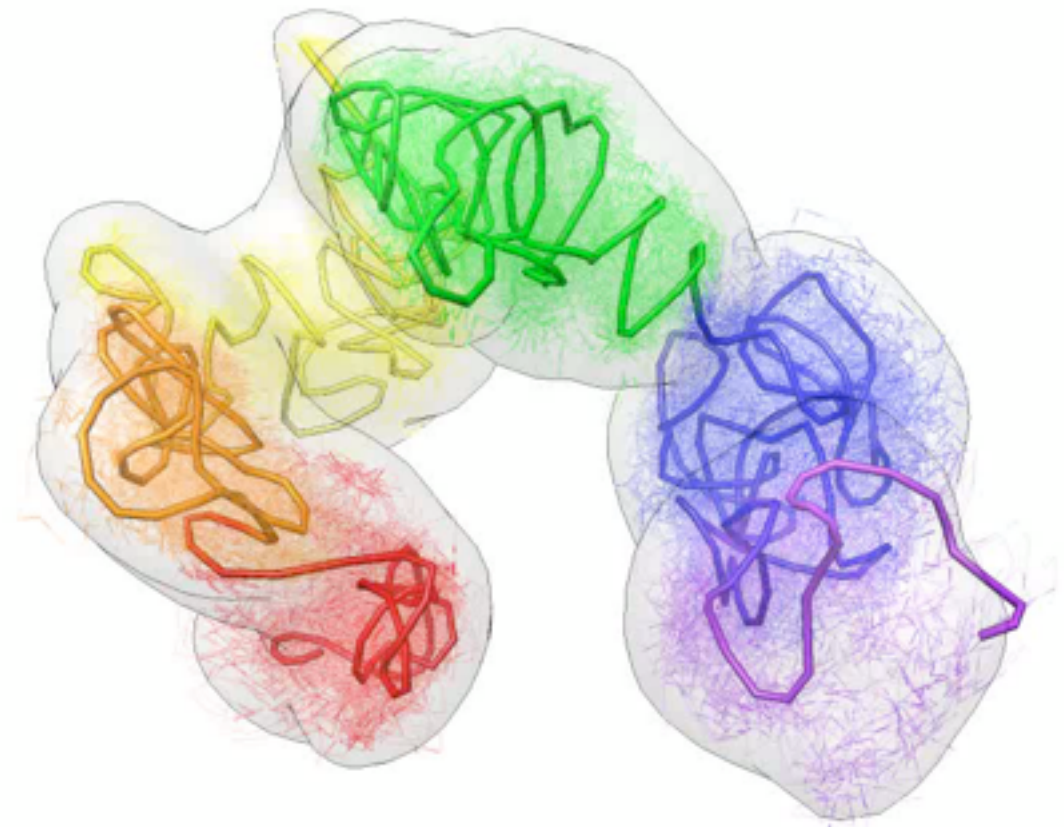
Human Chr2 (8,480,000 - 13,460,000)



T0

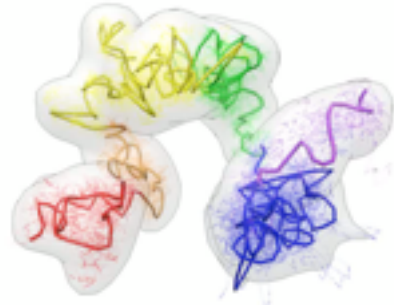


T60

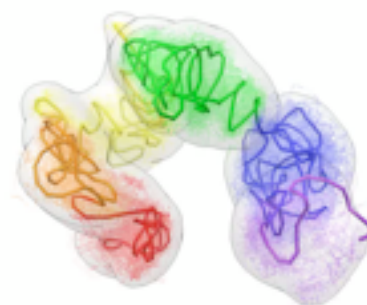


Structural expansion of TADs

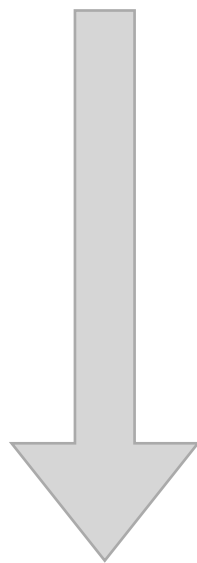
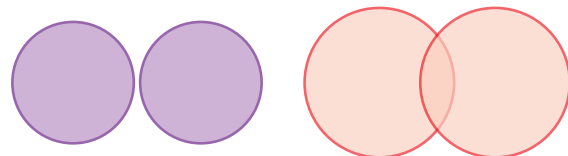
T0



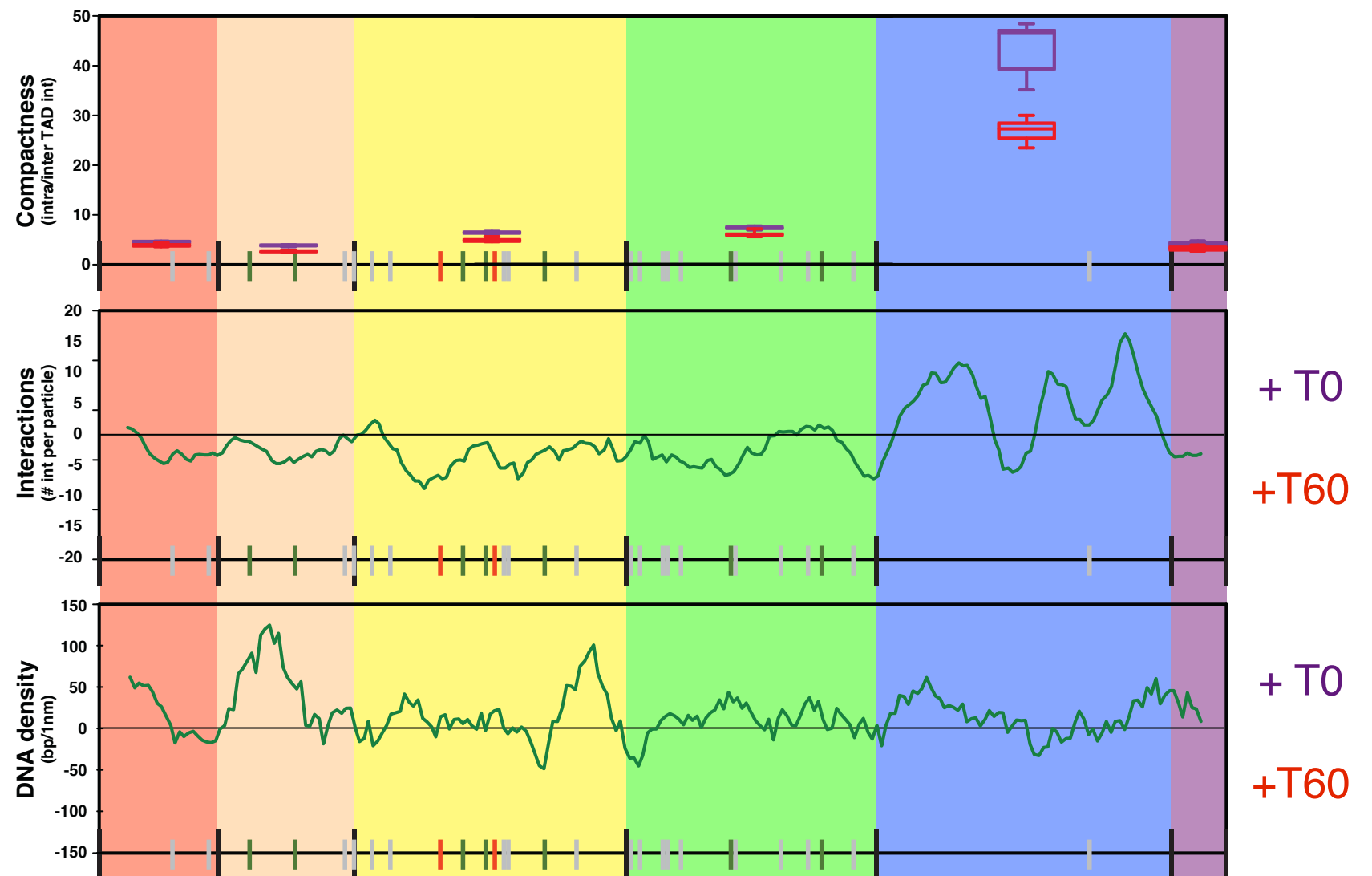
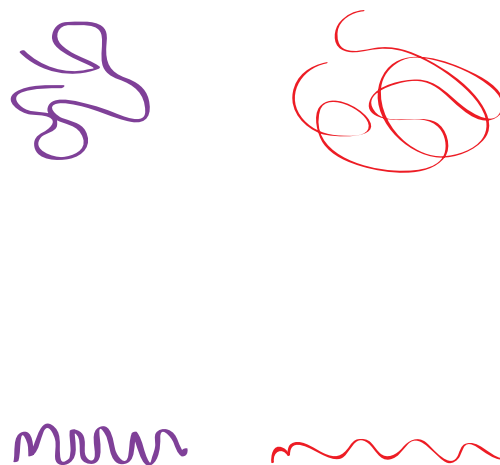
T60



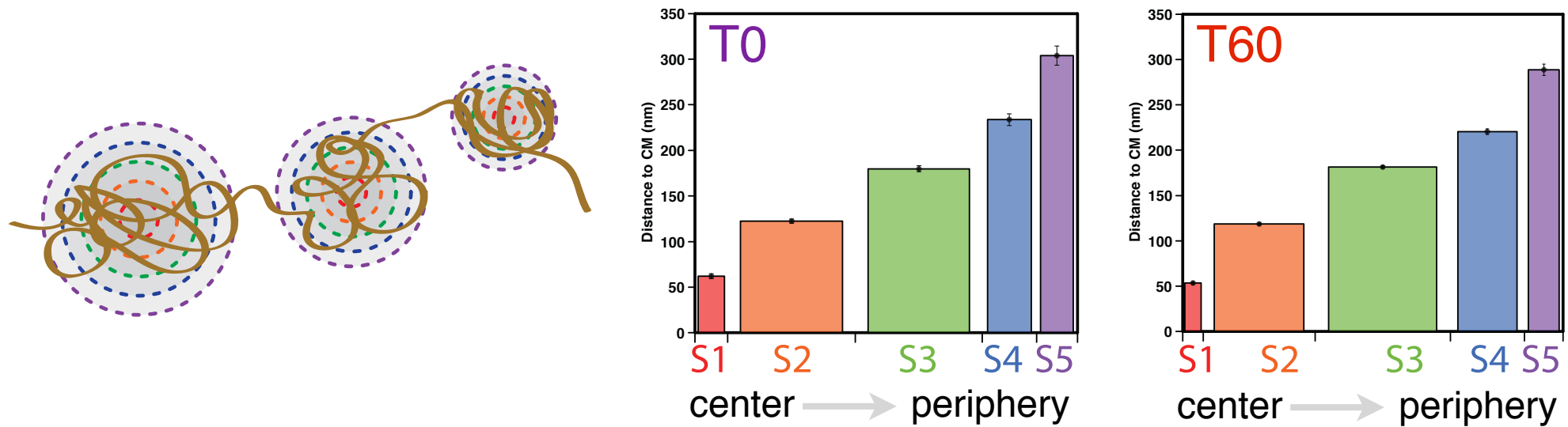
Global



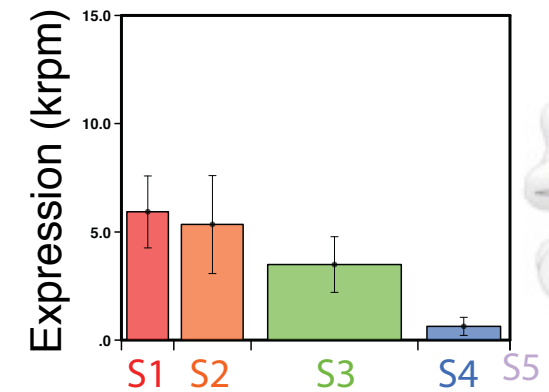
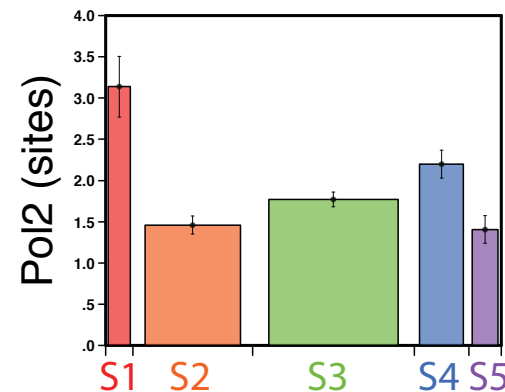
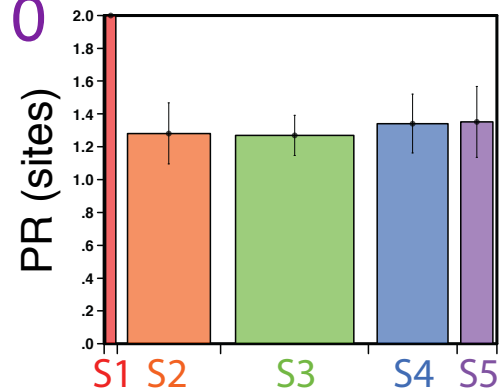
Local



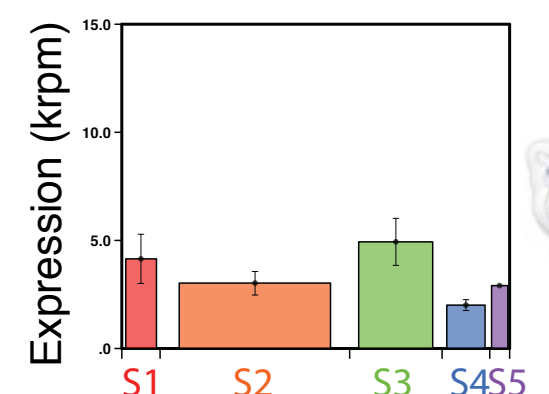
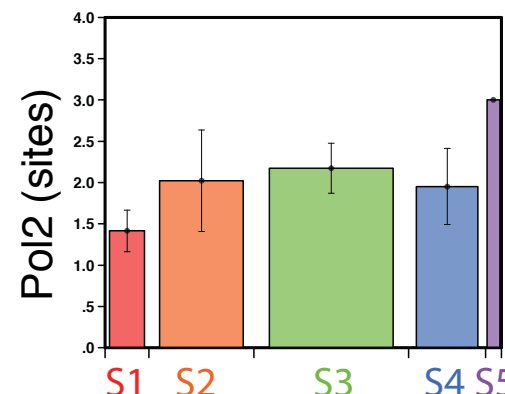
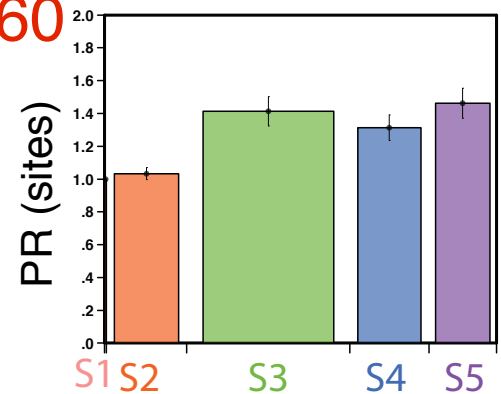
Functional TADs



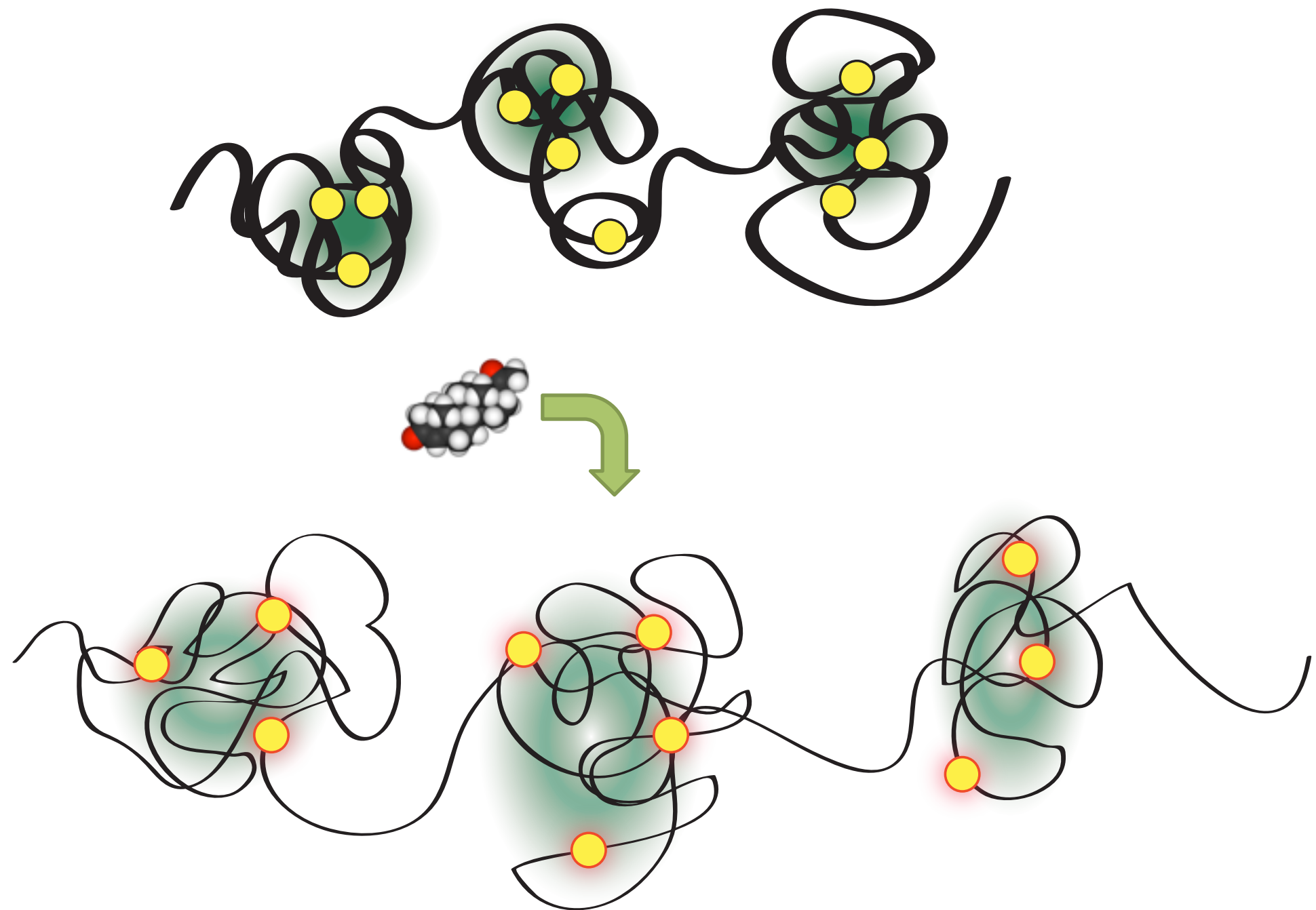
T0



T60



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>

