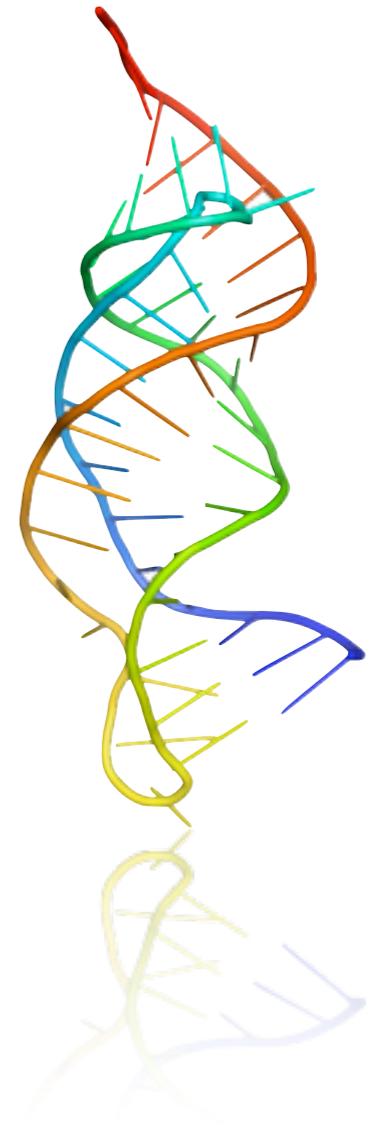
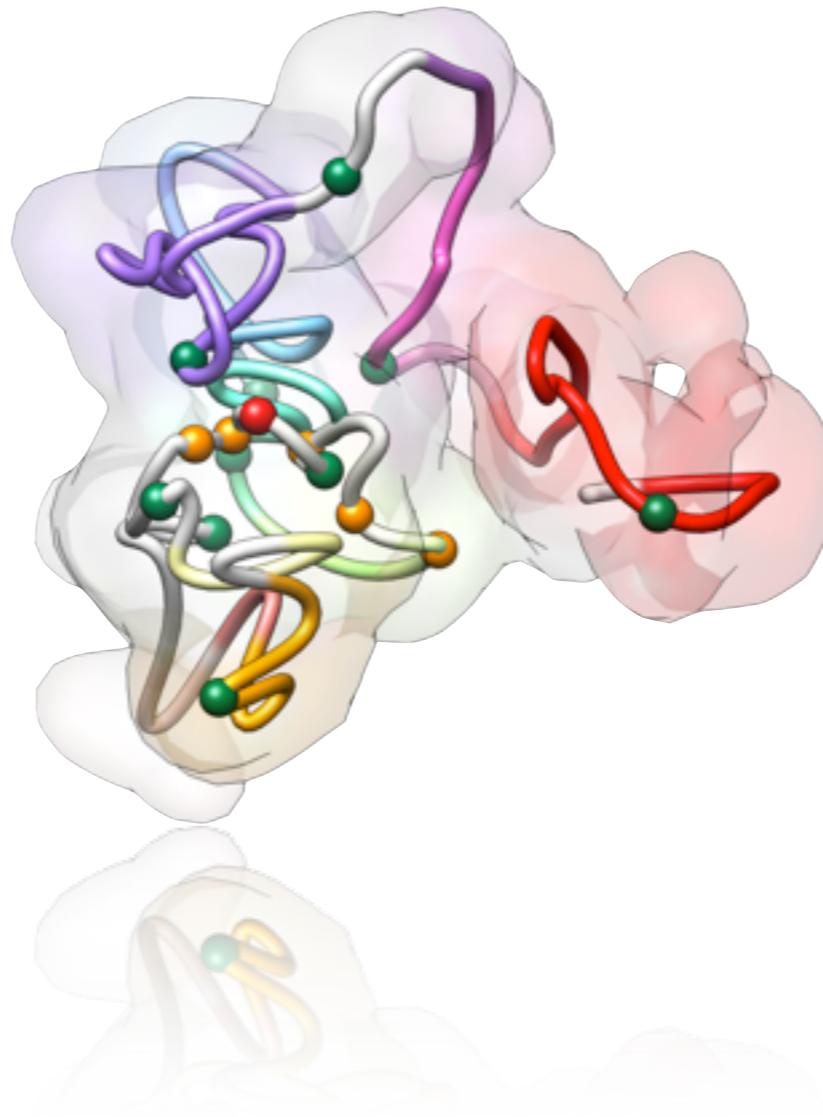
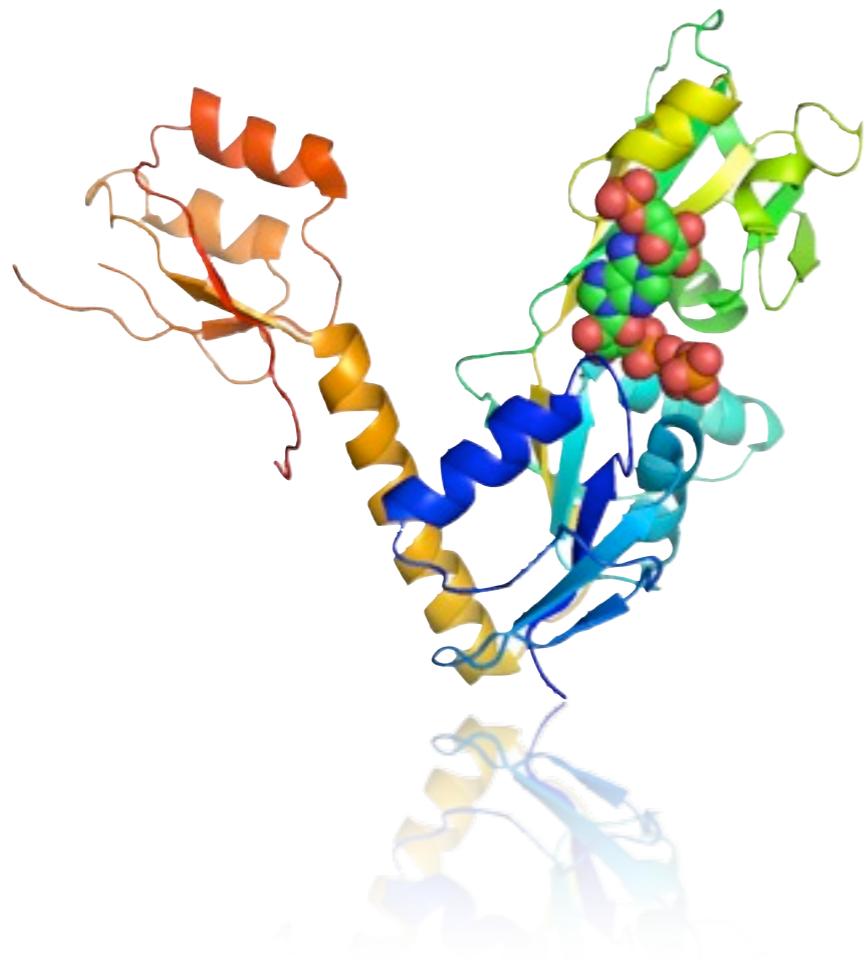


# Structure determination of genomes and genomic domains by satisfaction of spatial restraints

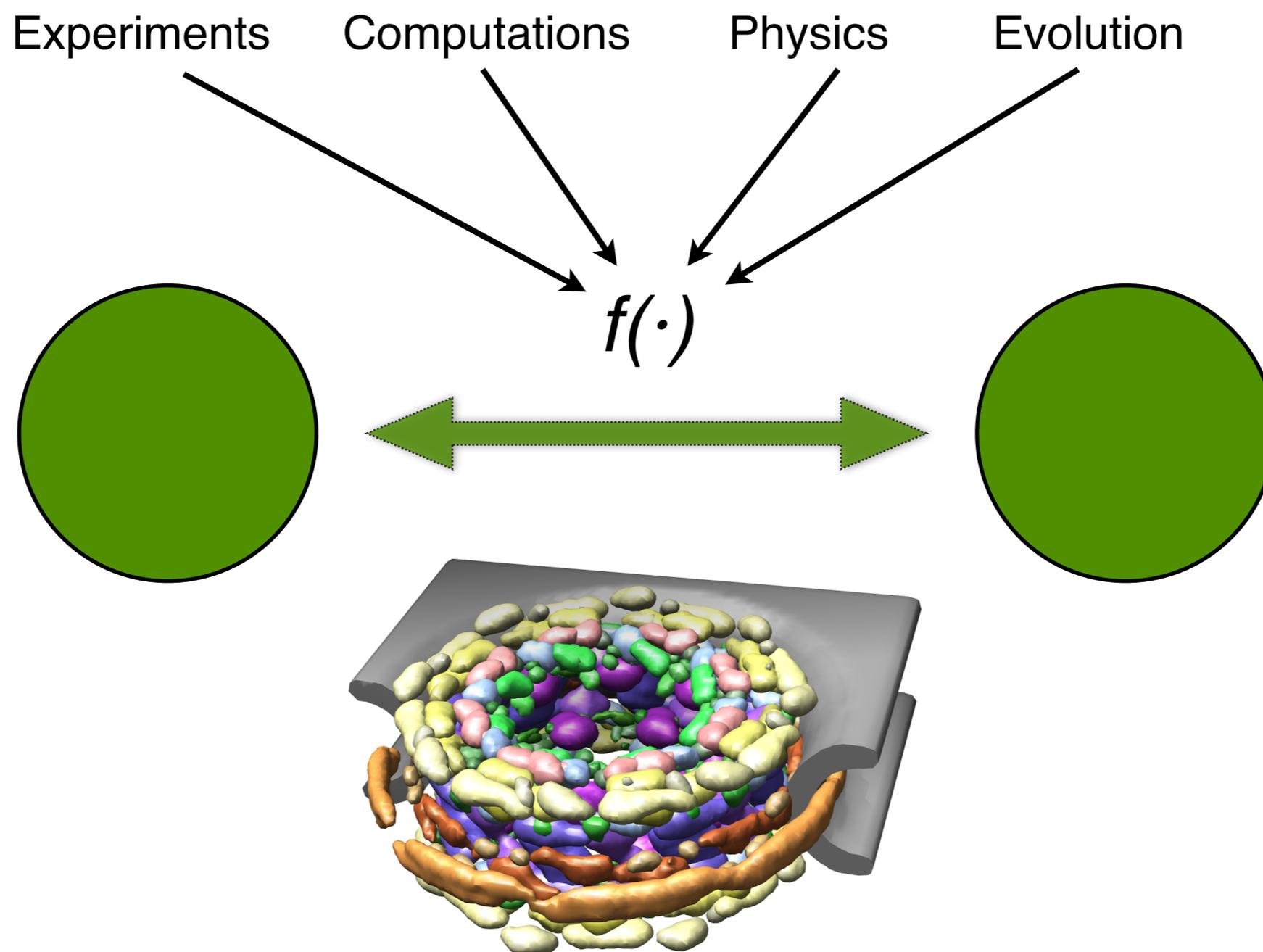
**Marc A. Marti-Renom**

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

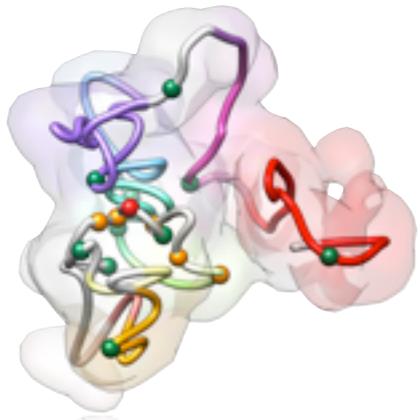


# Integrative Modeling Platform

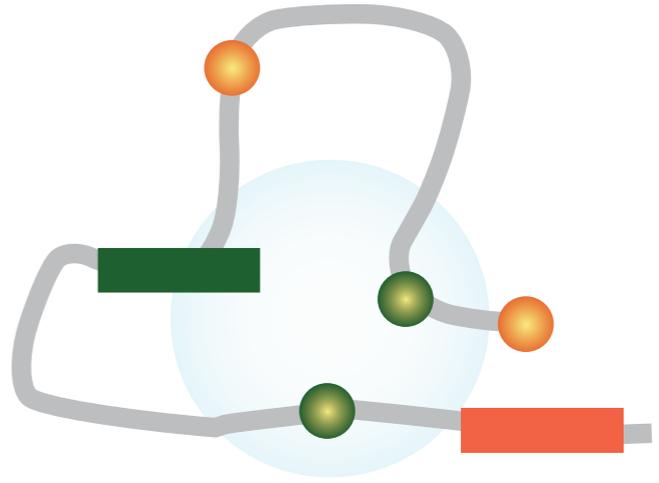
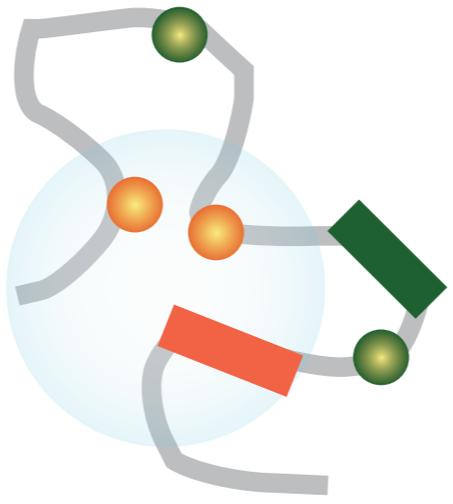
GENERALIZE software development  
<http://www.integrativemodeling.org>



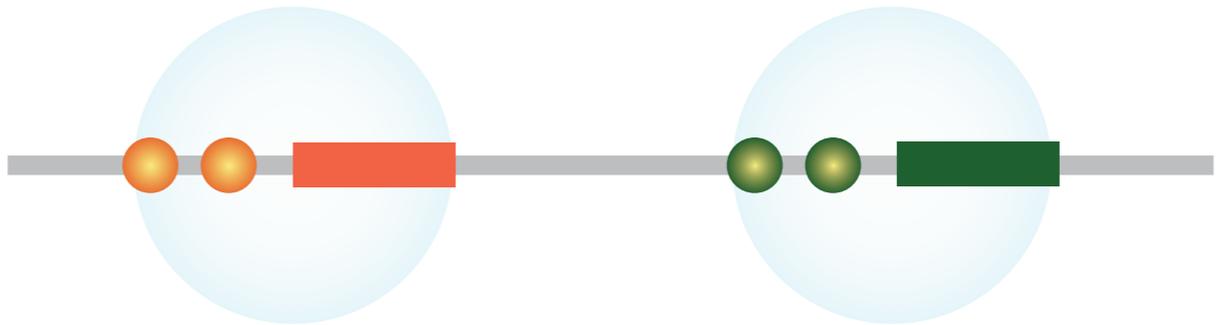
Alber, F. et al. (2007). *Nature*, 450(7170), 695–701  
Russel, D. et al. (2012). *PLoS Biology*, 10(1), e1001244.



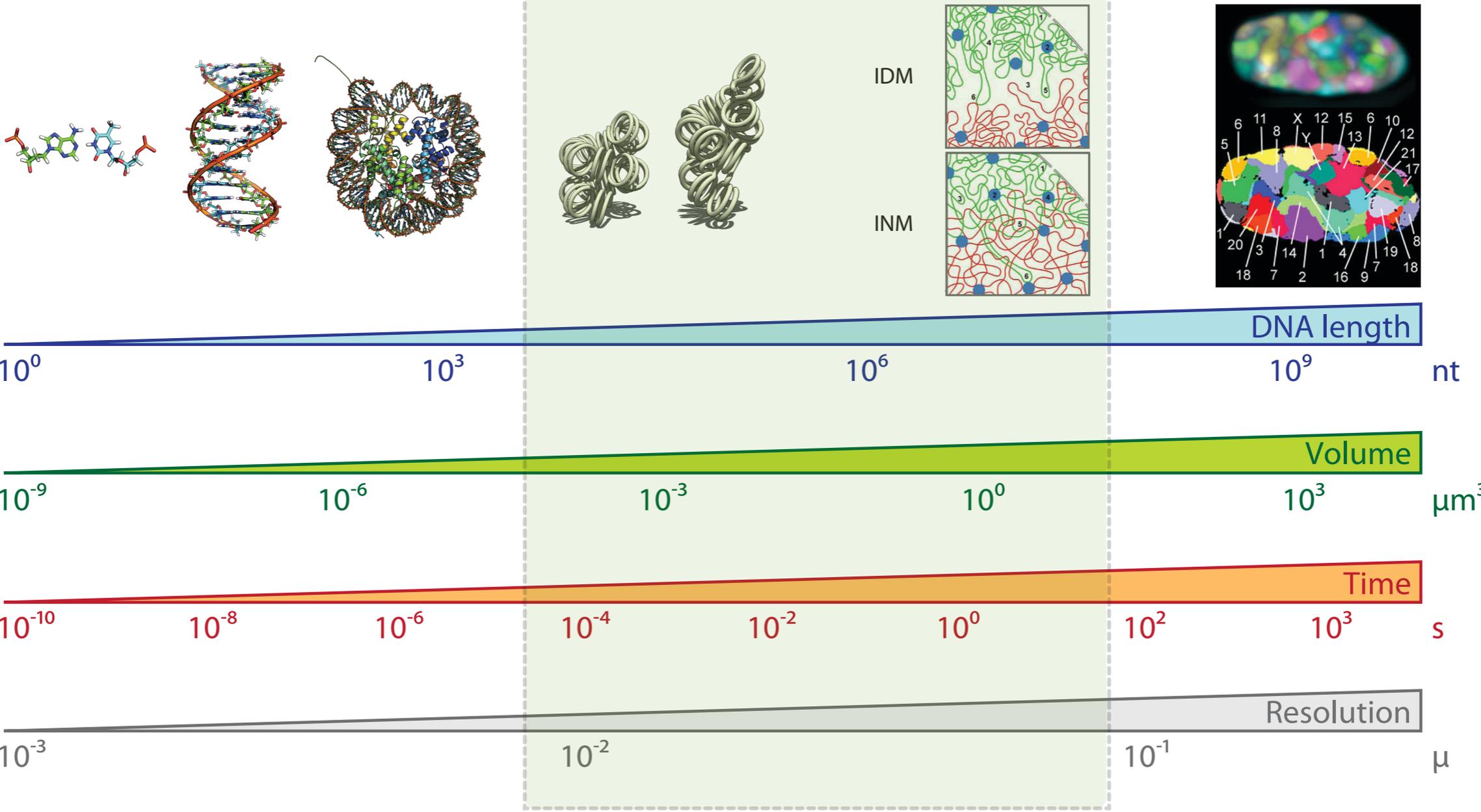
"Complex" genomes



"Simple" genomes

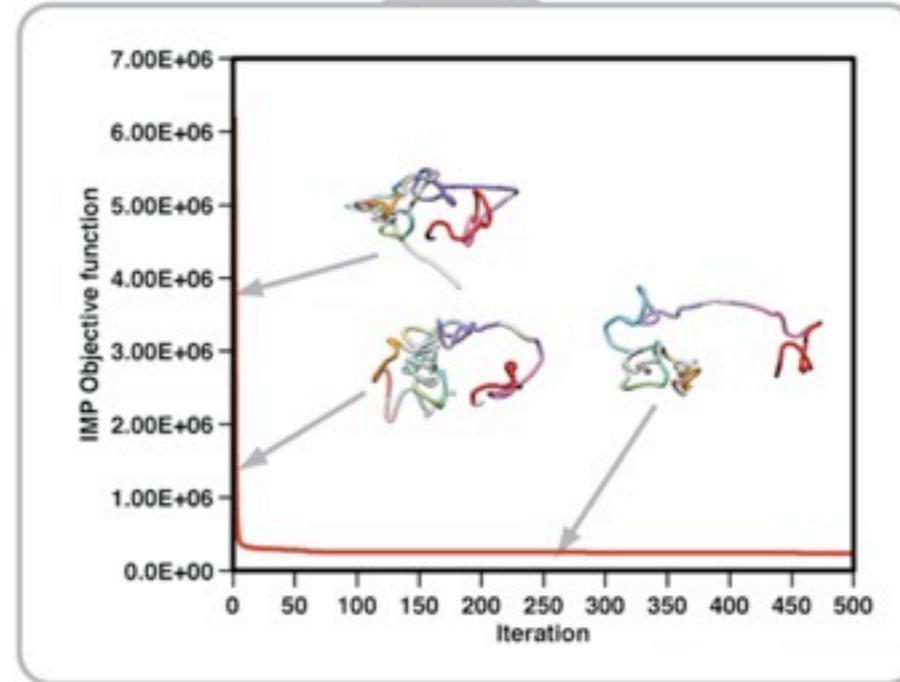
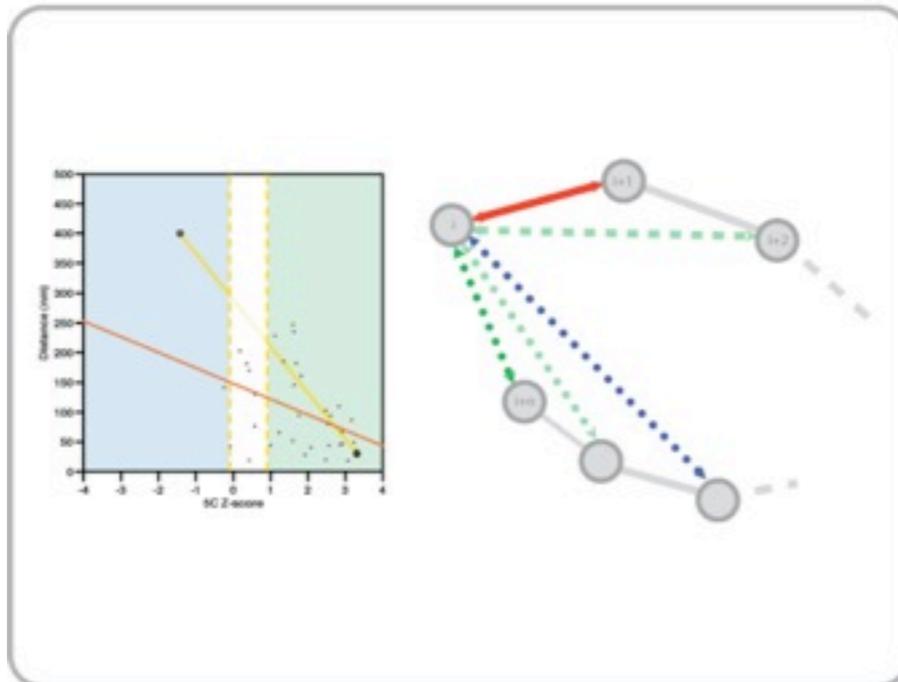
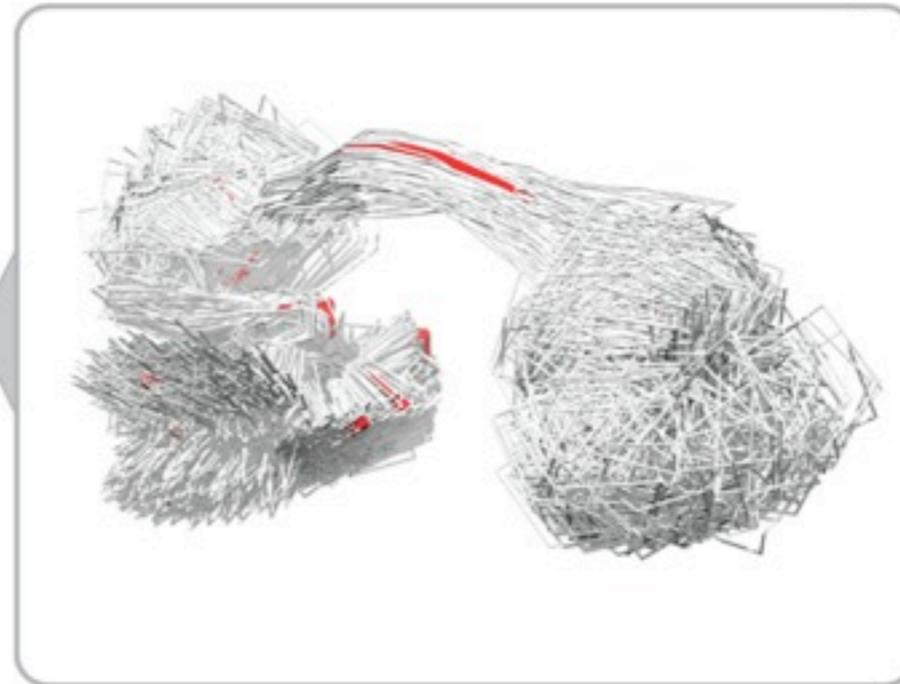
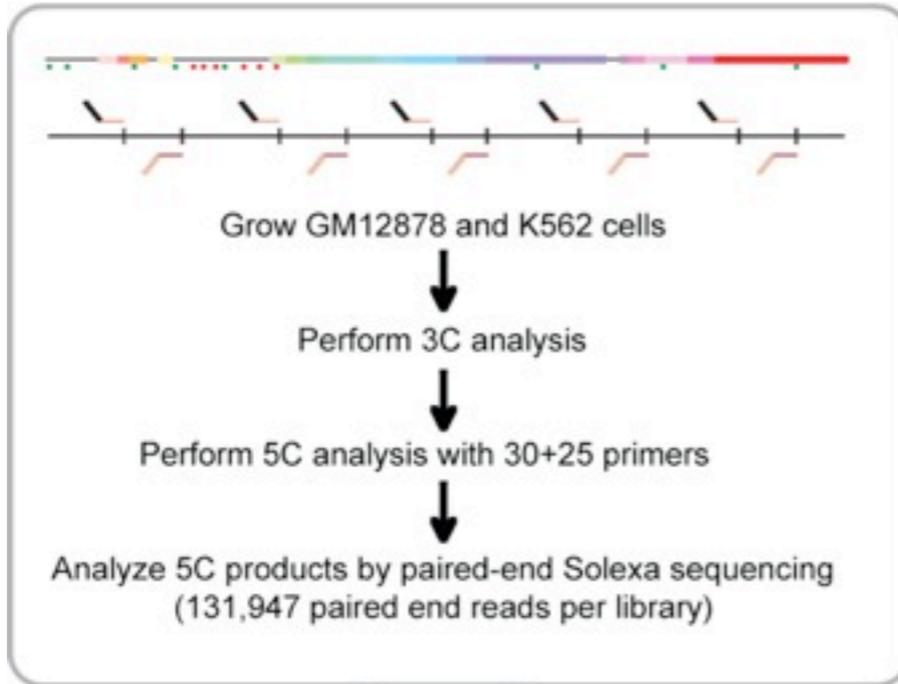


# Knowledge



Adapted from:  
 Langowski and Heermann. *Semin Cell Dev Biol* (2007) vol. 18 (5) pp. 659-67

# Experiments

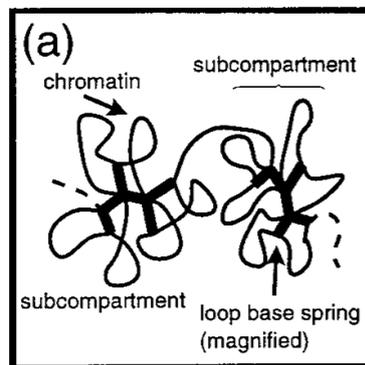


Computation

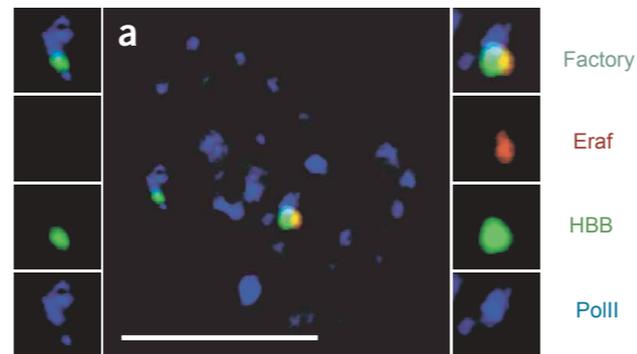
# The "Chromatin Globule" model

D. Baù et al. *Nat Struct Mol Biol* (2011) 18:107-14

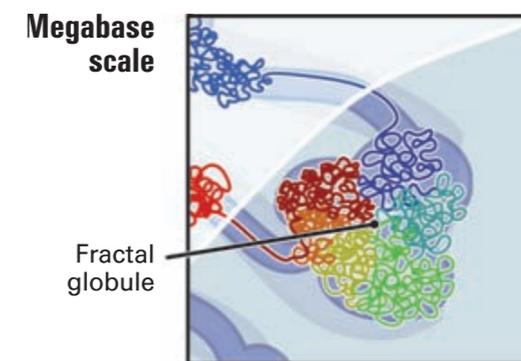
A. Sanyal et al. *Current Opinion in Cell Biology* (2011) 23:325-33.



Münkel et al. *JMB* (1999)



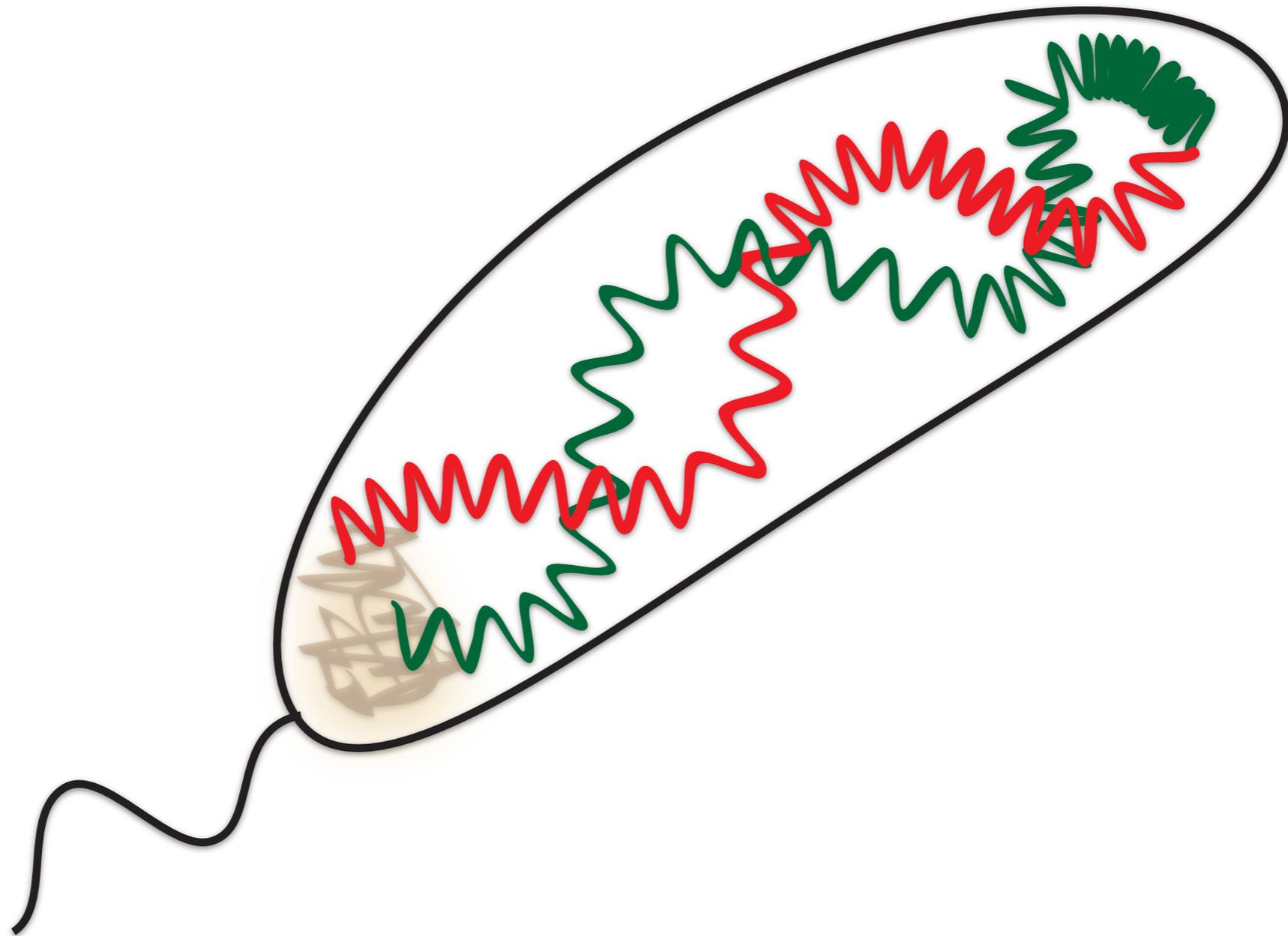
Osborne et al. *Nat Genet* (2004)

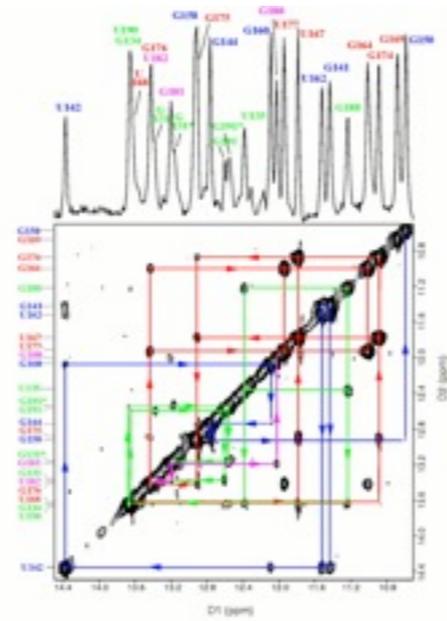
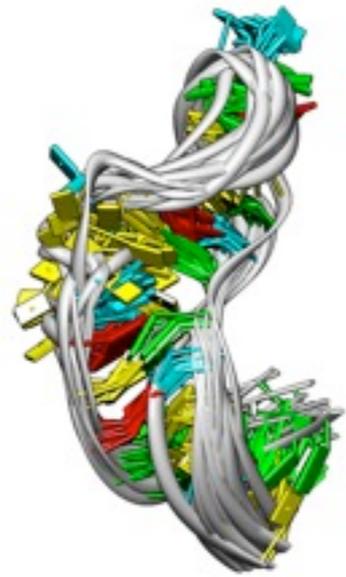


Lieberman-Aiden et al. *Science* (2009)

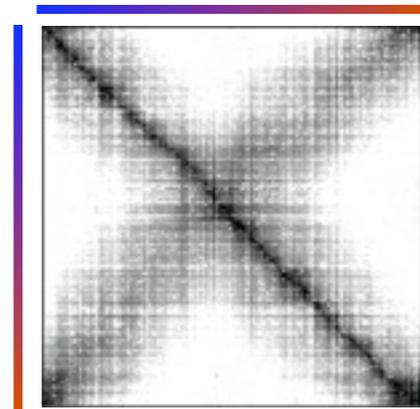
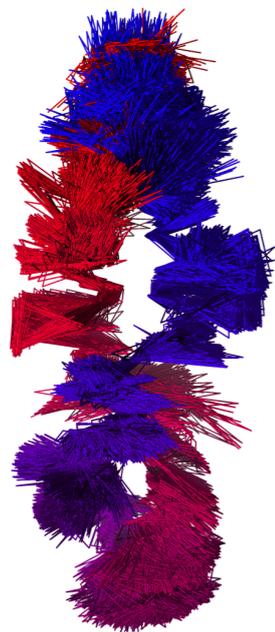
# Caulobacter crescentus 3D genome

M.A. Umbarger, et al. *Molecular Cell* (2011) 44:252–264





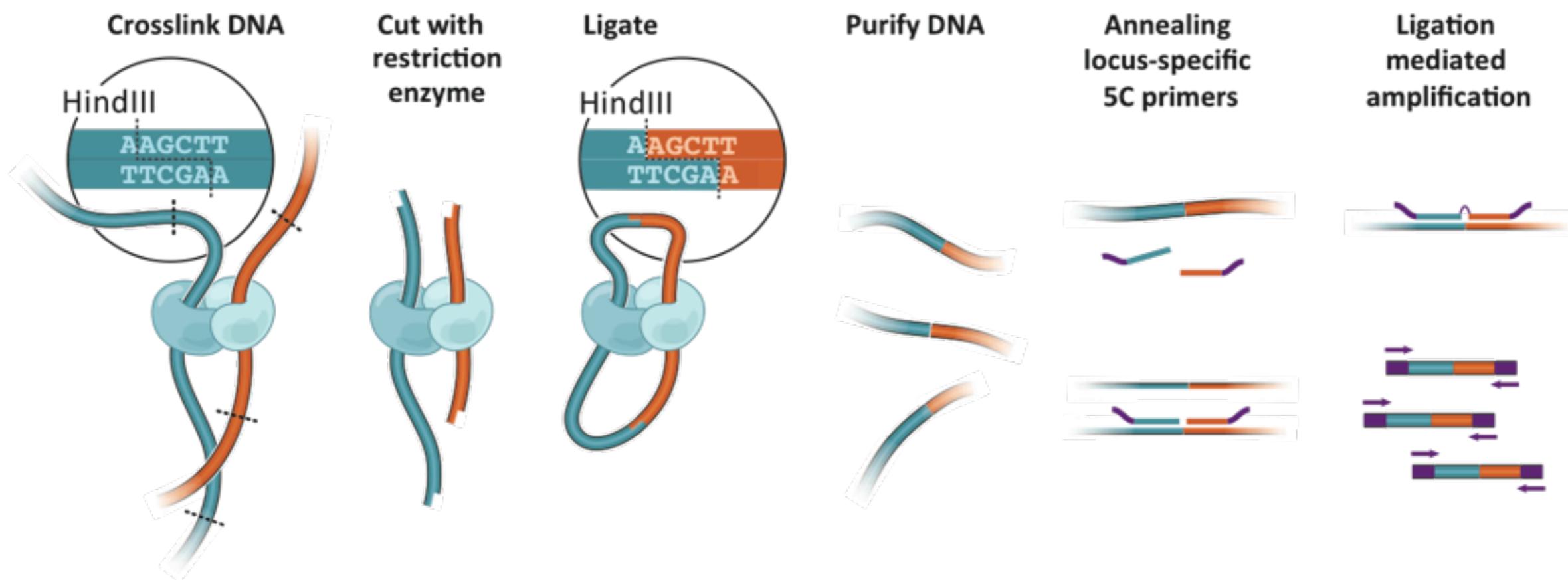
## Biomolecular structure determination 2D-NOESY data



## Chromosome structure determination 5C data

# 5C technology

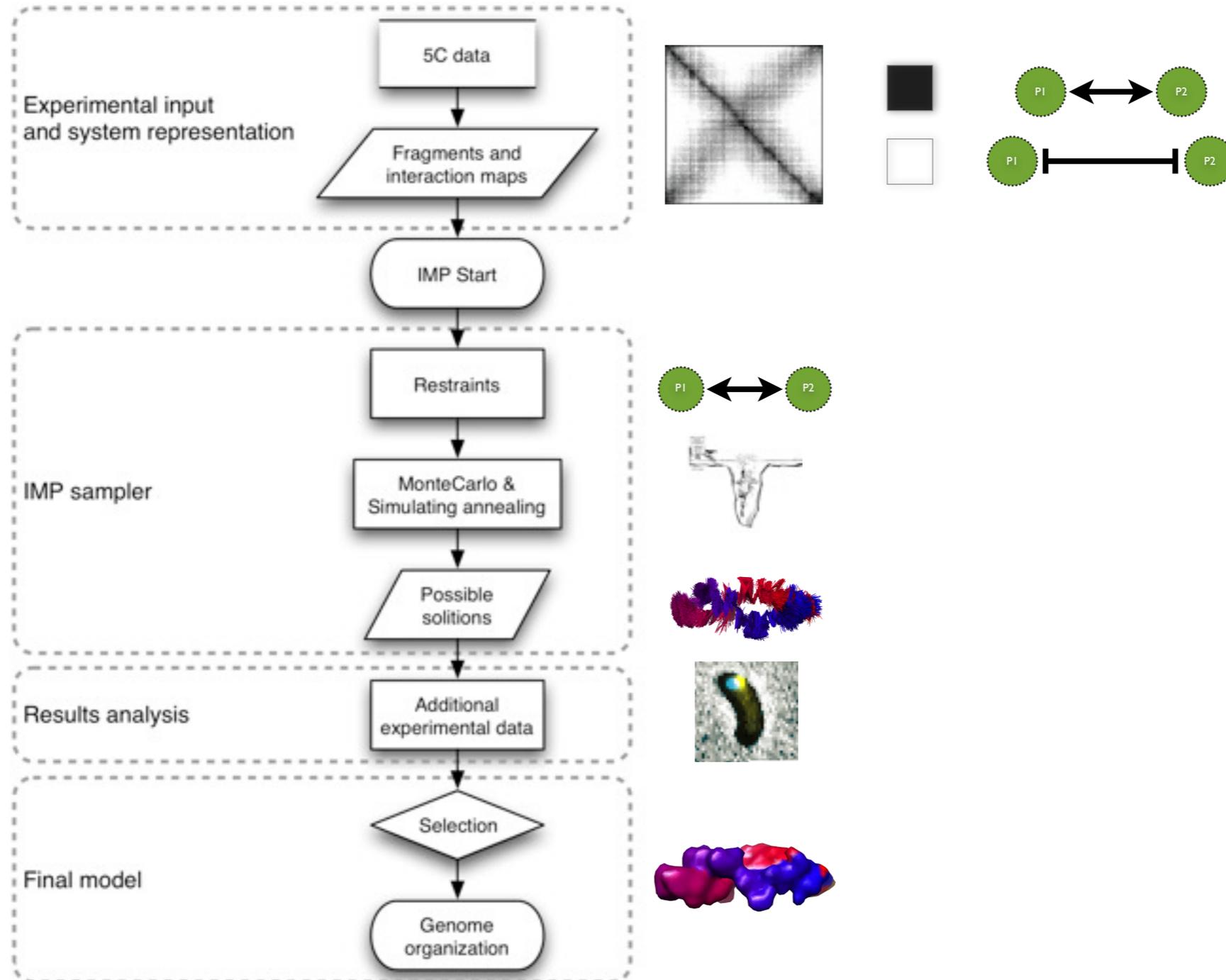
<http://my5C.umassmed.edu>



*Dostie et al. Genome Res (2006) vol. 16 (10) pp. 1299-309*

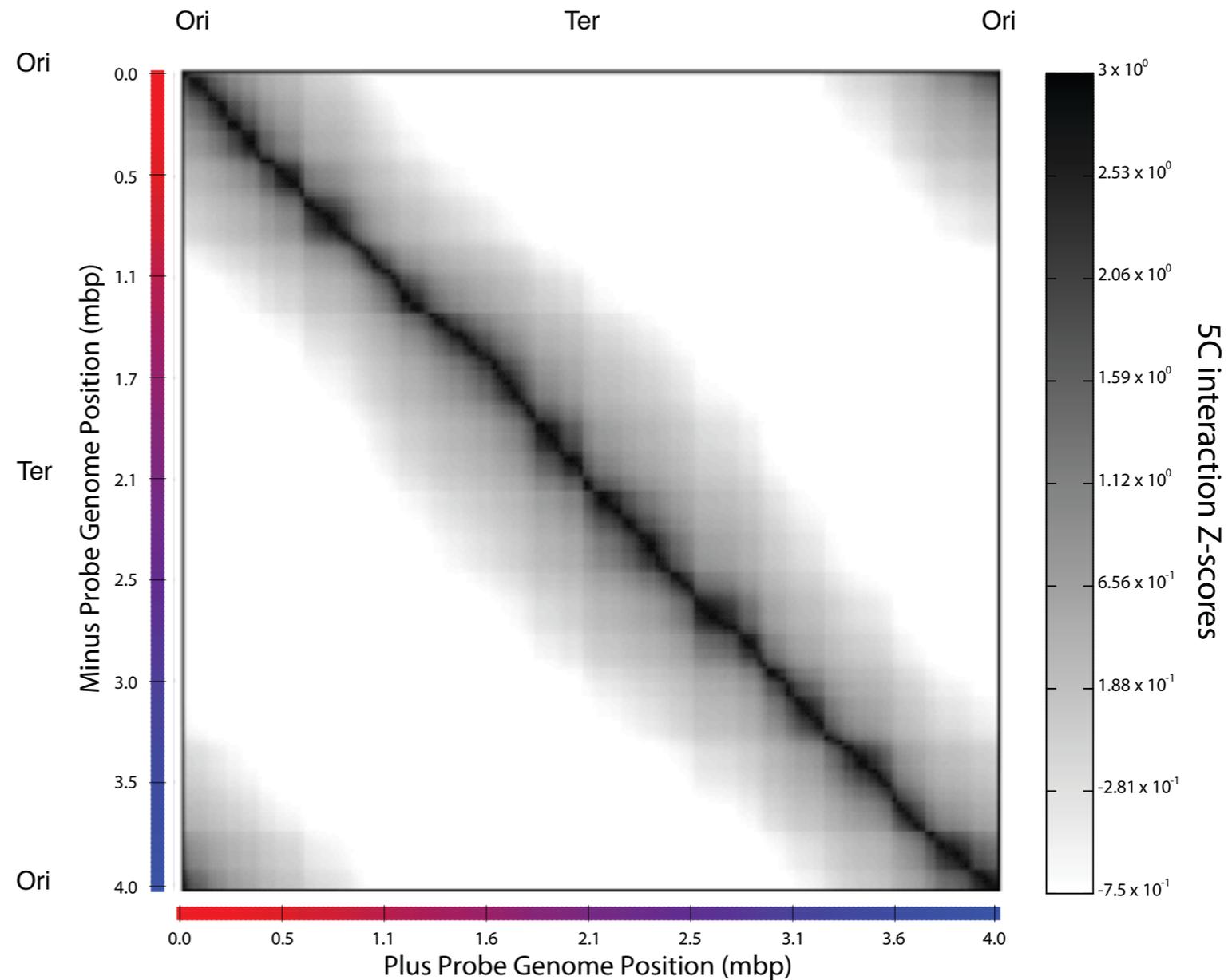
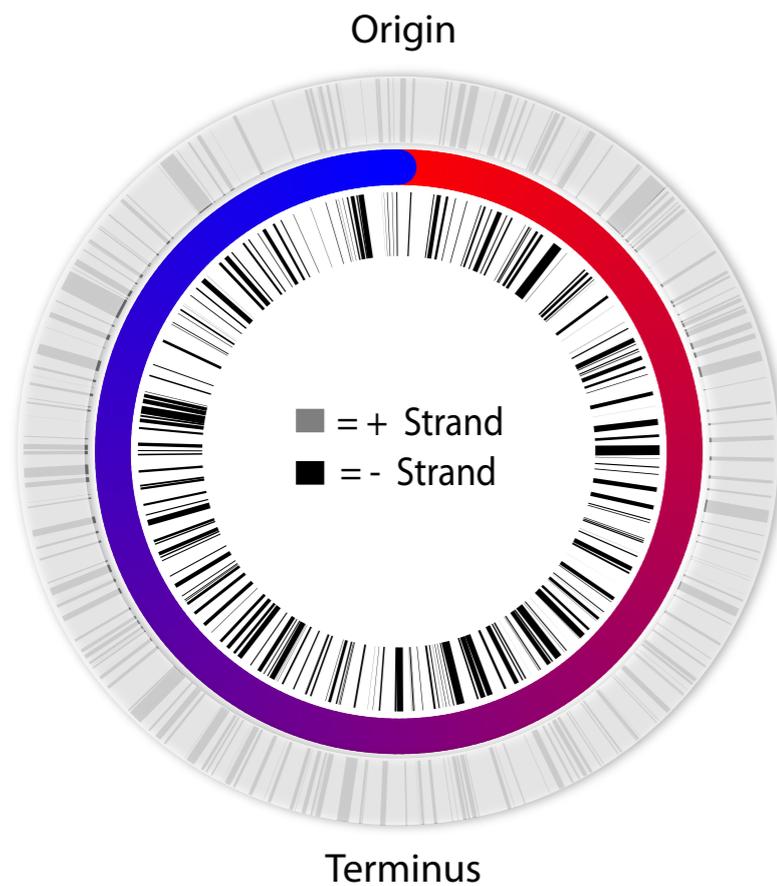
# Integrative Modeling

<http://www.integrativemodeling.org>



# The 3D architecture of *Caulobacter Crescentus*

4,016,942 bp & 3,767 genes

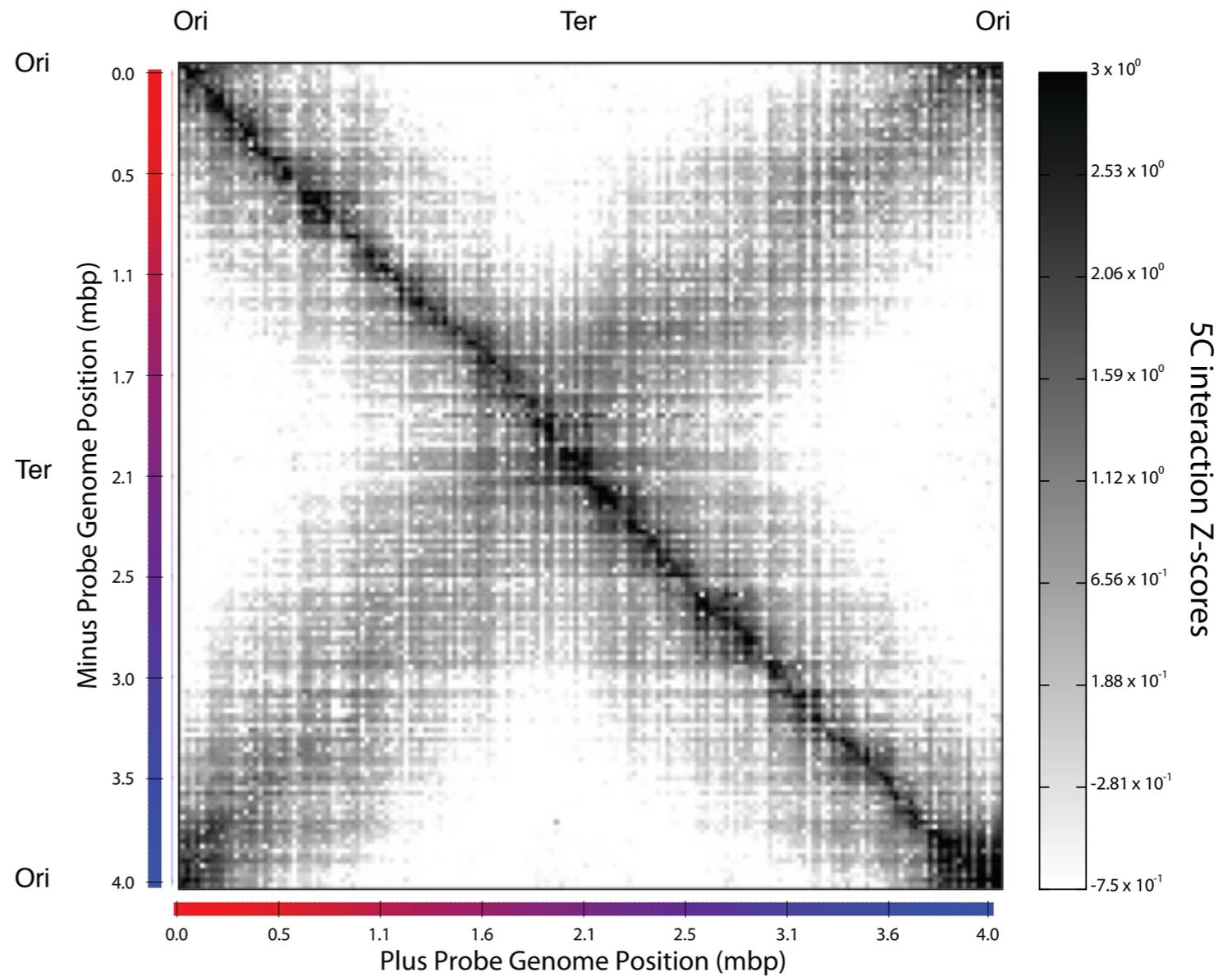
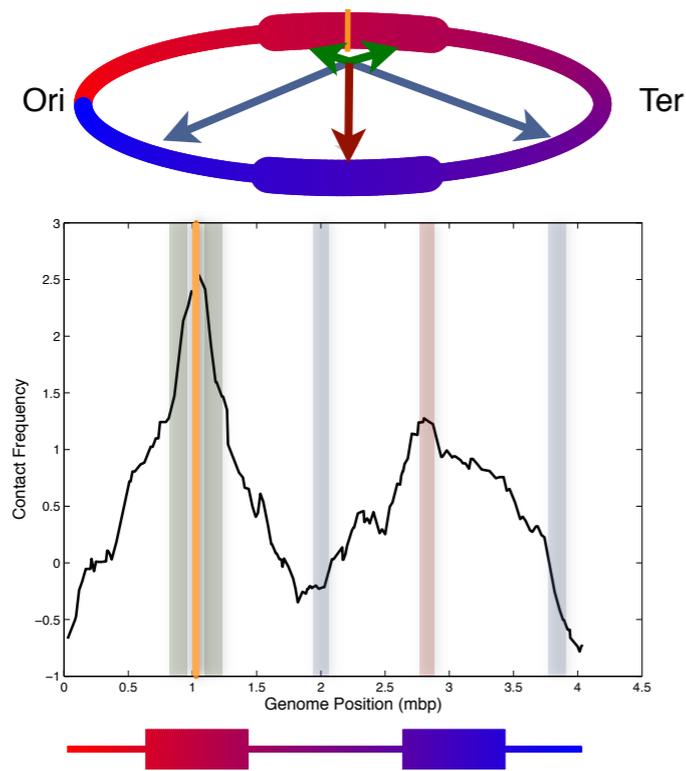
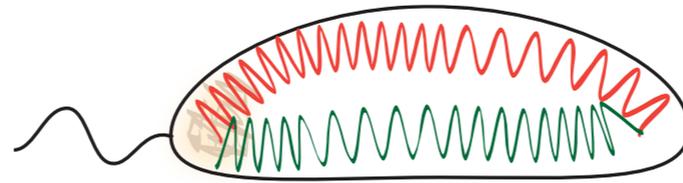


169 5C primers on + strand  
170 5C primers on - strand  
**28,730 chromatin interactions**

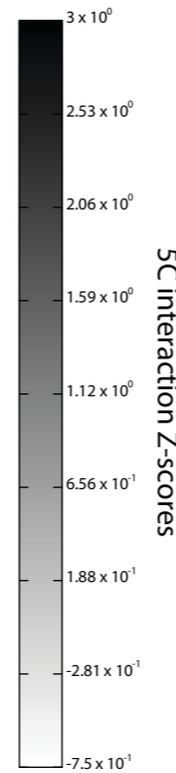
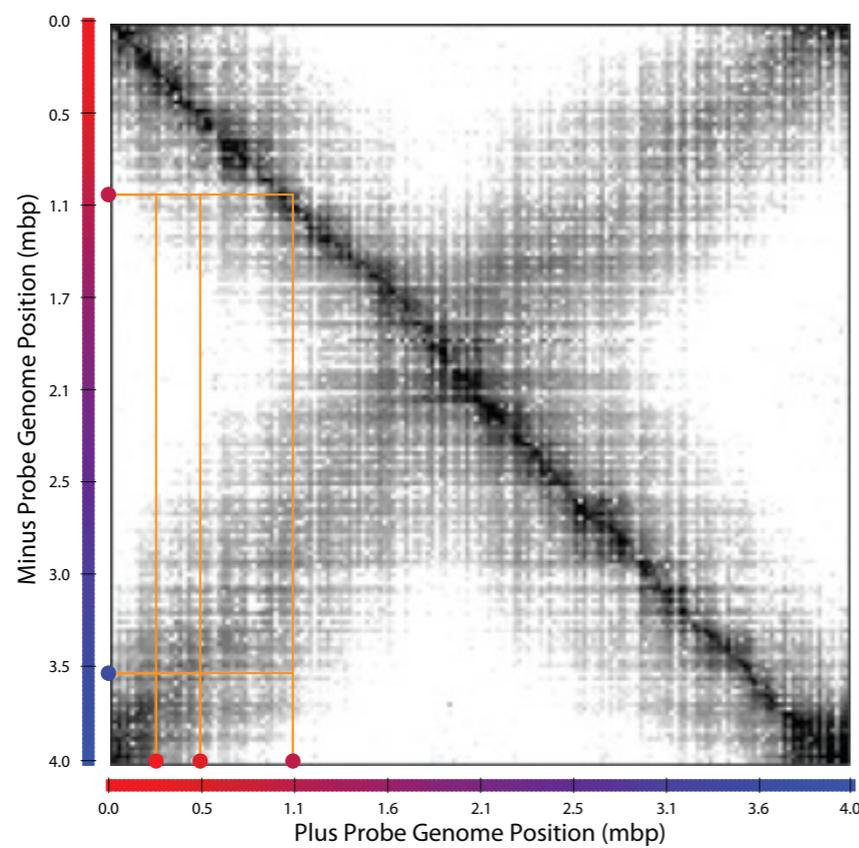
**~ 13Kb**

# 5C interaction matrix

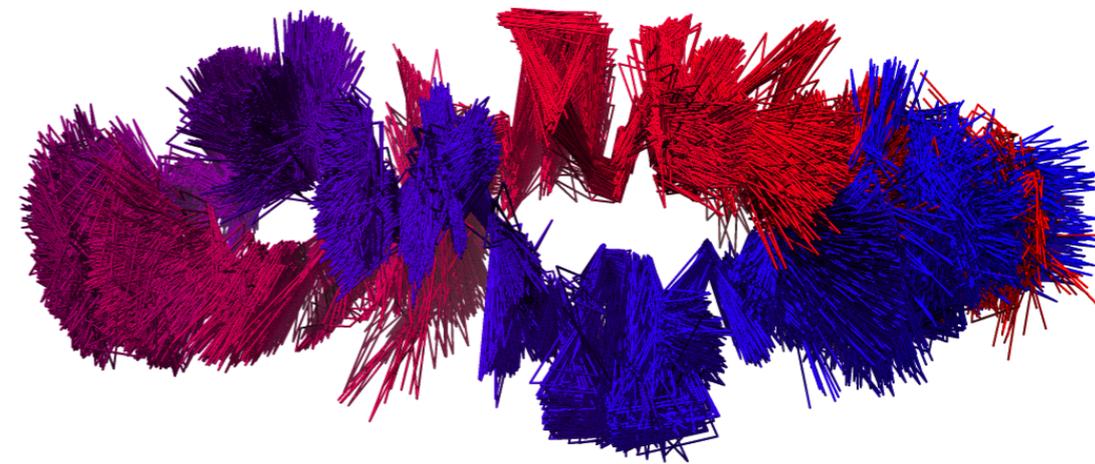
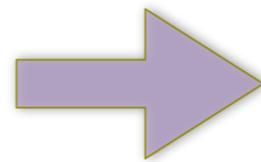
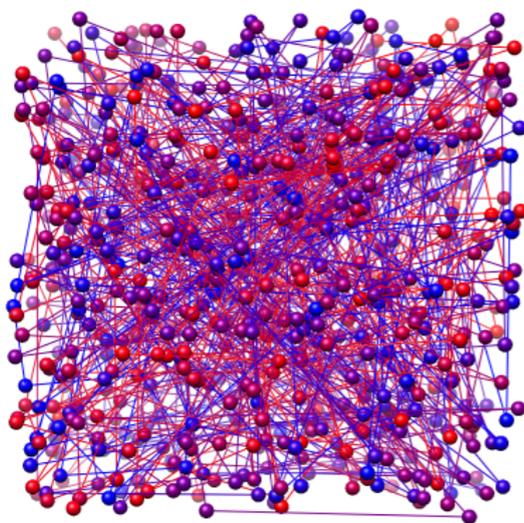
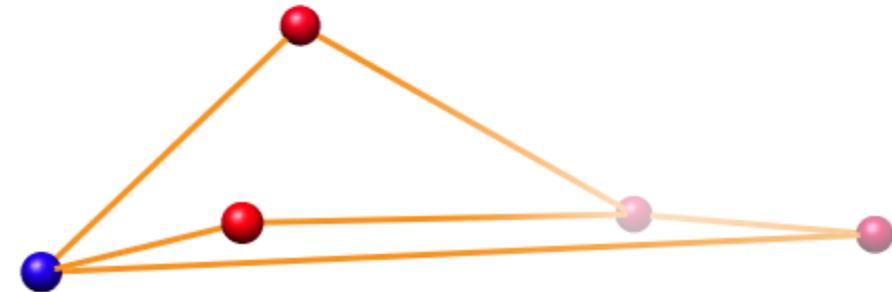
ELLIPSOID for *Caulobacter crescentus*



# 3D model building with the 5C + IMP approach



339 mers



# Genome organization in *Caulobacter crescentus*

Arms are helical

Resolution

Centromer-like

*dif* site  $47 \pm 17$  Kb from Ter

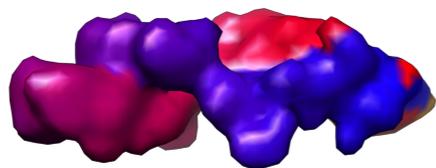
*parS* sites  $25 \pm 17$  Kb from Ori

Cluster 1

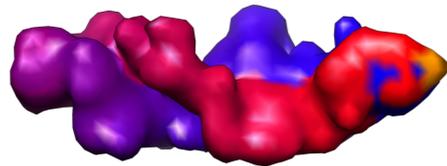
Cluster 2

Cluster 3

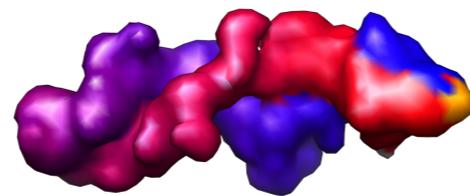
Cluster 4



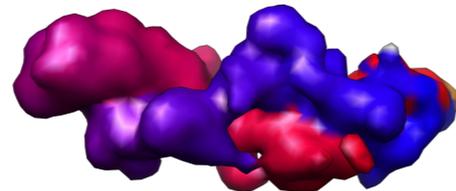
180°



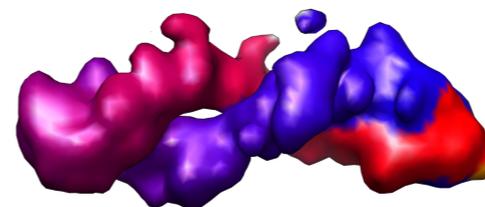
500 nm



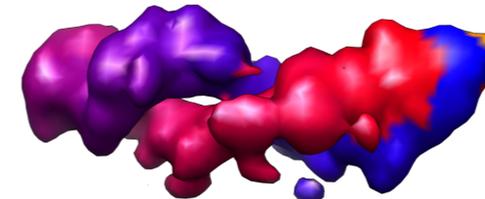
180°



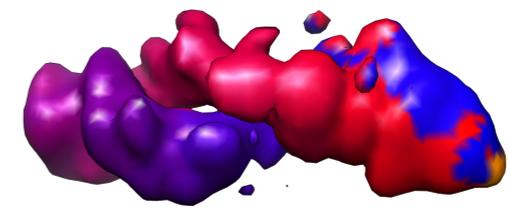
500 nm



180°



500 nm



180°

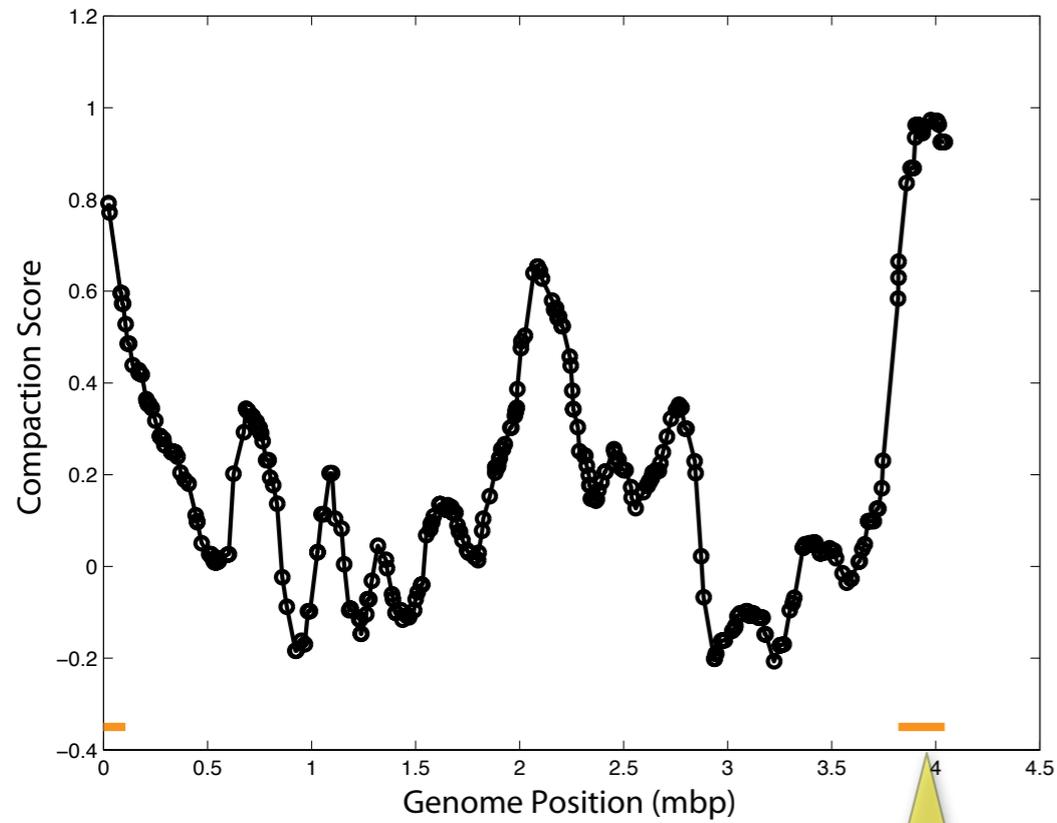


500 nm

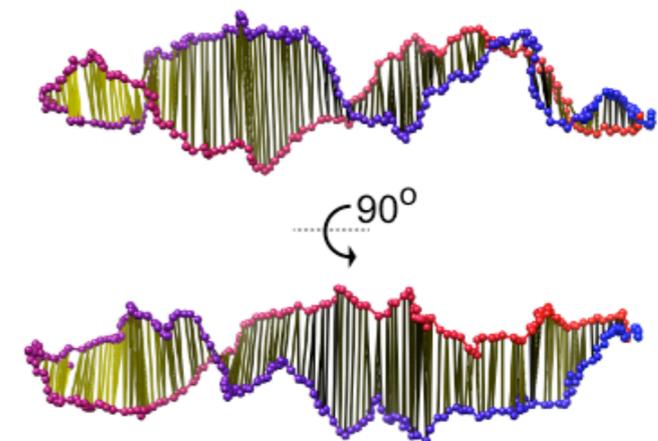
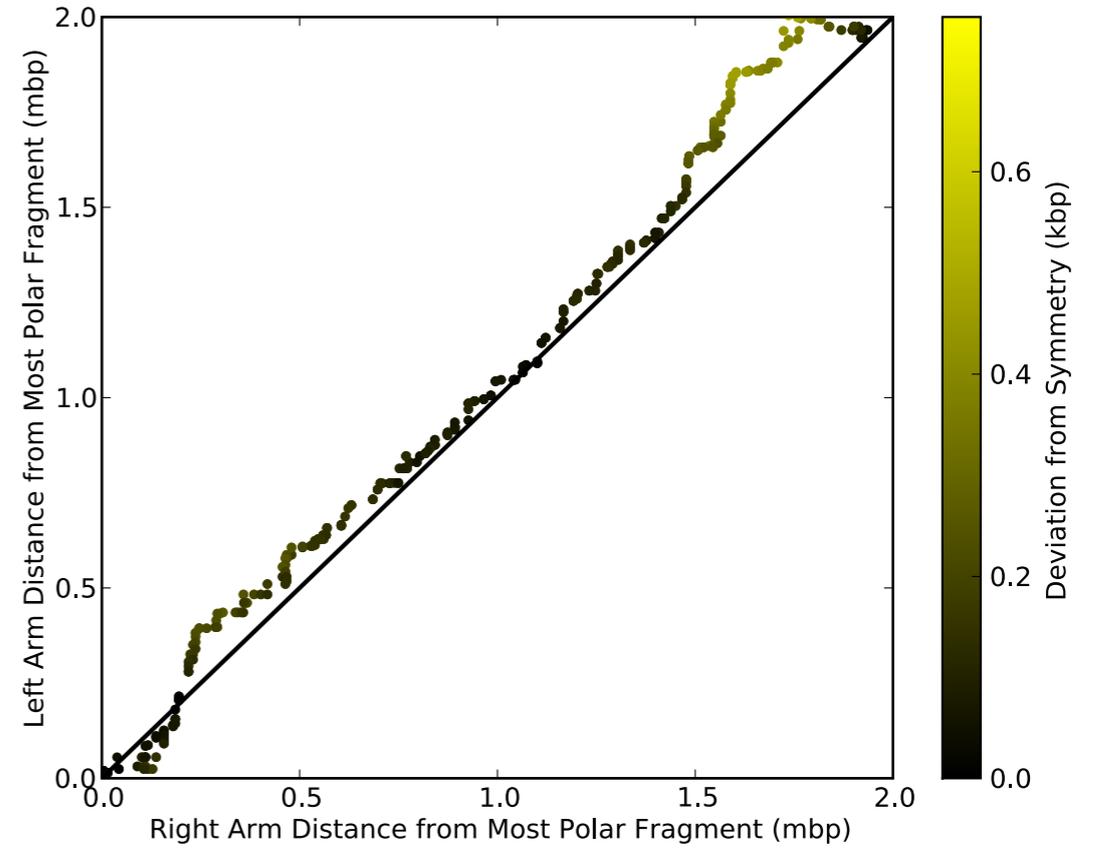
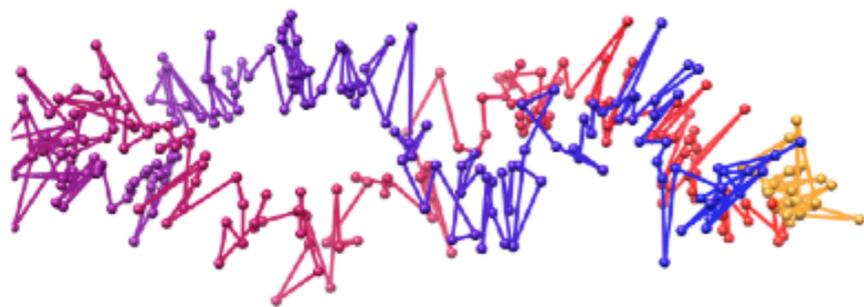
**MIRRORS!**

# *parS* sites initiate compact chromatin domain

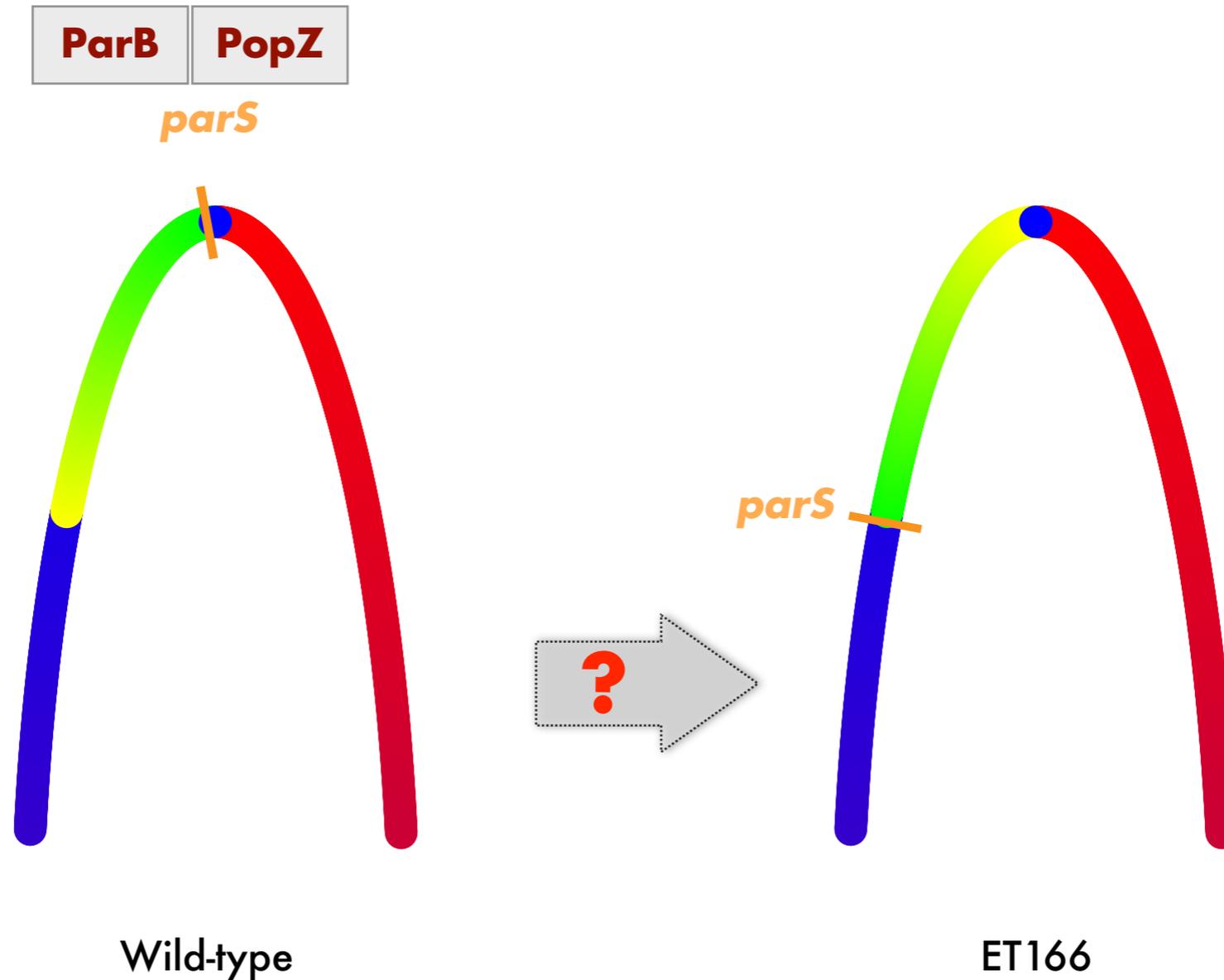
# Chromosome arms are equidistant to the cell center



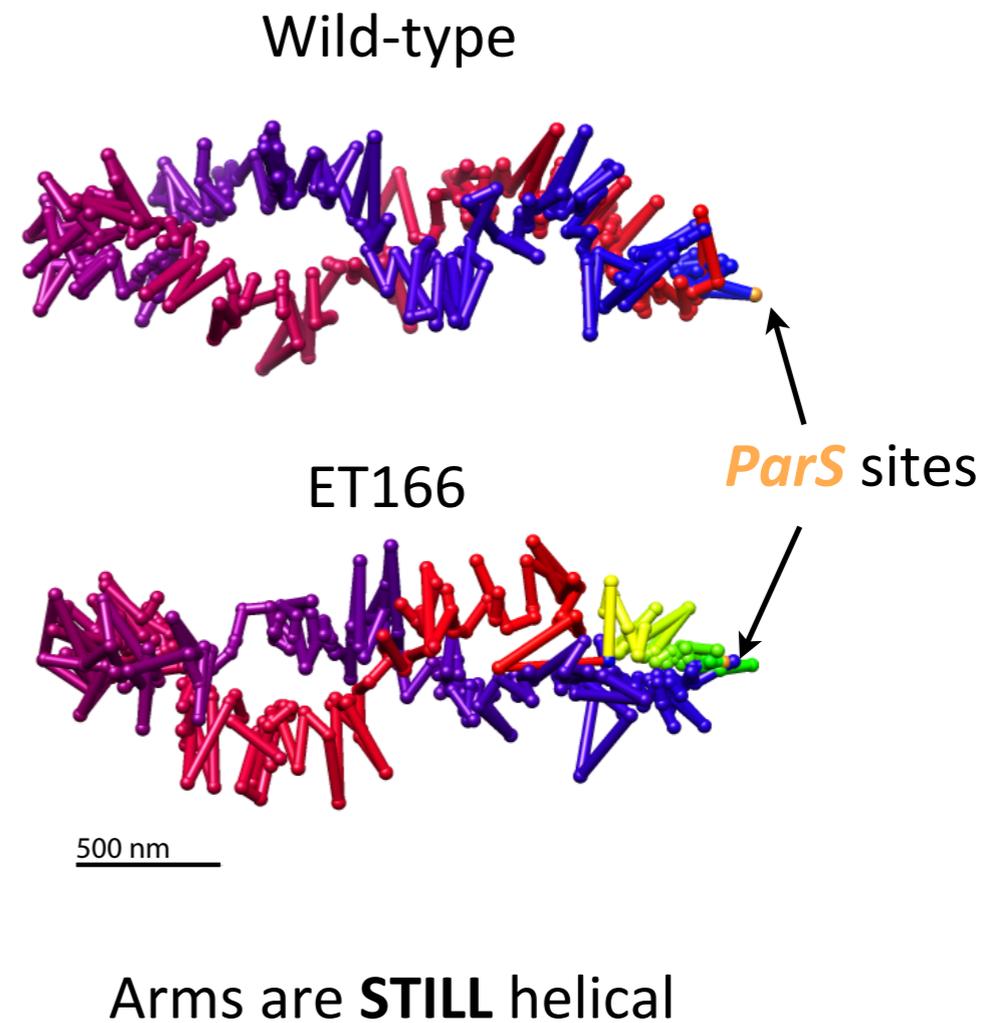
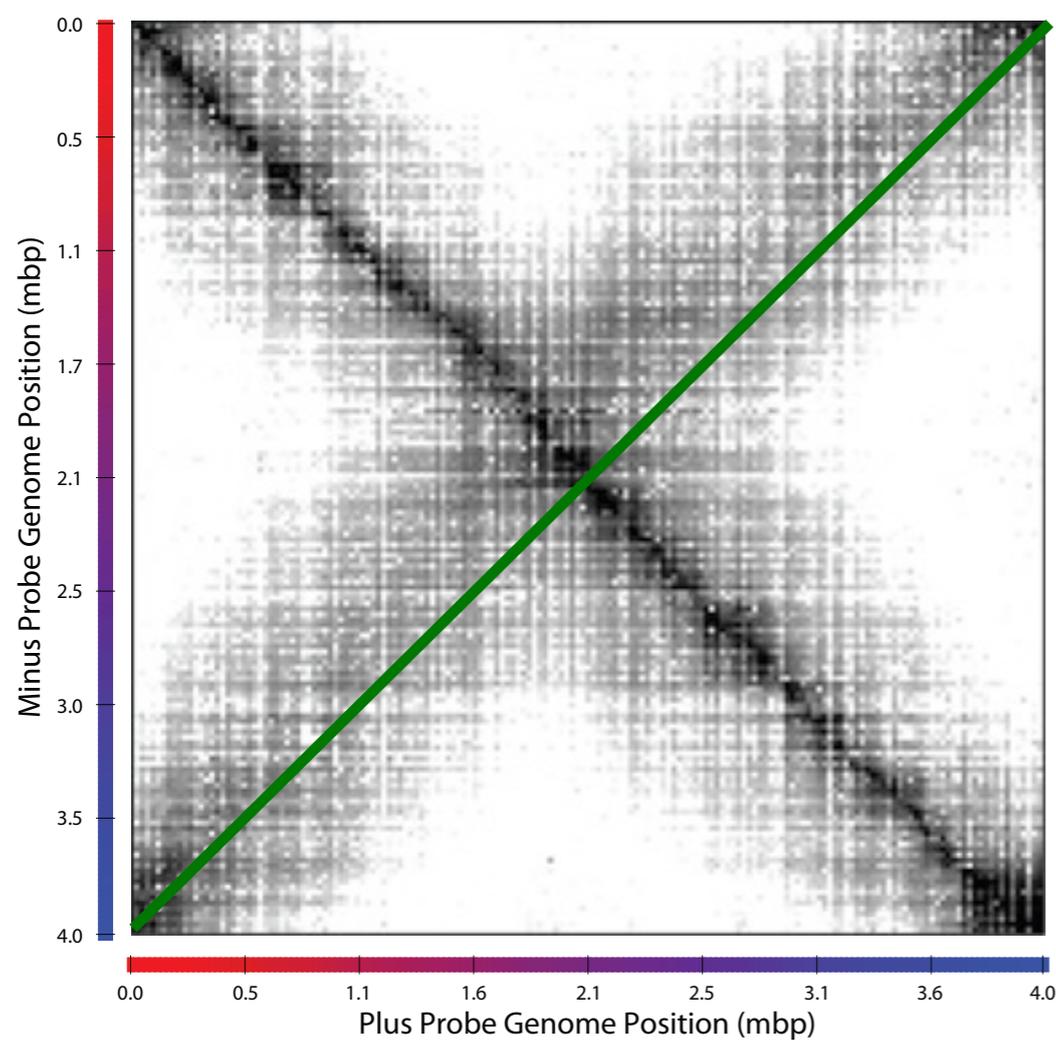
100-200Kb



# Moving the *parS* sites 400 Kb away from Ori

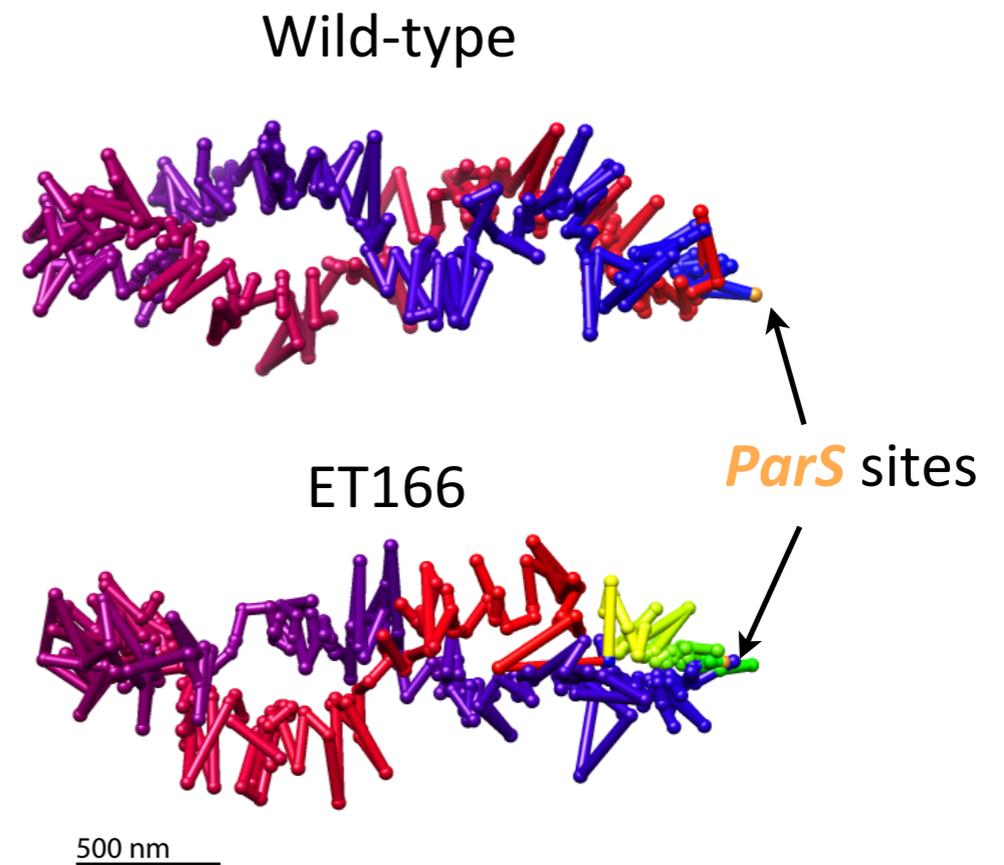
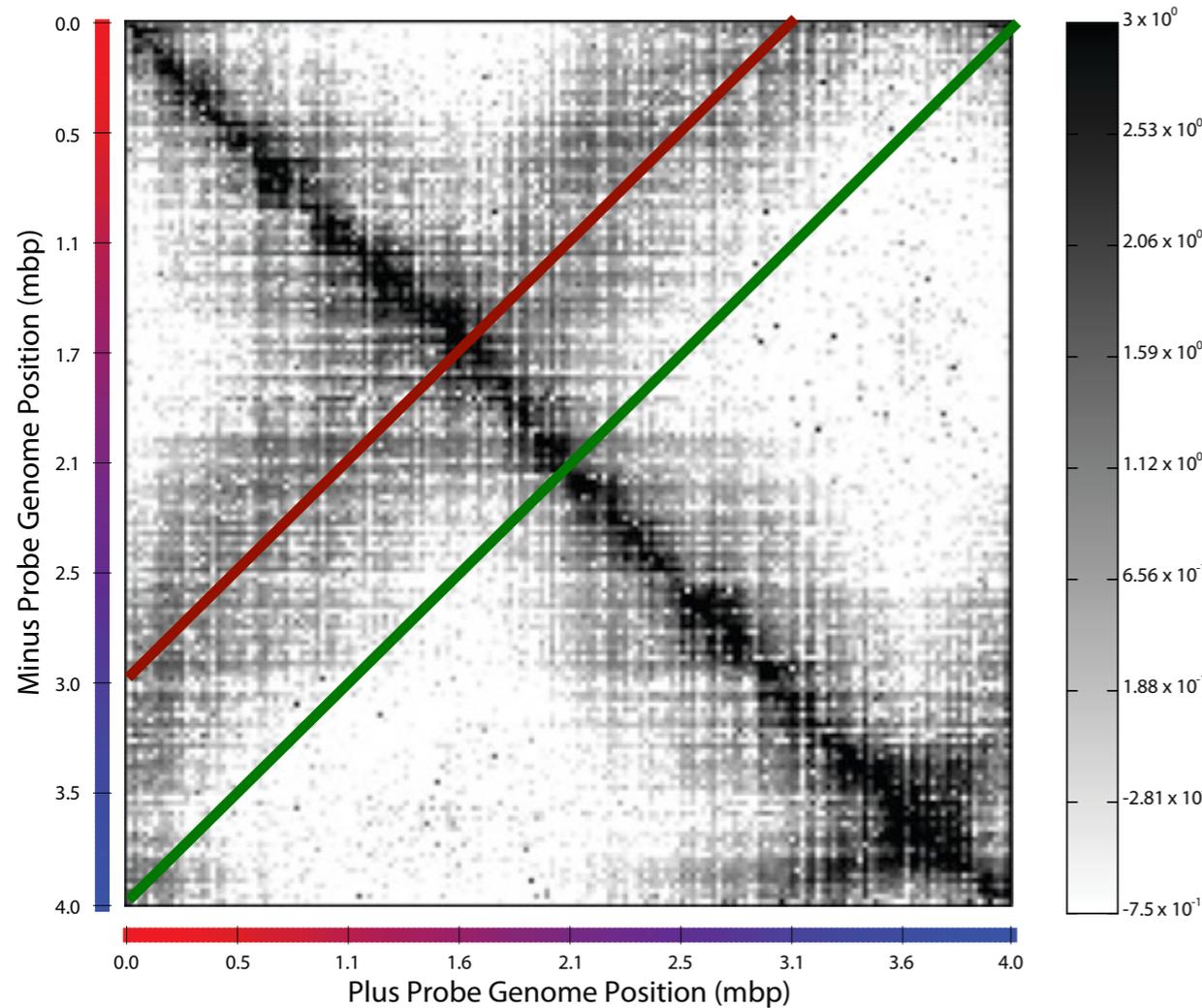


# Moving the *parS* sites results in whole genome rotation!



**Structure & function PRESERVED!!!**

# Moving the *parS* sites results in whole genome rotation!

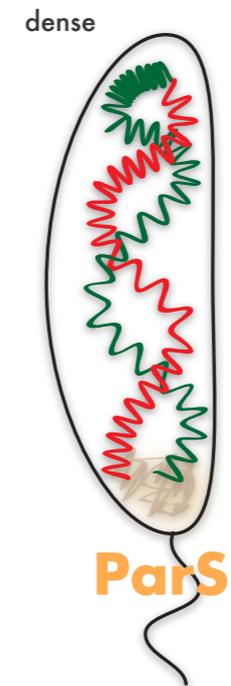
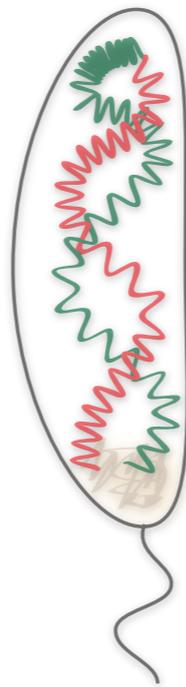
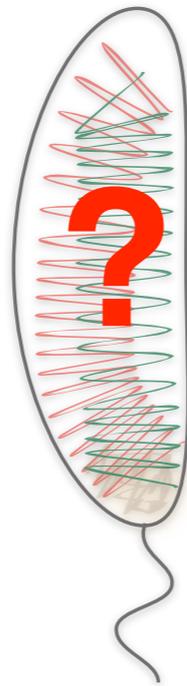
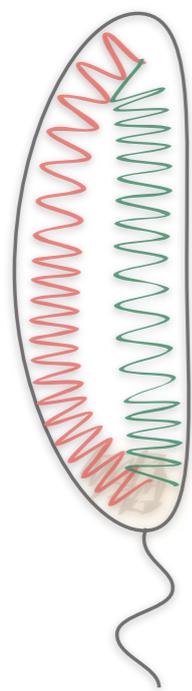
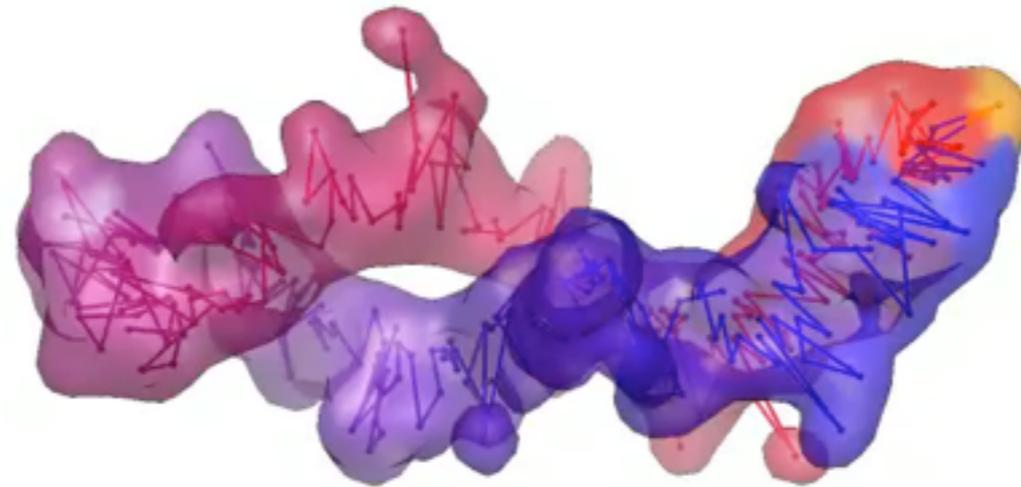


Arms are **STILL** helical

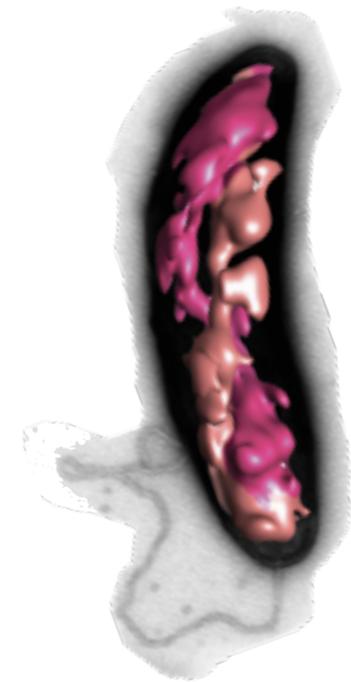
**Structure & function PRESERVED!!!**

# Genome architecture in Caulobacter

M.A. Umbarger, et al. *Molecular Cell* (2011) 44:252-264

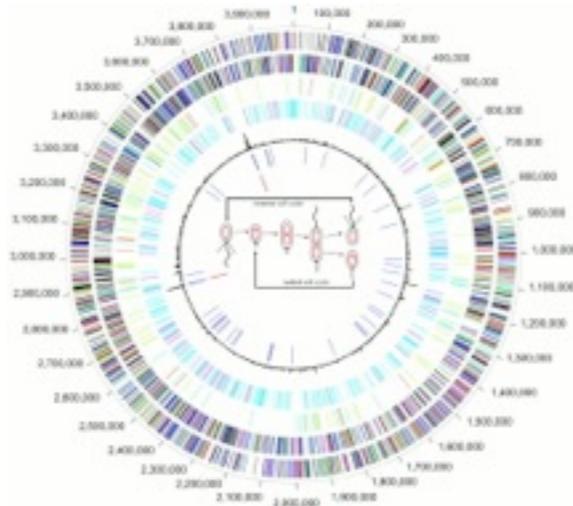


dense

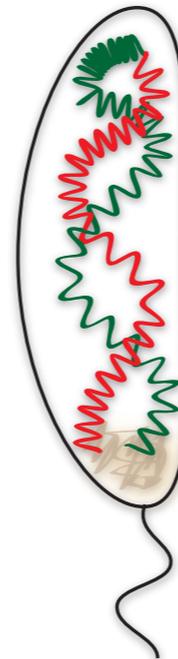
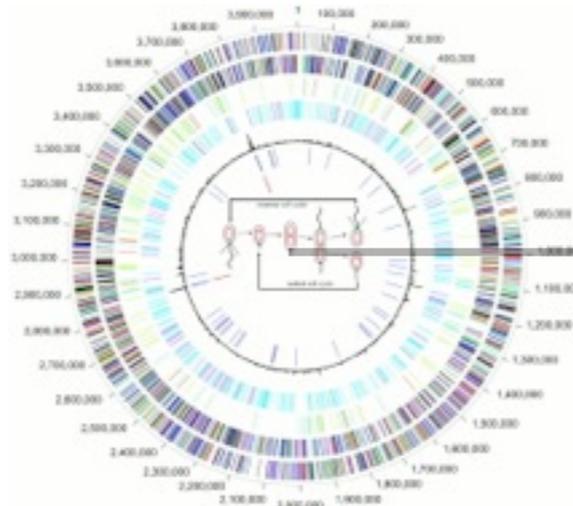


# From Sequence to Function

D. Baù and M.A. Marti-Renom *Chromosome Res* (2011) 19:25-35.



**Function!**



**Funtion!**

# Acknowledgments



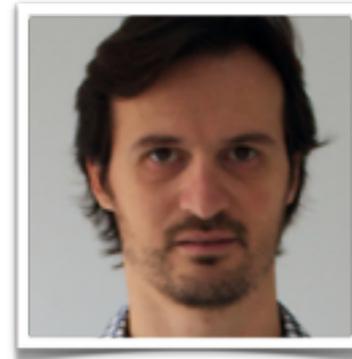
**Mark Umbarger**

PhD fellow  
Harvard



**Esteban Toro**

PhD fellow  
Stanford



**Davide Baù**

Staff Scientist  
CNAG



**Job Dekker**

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Stanford University School of Medicine,  
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<http://marciuslab.org>  
<http://integrativemodeling.org>  
<http://cnag.cat> · <http://crg.cat>