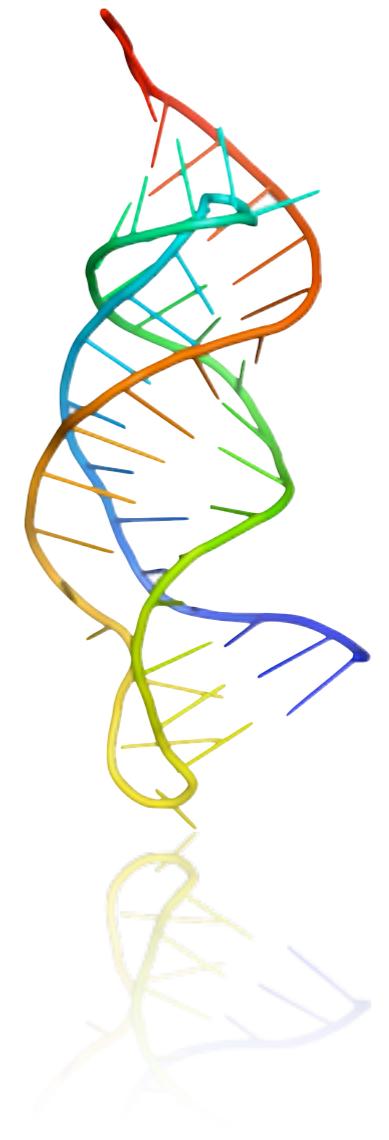
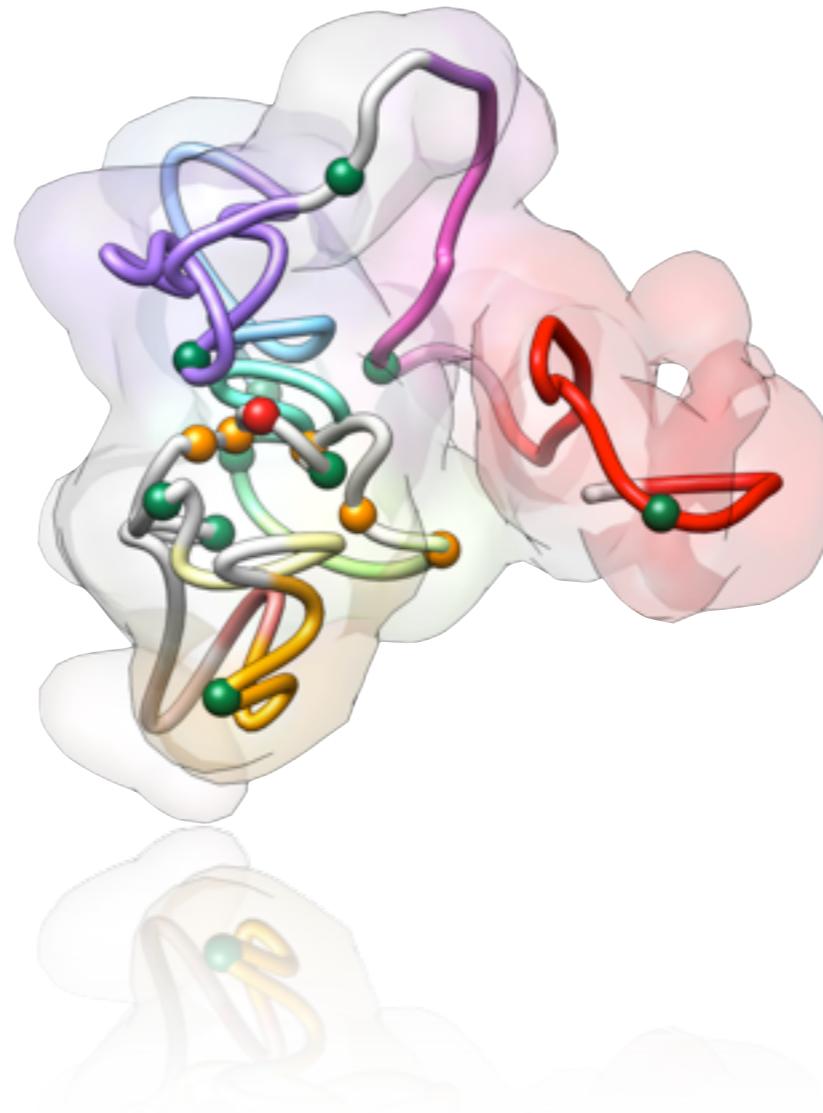
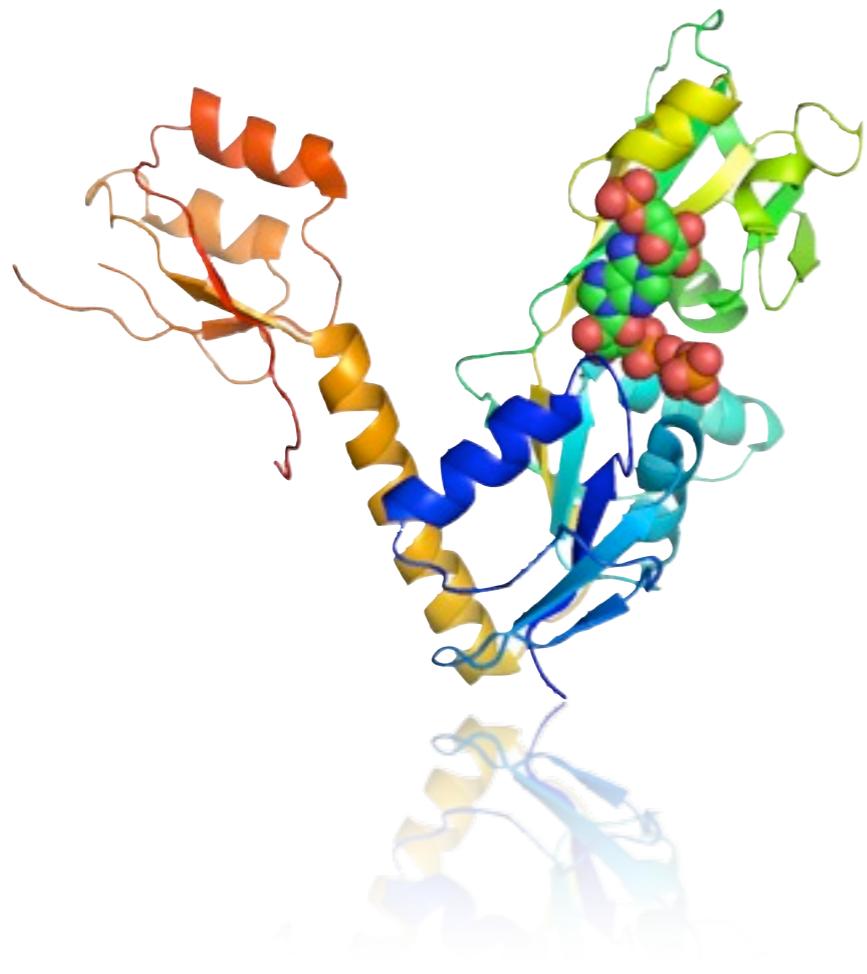


Structure determination of genomes and genomic domains by satisfaction of spatial restraints

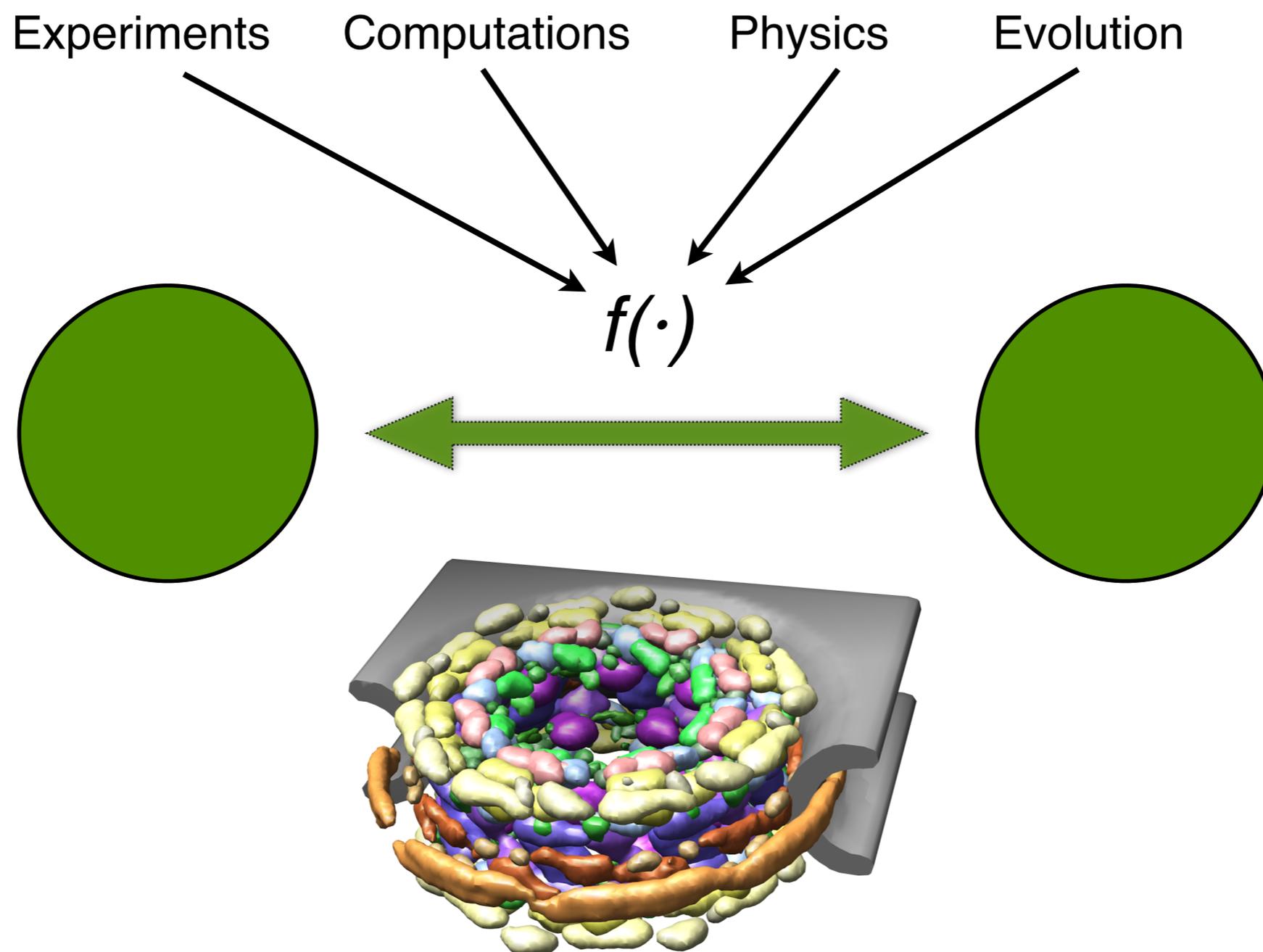
Marc A. Marti-Renom

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

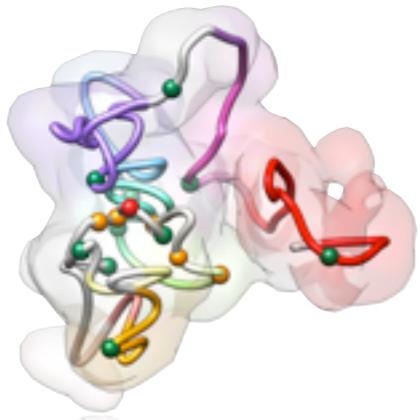


Integrative Modeling Platform

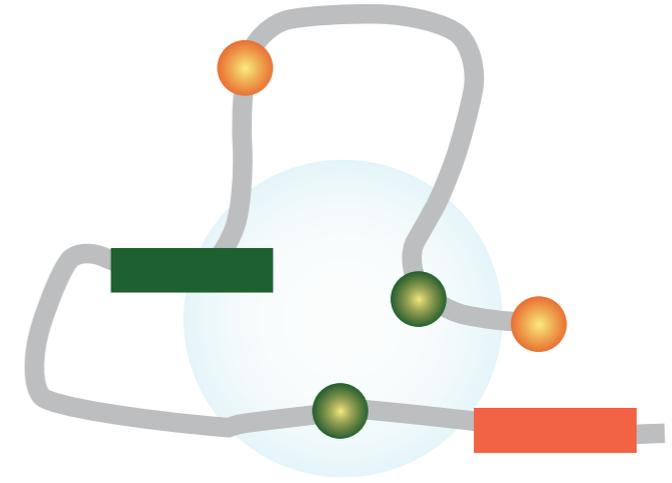
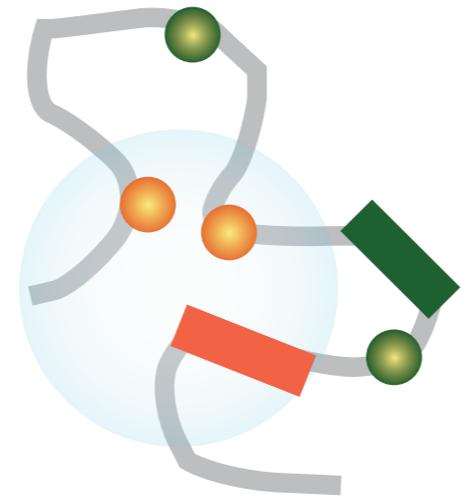
GENERALIZE software development
<http://www.integrativemodeling.org>



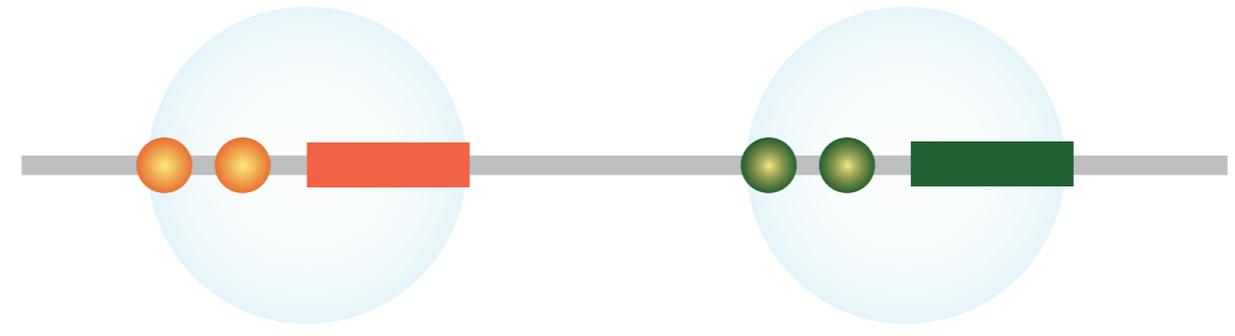
Alber, F. et al. (2007). *Nature*, 450(7170), 695–701
Russel, D. et al. (2012). *PLoS Biology*, 10(1), e1001244.



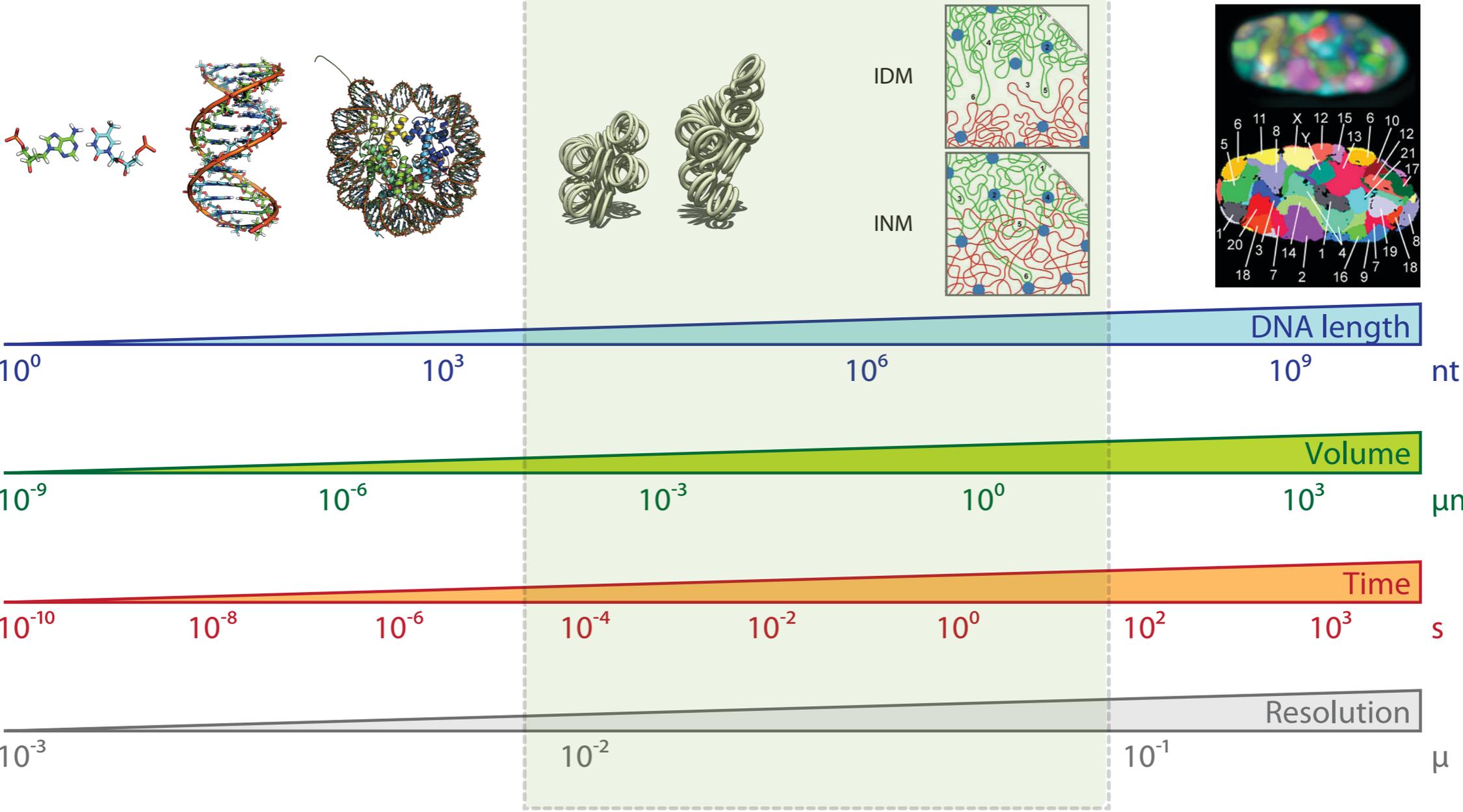
"Complex" genomes



"Simple" genomes



Knowledge

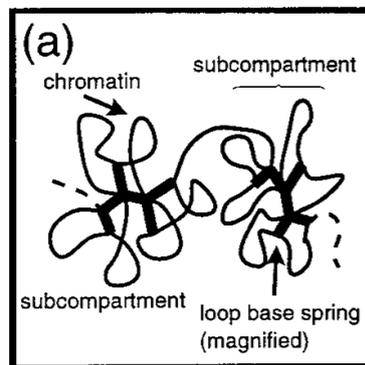


Adapted from:
Langowski and Heermann. *Semin Cell Dev Biol* (2007) vol. 18 (5) pp. 659-67

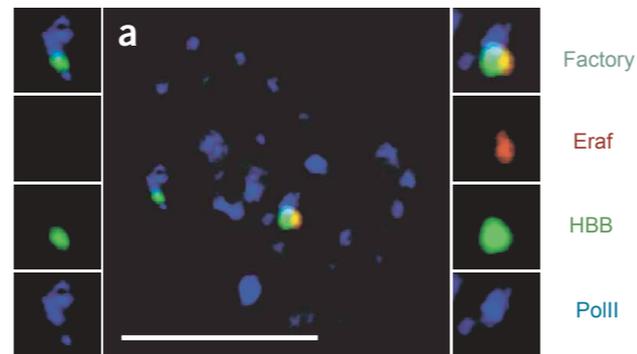
The "Chromatin Globule" model

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

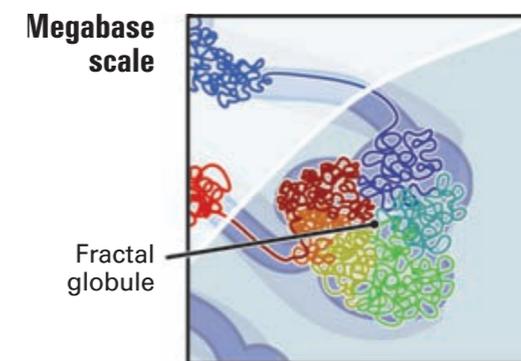
A. Sanyal et al. Current Opinion in Cell Biology (2011) 23:325-33.



Münkel et al. JMB (1999)



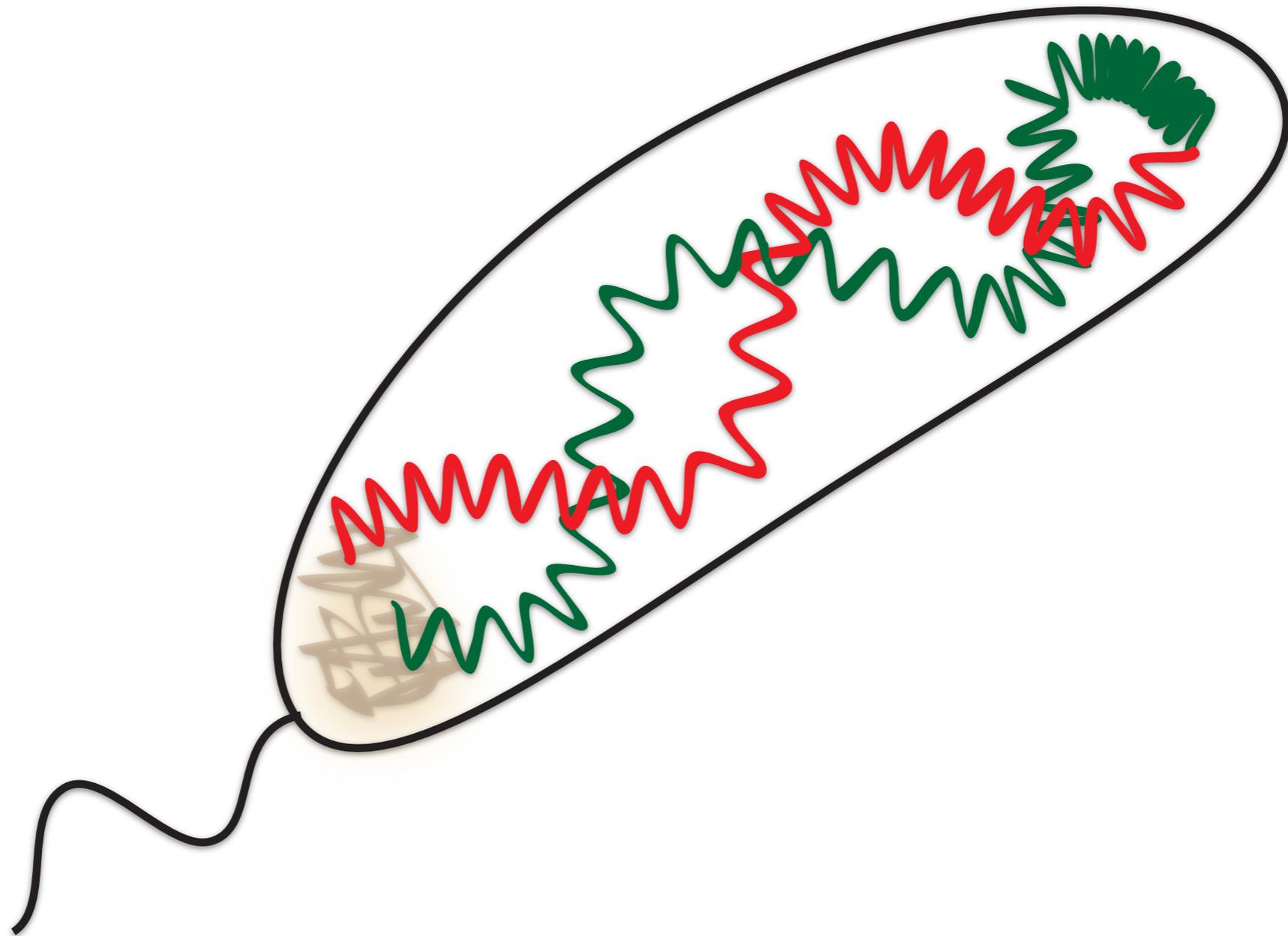
Osborne et al. Nat Genet (2004)

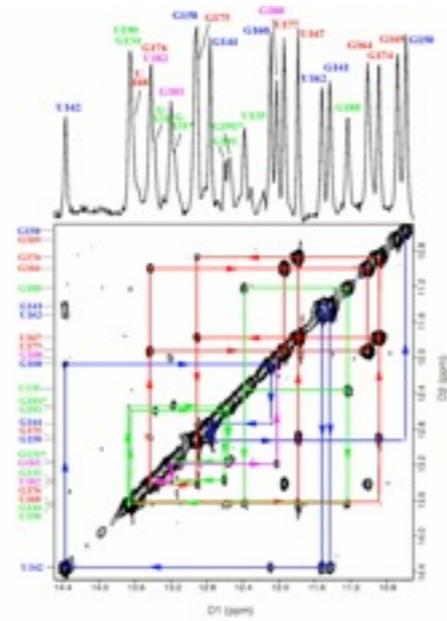
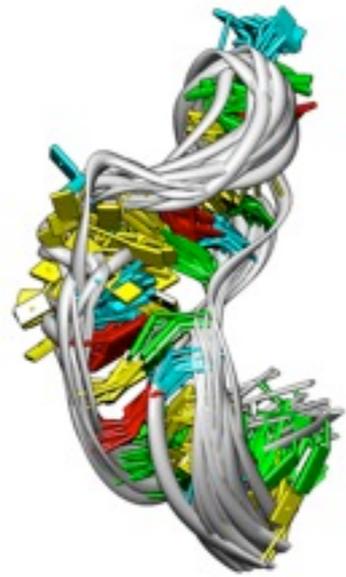


Lieberman-Aiden et al. Science (2009)

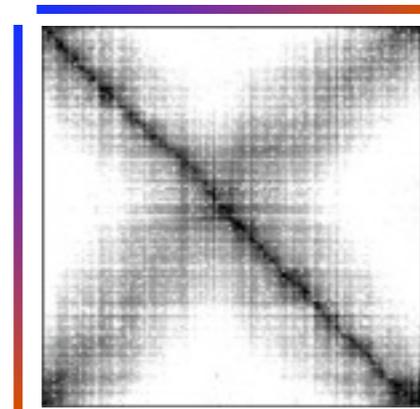
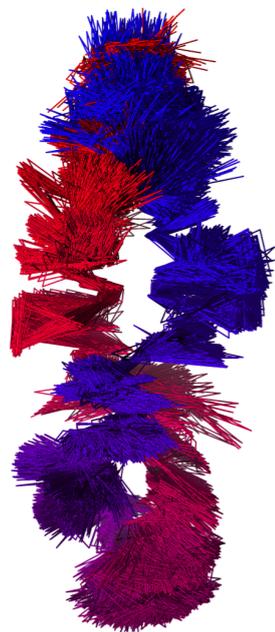
Caulobacter crescentus 3D genome

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





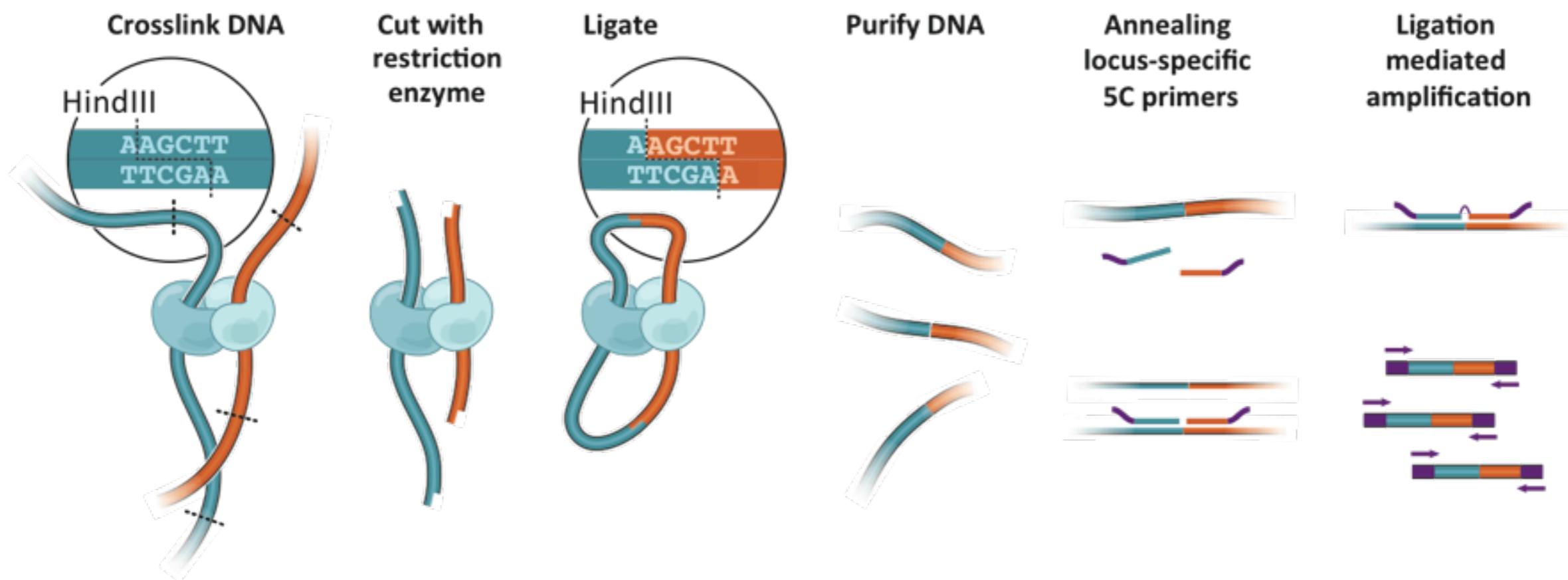
Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 5C data

5C technology

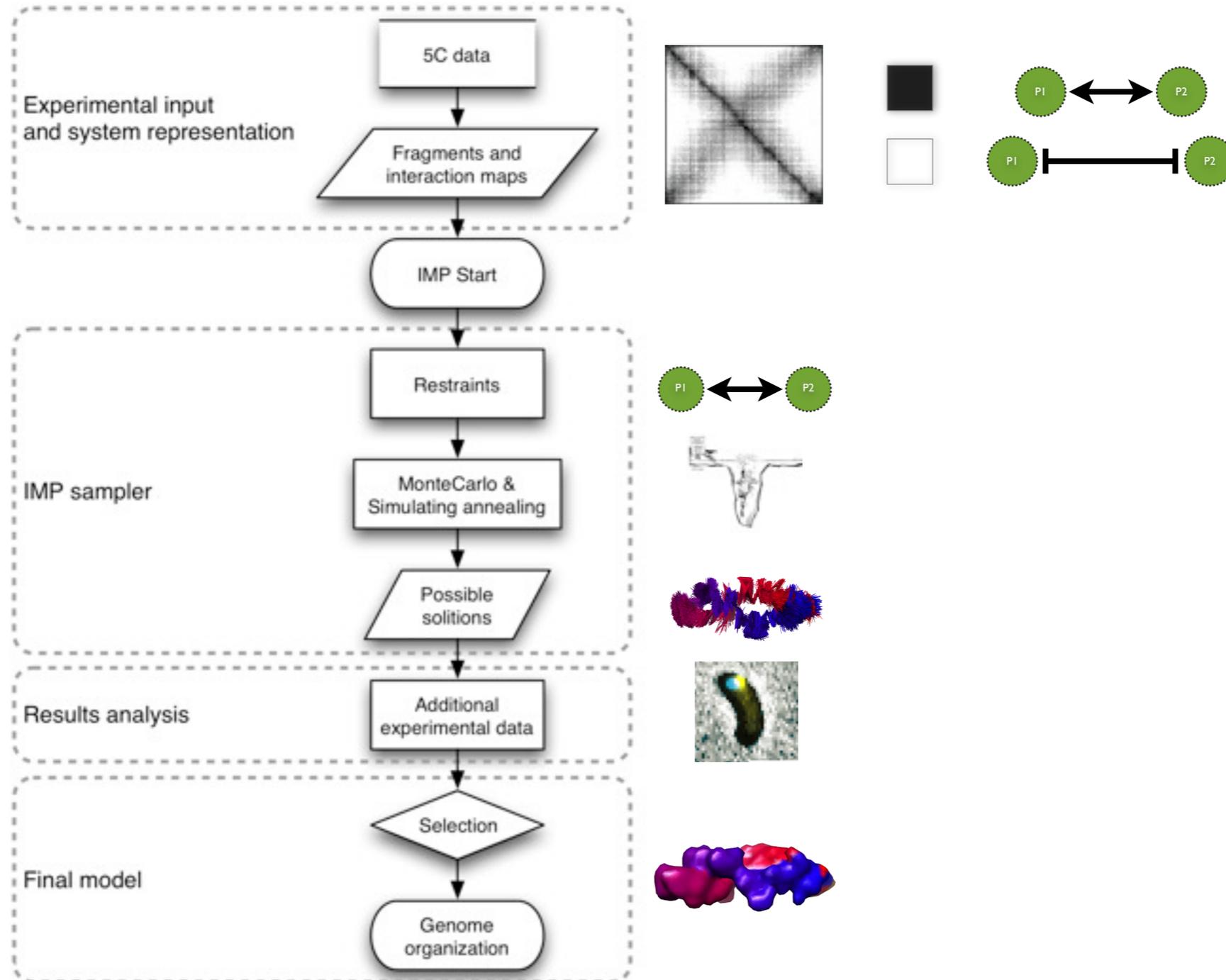
<http://my5C.umassmed.edu>



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

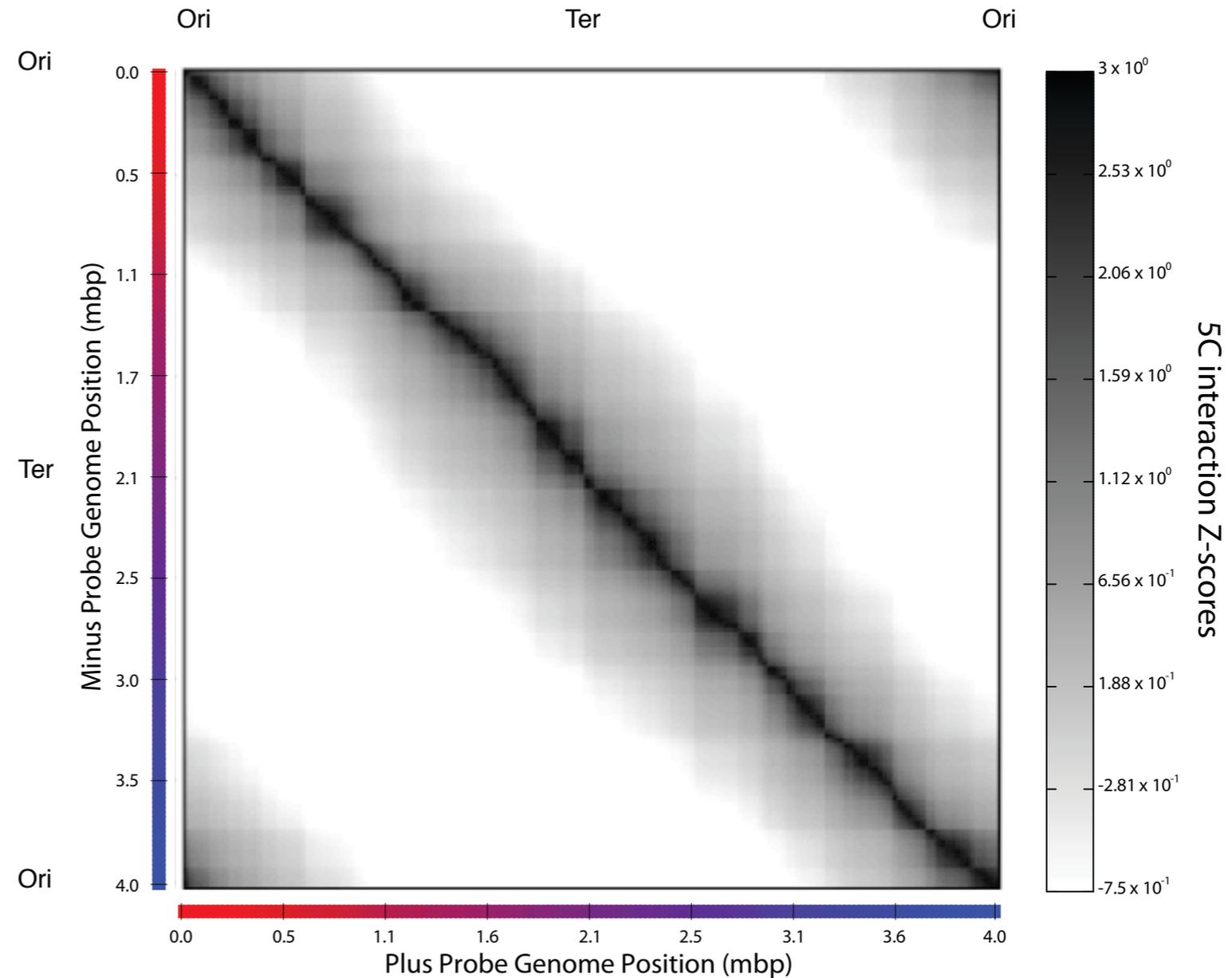
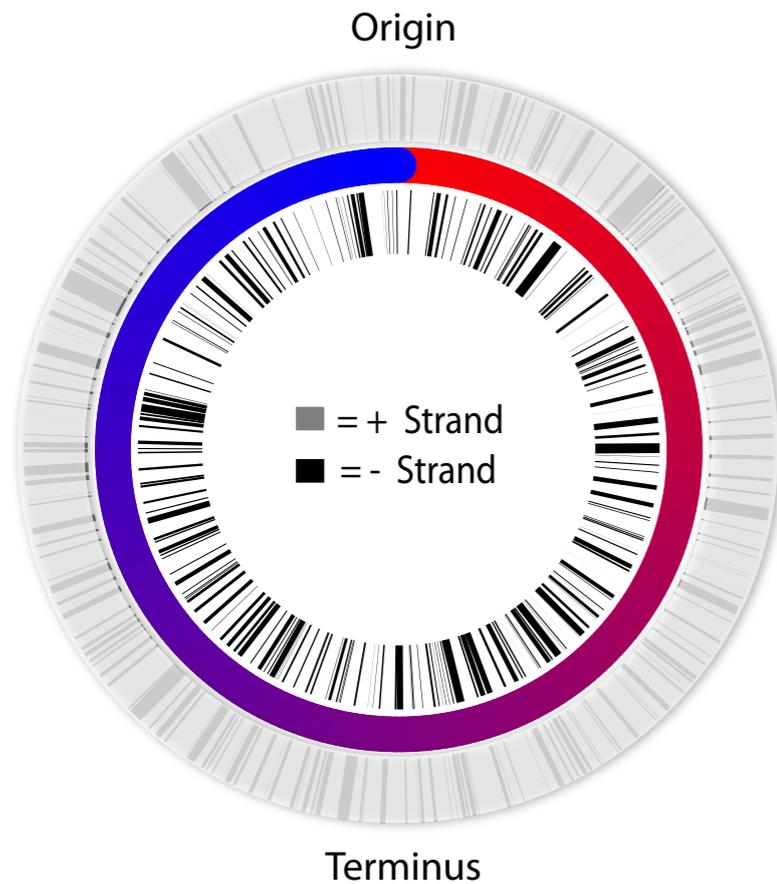
Integrative Modeling

<http://www.integrativemodeling.org>



The 3D architecture of *Caulobacter Crescentus*

4,016,942 bp & 3,767 genes

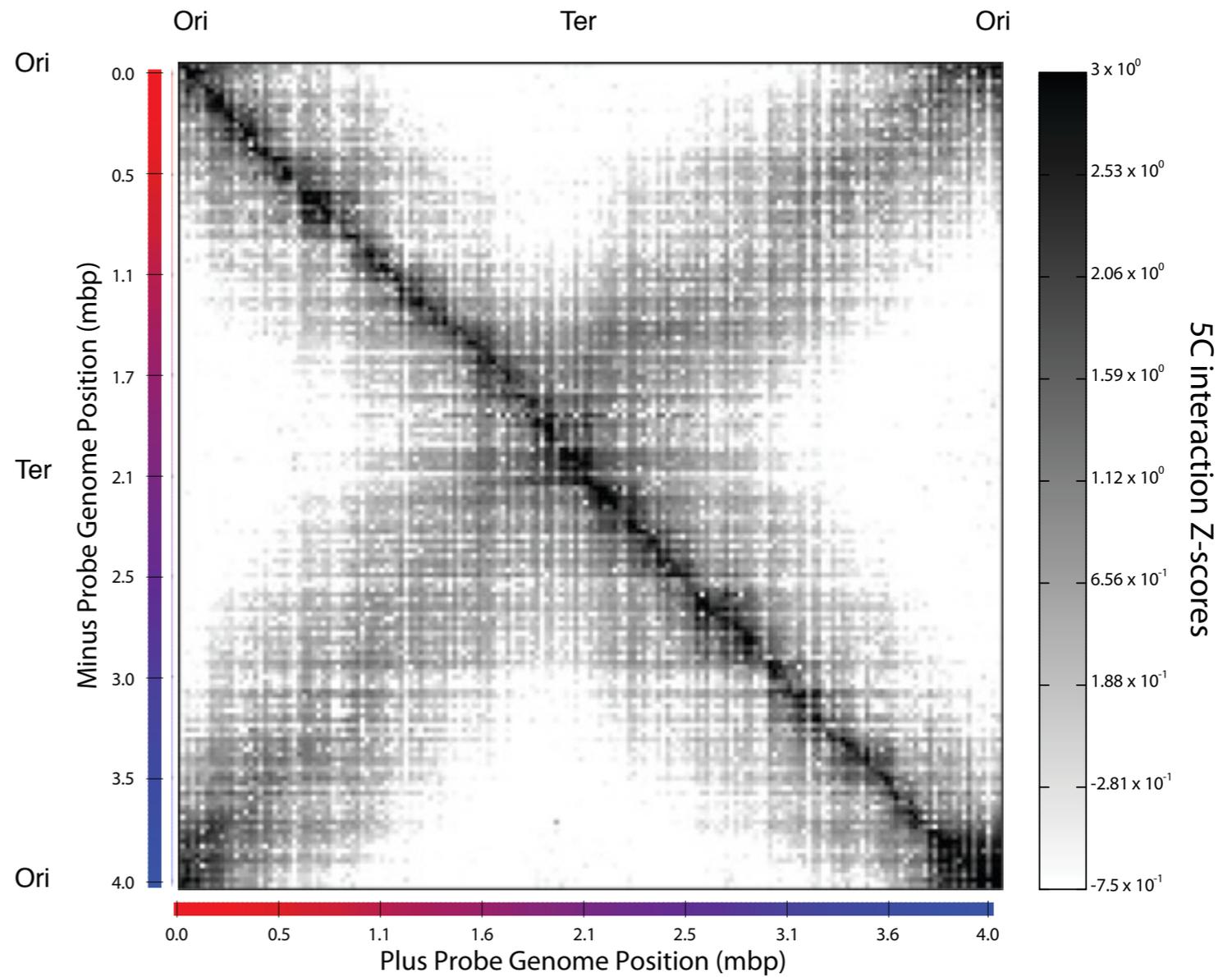
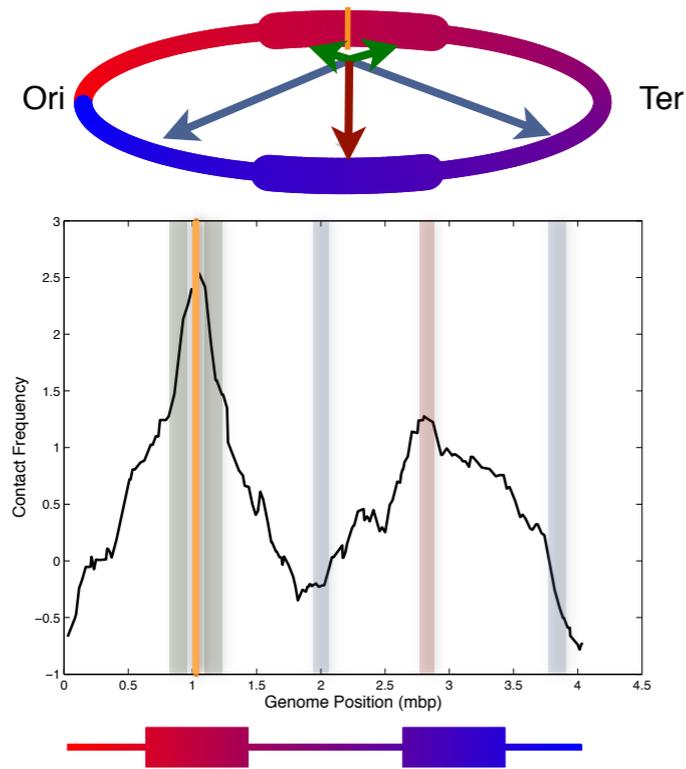
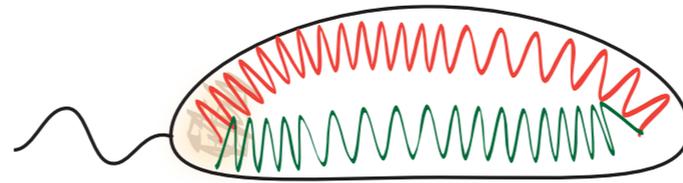


169 5C primers on + strand
170 5C primers on - strand
28,730 chromatin interactions

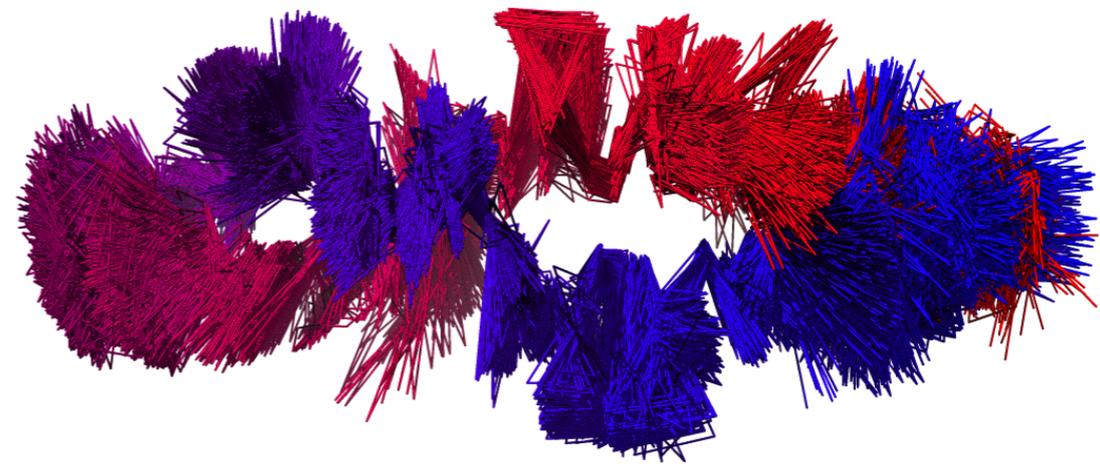
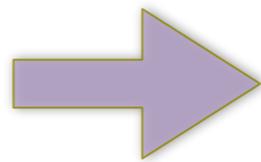
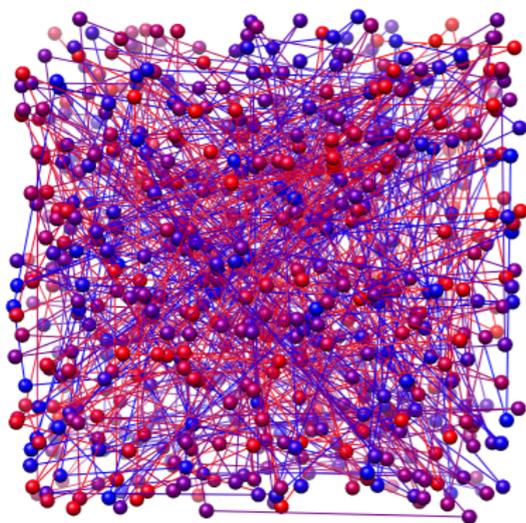
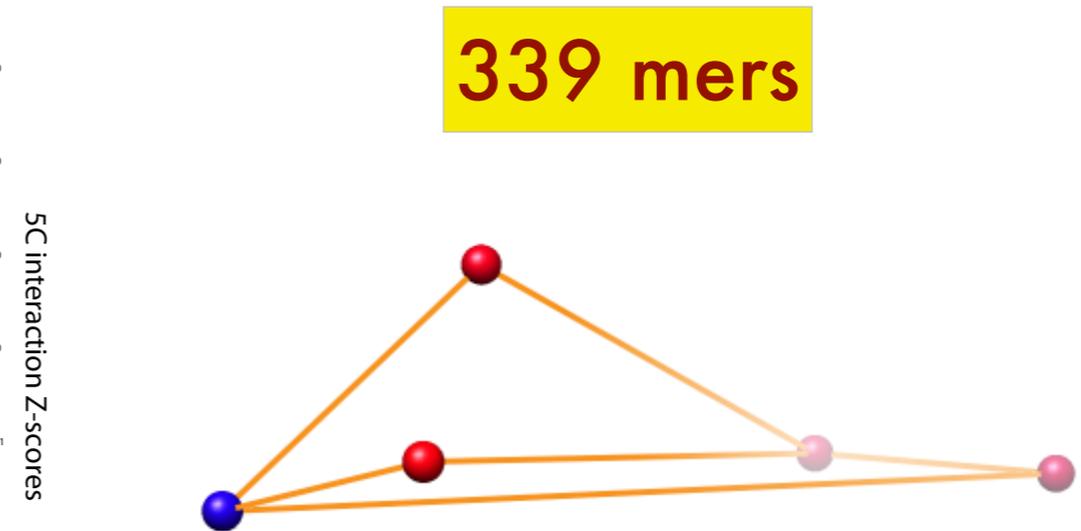
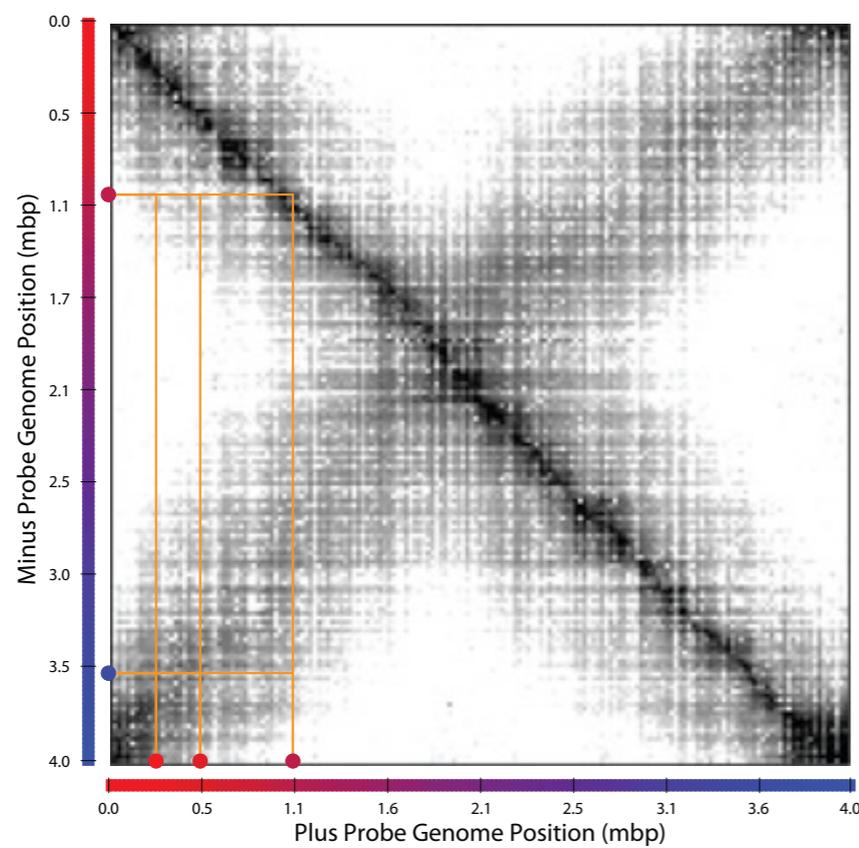
~ 13Kb

5C interaction matrix

ELLIPSOID for *Caulobacter crescentus*



3D model building with the 5C + IMP approach



Genome organization in *Caulobacter crescentus*

Arms are helical

Resolution

Centromer-like

dif site 47 ± 17 Kb from Ter

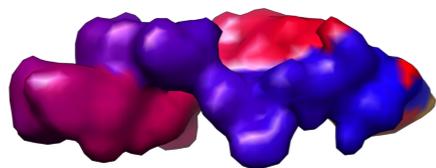
parS sites 25 ± 17 Kb from Ori

Cluster 1

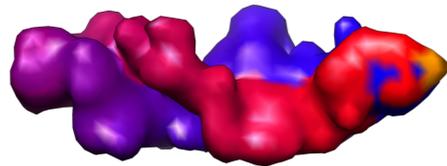
Cluster 2

Cluster 3

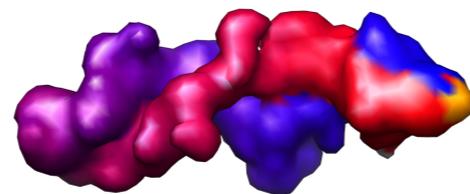
Cluster 4



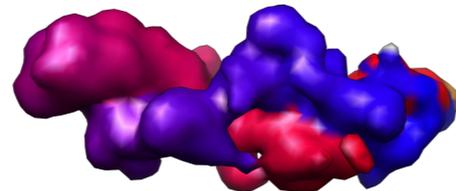
180°



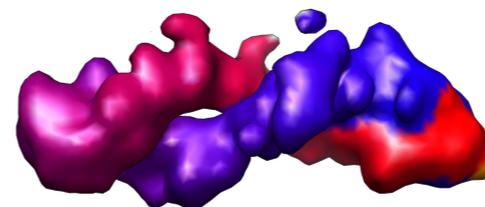
500 nm



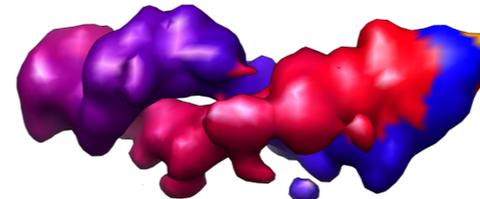
180°



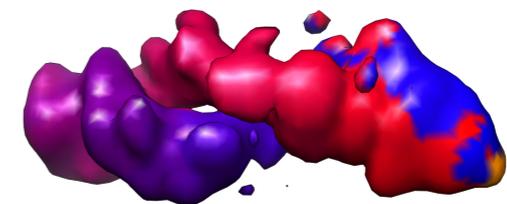
500 nm



180°



500 nm



180°

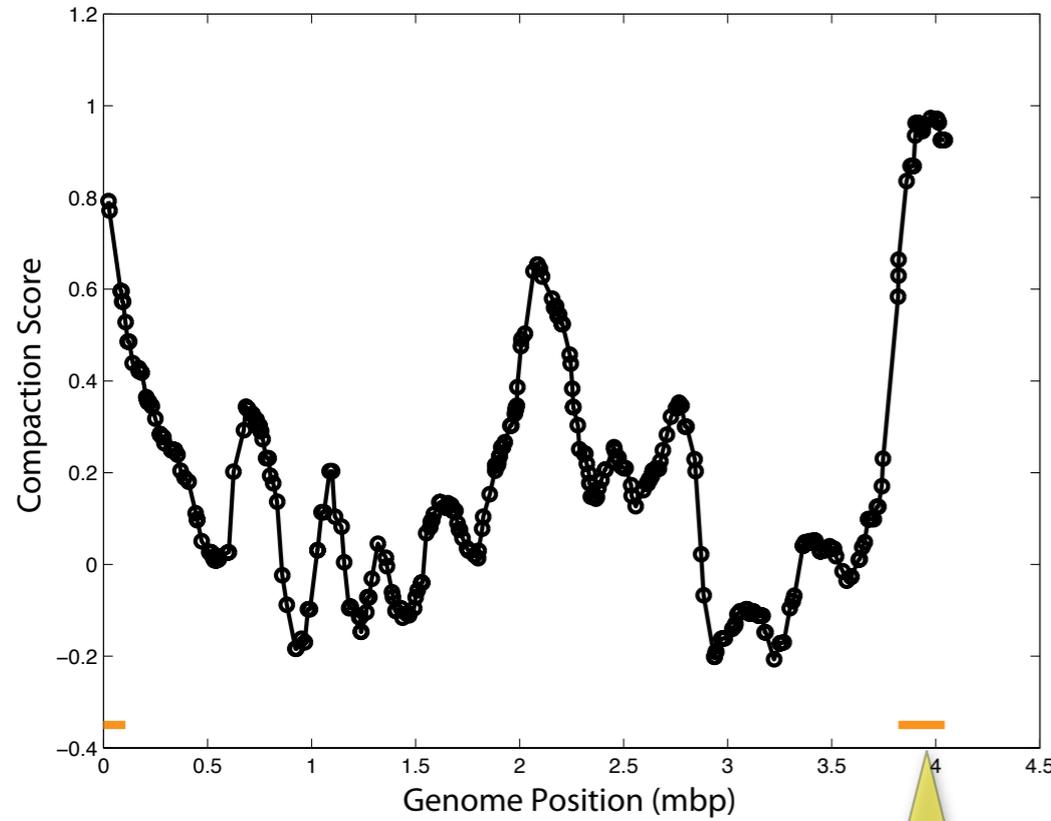


500 nm

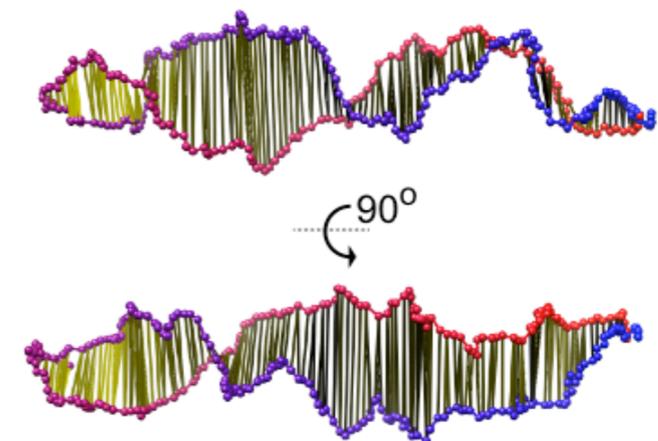
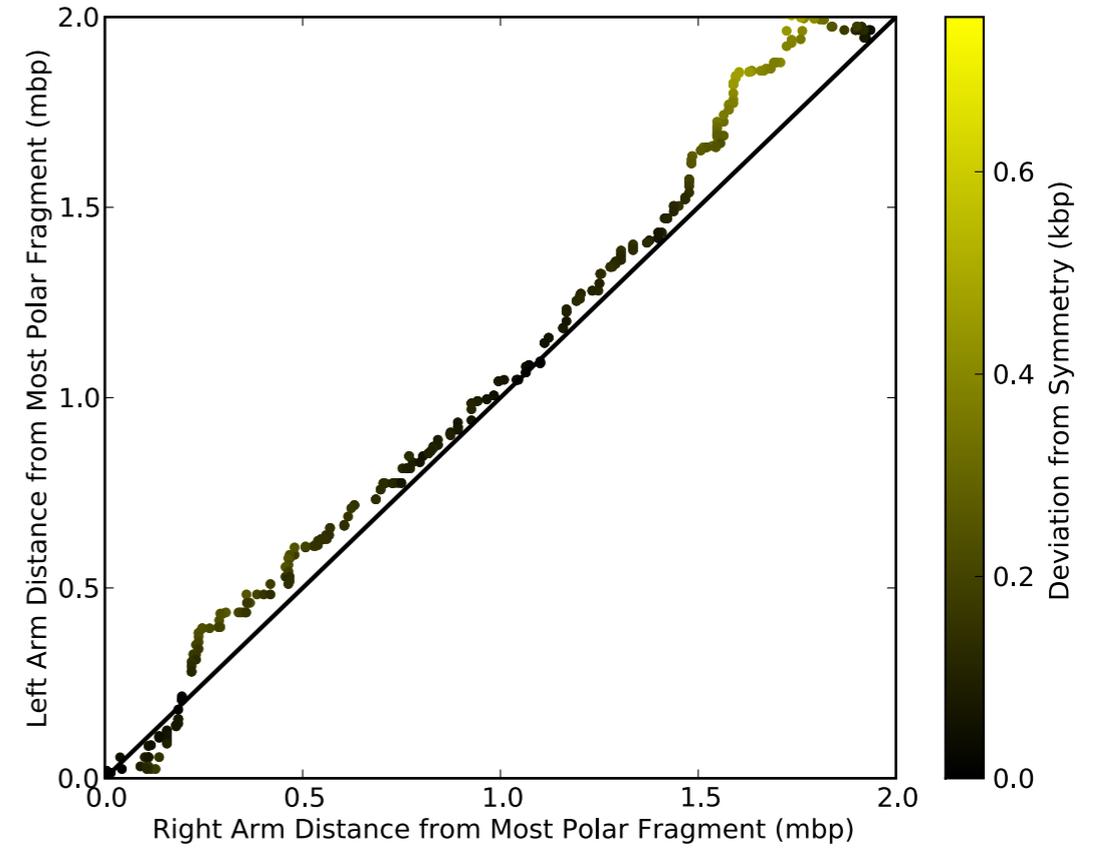
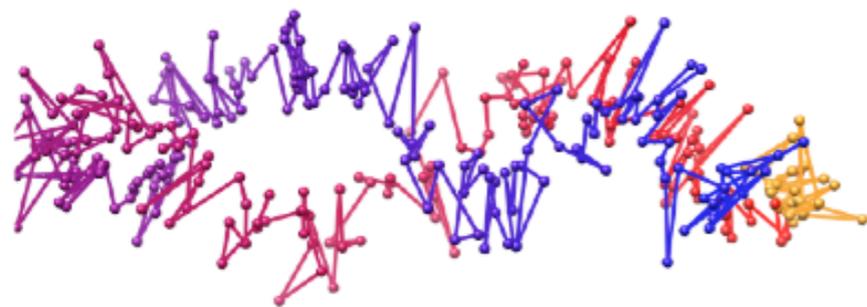
MIRRORS!

parS sites initiate compact chromatin domain

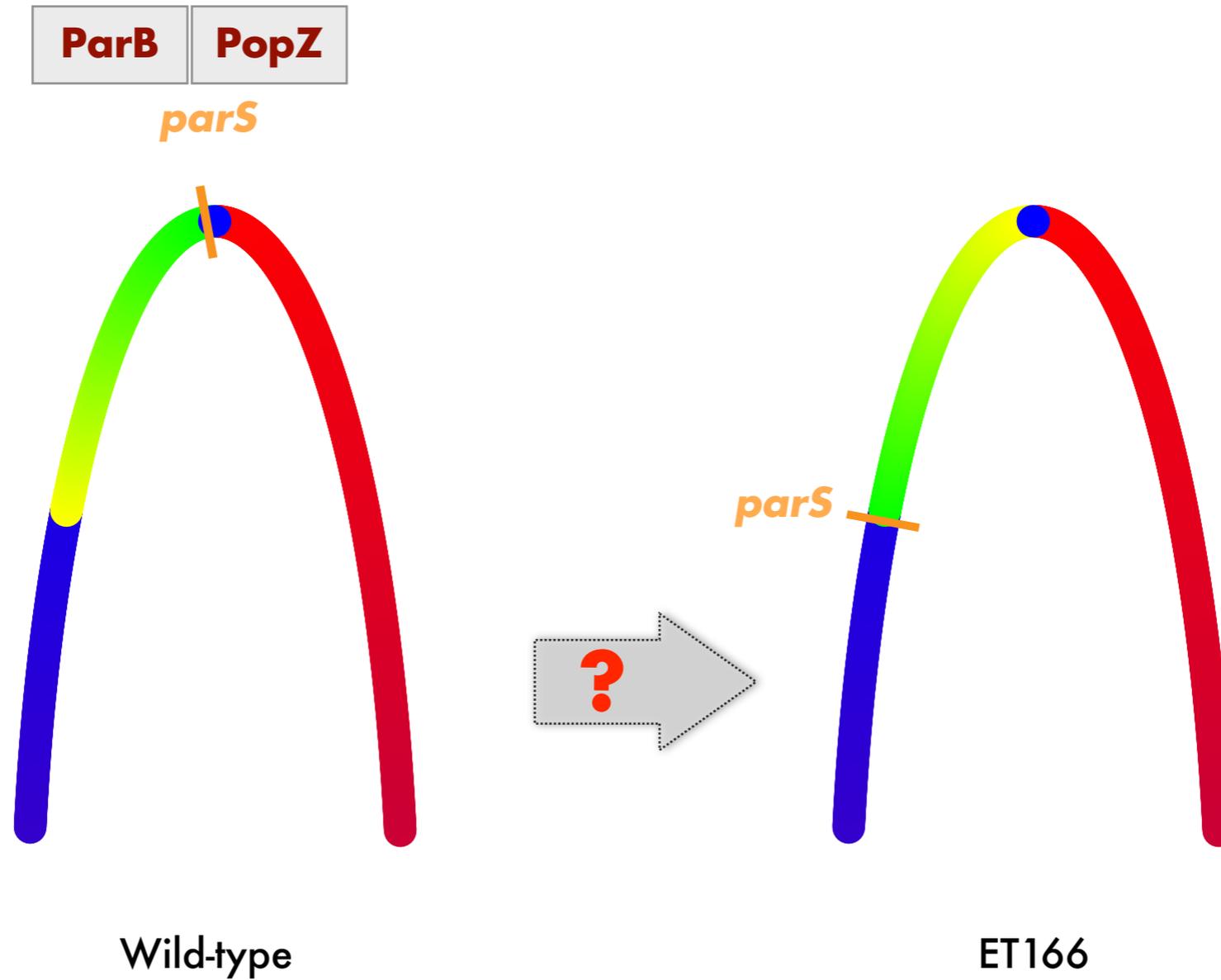
Chromosome arms are equidistant to the cell center



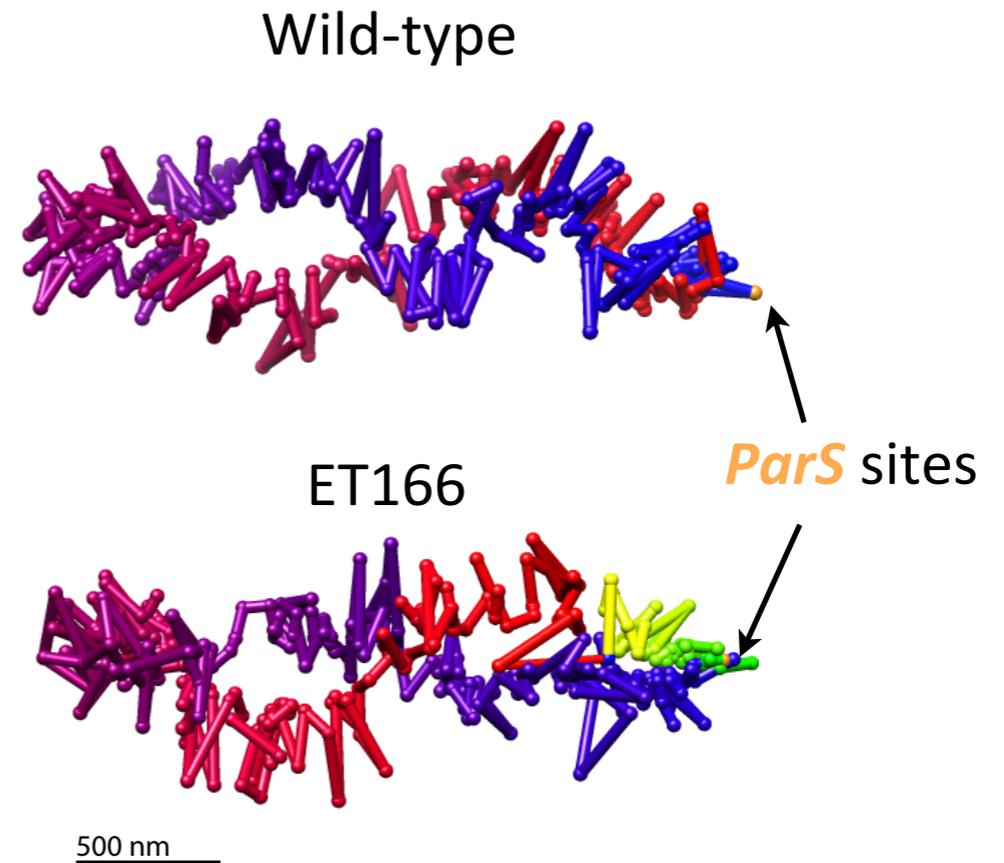
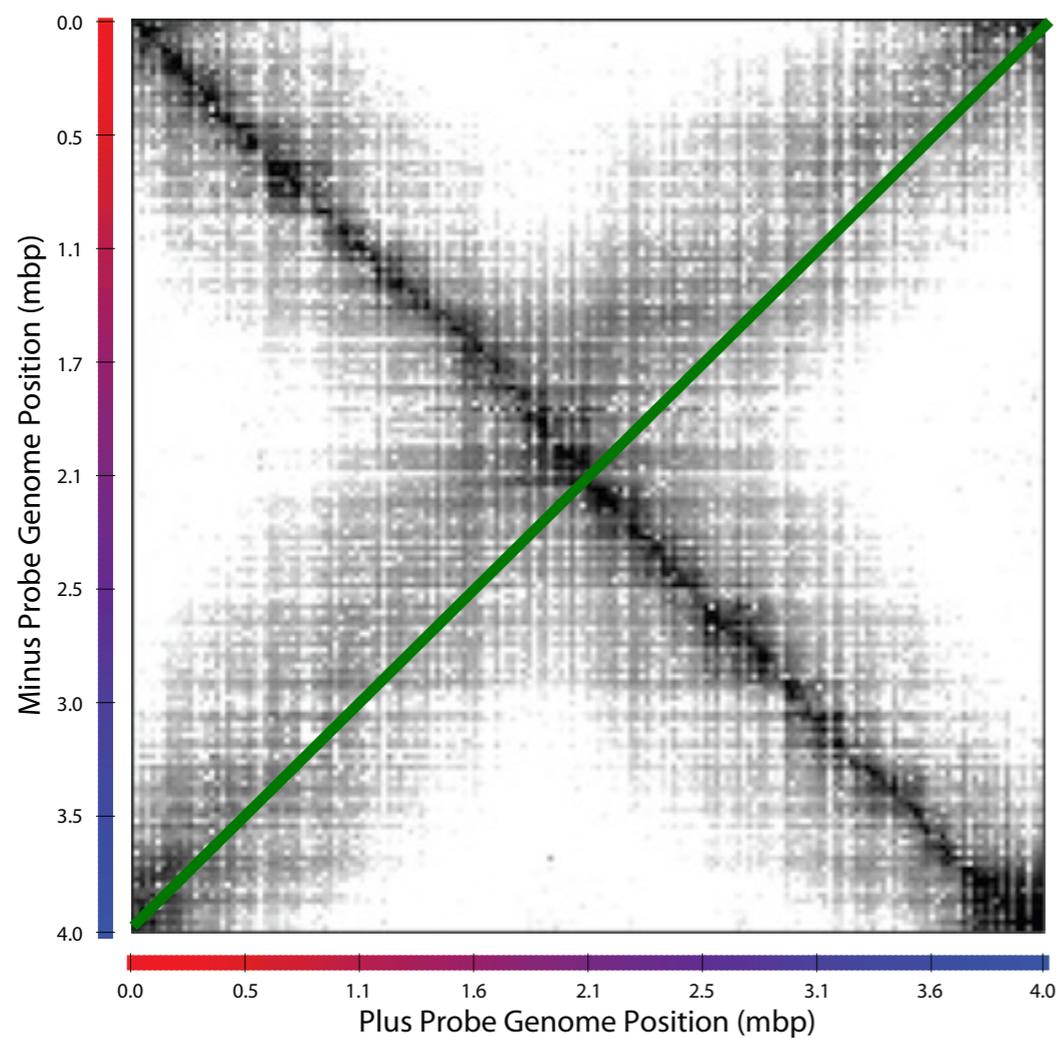
100-200Kb



Moving the *parS* sites 400 Kb away from Ori



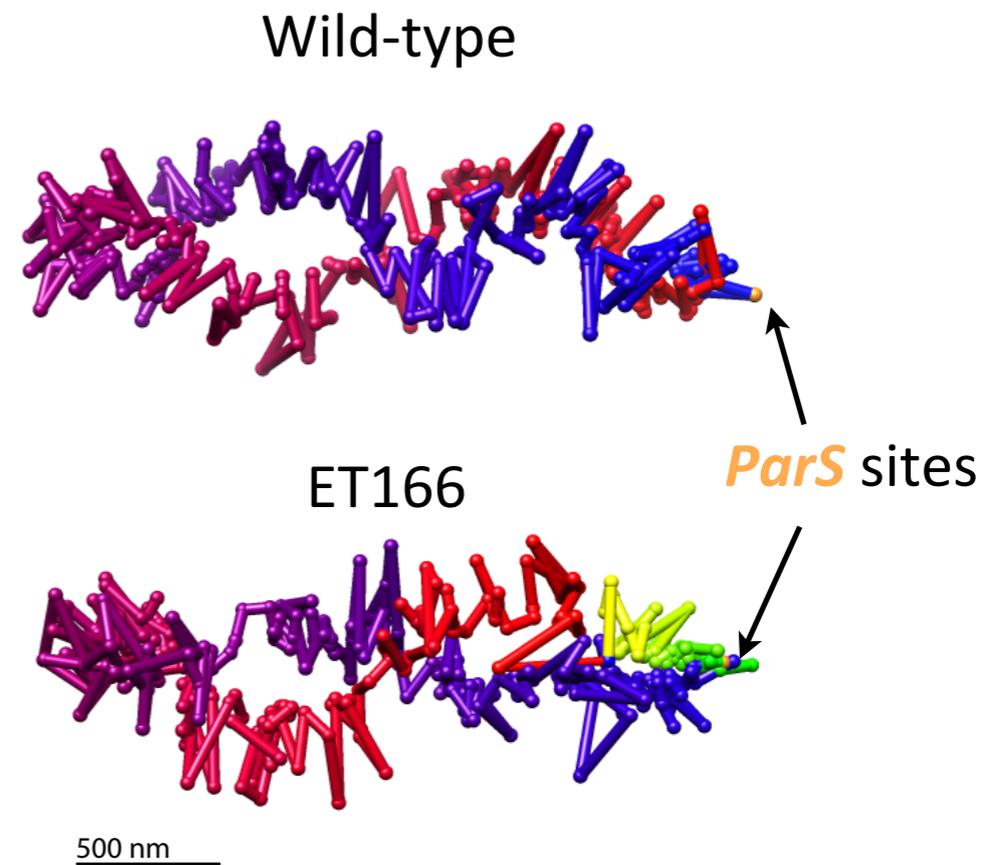
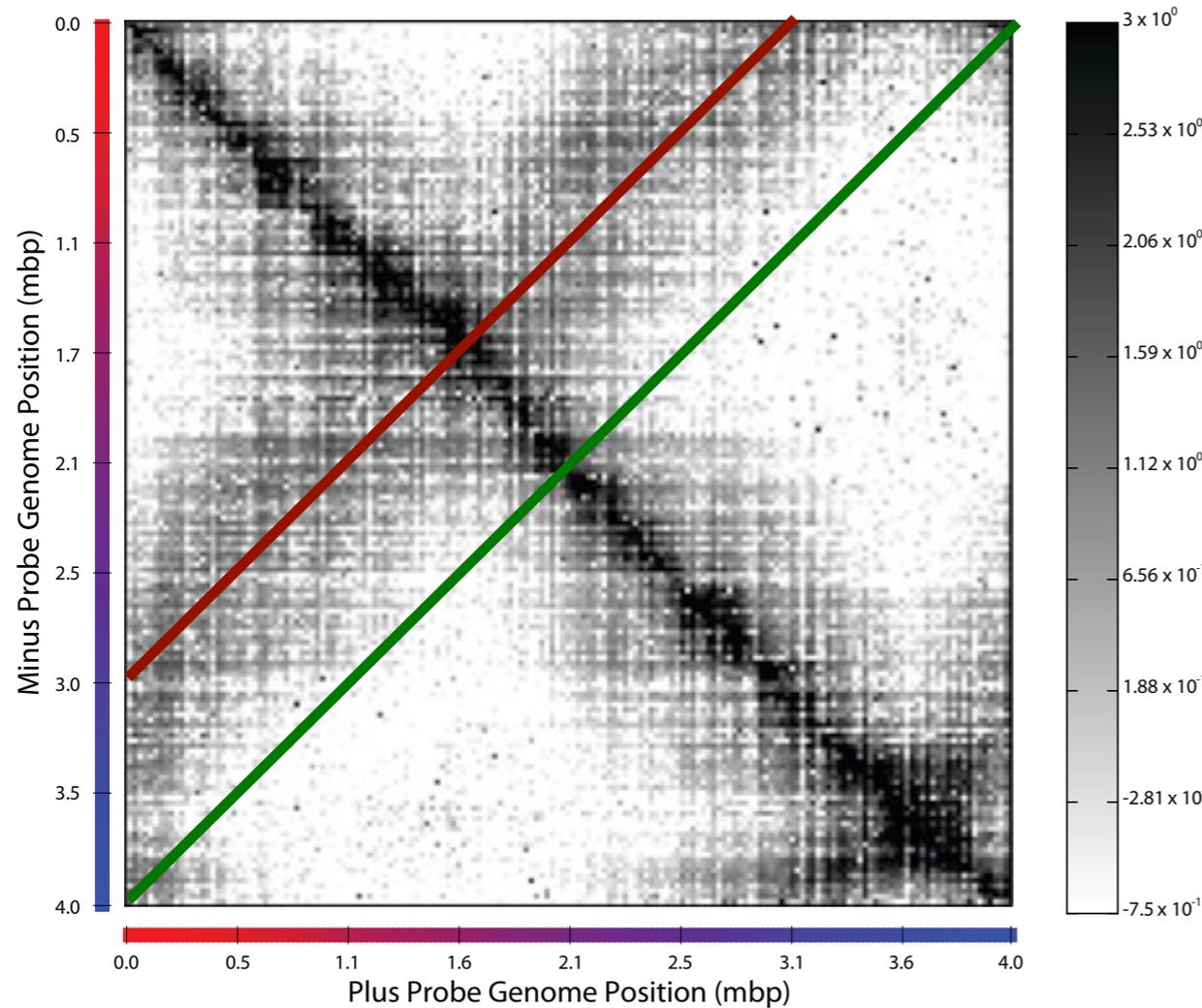
Moving the *parS* sites results in whole genome rotation!



Arms are **STILL** helical

Structure & function PRESERVED!!!

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

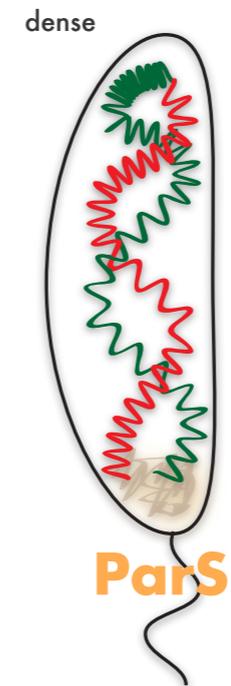
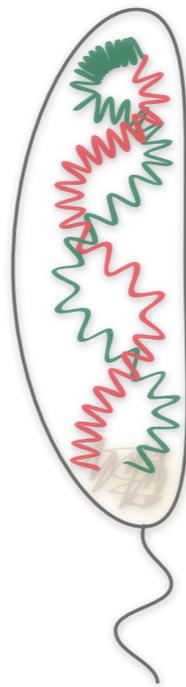
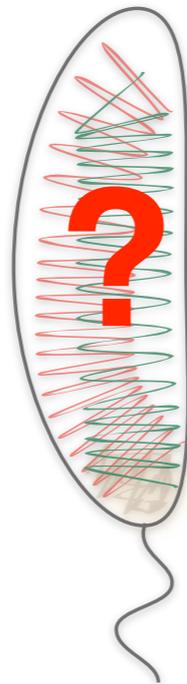
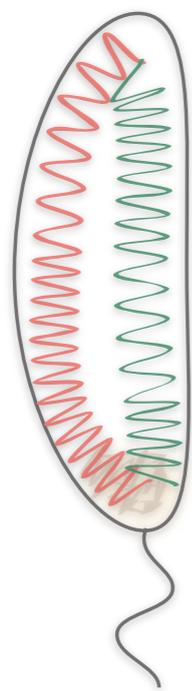
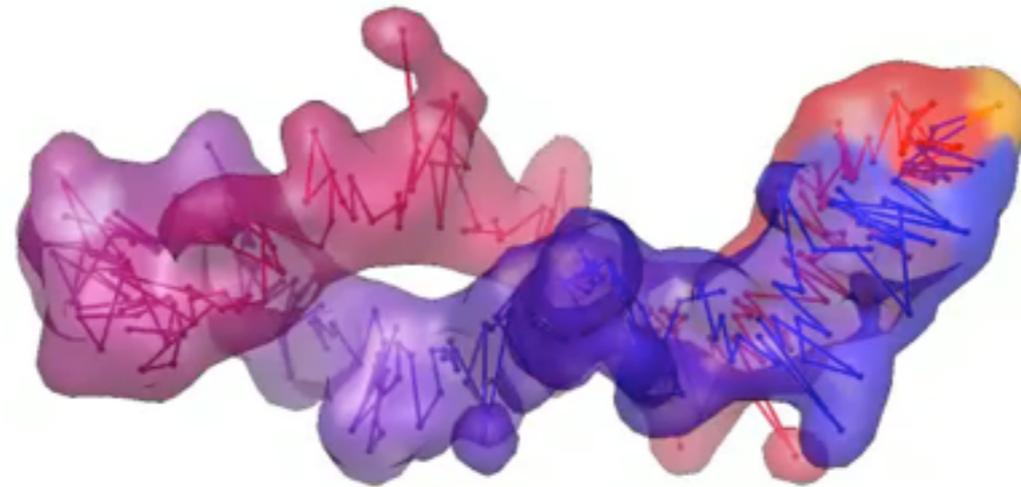


Arms are **STILL** helical

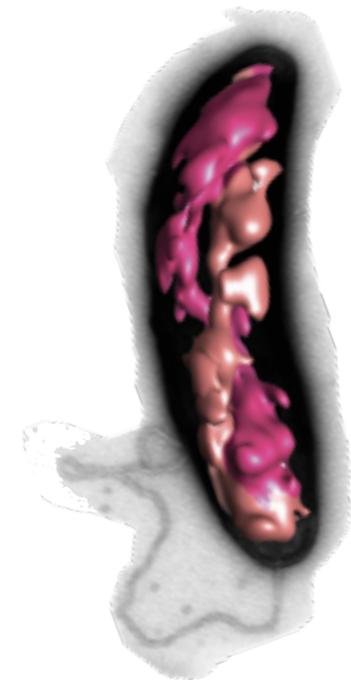
Structure & function PRESERVED!!!

Genome architecture in Caulobacter

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

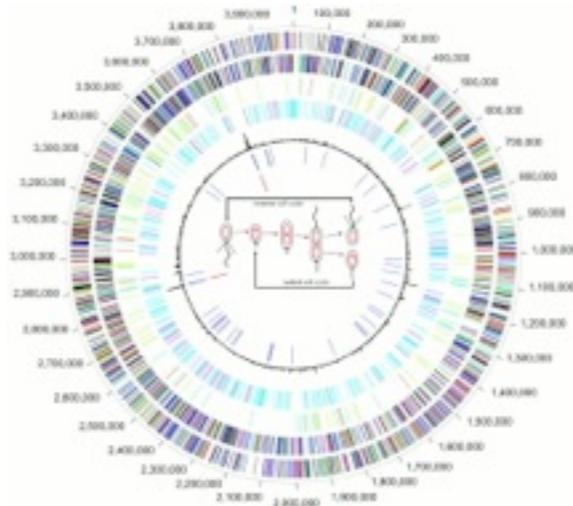


dense

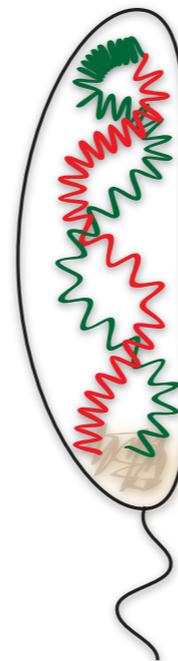
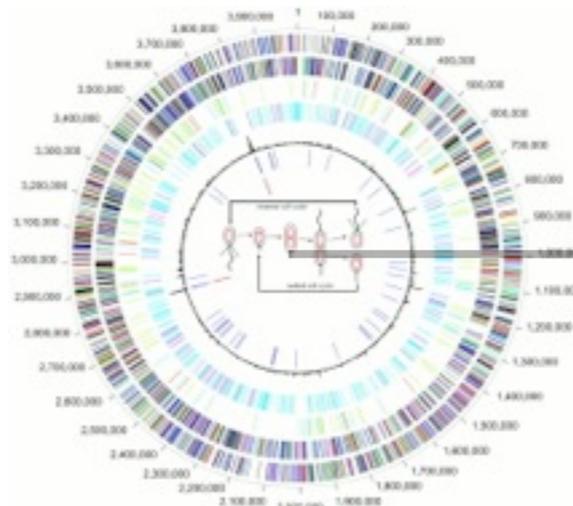


From Sequence to Function

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



Function!



Funtion!

Acknowledgments



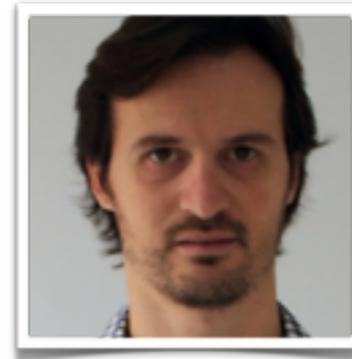
Mark Umbarger

PhD fellow
Harvard



Esteban Toro

PhD fellow
Stanford



Davide Baù

Staff Scientist
CNAG



Job Dekker

Program in Gene Function and Expression
Department of Biochemistry and Molecular Pharmacology
University of Massachusetts Medical School
Worcester, MA, USA



George M. Church

Department of Genetics,
Harvard Medical School,
Boston, MA. USA



Lucy Shapiro

Department of Developmental Biology,
Stanford University School of Medicine,
Stanford, CA. USA



Marc A. Marti-Renom

Genome Biology Group (CNAG)
Structural Genomics Group (CRG)
Barcelona, Spain.

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