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





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http://sgu.bioinfo.cipf.es

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								DNA length	
10 <sup>0</sup>	10 <sup>°</sup> 10 <sup>3</sup>			10 <sup>6</sup>				10 <sup>9</sup>	nt
								Volume	
10 <sup>-9</sup>	10 <sup>-6</sup>		10 <sup>-3</sup>		10 <sup>0</sup>			10 <sup>3</sup>	μm <sup>3</sup>
								Time	
10 <sup>-10</sup>	10 <sup>-8</sup>	10 <sup>-6</sup>	10 <sup>-4</sup>	10 <sup>-2</sup>		10 <sup>°</sup>	10 <sup>2</sup>	10 <sup>3</sup>	S
							Resolution		
10 <sup>-3</sup>			10 <sup>-2</sup>				10 <sup>-1</sup>		μ
		Lang	owski and He	eermann. Se 2	emin Ce	ll Dev Biol (20	07) vol. 1	Adapted from: 18 (5) pp. 659-67	



#### Biomolecular structure determination 2D-NOESY data





## Chromosome structure determination 5C data

## **Integrative Modeling**

http://www.integrativemodeling.org



## Human $\alpha$ -globin domain

#### ENm008 genomic structure and environment

ENCODE Consortium. Nature (2007) vol. 447 (7146) pp. 799-816



The ENCODE data for ENm008 region was obtained from the UCSC Genome Browser tracks for: RefSeq annotated genes, Affymetrix/CSHL expression data (Gingeras Group at Cold Spring Harbor), Duke/NHGRI DNasel Hypersensitivity data (Crawford Group at Duke University), and Histone Modifications by Broad Institute ChIP-seq (Bernstein Group at Broad Institute of Harvard and MIT).

## The "Chromatin Globule" model

Baù et al. (2011) Nat Struct Mol Biol 18:107-14 Sanyal, A., et al. (2011). Current Opinion in Cell Biology 23:325–33







Münkel et al. JMB (1999)



al. Science (2009)



Phillips and Corces. Cell (2009)

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l folding of the α-globin gene ion of chromatin globules

#### The 3D architecture of Caulobacter Crescentus

4,016,942 bp & 3,767 genes



Nierman W C et al. PNAS 2001 98:4136-4141

#### The 3D architecture of *Caulobacter Crescentus*

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#### **5C interaction matrix**

**ELLIPSOID** for Caulobacter cresentus



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







#### Genome organization in Caulobacter crescentus



Friday, September 30, 11

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



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





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





### **From Sequence to Function**

#### Genome architecture in Caulobacter





## OPEN POSITIONS 102012 Acknowledgments



D. Baù, A. Sanyal, B. Lajoie, E. Capriotti, M. Byron, J. Lawrence, J. Dekker\*, and M.A. Marti-Renom\* Nature Structural & Molecular Biology (2011) 18(1):107-14

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