### 3DGENOMICS

Marc A. Marti-Renom Structural Genomics Group (ICREA, CNAG-CRG)

http://marciuslab.org
http://3DGenomes.org
http://cnag.crg.eu







### Resolution Gap

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

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### Level I: Radial genome organization

Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



### Level II: Euchromatin vs heterochromatin



### Level III: Lamina-genome interactions



### Level IV: Higher-order organization

Dekker, J., Marti-Renom, M. A. & Mirny, L. A. Nat Rev Genet 14, 390–403 (2013).



### TADs are functional units

Lupiáñez, et al. (2015). Cell, 1–15.



### TADs are functional units

Hnisz, D., et al. (2016). Science, on line



### Level V: Chromatin loops





### Level V: Loop-extrusion as a driving force

Fudenberg, G., Imakaev, M., Lu, C., Goloborodko, A., Abdennur, N., & Mirny, L. A. (2015). Formation of Chromosomal Domains by Loop Extrusion. bioRxiv.



### Level VI: Nucleosome



### Complex genome organization

Cavalli, G. & Misteli, T. Functional implications of genome topology. Nat Struct Mol Biol 20, 290–299 (2013).



## H chical genome organisation





Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293. Rao, S. S. P., et al. (2014). Cell, 1–29.

### Resolution Gap

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

Knowl	edge								
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### Chromosome Conformation Capture

Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311. Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293.



### Chromosome Conformation Capture



Hakim, O., & Misteli, T. (2012). SnapShot: Chromosome Confirmation Capture. Cell, 148(5), 1068–1068.e2.

# srmation Capture \_\_\_\_\_assembly



Kaplan, N., & Dekker, J. (2013). High-throughput genome scaffolding from in vivo DNA interaction frequency. Nature

### Great apes lymphoblast maps Chromosome 14







GGO8 has an inversion of the region corresponding to HSA8:30.0-86.9Mb Aylwyn Scally (Department of Genetics, University of Cambridge)

## Chromosome Conformation Capture for meta genomics



Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Michelmore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/ peerj.preprints.260v1

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

**Experiments** 



Computation

### Structure determination using Hi-C data



### Biomolecular structure determination 2D-NOESY data



Chromosome structure determination 3C-based data



### http://3DGenomes.org





Serra, Baù, et al. (2017). PLOS CompBio



### Structuring the **COLORs** of chromatin

Serra, Baù et al. (2017) PLOS CompBio.





### Fly Chromatin **COLORs**

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







### Fly Chromatin **COLORs**

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





~200 regions of ~5Mb each 2Kb resolution

### Structural properties

50 1Mb regions. 10 enriched for each color.



### Structural **COLORs**



### Structural **COLORs**



### Structural **COLORs**



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🗊 Nucleosome 🌒 Histones H2A/H2B 🛛 🗧 Histone H1 🛛 🌒 PRBS







David Castillo Yasmina Cuartero Irene Farabella Silvia Galan Mike Goodstadt Julen Mendieta Francesca Mugianesi Juan Rodríguez François Serra Paula Soler Aleksandra Sparavier Marco di Stefano

#### http://sgt.cnag.cat/www/presentations/



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