

Centre Nacional d'Anàlisi Genòmic

## 3DGenomics

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Barcelona, 9 Nov 2017

centre nacional d'anàlisi genòmica  
centro nacional de análisis genómico

**cnag**

The **CNAG** is a non-profit organization created on 2010 and integrated in the Barcelona Science Park. It is funded by the Spanish Ministry of Economy and Competitiveness and the Catalan Government through the Economy and Knowledge Department and the Health Department (30 M€ initial funding, 2010-2012, but was extended 2010-2015). Competitive grants and contractual research with the private sector provide additional funds.

## Our Mission

To carry out large-scale projects in genome analysis that will lead to significant improvements in people's health and quality of life, in collaboration with the Catalan, Spanish, European and International research and clinical community.

## Our Vision

To be a large-scale, high quality sequence analysis center and to be a world reference center for genomic analysis.

# The CNAG's Genomehenge 2017



## Sequencing capacity

- >2000 Gbases/day = 20 human genomes per day at 30x coverage

## Sequencing

- 4 Illumina HiSeq2000
- 2 Illumina HiSeq2500
- 1 Illumina HiSeq4000
- 1 Illumina MiSeq
- 3 Oxford Nanopores Minlons

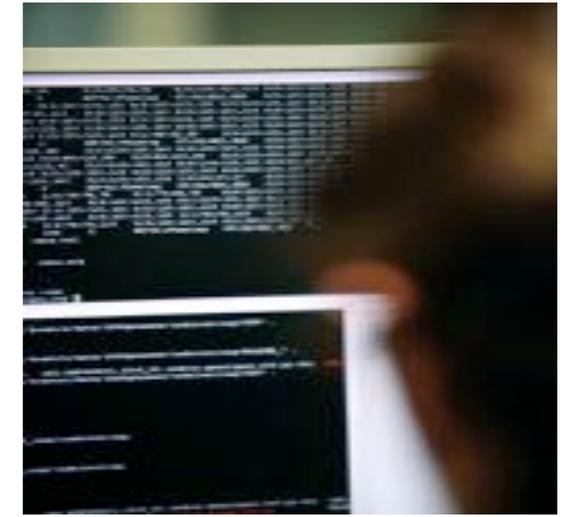


## Computing

- 3552 cores
- 3.7 PB disk + 3 PB tape
- 35,5 TB RAM
- Barcelona SuperComputing Center - 10 x 10 Gb/s



## How we work – Our process



### Biological Resources

- Reception
- Quality control
- Conditioning
- Storage

### Sequencing

- Sample Preparation
- Sequencing Production
- Methods Development

### Informatics

- Bioinformatic Analysis
- Bioinformatic Development
- Genome Biology
- Applied Genomics
- Biomedical Genomics
- Structural Genomics
- Population Genomics
- Databases

**LIMS + QC**

# CNAG's Sequencing Applications

## DNA

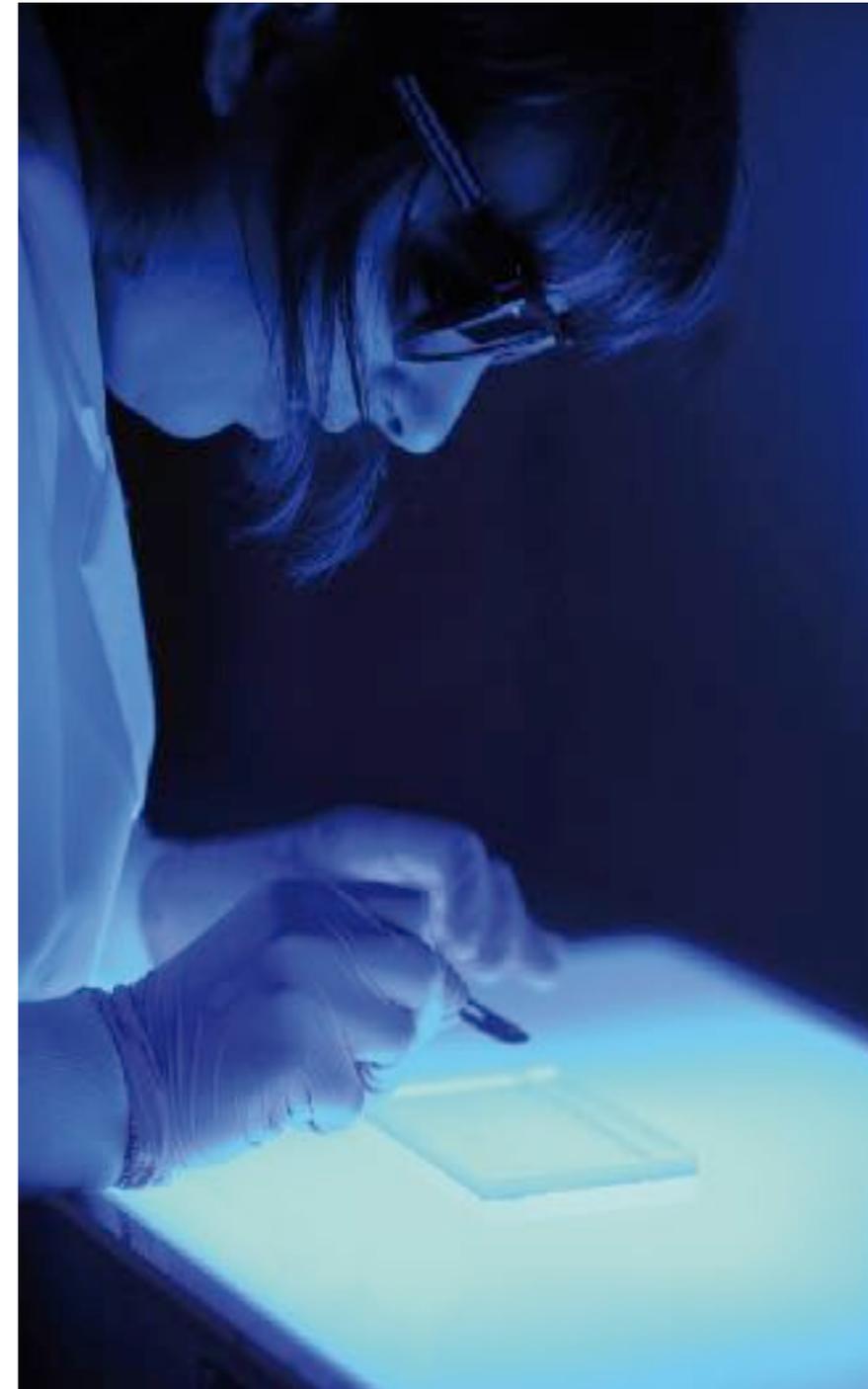
- Whole genome sequencing
  - No PCR
  - Double size selection
    - Low input
- Targeted sequencing
  - Exome & custom capture
    - Low input
    - FFPE
- Refined protocols
  - GBS

## RNA

- Regular Illumina protocols
  - polyA+, ribo minus, directionality
- Single cell

## DNA methylation

- Whole genome bisulphite sequencing
  - BS and oxBS
    - Low input



Contact [projectmanager@cnag.crg.eu](mailto:projectmanager@cnag.crg.eu)

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**CRG**<sup>®</sup>  
Centre  
for Genomic  
Regulation

# Informatics Resources

## Production Bioinformatics

- Primary run analysis and verification
- QC systems and LIMS

## Analysis Production

- Alignment, variant calling and annotation
- Analysis and interpretation

## Statistical Genomics

- DNA methylation pipeline
- RNA analysis pipeline

## *de novo* Assembly and Annotation

- Pipeline for *de novo* assembly
- Pipeline for genome annotation

## Algorithm Development

- Development and improvement of alignment and assembly methods - GEM
- Data compression

## Structural Genomics

- Modelling of 3-d structure of genomes - HiC analysis

## Comparative Genomics

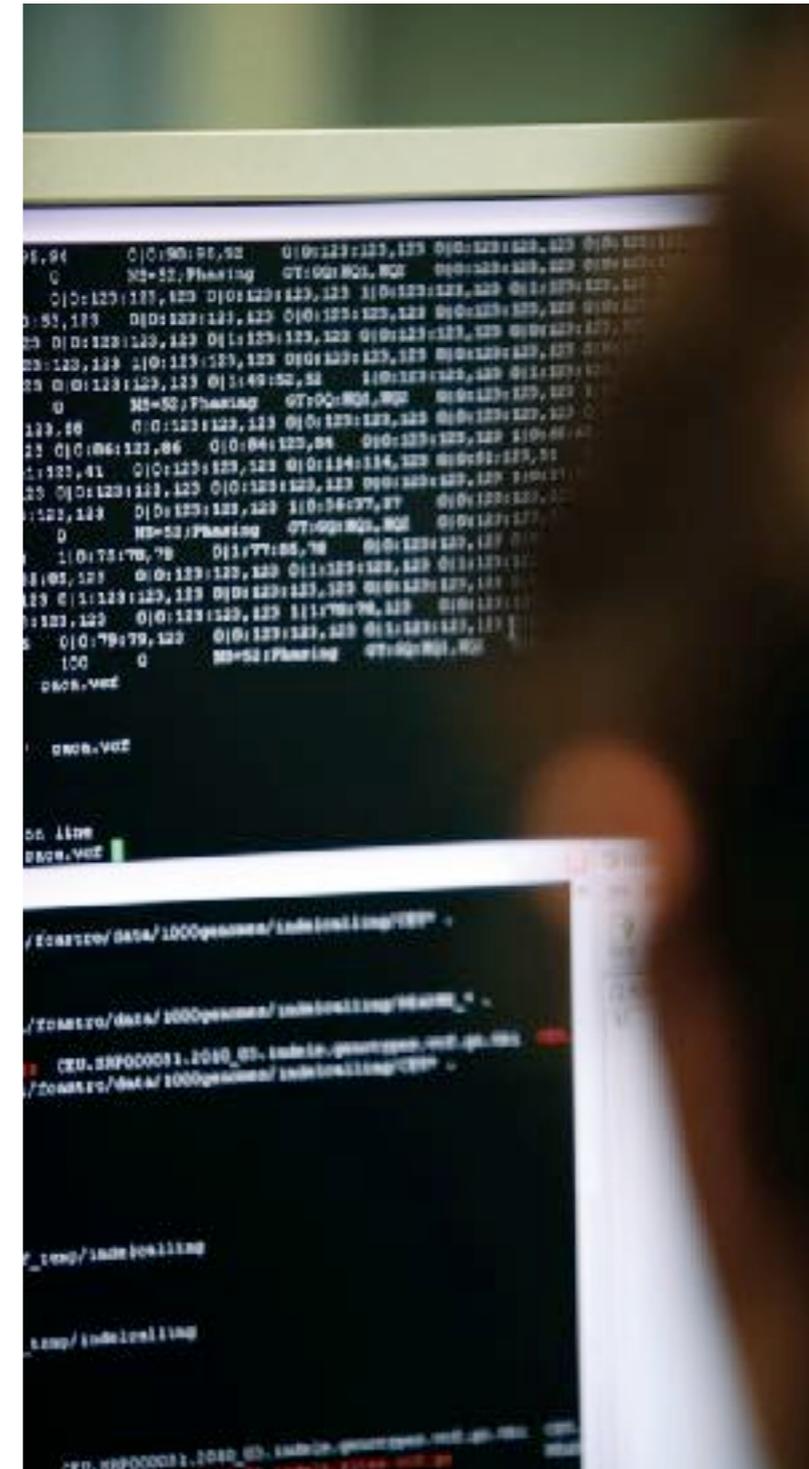
## Biomedical Genomics

- Advanced data mining

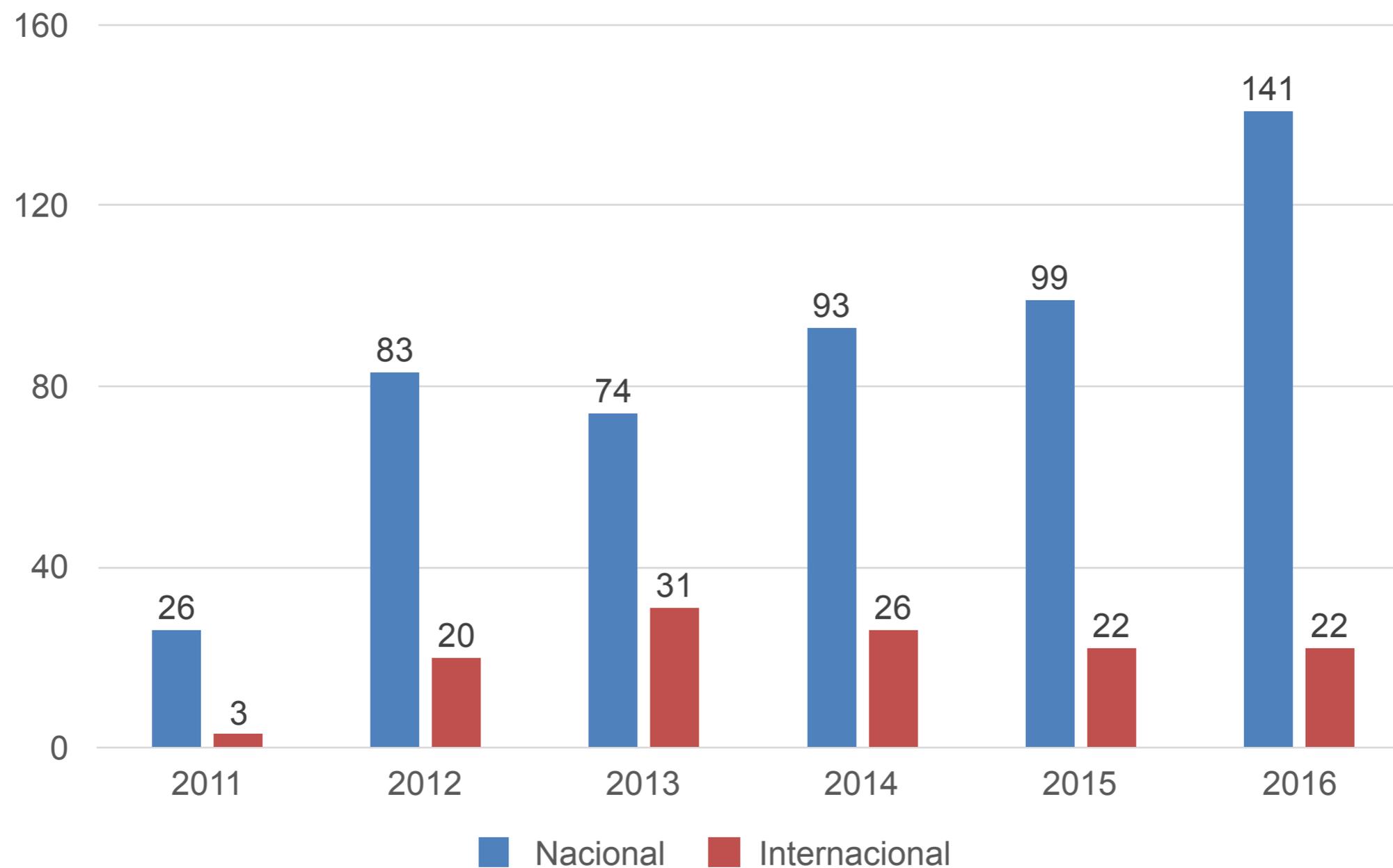
## Population Genomics

## Databases

- Storage and distribution of data

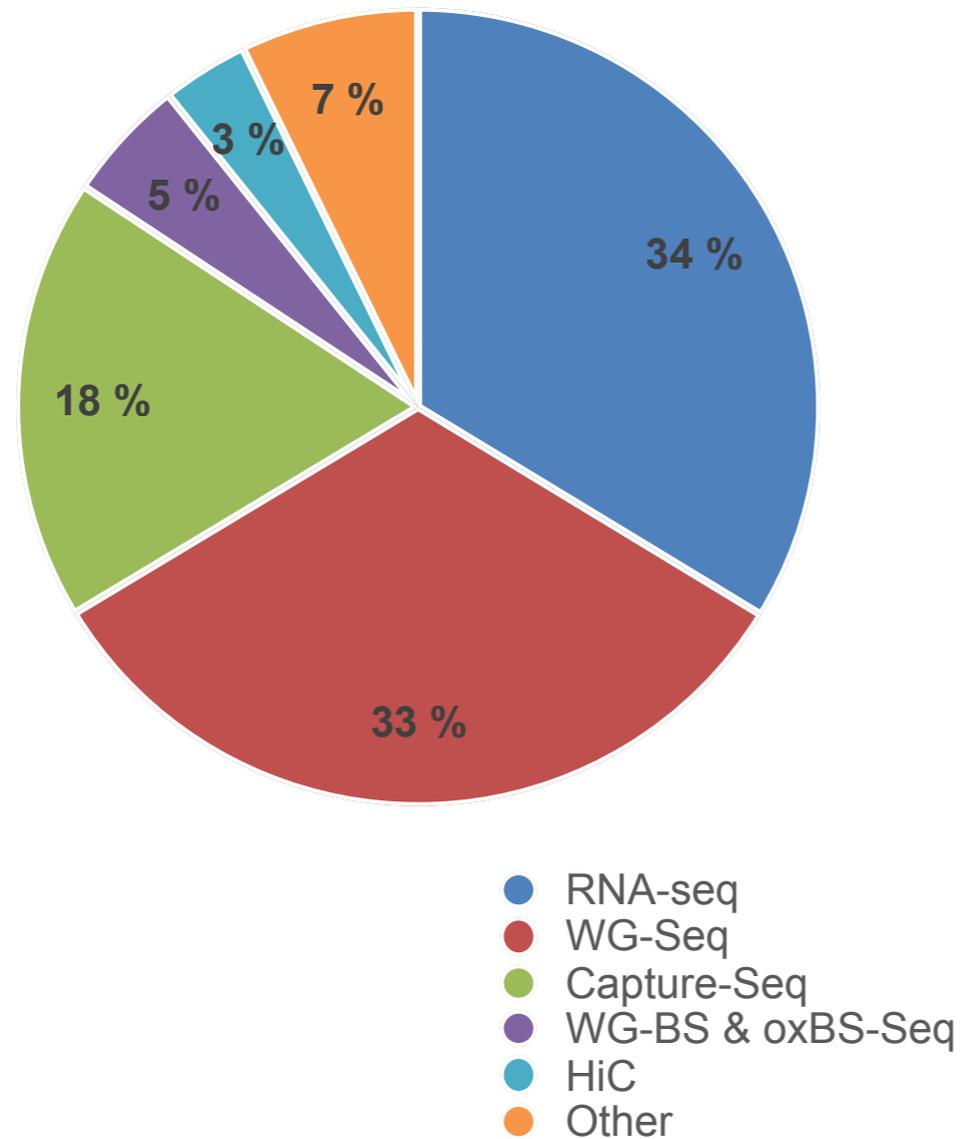


## CNAG-CRG Collaborators

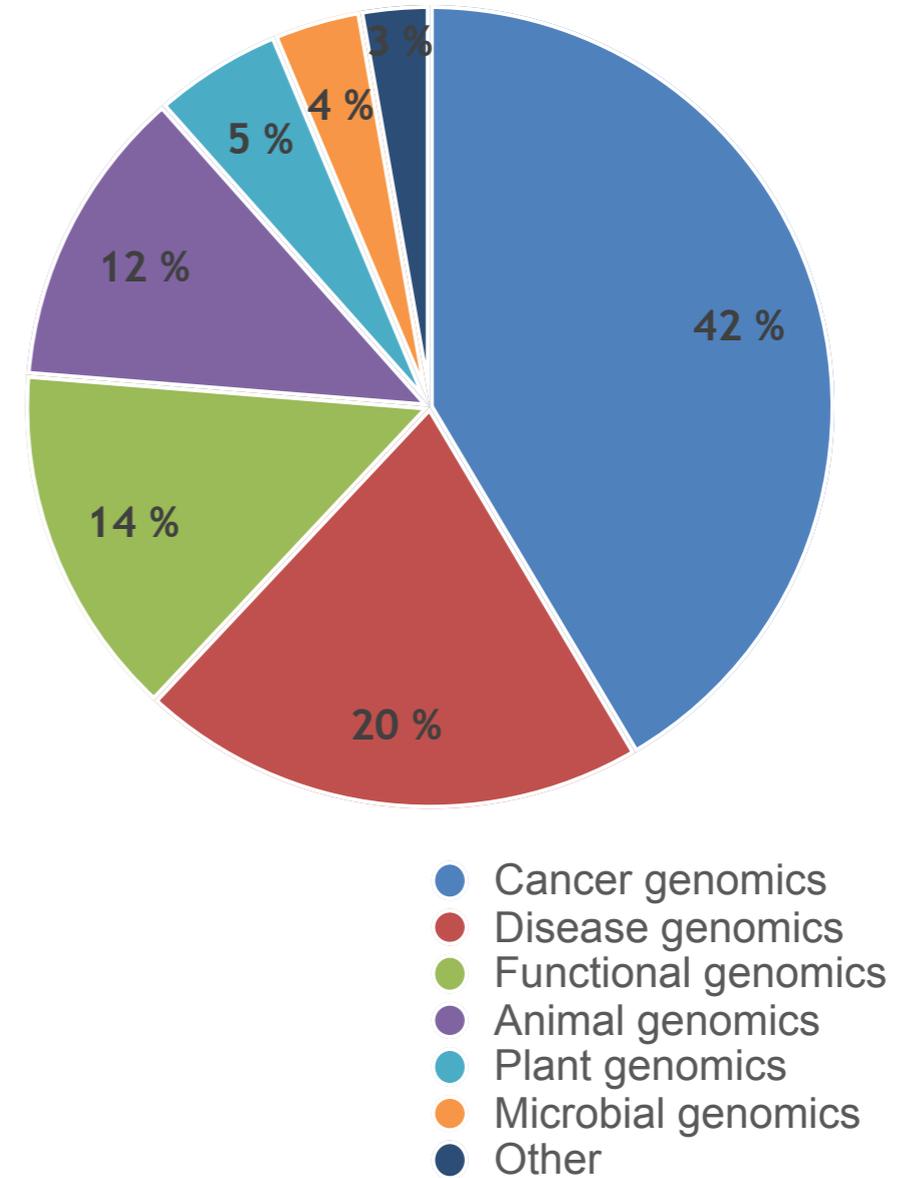


# Activity

## 2016 activity by application



## 2016 activity by research area



# Personalized Medicine

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Since its foundation, the CNAG-CRG is committed to translating discoveries into new applications that lead to health benefits.

In 2016, the center has accomplished 86 sequencing and/ or analysis projects with researchers from 18 Spanish Hospitals or Health Institutes.

Large ongoing Projects on Personalized Medicine:

***Proyecto piloto sobre uso clínico de medicina genómica en servicios públicos de salud de Navarra, Gobierno de Navarra, PI: Angel Alonso, Complejo Hospitalario de Navarra***

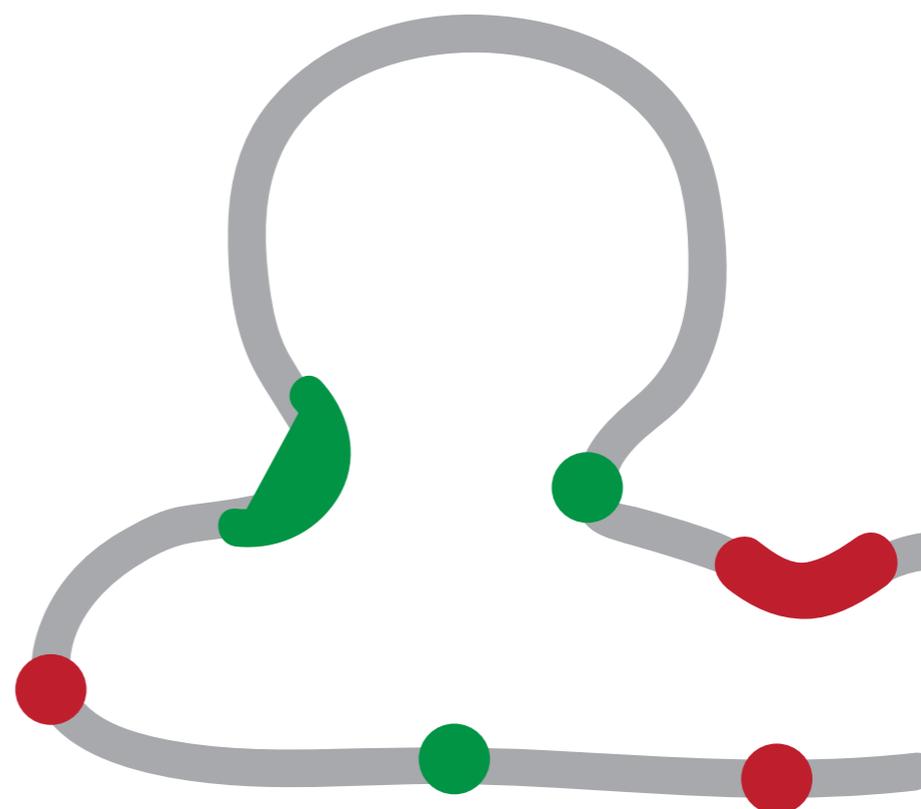
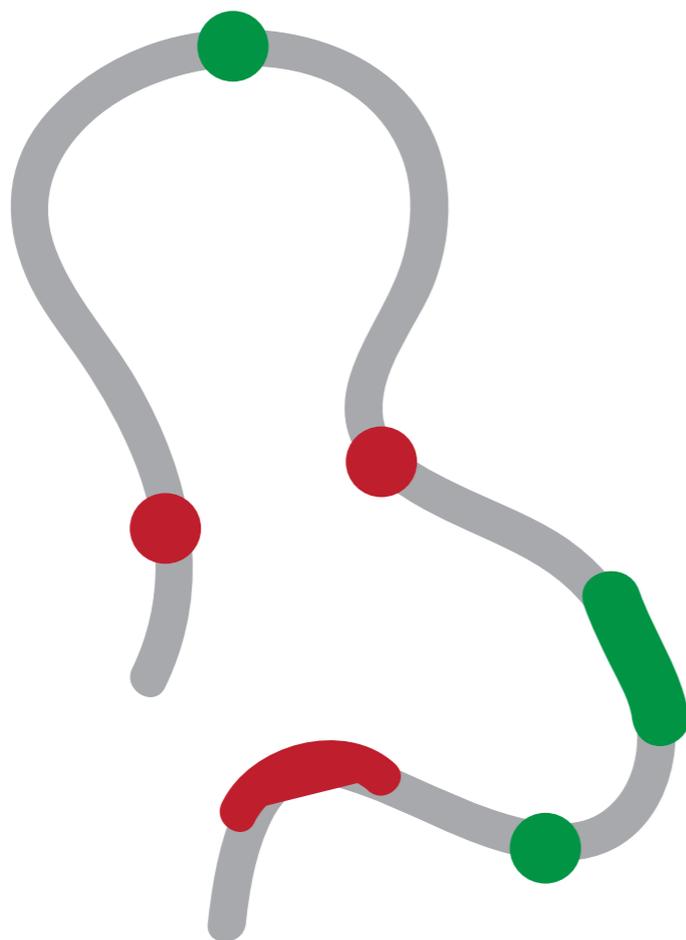
***MedPerCan: Pilot project in cancer personalized medicine, Generalitat de Catalunya PERIS 2017, PI: Elias Campo, IDIBAPS.***

***URDCat: Large scale Personalized Medicine Project on undiagnosed neurologic rare disorders, Generalitat de Catalunya, PERIS 2017, PI: L Pérez-Jurado, IMIM***

***GCAT: Genomes for Life, A Prospective Study of the Genomes of Catalonia, Ministerio de Sanidad y Departament de Salut de la Generalitat de Catalunya, PI: R de Cid, IGTP***

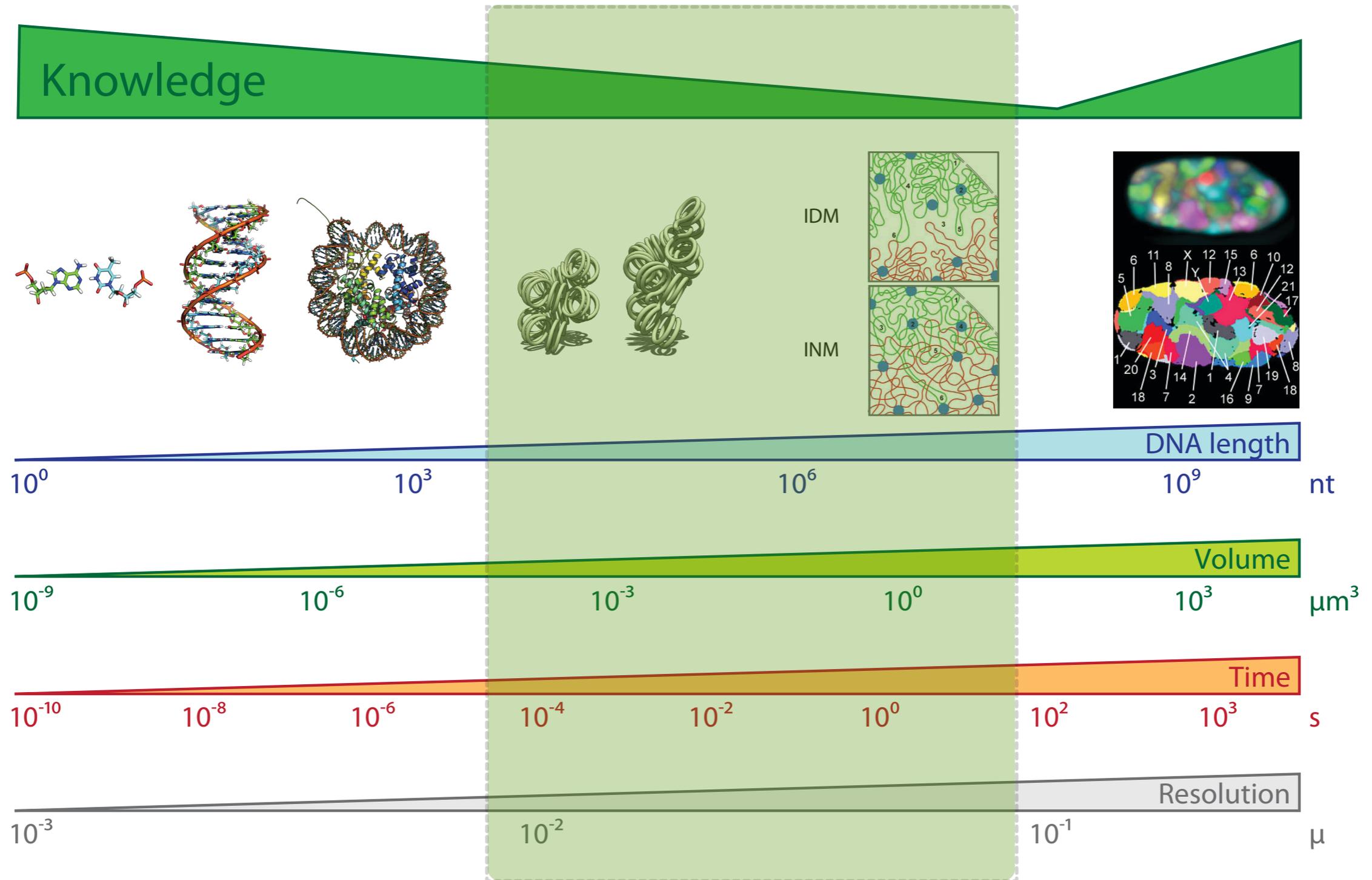






# Resolution Gap

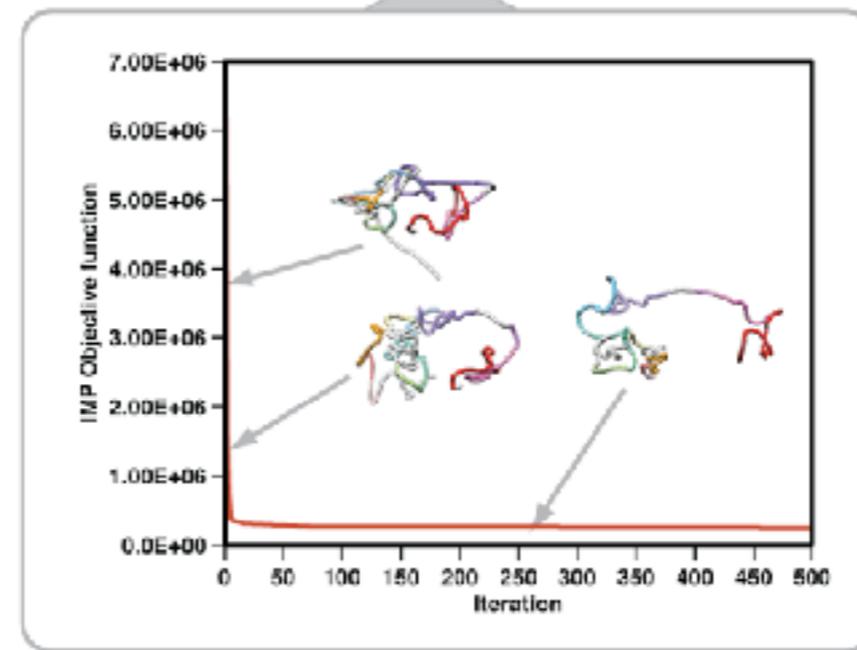
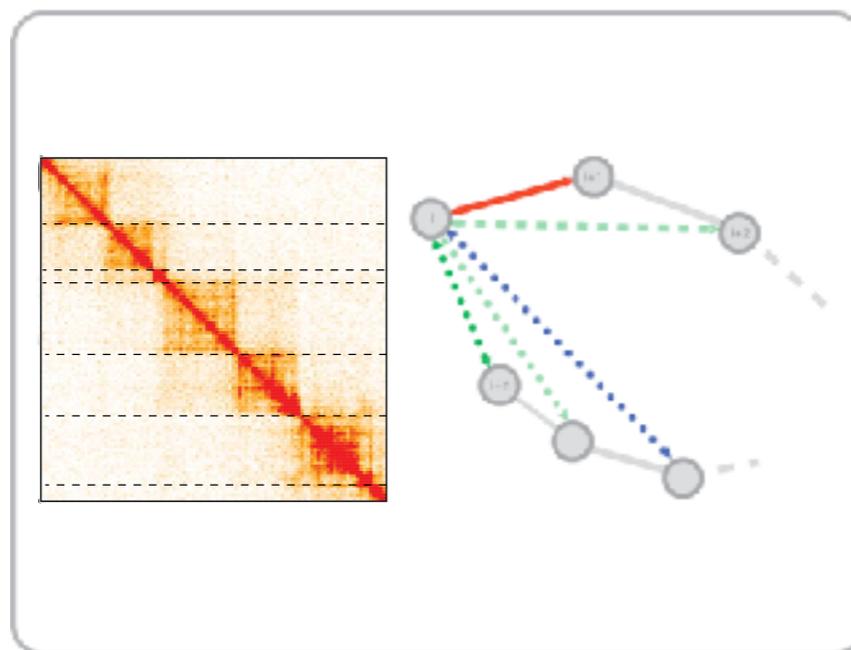
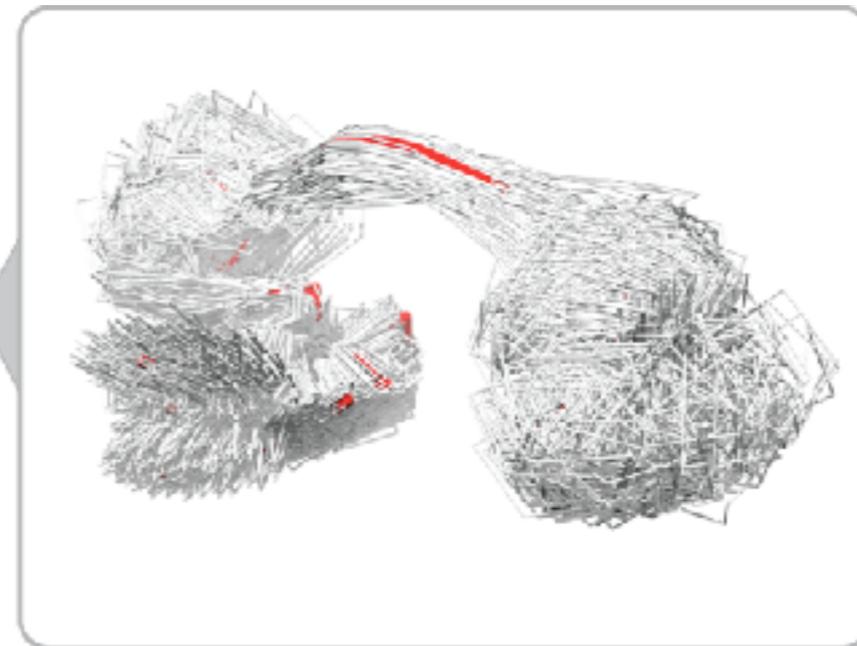
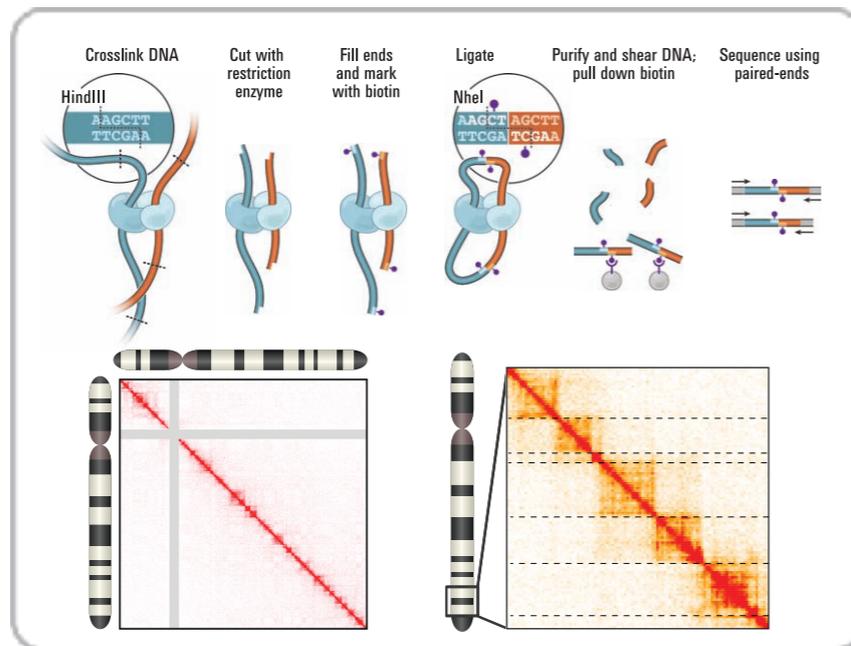
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol 7, e1002125 (2011)



# Hybrid Method

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

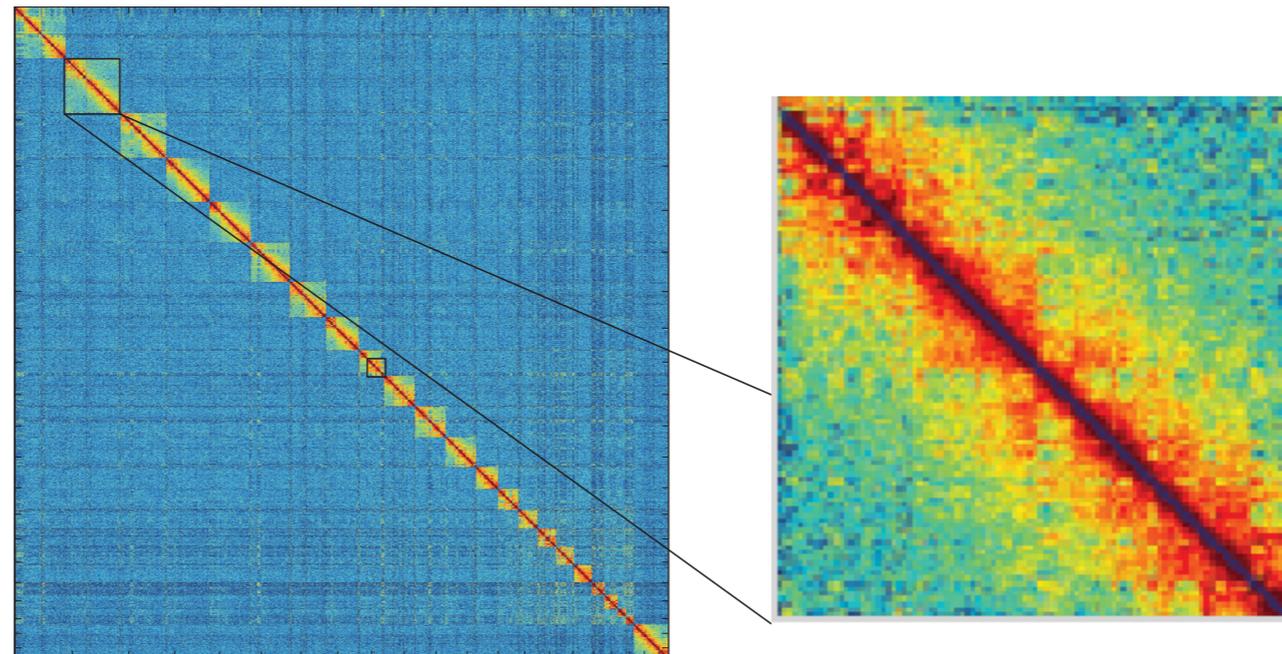
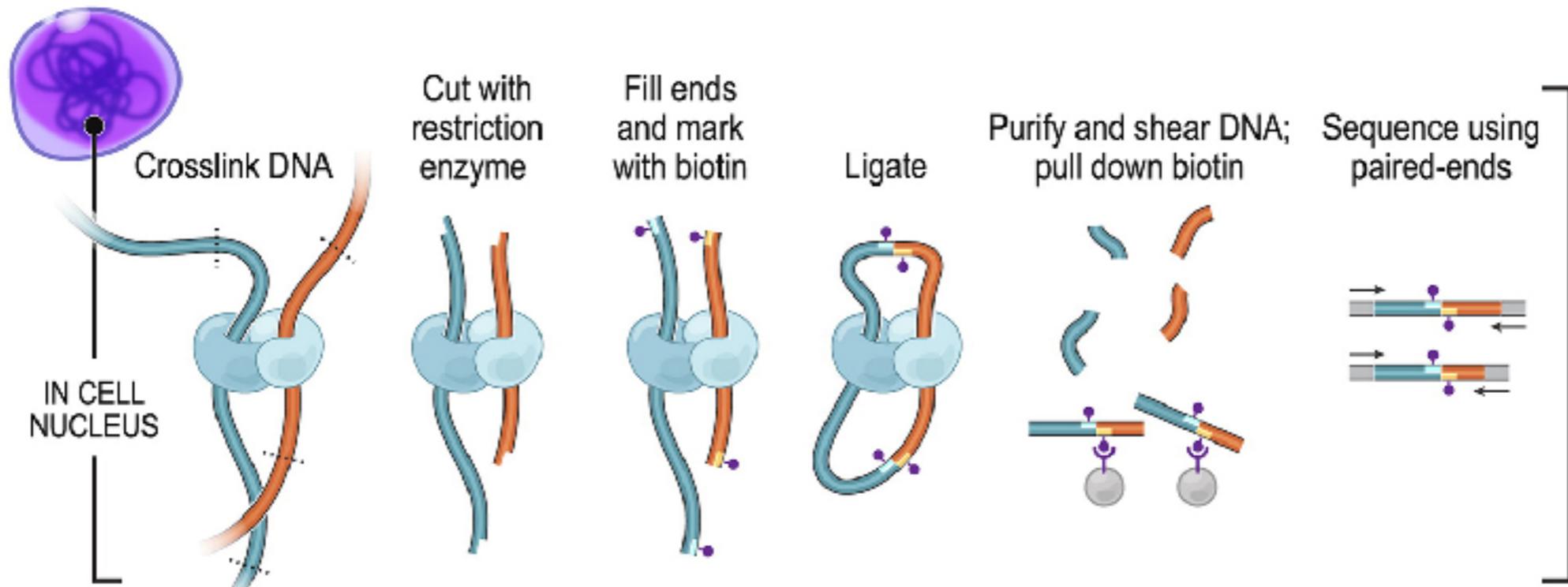
## Experiments



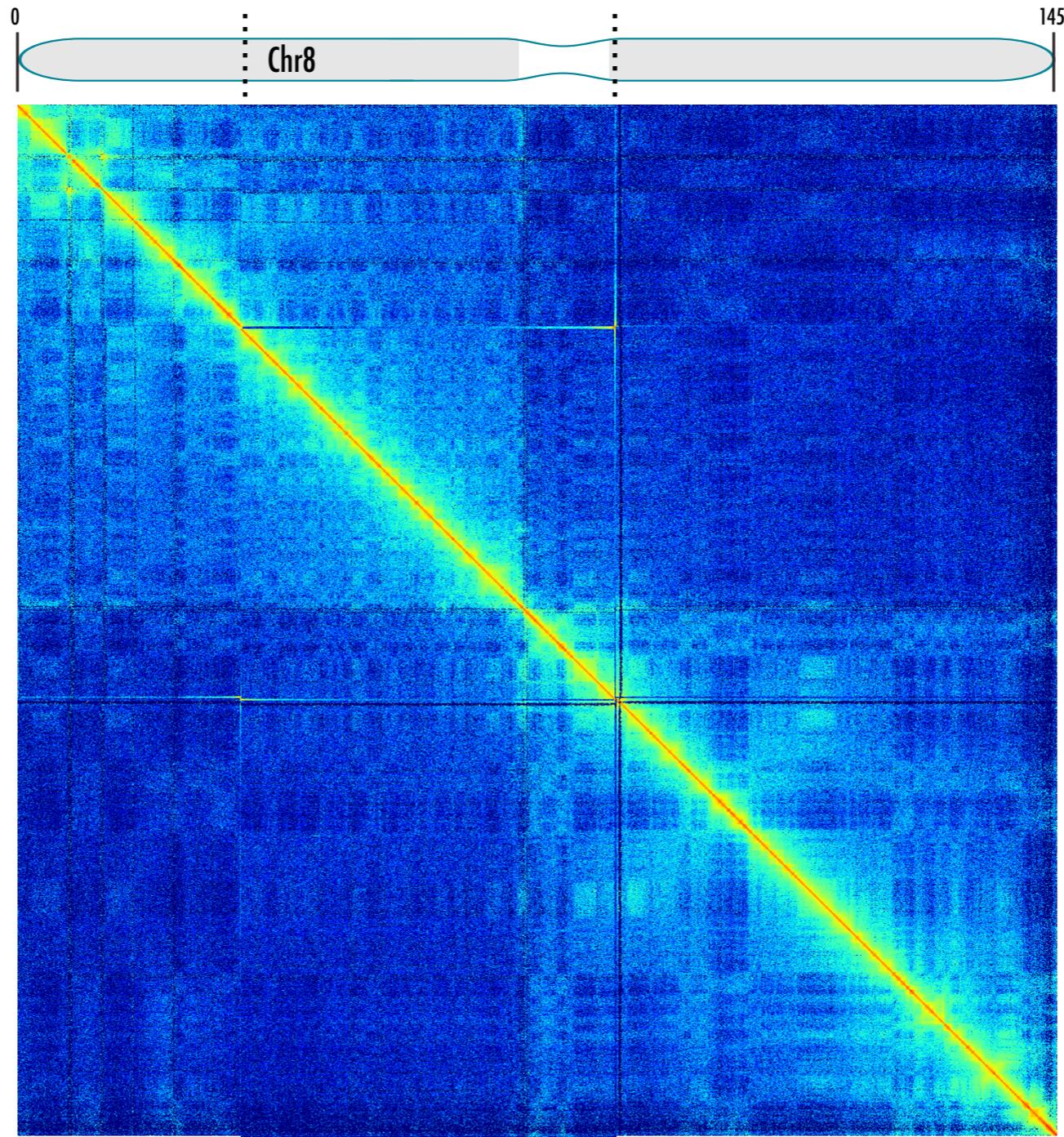
## Computation

# 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.

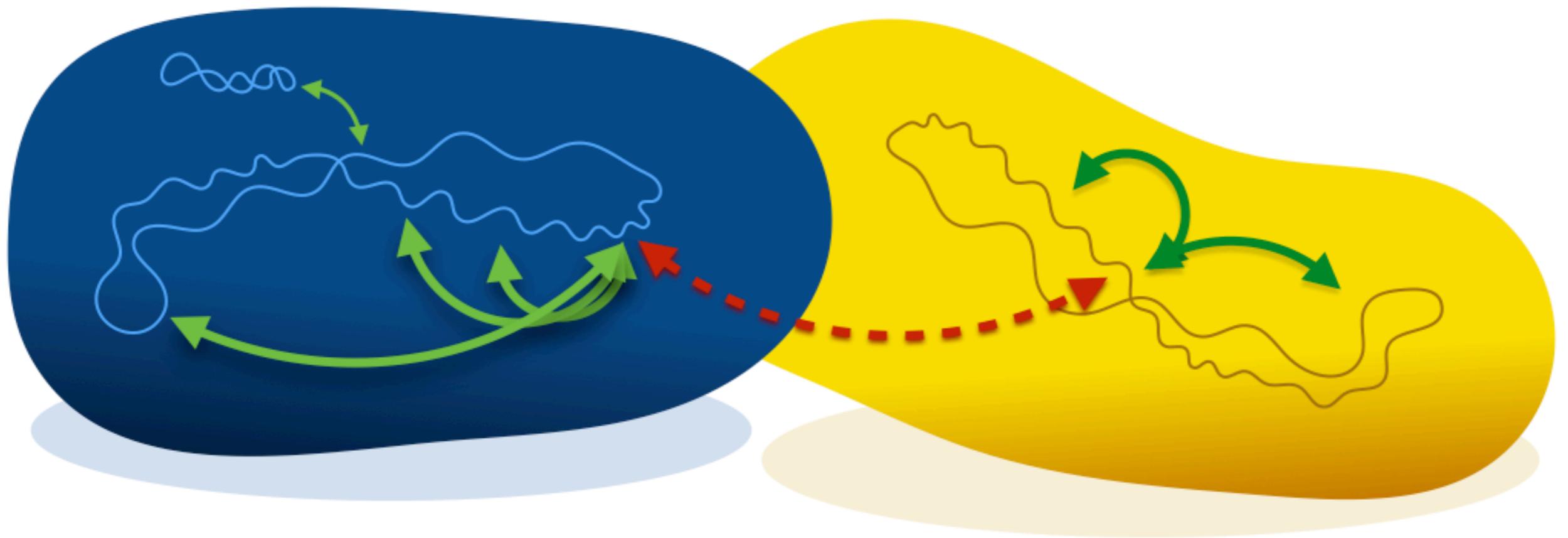


# Chromosome Conformation Capture for genome assembly



Chromosome 8 Gorilla

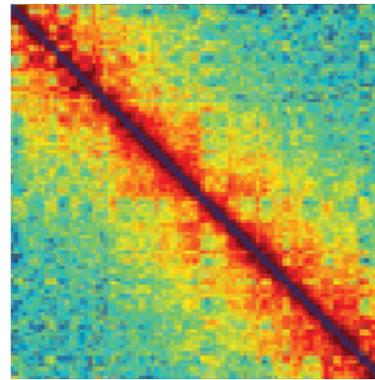
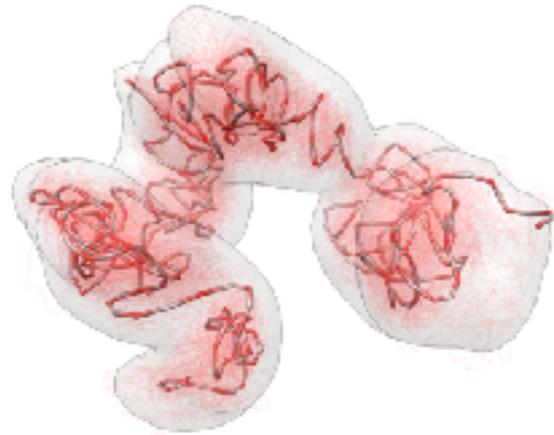
# Chromosome Conformation Capture for meta genomics



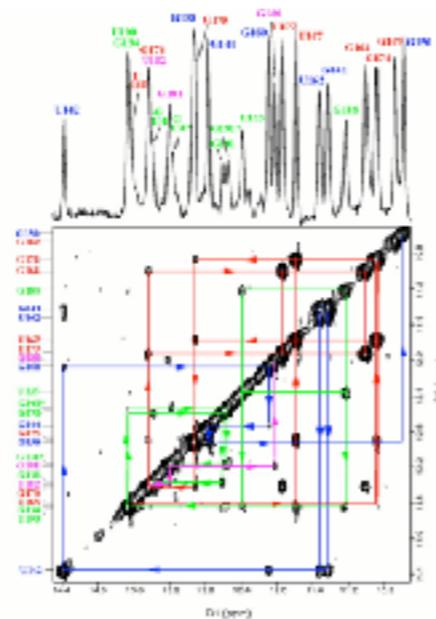
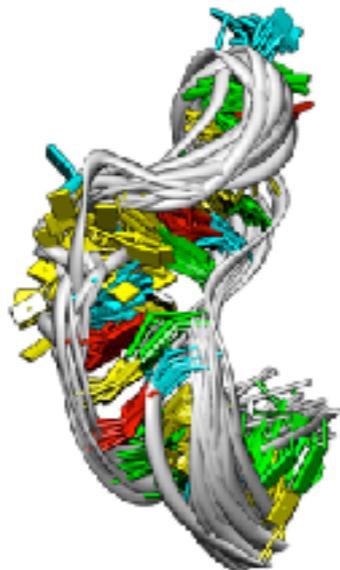
Beitel, C. W., Froenicke, L., Lang, J. M., Korf, I. F., Micheltore, R. W., Eisen, J. A., & Darling, A. E. (2014). Strain- and plasmid-level deconvolution of a synthetic metagenome by sequencing proximity ligation products. doi:10.7287/peerj.preprints.260v1

# Restraint-based Modeling

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



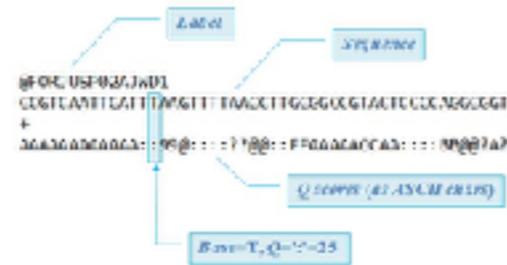
Chromosome structure determination  
3C-based data



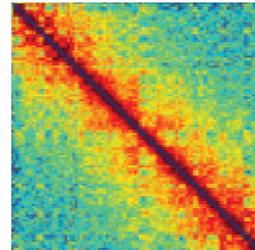
Biomolecular structure determination  
2D-NOESY data



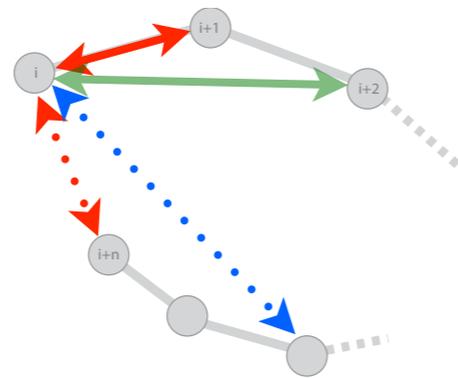
<http://3DGenomes.org>



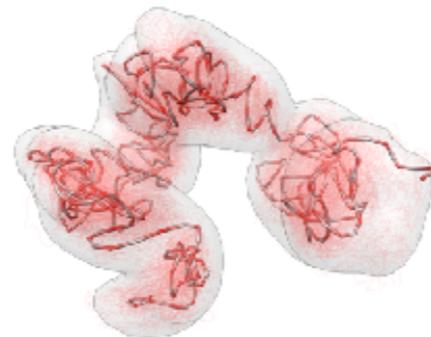
FastQ files to Maps



Map analysis



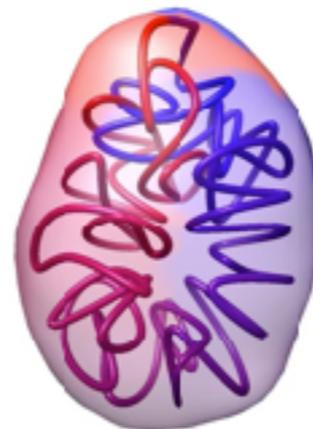
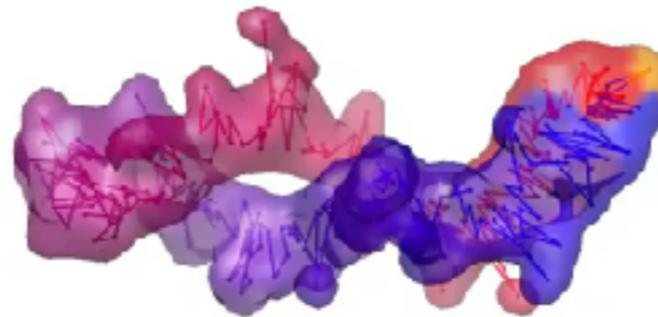
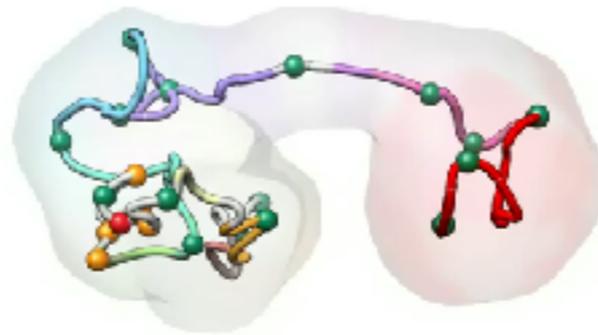
Model building



Model analysis

# TADbit previous applications...

Baù, D. et al. Nat Struct Mol Biol (2011)  
Umbarger, M. A. et al. Mol Cell (2011)  
Le Dily, F. et al. Genes & Dev (2014)  
Trussart M. et al. Nature Communication (2017)  
Cattoni et al. Nature Communication (2017)  
Stadhouders R. et al. Nature Genetics (2017) in press



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