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Using chromosome conformation capture to assemble genomes to perfection

Nadège Guiglielmoni, Antoine Limasset, Romain Koszul, Jean-François Flot

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Our goal

Using chromosome conformation capture

= information on DNA 3D structure

To assemble genomes

= obtain less fragmented genomes

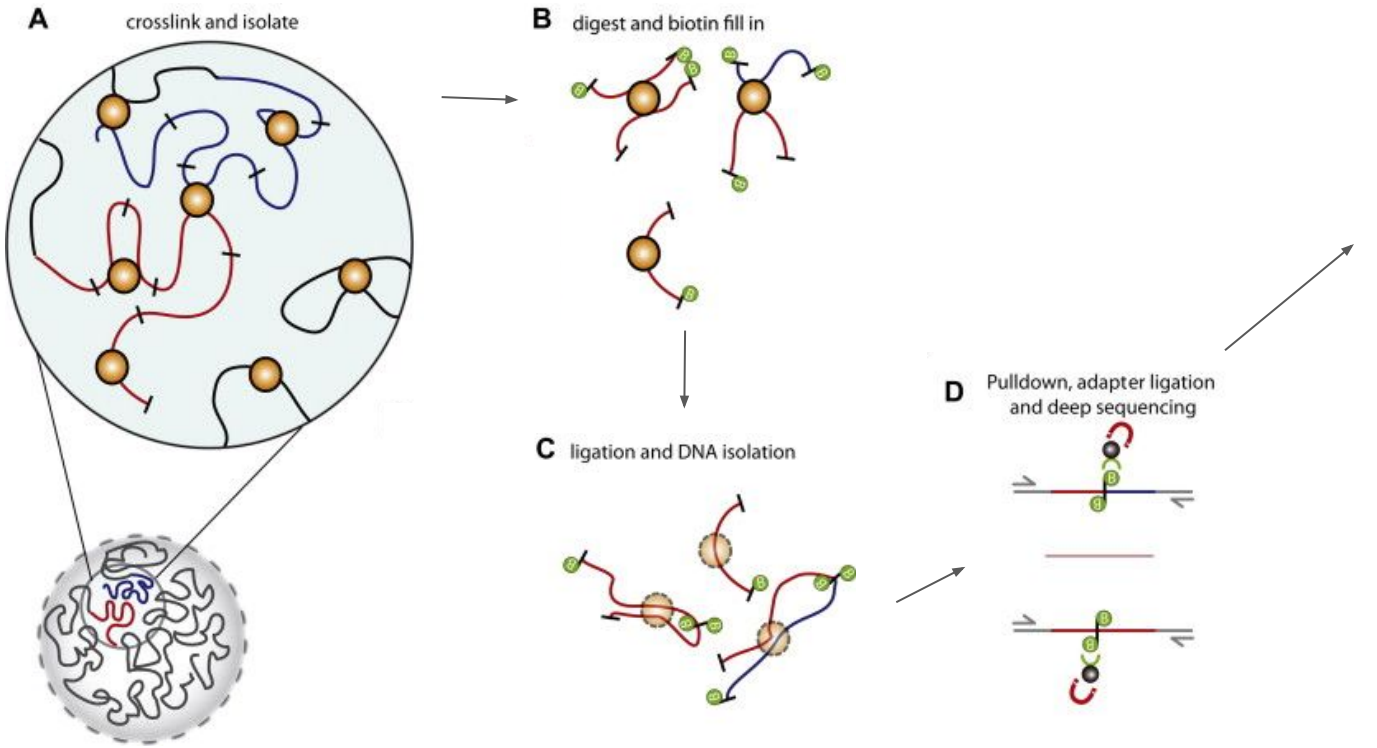
= phase haplotypes

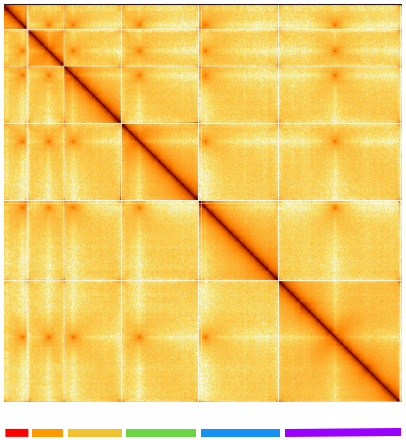
What is chromosome conformation capture ?

Chromosome Conformation Capture (3C)
Technique to study DNA 3D structure
Published in 2002 by Job Dekker
⟶ Hi-C : whole genome contacts (2009)

Capturing chromosome conformation. Dekker et al., 2002
Comprehensive mapping of long-range interactions reveals folding principles of the human genome.Lieberman-Aiden et al., 2009
Exploring the three-dimensional organization of genomes: Interpreting chromatin interaction data. Dekker et al., 2013

Chromosome conformation capture technique : Hi-C





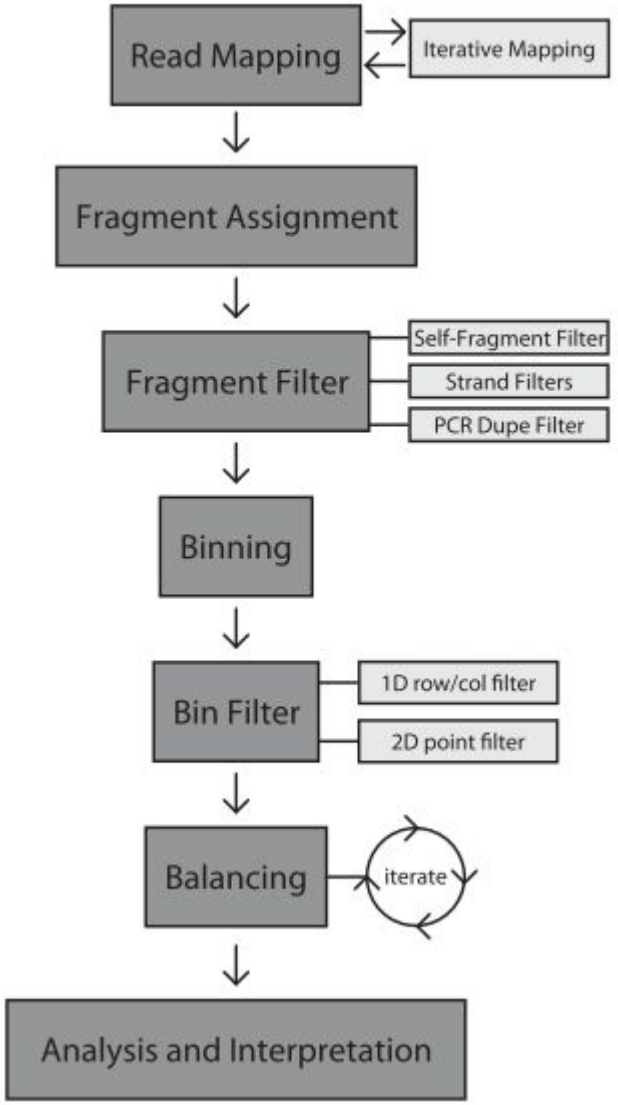
Partial map of
Lachancea cidri

Hi–C: A comprehensive technique to capture the conformation of genomes. Belton et al., 2012

Data processing

Steps :

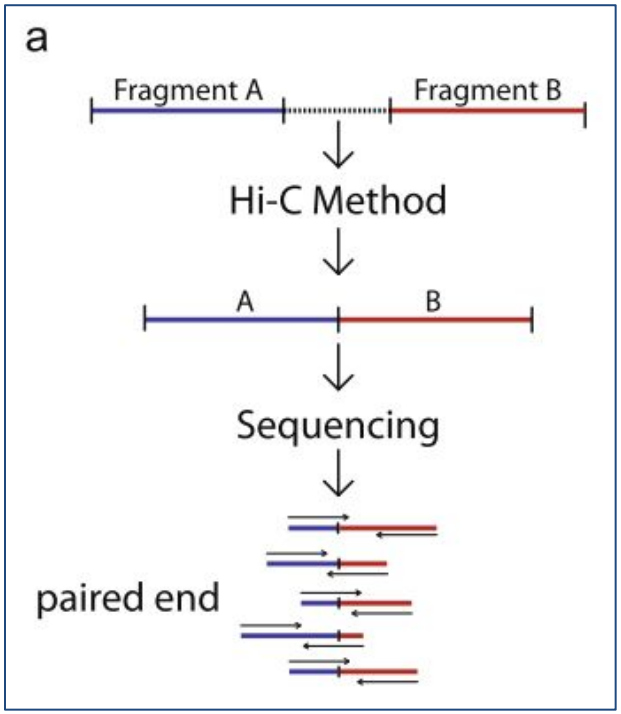
- ➔ Map reads on the genome
- ➔ Attribute fragments
- ➔ Eliminate non-chimeric reads
- ➔ Bin reads and build a map
- ➔ Normalize maps



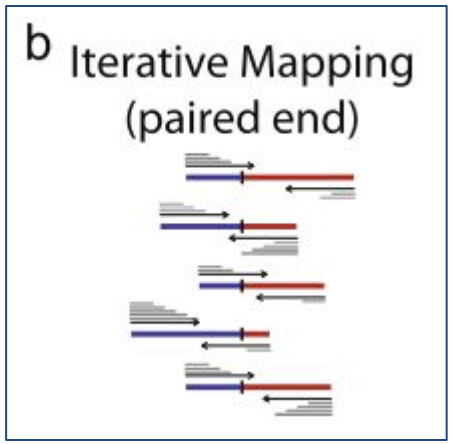
The Hitchhiker's guide to Hi-C analysis: Practical guidelines. Lajoie et al., 2015

Data processing

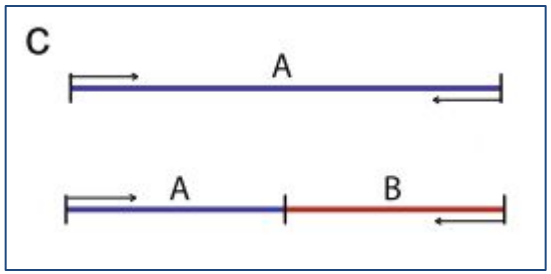
Raw data



Mapping

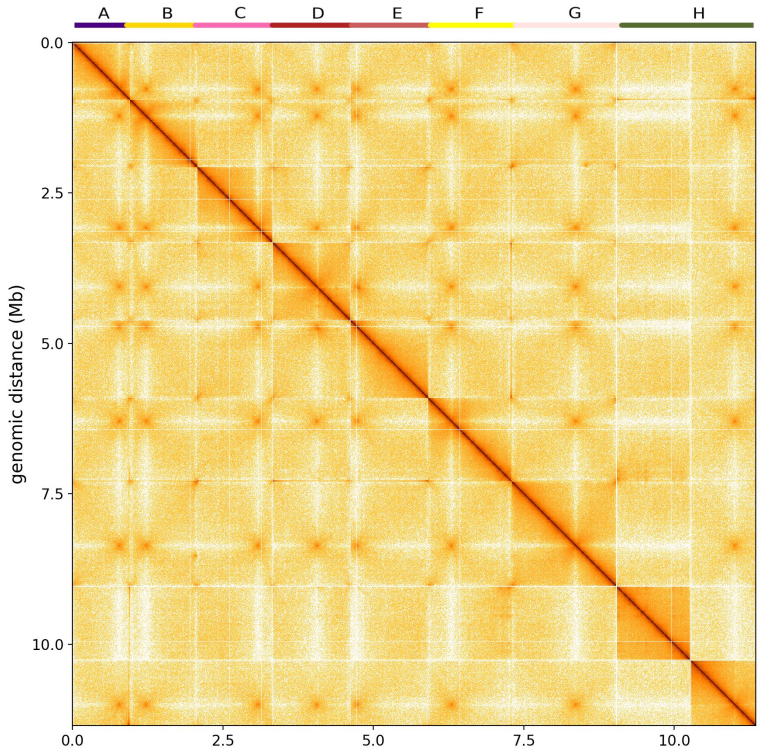


Filtering



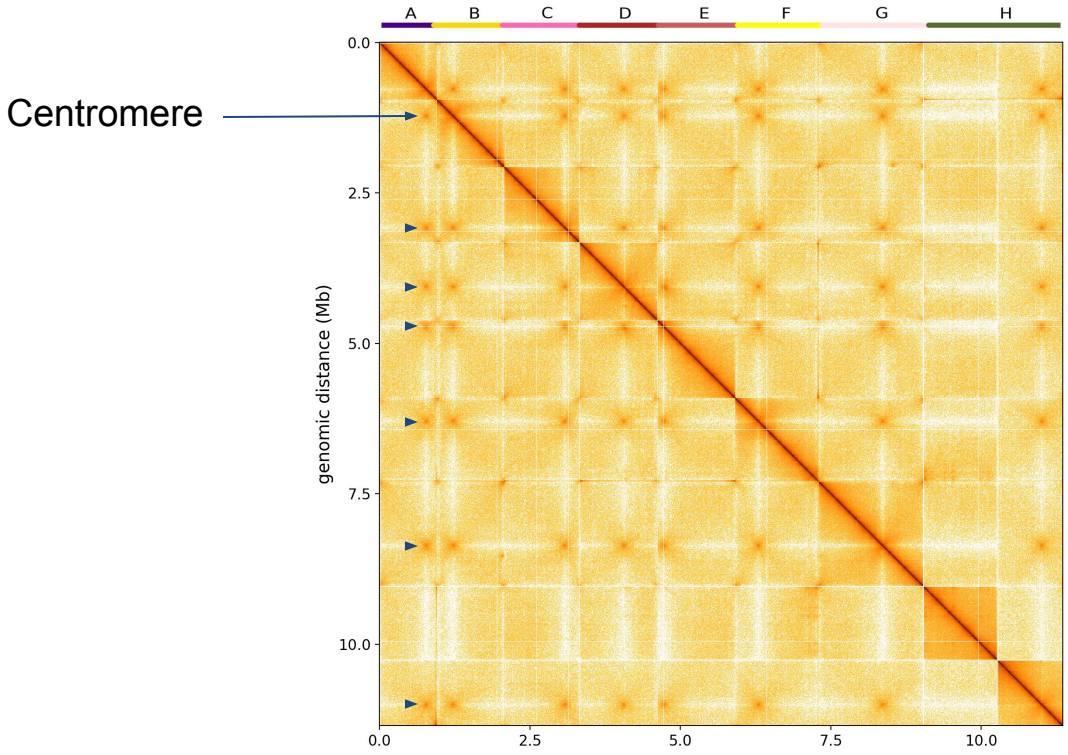
The Hitchhiker's guide to Hi-C analysis: Practical guidelines. Lajoie et al., 2015

Data processing : contact map



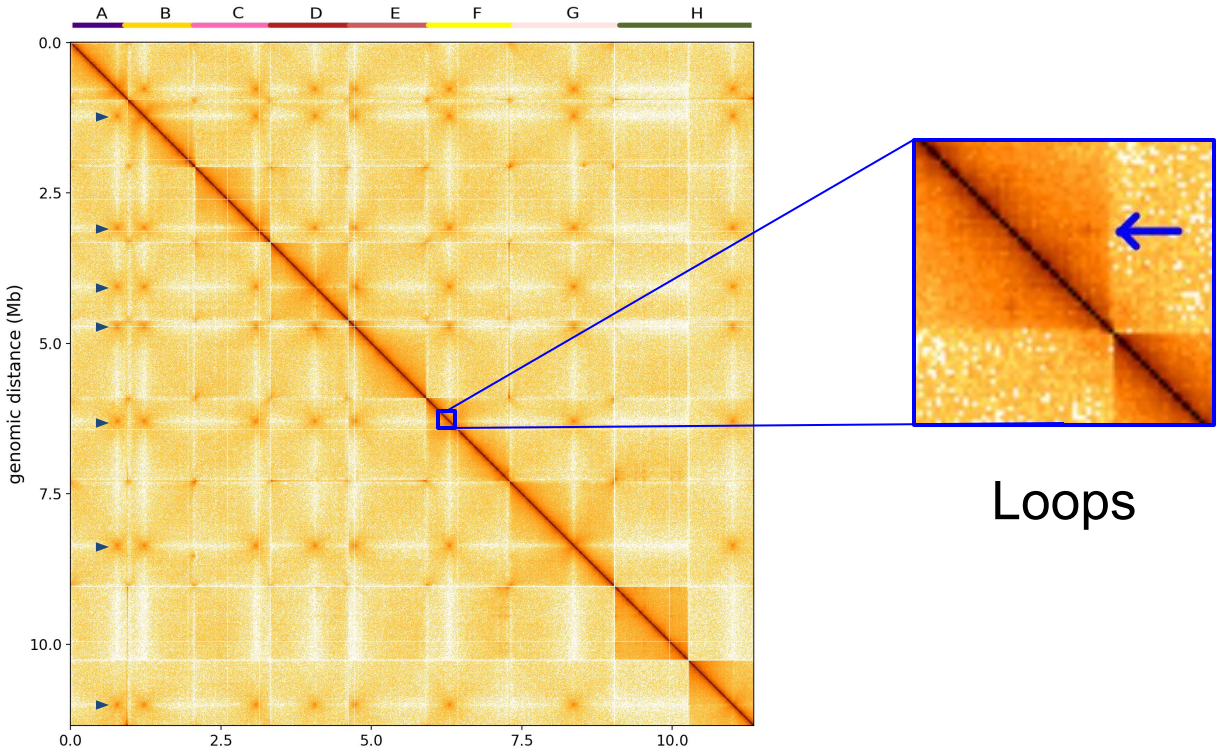
Yeast : *Lachancea kluyveri*

Data processing : contact map



Yeast : *Lachancea kluyveri*

Data processing : contact map



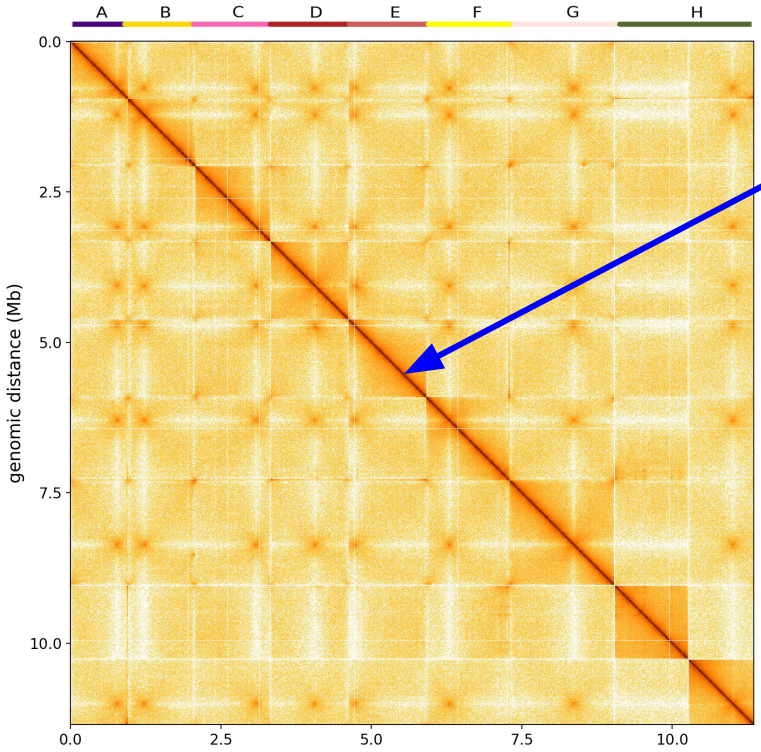
Loops

Yeast : Lachancea kluyveri

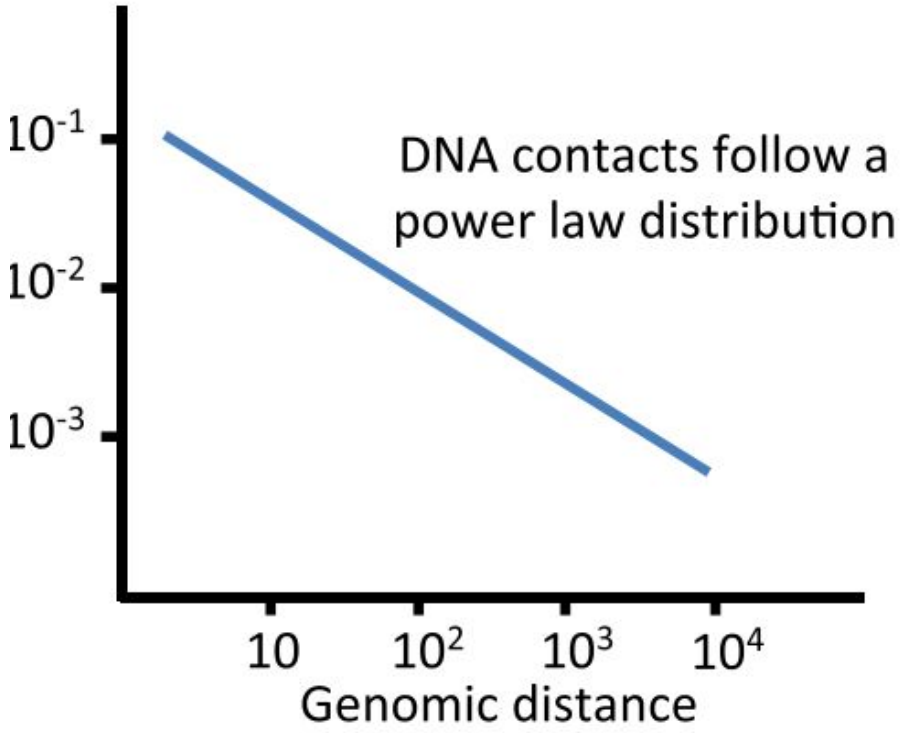
How can chromosome conformation capture data assist in genome assembly ?

➔ DNA 3D structure is linked to 1D structure

Genomic distance law



contact frequency = f(genomic distance)



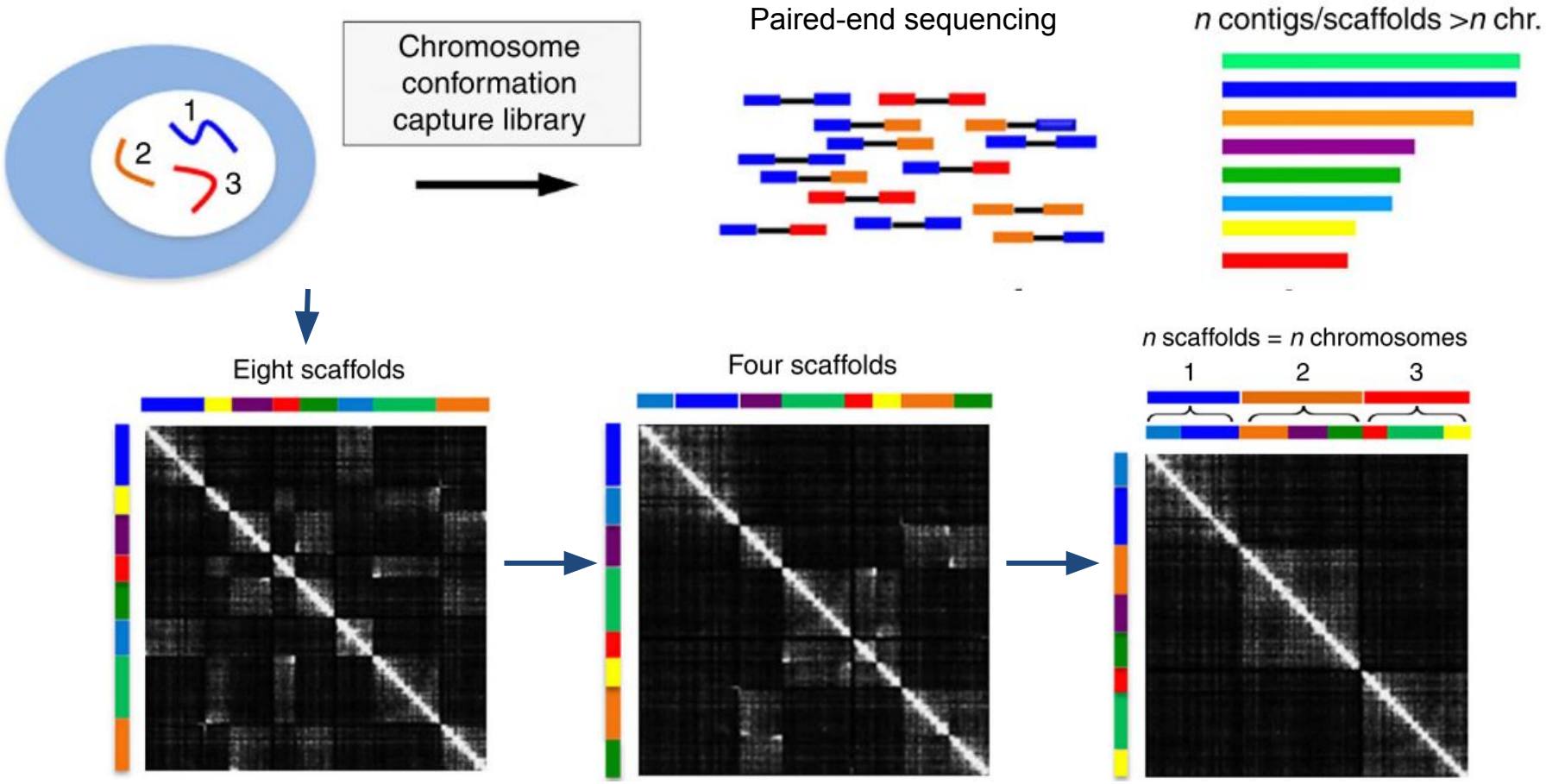
Contact genomics: scaffolding and phasing (meta)genomes using chromosome 3D physical signatures. Flot et al., 2015

Chromosome conformation capture in assembly

Tools to scaffold assemblies or reassemble with Hi-C data :

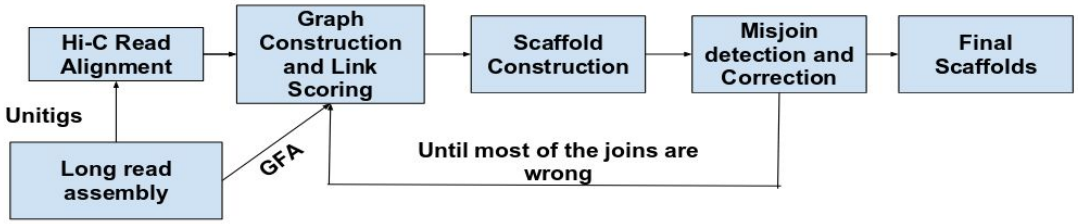
- GRAAL - instaGRAAL : reassemble to obtain a more likely genome according to contact data
- SALSA2 : scaffold by introducing Hi-C links in assembly graphs
- 3D-DNA, Lachesis...

GRAAL principle



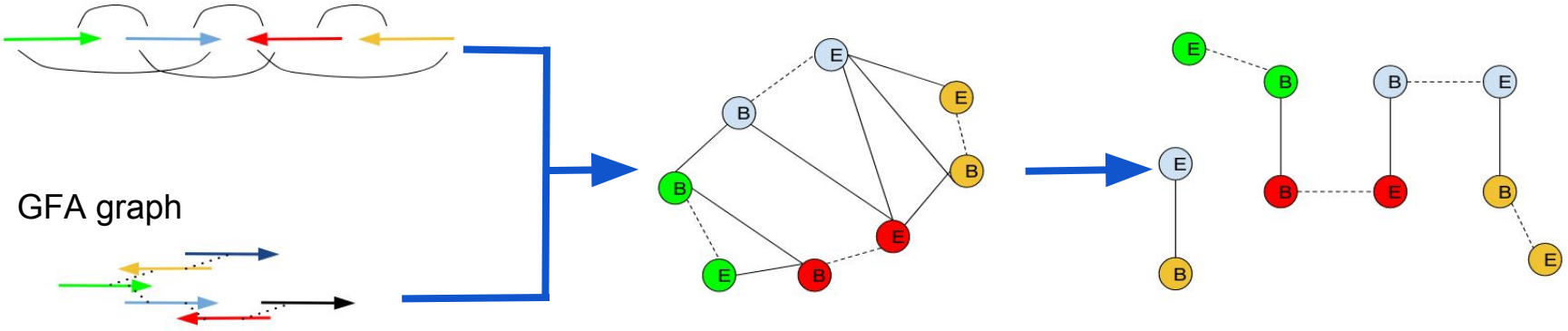
High-quality genome (re)assembly using chromosomal contact data. Marie-Nelly et al., 2014

SALSA2 principle



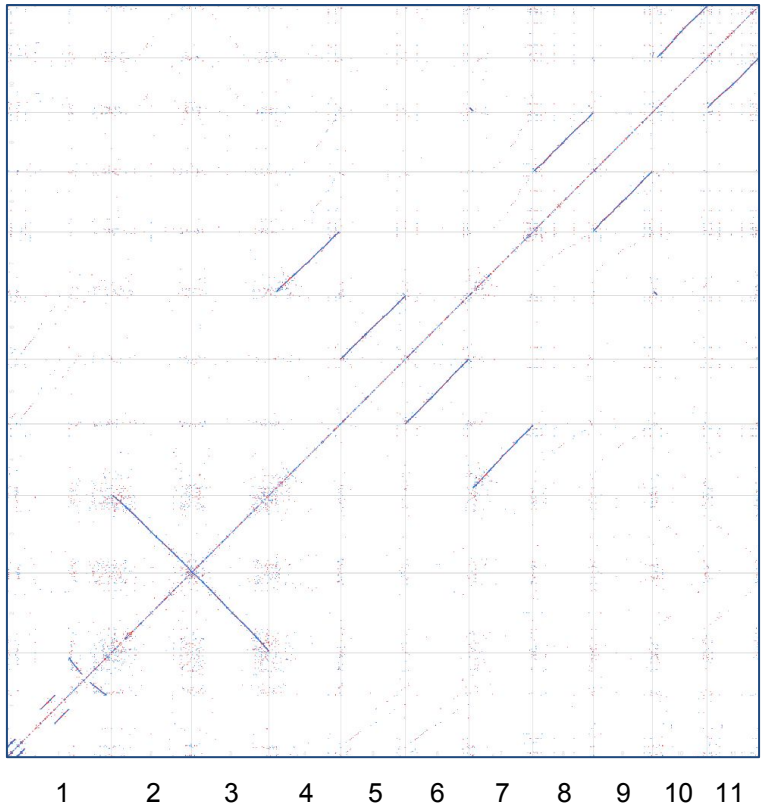
Hi-C data

GFA graph

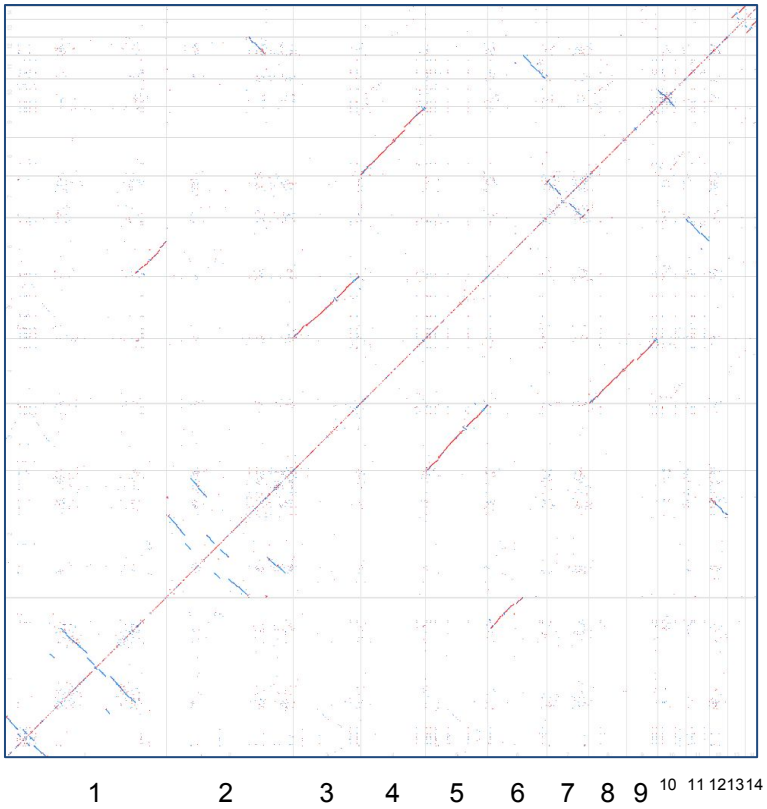


Integrating Hi-C links with assembly graphs for chromosome-scale assembly. Ghurye et al., 2018

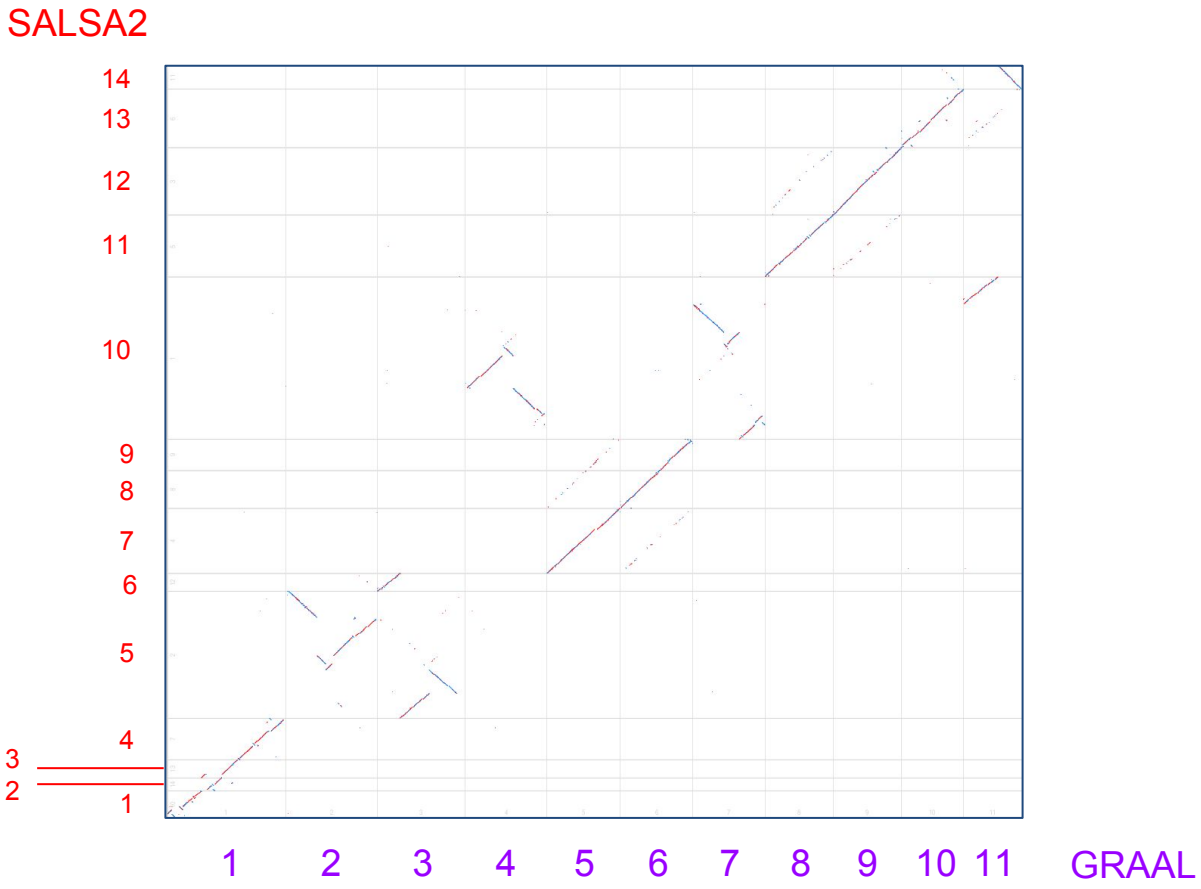
GRAAL reassembly of *Adineta vaga*



SALSA2 scaffolding of *Adineta vaga*



GRAAL vs SALSA2



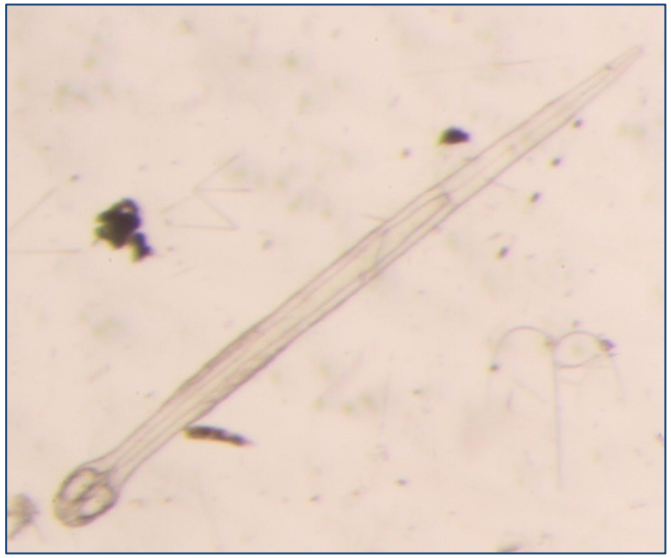
Our project

- Make a tool for genome scaffolding using 3C/Hi-C data

- Test our strategy by generating Hi-C data and assembling the genome of an organism

→ Chaetognaths

Focus on an organism : Chaetognaths



Also known as “arrow worms”

Currently classified as protostomians

Phylum : Chaetognatha
- Class : Sagittida
  - Orders : Aphragmophora
    Phragmophora
- Class: Spadella

IGNITE Innovative Training Network

Goal : study invertebrate non-model organisms

Motivation : invertebrate organisms represent the majority of animal diversity but remain understudied

Gathers biologists, bioinformaticians, computer scientists…

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Innovative Training Network
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Comparative genomics of non-model invertebrates
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