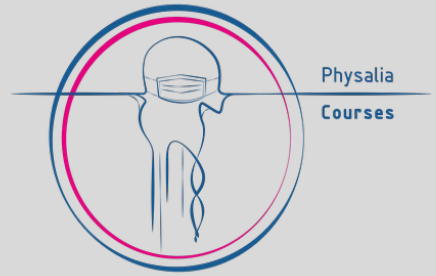
Hi-C processing

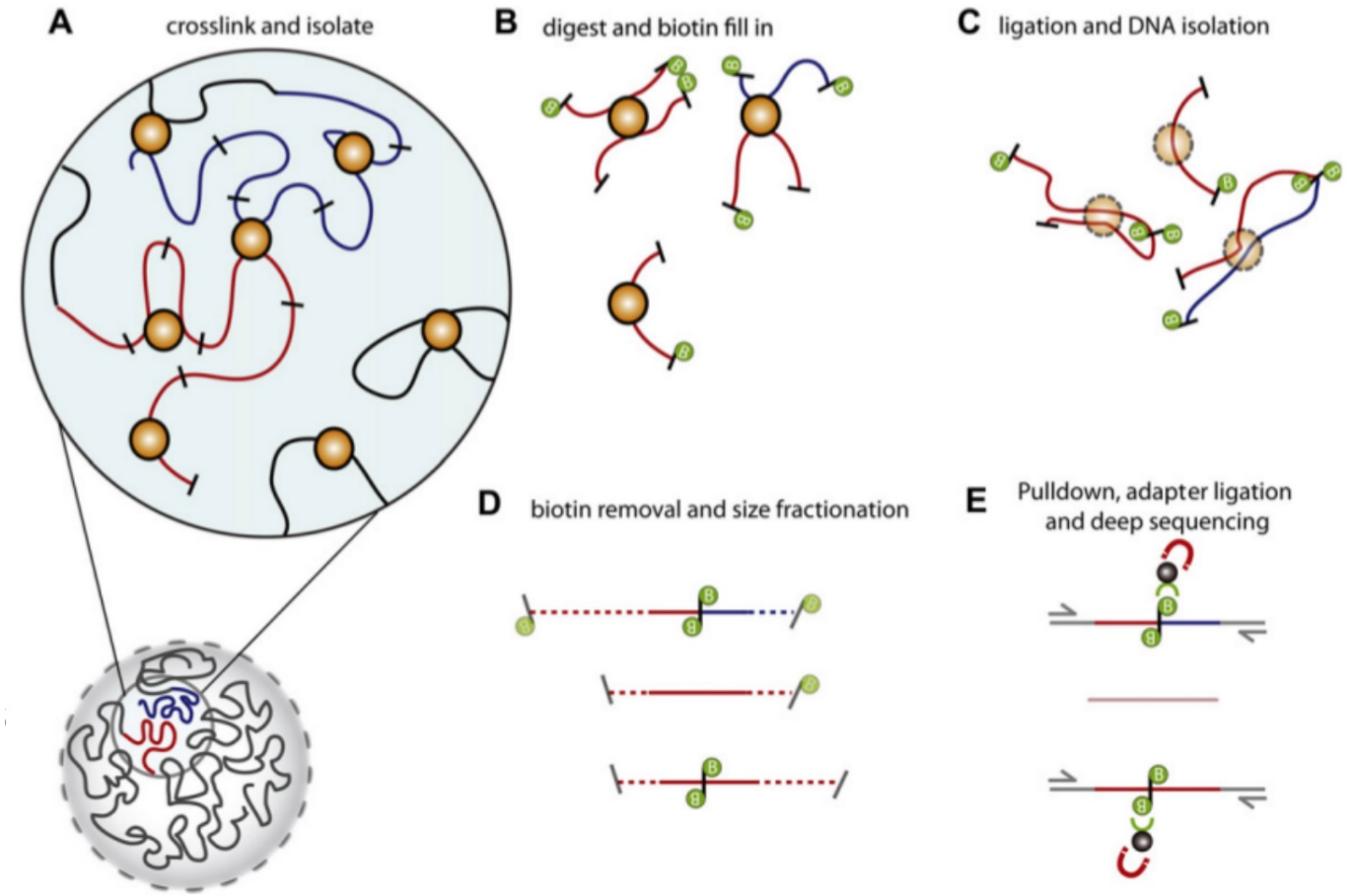
Epigenomics Data Analysis

Jacques Serizay

Physalia 2025

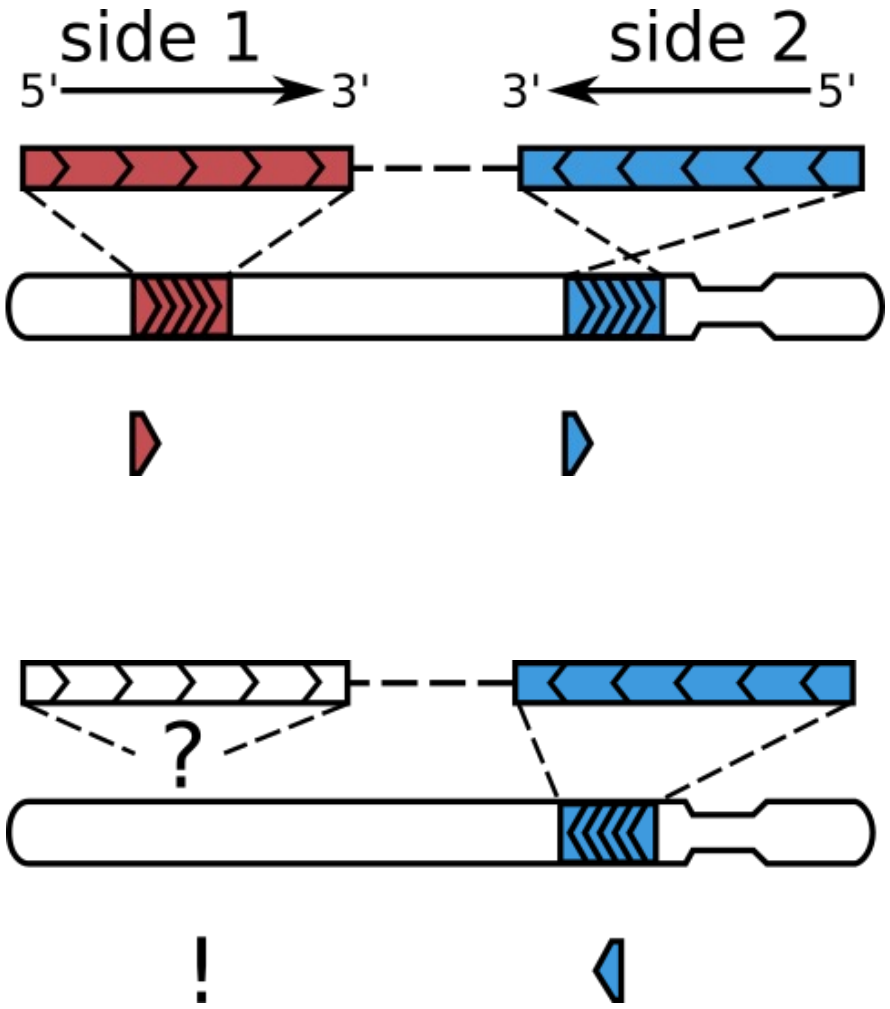


Hi-C experimental workflow



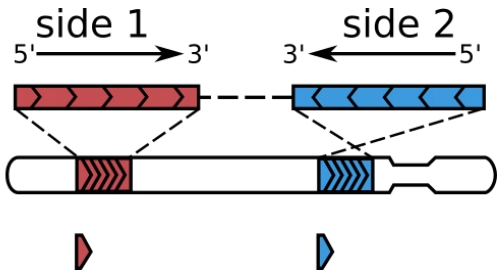
Belton et al., Methods 2012

Hi-C computational workflow



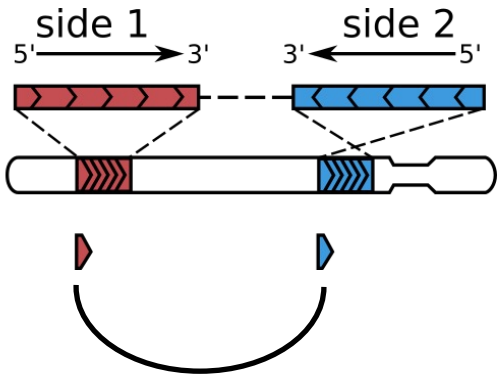
Open2C et al., Biorxiv 2023

Hi-C computational workflow



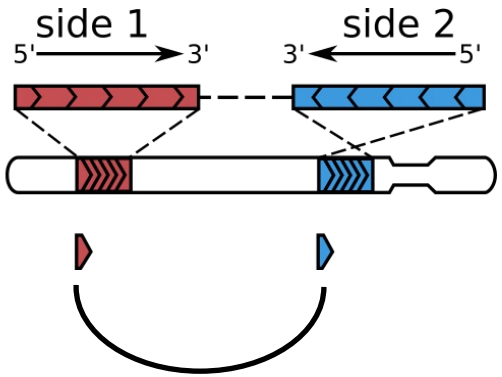
Open2C et al., Biorxiv 2023

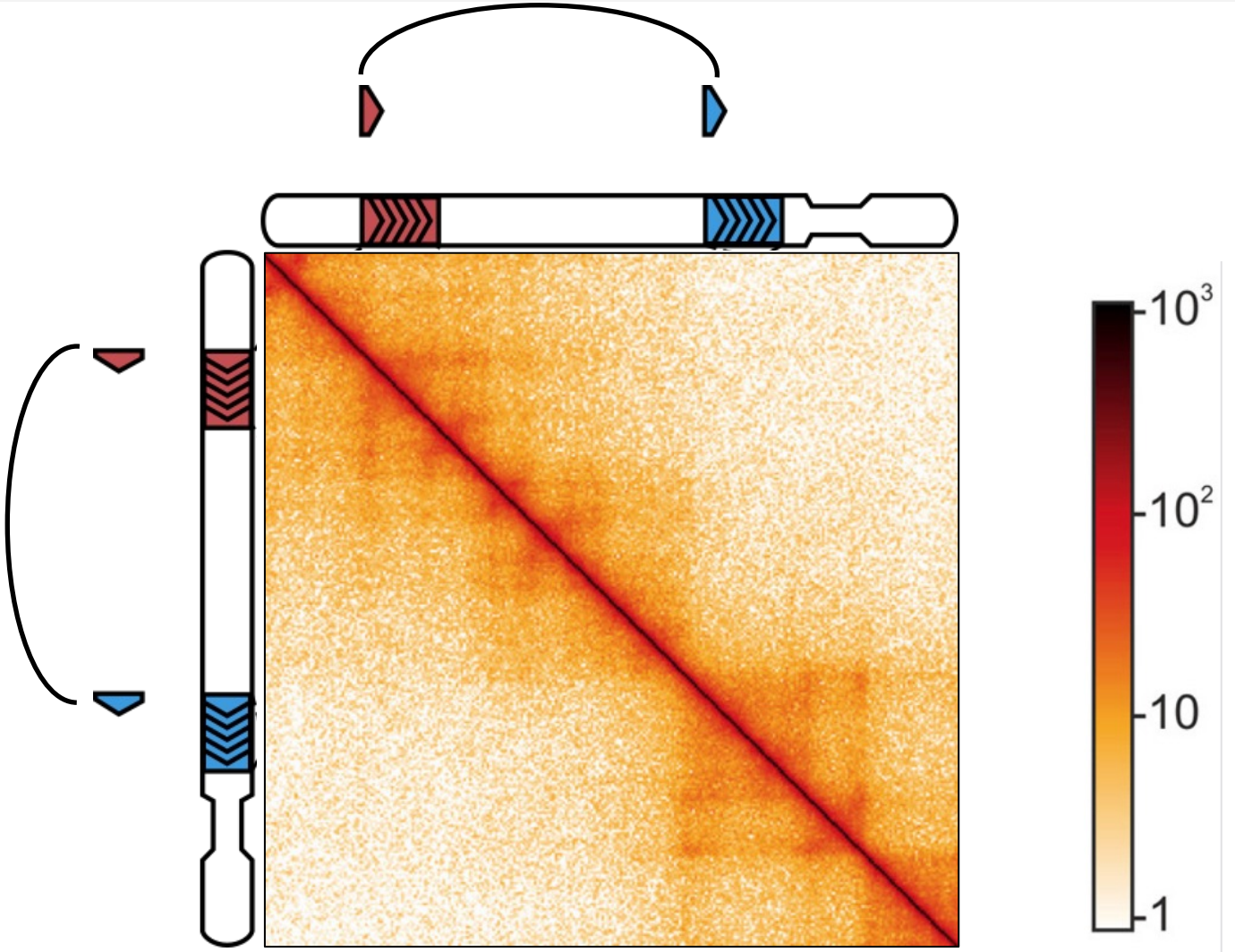
Hi-C computational workflow



Open2C et al., Biorxiv 2023

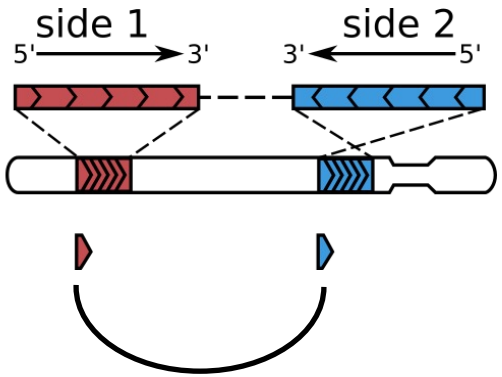
Hi-C computational workflow

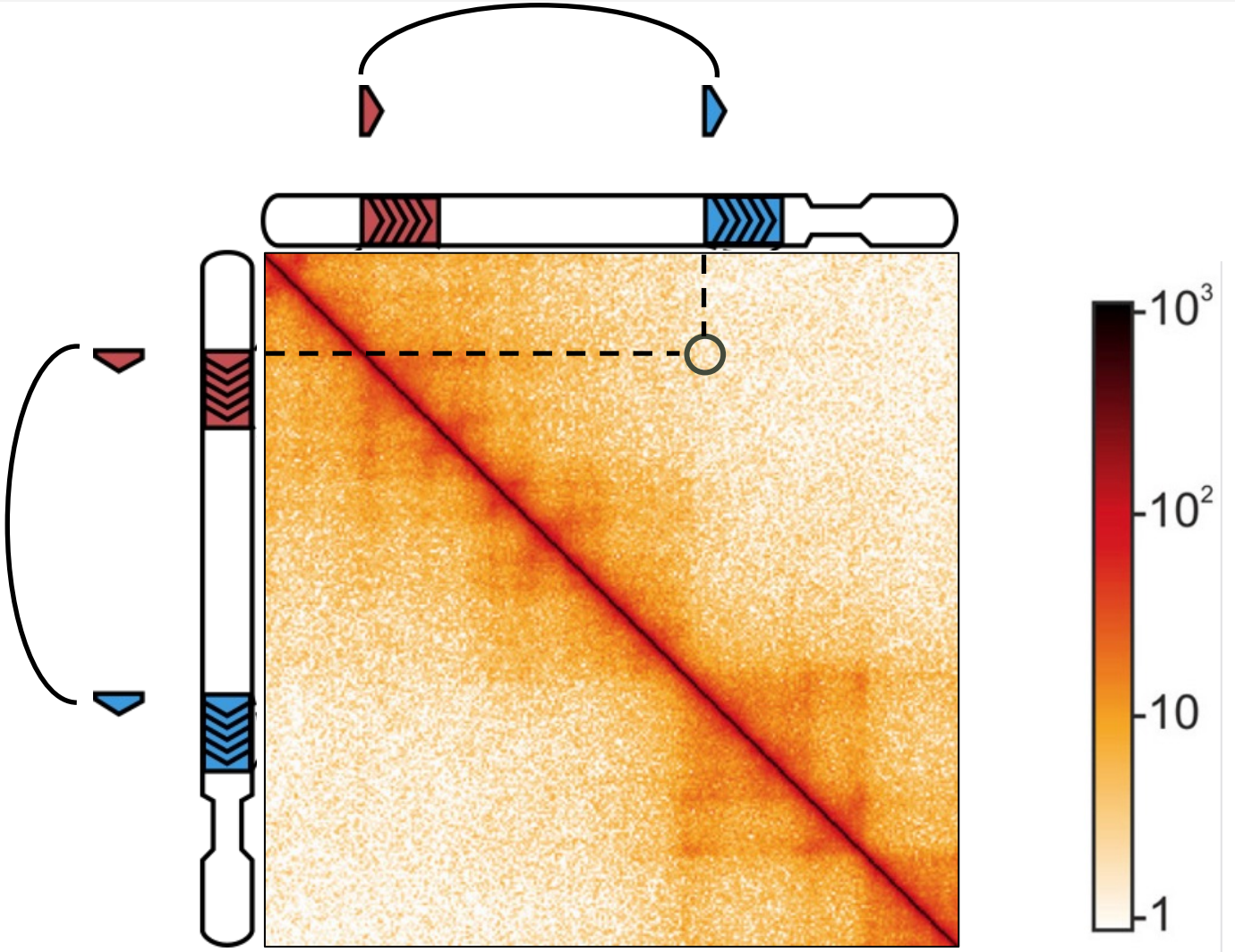




Open2C et al., Biorxiv 2023

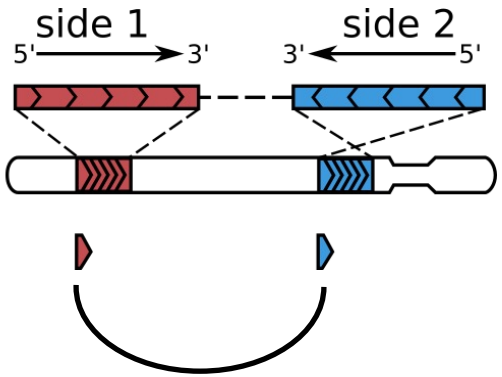
Hi-C computational workflow

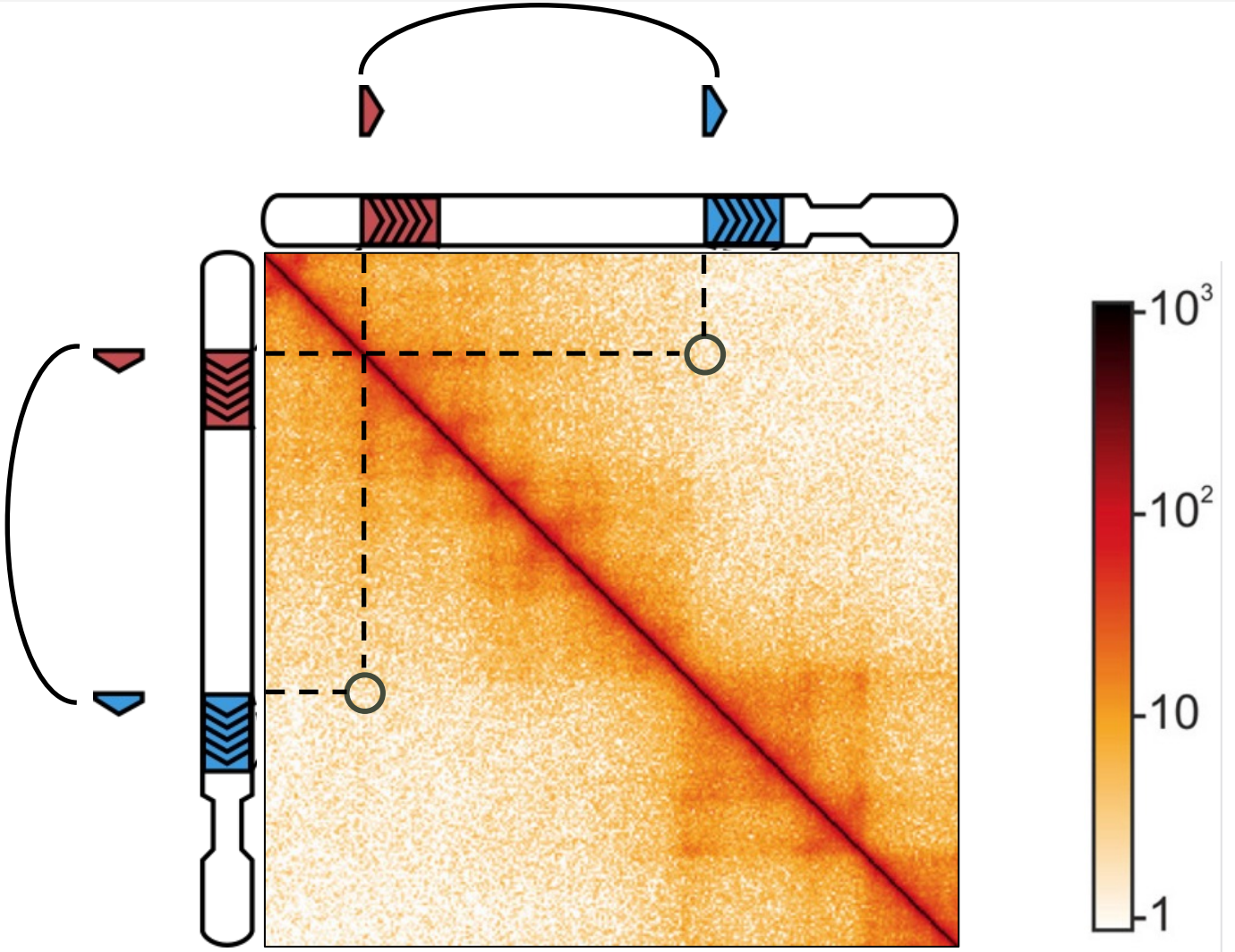




Open2C et al., Biorxiv 2023

Hi-C computational workflow



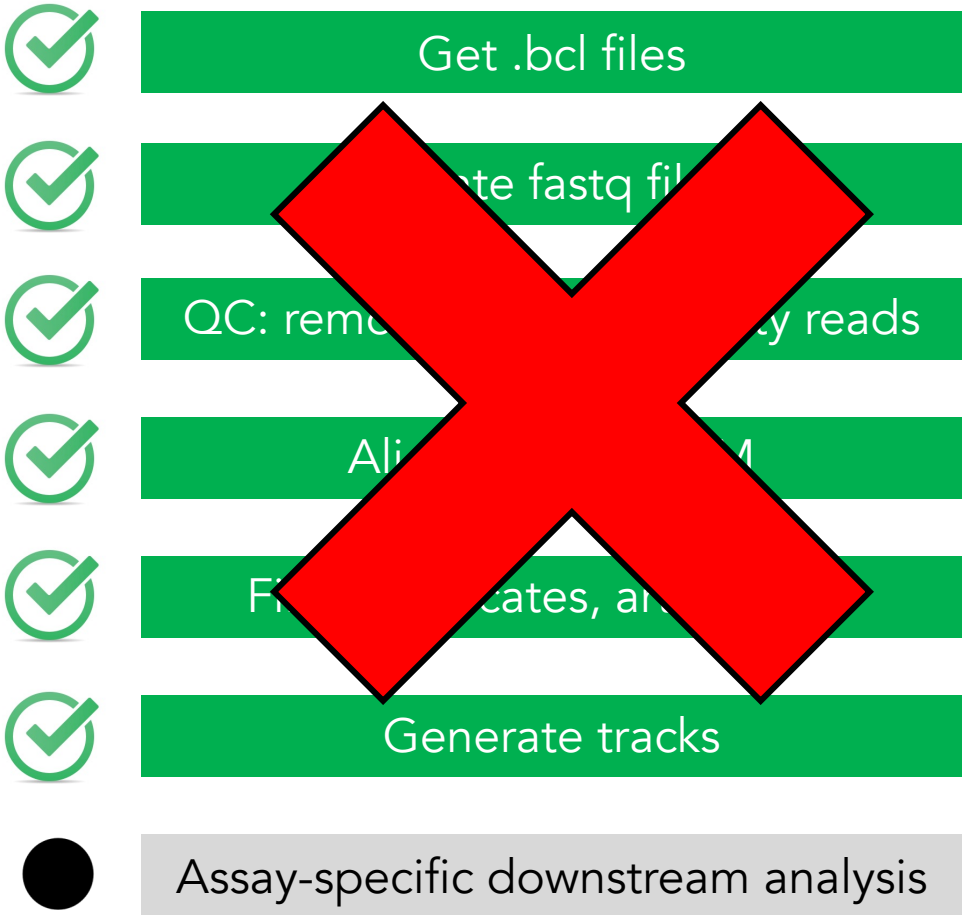


Open2C et al., Biorxiv 2023

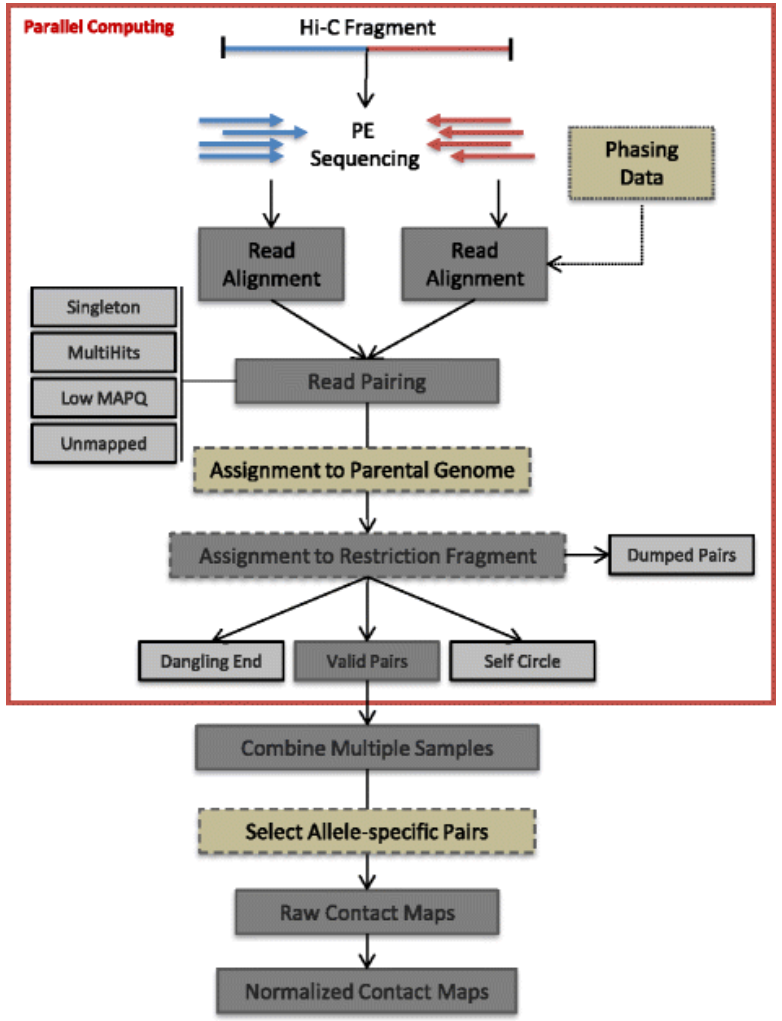
Hi-C pipeline

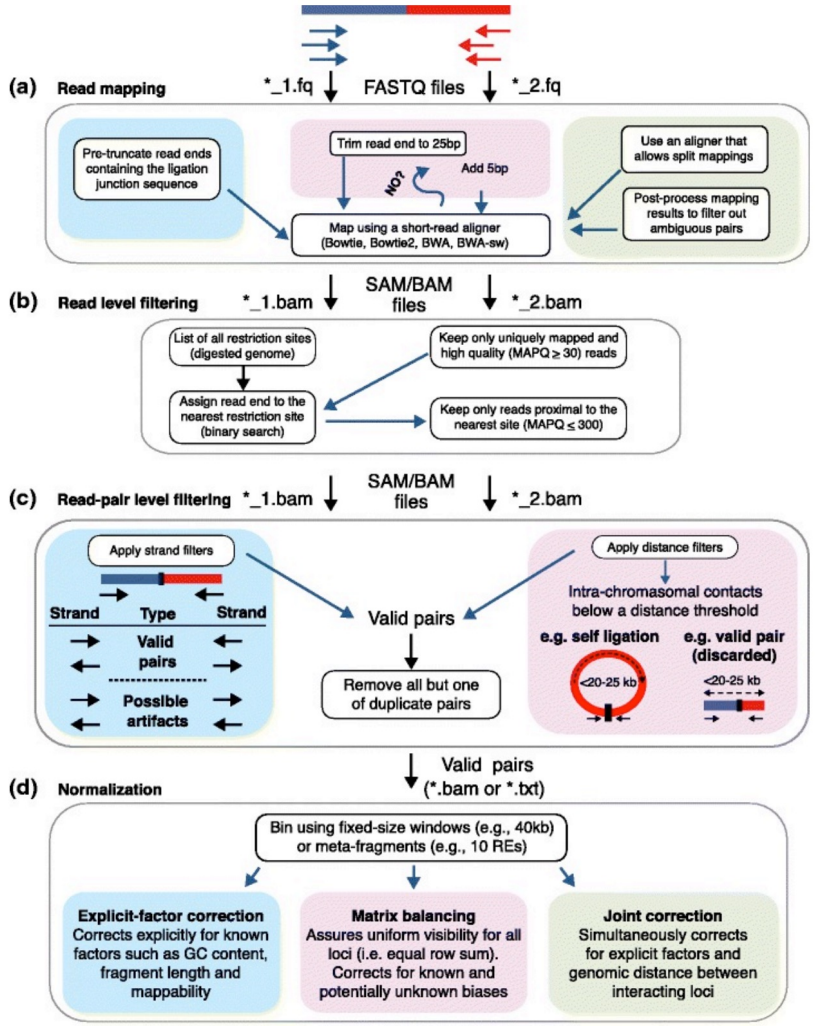
- [x] Get .bcl files
- [x] Create fastq files
- [x] QC: remove/trim low quality reads
- [x] Align fastq to BAM
- [x] Filter duplicates, artifacts, …
- [x] Generate tracks
- [ ] Assay-specific downstream analysis

Hi-C pipeline



Hi-C pipeline(s)





Servant et al., Genome Biol. 2015

Ay & Noble Genome Biol 2015

Hi-C pipeline(s) – 2015

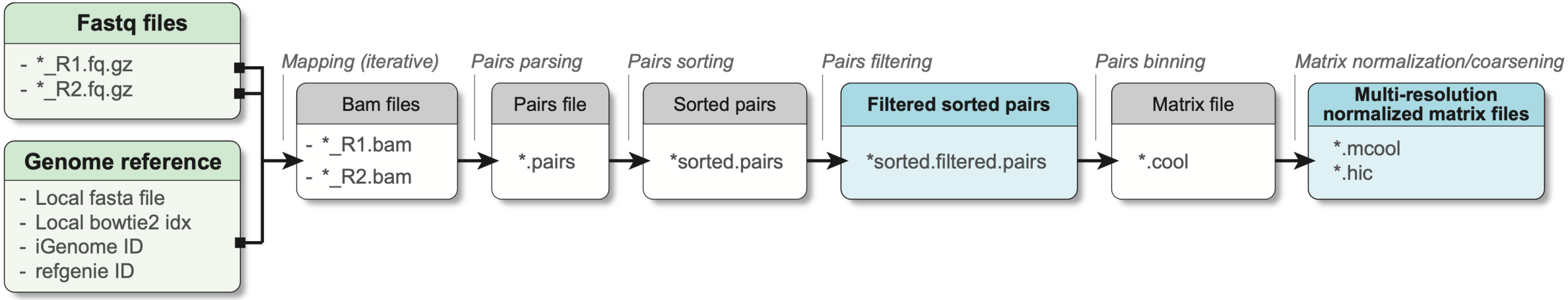
Tool	Short-read aligner(s)	Mapping improvement	Read filtering	Read-pair filtering	Normalization	Visualization	Confidence estimation	Implementation language(s)
HiCUP [46]	Bowtie/Bowtie2	Pre-truncation	✓	✓	–	–	–	Perl, R
Hiclib [47]	Bowtie2	Iterative	✓[a]	✓	Matrix balancing	✓	–	Python
HiC-inspector [131]	Bowtie	–	✓	✓	–	✓	–	Perl, R
HIPPIE [132]	STAR	✓[b]	✓	✓	–	–	–	Python, Perl, R
HiC-Box [133]	Bowtie2	–	✓	✓	Matrix balancing	✓	–	Python
HiCdat [122]	Subread	–[c]	✓	✓	Three options[d]	✓	–	C++, R
HiC-Pro [134]	Bowtie2	Trimming	✓	✓	Matrix balancing	–	–	Python, R
TADbit [120]	GEM	Iterative	✓	✓	Matrix balancing	✓	–	Python
HOMER [62]	–	–	✓	✓	Two options[e]	✓	✓	Perl, R, Java
Hicpipe [54]	–	–	–	–	Explicit-factor	–	–	Perl, R, C++
HiBrowse [69]	–	–	–	–	–	✓	✓	Web-based
Hi-Corrector [57]	–	–	–	–	Matrix balancing	–	–	ANSI C
GOTHiC [135]	–	–	✓	✓	–	–	✓	R
HiTC [121]	–	–	–	–	Two options[f]	✓	✓	R
chromoR [59]	–	–	–	–	Variance stabilization	–	–	R
HiFive [136]	–	–	✓	✓	Three options[g]	✓	–	Python
Fit-Hi-C [20]	–	–	–	–	–	✓	✓	Python

[a] Hiclib keeps the reads with only one mapped end (single-sided reads) for use in coverage computations
[b] HIPPIE states that it rescues chimeric reads. No details are given
[c] HiCdat reports no substantial improvement in successfully aligned read pairs when iterative mapping in Hiclib is used for *Arabidopsis thaliana* Hi-C data
[d] HiCdat provides three options for normalization: coverage and distance correction, HiCNorm and ICE
[e] HOMER provides two options for normalization: simpleNorm corrects for sequencing coverage only and norm corrects for coverage plus the genomic distance between loci
[f] HiTC provides two options for normalization: normLGF implements HiCNorm and normICE implements ICE algorithm from Hiclib
[g] HiFive provides three options - Probability, Express, and Binning - for normalization. The Express and Binning algorithms correspond to matrix balancing and explicit-factor correction schemes, respectively

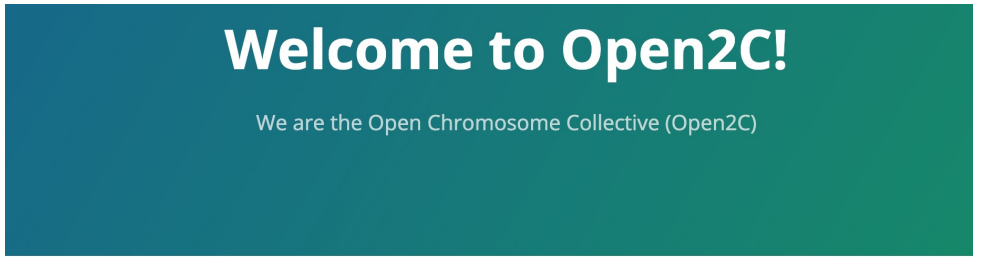
Servant et al., Genome Biol. 2015

Ay & Noble Genome Biol 2015

Common Hi-C processing steps



Open2C collective



Welcome to Open2C!

We are a group of computational biologists working on chromosome structure and interested in developing open source tools for the wider community.

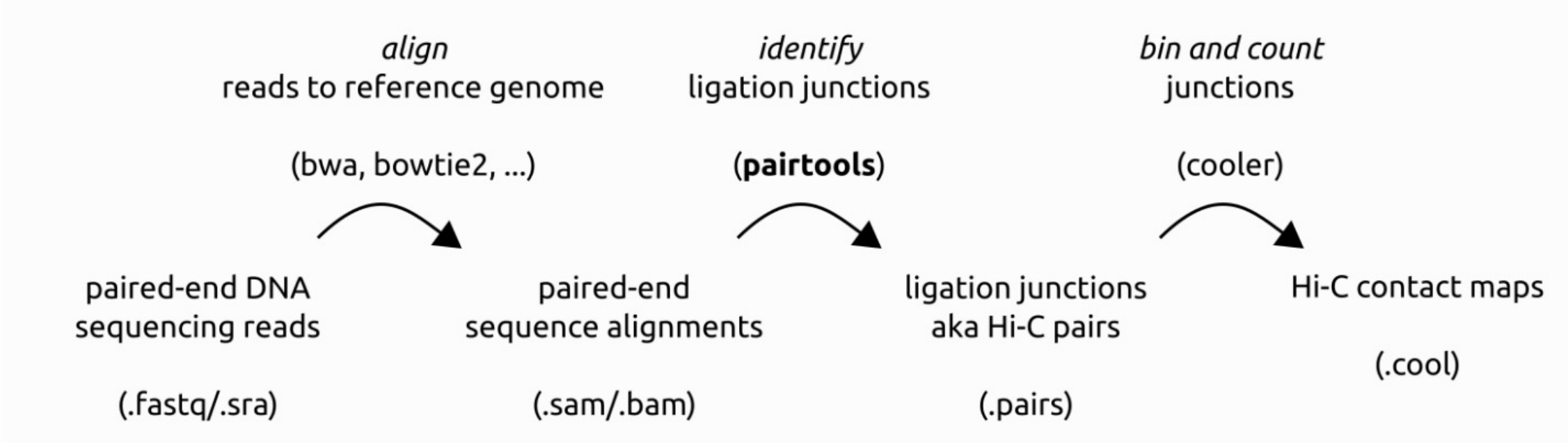
We are particularly interested in the 3D organization of chromosomes, and most of the tools are focused on the analysis of data obtained using Hi-C and related technologies. We like our tools to be easy to use, flexible, to facilitate active development of novel analytical approaches, and scalable, to make use of the latest and largest datasets.

🛠️ For analysis of Hi-C (and related) data, we have a suite of tools:

- cooler* for generation, normalization and storage of interaction matrices
- pairtools* for analysis and filtering of mapped reads
- cooltools* for extracting and quantifying features from Hi-C data, including: contacts vs. distance, compartments and saddles, insulation, and peaks
- coolpup.py for flexible pileup analysis
- distiller - a Nextflow pipeline for automation of Hi-C data processing, from reads to Cooler files
- quaich - a Snakemake pipeline for automated Hi-C postprocessing using **cooltools** and **coolpup.py**

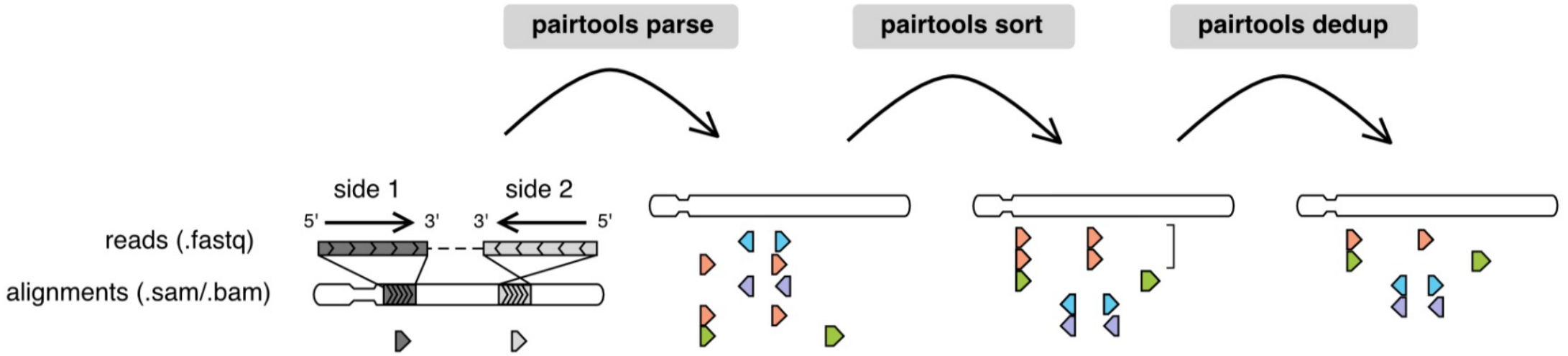
https://github.com/open2c/

Pairtools



https://pairtools.readthedocs.io/en/latest/

Pairtools



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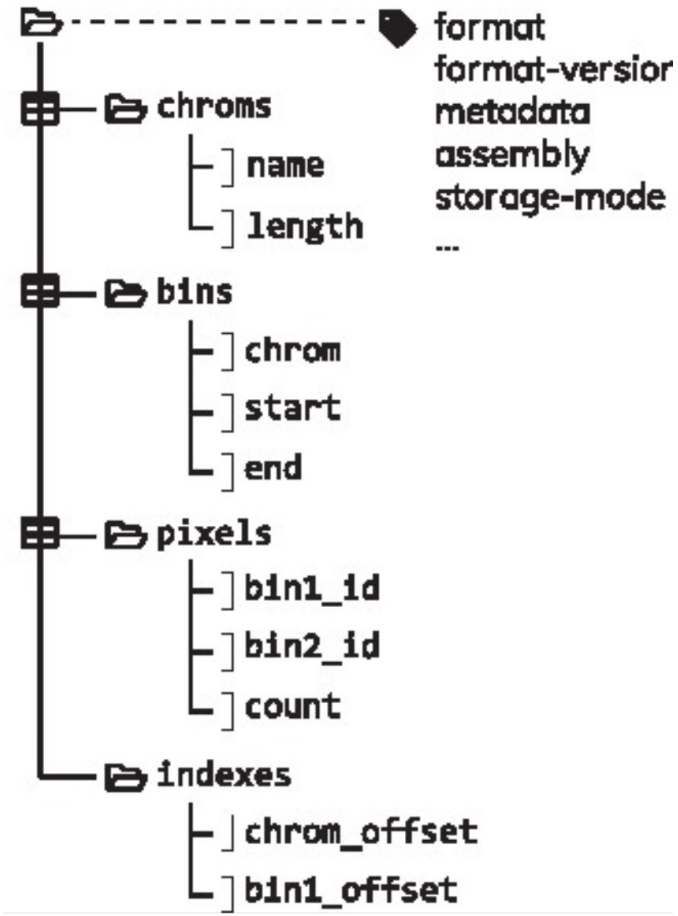
Cooler



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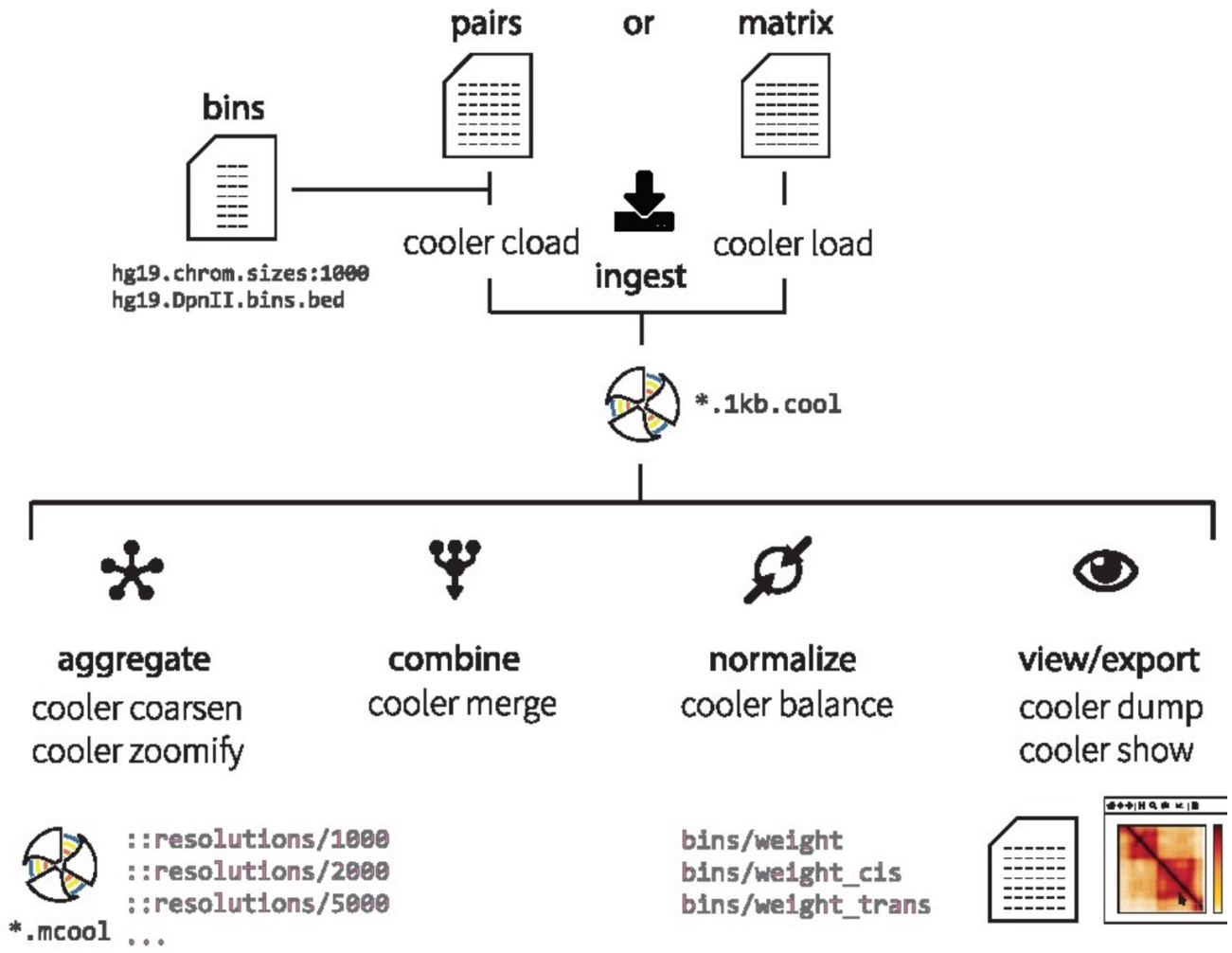
Cooler

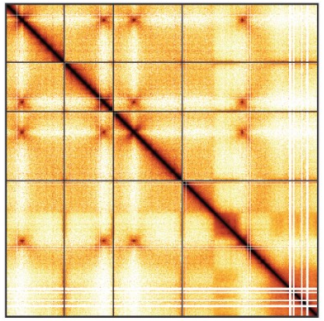


https://cooler.readthedocs.io/en/latest/

Handling Hi-C data in R

Orchestrating Hi-C analysis with Bioconductor

Package: OHCA
Authors: Jacques Serizay [aut, cre]
Compiled: 2024-11-11
Package version: 1.3.0
R version: R Under development (unstable) (2024-10-21 r87258)
BioC version: 3.21
License: MIT + file LICENSE

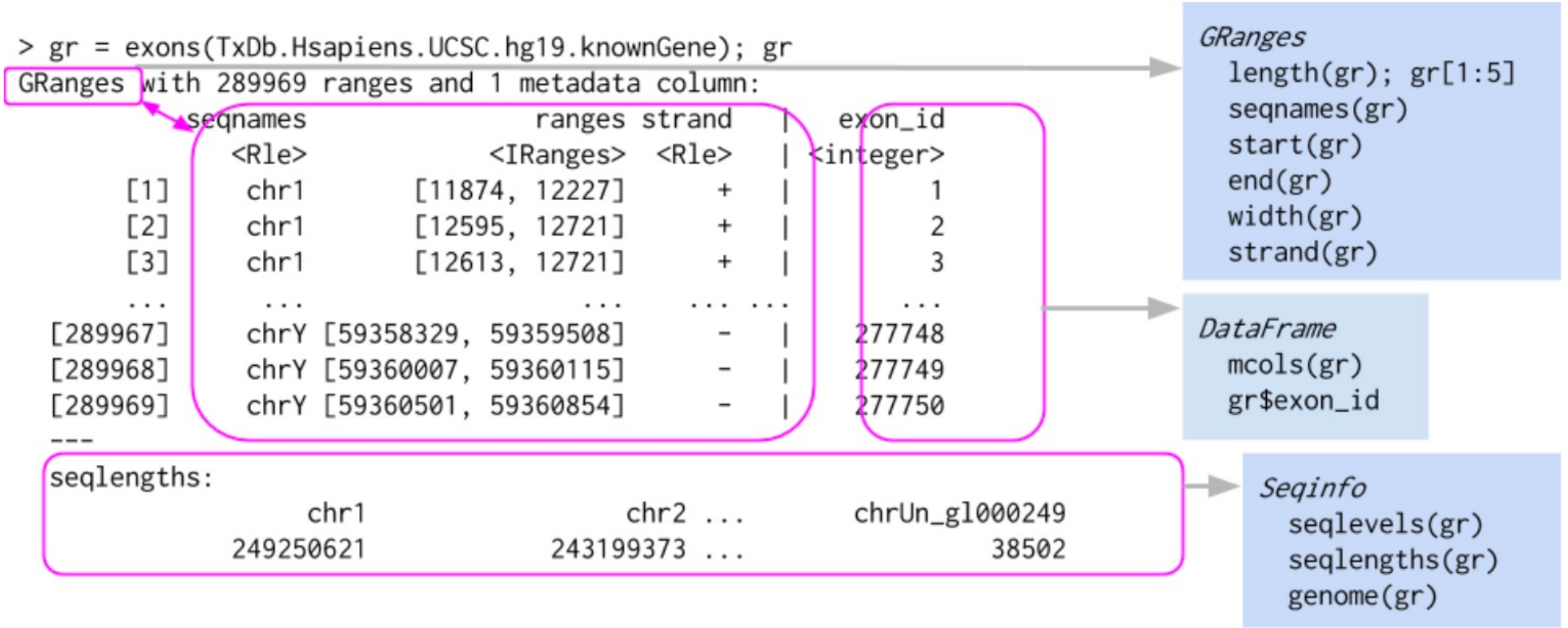


Welcome

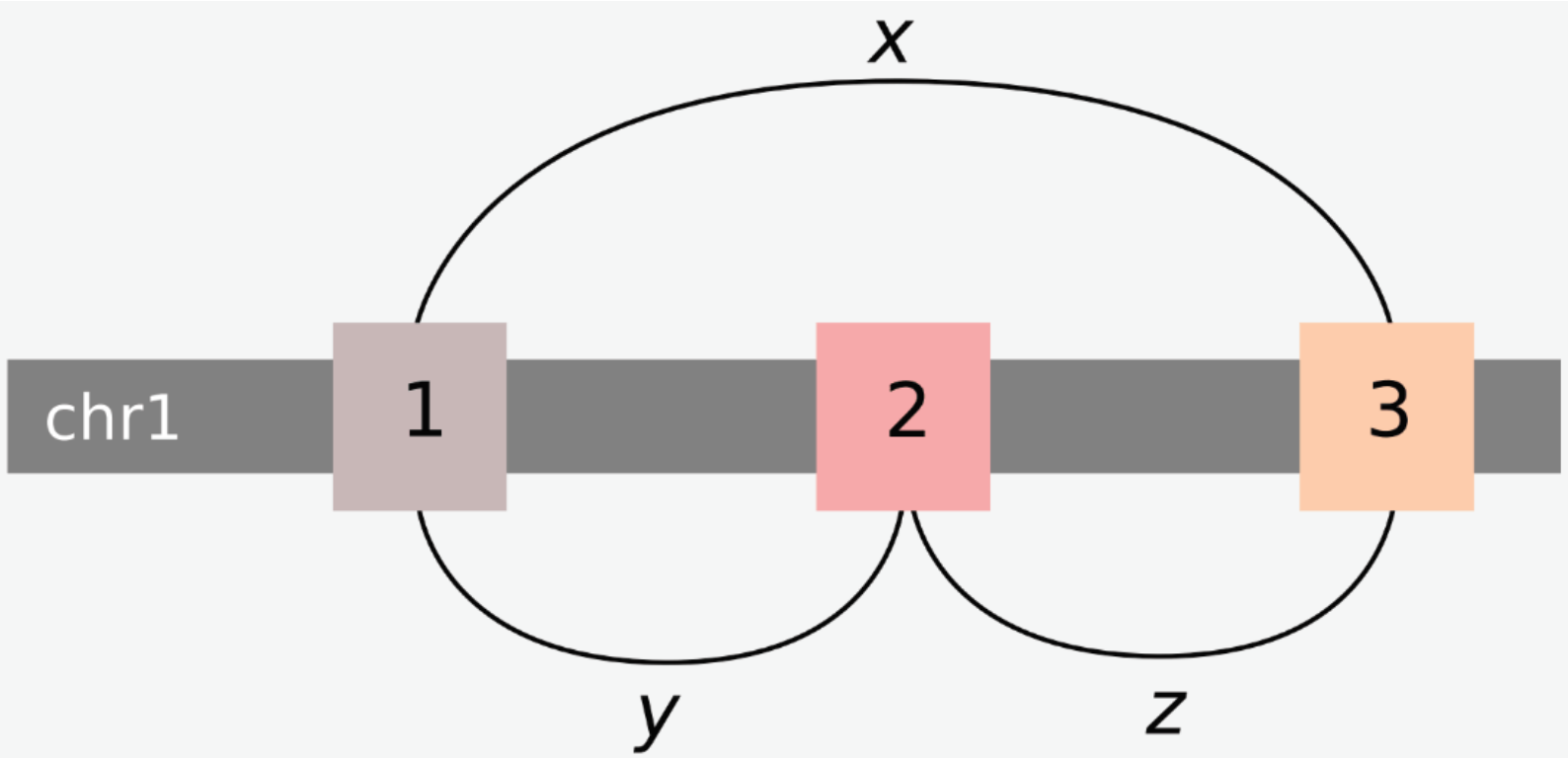
This is the landing page of the **"Orchestrating Hi-C analysis with Bioconductor"** book. **The primary aim of this book is to introduce the `R` user to Hi-C analysis**. This book starts with key concepts important for the analysis of chromatin conformation capture and then presents `Bioconductor` tools that can be leveraged to process, analyze, explore and visualize Hi-C data.

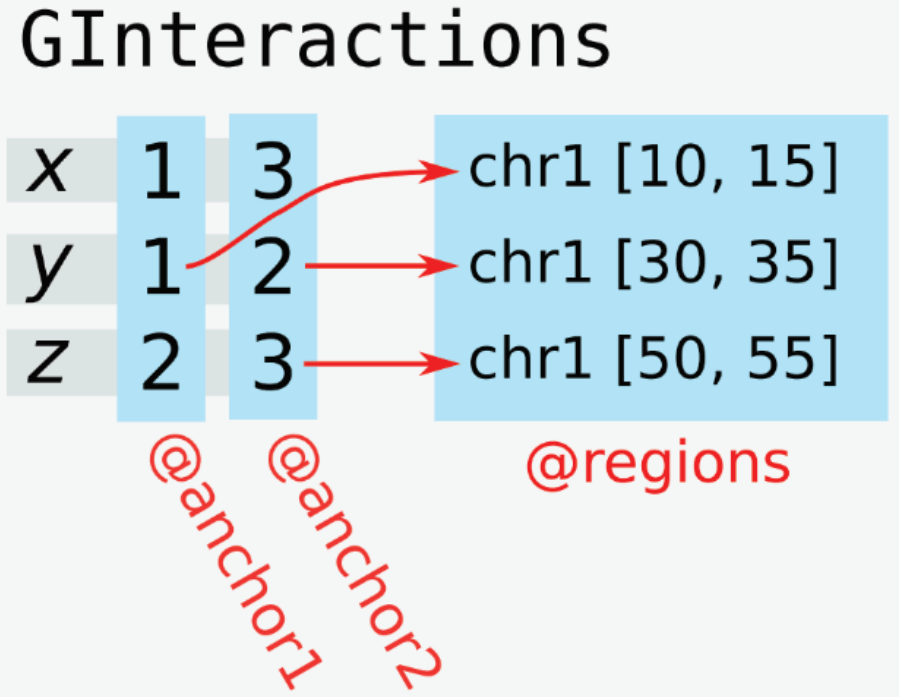
https://www.nature.com/articles/s41467-024-44761-x

Granges vs GInteractions



Granges vs GInteractions





Handling Hi-C files in R