
epical

Release 0.7.0

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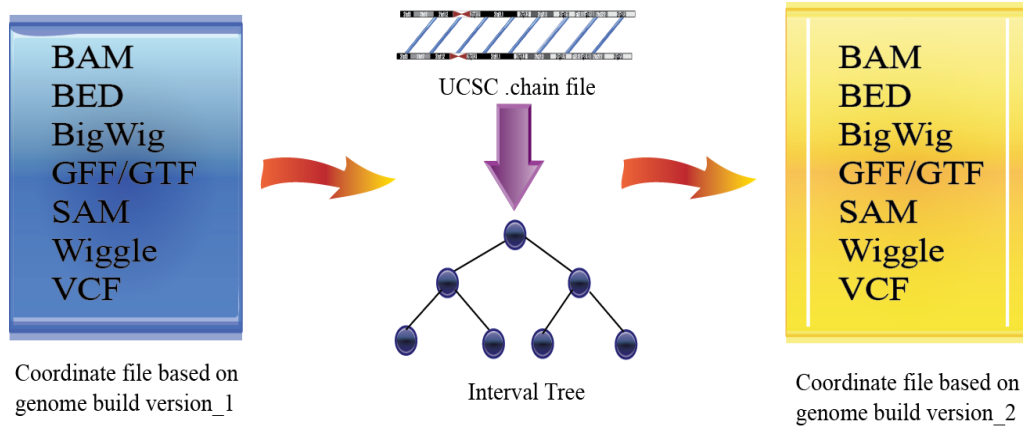
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CrossMap

Convert Genome Coordinates Between Assemblies

CrossMap is a program for genome coordinates conversion between *different assemblies* (such as hg18 (NCBI36) <=> hg19 (GRCh37)). It supports commonly used file formats including BAM, CRAM, SAM, Wiggle, BigWig, BED, GFF, GTF, MAF VCF, and gVCF.

HOW CROSSMAP WORKS?



RELEASE HISTORY

01/11/2024: Release version 0.7.0

1. Fix bugs for VCF variants liftover.
2. Handle non-DNA ALT alleles such as
3. Use [pyproject.toml](#) to replace “setup.py”.

Note: From v0.7.0 onwards, the main program `CrossMap.py` is now renamed to `CrossMap` due to the restriction on using “.” in the script name in the “pyproject.toml” file. To ensure compatibility with the previous pipelines, please include the following line in your `~/ .bashrc` file.

```
alias CrossMap.py='CrossMap'
```

07/21/2023: Release version 0.6.4

1. Fix bug when the sequence in BAM file is represented as “*”
2. Change code style

07/12/2022: Release version 0.6.4

1. Fix bug when the input bigwig file does not have coverage signal for some chromosomes.
2. When the input VCF file does not have CONTIG field, use long chromosome ID (e.g., “chr1”) as default.

03/04/2022: Release version 0.6.3

1. Fix bug in v0.6.2. “Alternative allele is empty”

02/22/2022: Release version 0.6.2

1. For insertions and deletions, the first nucleotide of the ALT allele (the 5th field in VCF file) is updated to the nucleotide at POS of the reference genome

11/29/2021: Release version 0.6.1

1. Same as v0.6.0. Remove unused modules from the lib folder.

11/16/2021: Release version 0.6.0

1. Use [argparse](#) instead of [optparse](#).
2. Use `os.path.getmtime` instead of `os.path.getctime` to check the timestamps of fasta file and its index file.
3. Add ‘`--unmap-file`’ option to `CrossMap.py bed` command.

4/16/2021: Release version 0.5.3/0.5.4

Add `CrossMap.py viewchain` to convert chain file into block-to-block, more readable format.

12/08/2020: Release version 0.5.2

Add ‘`--no-comp-alleles`’ flag to `CrossMap.py vcf` and `CrossMap.py gvcf`. If set, `CrossMap` does not check if the “reference allele” is different from the “alternative allele”.

08/19/2020: Release version 0.5.1

In `CrossMap.py region`: keep additional columns (columns after the 3rd column) of the original BED file after conversion.

08/14/2020: Release version 0.5.0

Add `CrossMap.py region` function to convert large genomic regions. Unlike the `CrossMap.py bed` function, which splits big genomic regions, `CrossMap.py region` tries to convert the big genomic region as a whole.

07/09/2020: Release version 0.4.3

Structural Variants VCF files often use INFO/END field to indicate the end of a deletion. v0.4.3 updates “END” coordinate in the INFO field.

05/04/2020: Release version 0.4.2

Support `GVCF` file conversion.

03/24/2020: Release version 0.4.1

Deal with consecutive TABs in the input MAF file.

10/09/2019: Release version 0.3.8

The University of California holds the copyrights in the UCSC chain files. As requested by UCSC, all UCSC-generated chain files will be permanently removed from this website and the `CrossMap` distributions.

07/22/2019: Release version 0.3.6

1. Support MAF (mutation annotation format).
2. Fix error “`TypeError: AlignmentHeader does not support item assignment (use header.to_dict())`” when lifting over BAM files. User does not need to downgrade `pysam` to 0.13.0 to lift over BAM files.

04/01/2019: Release version 0.3.4

Fix bugs when chromosome IDs (of the source genome) in chain file do not have ‘chr’ prefix (such as “GRCh37ToHg19.over.chain.gz”). This version also allows `CrossMap` to detect if a VCF mapping was inverted, and if so, reverse complements the alternative allele (Thanks to Andrew Yates). Improve wording.

01/07/2019: Release version 0.3.3

Version 0.3.3 is exactly the same as Version 0.3.2. The reason to release this version is that `CrossMap-0.3.2.tar.gz` was broken when uploading to pypi.

12/14/18: Release version 0.3.2

Fix the key error problem (e.g `KeyError: “sequence ‘b’7_K1270803v1_alt” not present`”). This error happens when a locus from the original assembly is mapped to an “alternative”, “unplaced” or “unlocalized” contig in the target assembly, and this “target contig” does not exist in your `target_ref.fa`. In version 0.3.2, such loci will be silently skipped and saved to the “.unmap” file.

11/05/18: Release version 0.3.0

1. v0.3.0 or newer will Support Python3. Previous versions support Python2.7.*
2. add `pyBigWig` as a dependency.

INSTALLATION

3.1 Install from PyPI

```
pip3 install CrossMap
```

3.2 Install from GitHub

```
pip3 install git+https://github.com/liguowang/CrossMap.git
```

3.3 Upgrade

```
pip3 install CrossMap --upgrade
```


INPUT AND OUTPUT

4.1 Chain file

A **chain file** describes a pairwise alignment between two reference assemblies. **UCSC** and **Ensembl** chain files are available:

UCSC chain files

- Chain files from hs1 (T2T-CHM13) to hg38/hg19/mm10/mm9 (ore vice versa): <https://hgdownload.soe.ucsc.edu/goldenPath/hs1/liftOver/>
- Chain files from hg38 (GRCh38) to hg19 and all other organisms: <http://hgdownload.soe.ucsc.edu/goldenPath/hg38/liftOver/>
- Chain File from hg19 (GRCh37) to hg17/hg18/hg38 and all other organisms: <http://hgdownload.soe.ucsc.edu/goldenPath/hg19/liftOver/>
- Chain File from mm10 (GRCm38) to mm9 and all other organisms: <http://hgdownload.soe.ucsc.edu/goldenPath/mm10/liftOver/>

Ensembl chain files

- Human to Human: ftp://ftp.ensembl.org/pub/assembly_mapping/homo_sapiens/
- Mouse to Mouse: ftp://ftp.ensembl.org/pub/assembly_mapping/mus_musculus/
- Other organisms: ftp://ftp.ensembl.org/pub/assembly_mapping/

4.2 User Input file

CrossMap supports the following file formats.

1. **BAM**, **CRAM**, or **SAM**
2. **BED** or **BED-like**. (BED file must have at least ‘chrom’, ‘start’, ‘end’)
3. **Wiggle** (“variableStep”, “fixedStep” and “bedGraph” formats are supported)
4. **BigWig**
5. **GFF** or **GTF**
6. **VCF**
7. **GVCF**
8. **MAF**

4.3 Output file

The format of output files depends on the input

Input_format	Output_format
BED	BED (Genome coordinates will be updated)
BAM	BAM (Genome coordinates, header section, all SAM flags, insert size will be updated)
CRAM	BAM (require pysam >= 0.8.2)
SAM	SAM (Genome coordinates, header section, all SAM flags, insert size will be updated)
Wiggle	BigWig
BigWig	BigWig
GFF	GFF (Genome coordinates will be updated to the target assembly)
GTF	GTF (Genome coordinates will be updated to the target assembly)
VCF	VCF (header section, Genome coordinates, reference alleles will be updated)
GVCF	GVCF (header section, Genome coordinates, reference alleles will be updated)
MAF	MAF (Genome coordinates and reference alleles will be updated)

USAGE

Run CrossMap -h or CrossMap --help print help message

```
$ CrossMap -h

usage: CrossMap [-h] [-v] {bed,bam,gff,wig,bigwig,vcf,gvcf,maf,region,viewchain} ...

CrossMap (v0.6.0) is a program to convert (liftover) genome coordinates between
↳different reference
assemblies (e.g., from human GRCh37/hg19 to GRCh38/hg38 or vice versa). Supported file
↳formats: BAM,
BED, BigWig, CRAM, GFF, GTF, VCF, MAF (mutation annotation format), SAM, Wiggle, and
↳VCF.

positional arguments:
  {bed,bam,gff,wig,bigwig,vcf,gvcf,maf,region,viewchain}
                                sub-command help
  bed
↳coordinates                    converts BED, bedGraph or other BED-like files. Only genome
                                (i.e., the first 3 columns) will be updated. Regions mapped to
↳multiple                      locations to the new assembly will be split. Use the "region"
                                command to
                                liftover large genomic regions. Use the "wig" command if you need
                                bedGraph/bigWig output.
  bam
↳header section,              converts BAM, CRAM, or SAM format file. Genome coordinates,
                                all SAM flags, insert size will be updated.
  gff
↳updated.                    converts GFF or GTF format file. Genome coordinates will be
  wig
↳be updated.                 converts Wiggle or bedGraph format file. Genome coordinates will
  bigwig                      converts BigWig file. Genome coordinates will be updated.
  vcf
↳alleles will                converts VCF file. Genome coordinates, header section, reference
                                be updated.
  gvcf
↳reference alleles           converts GVCf file. Genome coordinates, header section,
                                will be updated.
  maf
↳coordinates and             converts MAF (mutation annotation format) file. Genome
```

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```

    region          reference alleles will be updated.
    ↪Genome         converts big genomic regions (in BED format) such as CNV blocks.
    viewchain       coordinates will be updated.
    ↪block-to-block prints out the content of a chain file into a human readable,
                    format.

optional arguments:
  -h, --help          show this help message and exit
  -v, --version       show program's version number and exit

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

```

5.1 Convert BED format files

A **BED** (Browser Extensible Data) file is a tab-delimited text file describing genome regions or gene annotations. It consists of one line per feature, each containing 3-12 columns. CrossMap converts BED files with less than 12 columns to a different assembly by updating the chromosome and genome coordinates only; all other columns remain unchanged. Regions from the old assembly mapping to multiple locations to the new assembly will be split. For 12-columns BED files, all columns will be updated accordingly except the 4th column (name of bed line), 5th column (score value), and 9th column (RGB value describing the display color). 12-column BED files usually define multiple blocks (e.g., exons); if any of the exons fails to map to a new assembly, the whole BED line is skipped.

The input BED file can be plain text file, compressed file with extension of .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URL pointing to accessible remote files (<http://>, <https://> and <ftp://>). Compressed remote files are not supported. The output is a BED format file with exactly the same number of columns as the original one.

Standard **BED** format has 12 columns, but CrossMap also supports BED-like formats:

- **BED3**: The first three columns (“chrom”, “start”, “end”) of the BED format file.
- **BED6**: The first six columns (“chrom”, “start”, “end”, “name”, “score”, “strand”) of the BED format file.
- **Other**: Format has at least three columns (“chrom”, “start”, “end”) and no more than 12 columns. All other columns are arbitrary.

Note:

1. For BED-like formats mentioned above, CrossMap only updates the “chrom”, “start”, “end”, and “strand” columns. All other columns will be kept AS-IS.
2. Lines starting with ‘#’, ‘browser’, ‘track’ will be skipped.
3. Lines less than three columns will be skipped.
4. The 2nd and 3rd columns must be integers.
5. The “+” strand is assumed if no strand information is found.
6. For standard BED format (12 columns). If any of the defined exon blocks cannot be uniquely mapped to target assembly, the whole entry will be skipped.
7. The “input_chain_file” and “input_bed_file” can be regular or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file, local file or URL (<http://>, <https://>, <ftp://>) pointing to remote file.

8. If the `output_file` is not specified, results will be printed to screen (console). In this case, the original bed entries (including entries failed to convert) were also printed out.
9. If the input region cannot be consecutively mapped to the target assembly, it will be split.
10. The `*.unmap` file contains regions that cannot be unambiguously converted.

Typing `CrossMap bed -h` will print help message:

```
$ CrossMap bed -h

usage: CrossMap bed [-h] [--chromid {a,s,l}] [--unmap-file UNMAP_FILE]
                  input.chain input.bed [out_bed]

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
                      ↳ describes pairwise alignments between two genomes. The input chain file
                      ↳ can be a plain text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.bed           The input BED file. The first 3 columns must be "chrom", "start",
                      ↳ and "end".
                      ↳ extension of The input BED file can be plain text file, compressed file with
                      ↳ accessible .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URL pointing to
                      ↳ files are not remote files (http://, https:// and ftp://). Compressed remote
                      ↳ supported.
  out_bed             Output BED file. if argument is missing, CrossMap will write BED
                      ↳ file to the STDOUT.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style"
                      ↳ (eg. "chr1", "chrX"); "s" = "short style" (eg. "1", "X").
  --unmap-file UNMAP_FILE
                      ↳ file to save unmapped entries. This will be ignored if [out_bed]
                      ↳ was not provided.
```

Example 1

run `CrossMap bed` with **no** `output_file`:

```
$ CrossMap bed hg18ToHg19.over.chain.gz test.hg18.bed3

# Conversion results were printed to screen directly (column1-3 are hg18 based, column5-
↳ 7 are hg19 based)::
chr1 142614848 142617697 -> chr1 143903503 143906352
chr1 142617697 142623312 -> chr1 143906355 143911970
chr1 142623313 142623350 -> chr1 143911971 143912008
```

Example 2

run CrossMap bed with *output_file* (test.hg19.bed3) specified:

```
$ CrossMap bed hg18ToHg19.over.chain.gz test.hg18.bed3 test.hg19.bed3

$ cat test.hg19.bed3
chr1 143903503 143906352
chr1 143906355 143911970
chr1 143911971 143912008
```

Example 3

One input region was split because it cannot map consecutively to the target assembly:

```
$ CrossMap bed hg18ToHg19.over.chain.gz test.hg18.bed3

chr10 81369946 81370453 + -> chr10 81380000 81380507 ↵
↪ +
chr10 81370483 81371363 + -> chr10 81380539 81381419 ↵
↪ +
chr10 81371363 81371365 + -> chr10 62961832 62961834 ↵
↪ +
chr10 81371412 81371432 + (split.1:chr10:81371412:81371422:+) ↵
↪ chr10 62961775 62961785 +
chr10 81371412 81371432 + (split.2:chr10:81371422:81371432:+) ↵
↪ chrX 63278348 63278358 +
```

Example 4

BedGraph format file can be converted using either CrossMap bed or CrossMap wig; however, the output formats are different:

- Use CrossMap bed command to convert a bedGraph file, the output is a **bedGraph** file.
- Use CrossMap wig command to convert a bedGraph file, the output is a **bigWig** file.

```
$ CrossMap bed hg19ToHg38.over.chain.gz 4_hg19.bgr

chrX 5873316 5873391 2.0 -> chrX 5955275 5955350 2.0
chrX 5873673 5873710 0.8 -> chrX 5955632 5955669 0.8
chrX 5873710 5873785 1.4 -> chrX 5955669 5955744 1.4
chrX 5873896 5873929 0.9 -> chrX 5955855 5955888 0.9
chrX 5873929 5874004 1.5 -> chrX 5955888 5955963 1.5
chrX 5874230 5874471 0.3 -> chrX 5956189 5956430 0.3
chrX 5874471 5874518 0.9 -> chrX 5956430 5956477 0.9

$ python3 CrossMap wig hg19ToHg38.over.chain.gz 4_hg19.bgr output_hg38
@ 2018-11-06 00:09:11: Read chain_file: hg19ToHg38.over.chain.gz
@ 2018-11-06 00:09:12: Liftover wiggle file: 4_hg19.bgr ==> output_hg38.bgr
@ 2018-11-06 00:09:12: Merging overlapped entries in bedGraph file ...
@ 2018-11-06 00:09:12: Sorting bedGraph file:output_hg38.bgr
@ 2018-11-06 00:09:12: Writing header to "output_hg38.bw" ...
@ 2018-11-06 00:09:12: Writing entries to "output_hg38.bw" ...
```

Example 5

Use CrossMap region command to convert large genomic regions (such as CNV blocks) in BED format.

```
# a genomic region of 3.48Mb
$ cat test.bed
chr2    239716679      243199373
```

If we use `CrossMap bed` command to convert this 3.48 Mb region. It will be split into 74 small blocks:

```
$CrossMap bed GRCh37_to_GRCh38.chain.gz test.bed

chr2    239716679      243199373      (split.1:chr2:239716679:239801978:+)    chr2    ↵
↪238808038      238893337
chr2    239716679      243199373      (split.2:chr2:239831978:240205681:+)    chr2    ↵
↪238910282      239283985
chr2    239716679      243199373      (split.3:chr2:240205681:240319336:+)    chr2    ↵
↪239283986      239397641
... (split 74 times)
```

If we use `CrossMap region` command to convert this 3.48Mb region. Note: `-r` (the minimum ratio of bases that must remap) is 0.85 by default:

```
$CrossMap region GRCh37_to_GRCh38.chain.gz test.bed

chr2    239716679      243199373      ->      chr2    238808038      242183529    ↵
↪map_ratio=0.9622
```

If we increase `-r` to 0.99, this region will fail:

```
$CrossMap region GRCh37_to_GRCh38.chain.gz test.bed -r 0.99

chr2    239716679      243199373      Fail      map_ratio=0.9622
```

5.2 Convert BAM/CRAM/SAM format files

SAM (Sequence Alignment Map) format is a generic format for storing sequencing alignments, and **BAM** is the binary and compressed version of SAM (Li et al., 2009). **CRAM** was designed to be an efficient reference-based alternative to the **SAM** and **BAM** file formats. Most high-throughput sequencing (HTS) alignments were in SAM/BAM format and many HTS analysis tools work with SAM/BAM format. `CrossMap` updates chromosomes, genome coordinates, header sections, and all SAM flags accordingly. `CrossMap`'s version number is inserted into the header section, along with the names of the original BAM file and the chain file. For pair-end sequencing, insert size is also recalculated. The input BAM file should be sorted and indexed properly using `Samtools` (Li et al., 2009). The output format is determined by the input format, and the BAM output will be sorted and indexed automatically.

Typing `CrossMap bam -h` will print help message:

```
$ CrossMap bam -h

usage: CrossMap bam [-h] [-m INSERT_SIZE] [-s INSERT_SIZE_STDEV] [-t INSERT_SIZE_FOLD] [-a]
                    [--chromid {a,s,l}]
                    input.chain input.bam [out_bam]

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html) ↵
```

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```

↳describes pairwise alignments between two genomes. The input chain file
↳can be a plain text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
input.bam Input BAM file (https://genome.ucsc.edu/FAQ/FAQformat.html
↳#format5.1).
out_bam Output BAM file. if argument is missing, CrossMap will write BAM
↳file to the STDOUT.

optional arguments:
-h, --help show this help message and exit
-m INSERT_SIZE, --mean INSERT_SIZE
Average insert size of pair-end sequencing (bp).
-s INSERT_SIZE_STDEV, --stdev INSERT_SIZE_STDEV
Stanadard deviation of insert size.
-t INSERT_SIZE_FOLD, --times INSERT_SIZE_FOLD
A mapped pair is considered as "proper pair" if both ends mapped
↳to different strand and the distance between them is less then '-t' * stdev
↳from the mean.
-a, --append-tags Add tag to each alignment in BAM file. Tags for pair-end
↳alignments include:
QF = QC failed, NN = both read1 and read2 unmapped, NU = read1
↳unmapped,
read2 unique mapped, NM = read1 unmapped, multiple mapped, UN =
↳read1
uniquely mapped, read2 unmap, UU = both read1 and read2 uniquely
↳mapped, UM =
read1 uniquely mapped, read2 multiple mapped, MN = read1
↳multiple mapped,
read2 unmapped, MU = read1 multiple mapped, read2 unique mapped,
↳MM = both
read1 and read2 multiple mapped. Tags for single-end alignments
↳include: QF =
QC failed, SN = unmaped, SM = multiple mapped, SU = uniquely
↳mapped.
--chromid {a,s,l} The style of chromosome IDs. "a" = "as-is"; "l" = "long style"
↳(eg. "chr1",
"chrX"); "s" = "short style" (eg. "1", "X").

```

Example

Convert BAM from hg19 to hg18:

```

# add optional tags using '-a' (recommend always use '-a' option)

$ CrossMap bam -a ../data/hg19ToHg18.over.chain.gz test.hg19.bam test.hg18
Insert size = 200.000000
Insert size stdev = 30.000000
Number of stdev from the mean = 3.000000
Add tags to each alignment = True
@ 2016-10-07 15:29:06: Read chain_file: ../data/hg19ToHg18.over.chain.gz

```

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```
@ 2016-10-07 15:29:07: Liftover BAM file: test.hg19.bam ==> test.hg18.bam
@ 2016-10-07 15:29:14: Done!
@ 2016-10-07 15:29:14: Sort "test.hg18.bam" ...
@ 2016-10-07 15:29:15: Index "test.hg18.sorted.bam" ...
Total alignments:99914
    QC failed: 0
    R1 unique, R2 unique (UU): 96094
    R1 unique, R2 unmapp (UN): 3579
    R1 unique, R2 multiple (UM): 0
    R1 multiple, R2 multiple (MM): 0
    R1 multiple, R2 unique (MU): 233
    R1 multiple, R2 unmapped (MN): 8
    R1 unmap, R2 unmap (NN): 0
    R1 unmap, R2 unique (NU): 0
    R1 unmap, R2 multiple (NM): 0
```

BAM/SAM header sections was updated:

```
$ samtools view -H test.hg19.bam
@SQ      SN:chr1 LN:249250621
@SQ      SN:chr2 LN:243199373
@SQ      SN:chr3 LN:198022430
...
@SQ      SN:chrX LN:155270560
@SQ      SN:chrY LN:59373566
@SQ      SN:chrM LN:16571
@RG      ID:Sample_618545BE      SM:Sample_618545BE      LB:Sample_618545BE
↳PL:Illumina
@PG      ID:bwa PN:bwa VN:0.6.2-r126

$ samtools view -H test.hg18.bam
@HD      VN:1.0 SO:coordinate
@SQ      SN:chr1 LN:247249719
@SQ      SN:chr10 LN:135374737
@SQ      SN:chr11 LN:134452384
...
@SQ      SN:chrX LN:154913754
@SQ      SN:chrX_random LN:1719168
@SQ      SN:chrY LN:57772954
@RG      ID:Sample_618545BE      SM:Sample_618545BE      LB:Sample_618545BE
↳PL:Illumina
@PG      PN:bwa ID:bwa VN:0.6.2-r126
@PG      ID:CrossMap VN:0.5.0
@CO      Liftover from original BAM/SAM file: test.hg19.bam
@CO      Liftover is based on the chain file: ../test/hg19ToHg18.over.chain.gz
```

Optional tags:

Q

QC. QC failed.

N

Unmapped. Originally unmapped or originally mapped but failed to lift over to new assembly.

M

Multiple mapped. Alignment can be lifted over to multiple places.

U

Unique mapped. Alignment can be lifted over to only 1 place.

Tags for pair-end sequencing include:

- QF = QC failed
- NN = both read1 and read2 unmapped
- NU = read1 unmapped, read2 unique mapped
- NM = read1 unmapped, multiple mapped
- UN = read1 uniquely mapped, read2 unmap
- UU = both read1 and read2 uniquely mapped
- UM = read1 uniquely mapped, read2 multiple mapped
- MN = read1 multiple mapped, read2 unmapped
- MU = read1 multiple mapped, read2 unique mapped
- MM = both read1 and read2 multiple mapped

Tags for single-end sequencing include:

- QF = QC failed
- SN = unmaped
- SM = multiple mapped
- SU = uniquely mapped

Note:

1. All alignments (mapped, partial mapped, unmapped, QC failed) will write to one file. Users can filter them by tags.
 2. The header section will be updated to the target assembly.
 3. Genome coordinates and all SAM flags in the alignment section will be updated to the target assembly.
 4. If the input is a CRAM file, pysam version should $\geq 0.8.2$
 5. Optional fields in the alignment section will not update.
-

5.3 Convert Wiggle format files

Wiggle (WIG) format is useful in displaying continuous data such as GC content and the reads intensity of high-throughput sequencing data. BigWig is a self-indexed binary-format Wiggle file and has the advantage of supporting random access. Input wiggle data can be in variableStep (for data with irregular intervals) or fixedStep (for data with regular intervals). Regardless of the input, the output files are always in bedGraph format.

Typing `CrossMap wig -h` will print help message:

```
$ CrossMap wig -h

usage: CrossMap wig [-h] [--chromid {a,s,l}] input.chain input.wig out_wig

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
  ↪ describes          pairwise alignments between two genomes. The input chain file can
  ↪ be a plain         text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.wig           The input wiggle/bedGraph format file
  ↪ "variableStep" and (http://genome.ucsc.edu/goldenPath/help/wiggle.html). Both
  ↪ file can be        "fixedStep" wiggle lines are supported. The input wiggle/bedGraph
  ↪ .bz2 and           plain text file, compressed file with extension of .gz, .Z, .z, .bz,
  ↪ https:// and       .bzip2, or even a URL pointing to accessible remote files (http://,
  ftp://). Compressed remote files are not supported.
  out_wig             Output bedGraph file. Regardless of the input is wiggle or bedGraph,
  ↪ the output         file is always in bedGraph format.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
  ↪ "chr1",           "chrX"); "s" = "short style" (eg. "1", "X").
```

Note: To improve performance, this script calls GNU “sort” command internally. If the “sort” command is not callable, CrossMap will exit.

5.4 Convert BigWig format files

If an input file is in BigWig format, the output is BigWig format if UCSC’s ‘wigToBigWig’ executable can be found; otherwise, the output file will be in bedGraph format.

After v0.3.0, UCSC’s wigToBigWig command is no longer needed.

Typing `CrossMap bigwig -h` will print help message:

```
$ CrossMap bigwig -h

usage: CrossMap bigwig [-h] [--chromid {a,s,l}] input.chain input.bw output.bw

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
  ↪ describes          pairwise alignments between two genomes. The input chain file can
```

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```

→ be a plain          text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
input.bw              The input bigWig format file
                      (https://genome.ucsc.edu/goldenPath/help/bigWig.html).
output.bw             Output bigWig file.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
→ "chr1",
                      "chrX"); "s" = "short style" (eg. "1", "X").

```

Example (Convert BigWig file from hg18 to hg19):

```

$ python CrossMap bigwig hg19ToHg18.over.chain.gz test.hg19.bw test.hg18
@ 2013-11-17 22:12:42: Read chain_file: ../data/hg19ToHg18.over.chain.gz
@ 2013-11-17 22:12:44: Liftover bigwig file: test.hg19.bw ==> test.hg18.bgr
@ 2013-11-17 22:15:38: Merging overlapped entries in bedGraph file ...
@ 2013-11-17 22:15:38: Sorting bedGraph file:test.hg18.bgr
@ 2013-11-17 22:15:39: Convert wiggle to bigwig ...

```

Note: To improve performance, this script calls GNU “sort” command internally. If “sort” command does not exist, CrossMap will exit.

5.5 Convert GFF/GTF format files

GFF (General Feature Format) is another plain text file used to describe gene structure. **GTF** (Gene Transfer Format) is a refined version of GTF. The first eight fields are the same as GFF. Plain text, compressed plain text, and URLs pointing to remote files are all supported. Only chromosome and genome coordinates are updated. The format of the output is determined from the input.

Typing `CrossMap gff -h` will print help message:

```

$ CrossMap gff -h

usage: CrossMap gff [-h] [--chromid {a,s,l}] input.chain input.gff [out_gff]

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
→ describes           pairwise alignments between two genomes. The input chain file can
→ be a plain          text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
input.gff             The input GFF (General Feature Format,
→ Transfer Format,     http://genome.ucsc.edu/FAQ/FAQformat.html#format3) or GTF (Gene
→ GFF/GTF file       http://genome.ucsc.edu/FAQ/FAQformat.html#format4) file. The input
                      can be plain text file, compressed file with extension of .gz, .Z, .

```

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```

→z, .bz, .bz2
and .bzip2, or even a URL pointing to accessible remote files.
→(http://, https://
and ftp://). Compressed remote files are not supported.
out_gff      Output GFF/GTF file. if argument is missing, CrossMap will write.
→GFF/GTF file to
the STDOUT.

optional arguments:
-h, --help      show this help message and exit
--chromid {a,s,l} The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
→"chr1",
"chrX"); "s" = "short style" (eg. "1", "X").

```

Example (Convert GTF file from hg19 to hg18):

```

$ python CrossMap gff hg19ToHg18.over.chain.gz test.hg19.gtf test.hg18.gtf
@ 2013-11-17 20:44:47: Read chain_file: ../data/hg19ToHg18.over.chain.gz

$ head test.hg19.gtf
chr1  hg19_refGene  CDS      48267145      48267291      0.000000      -      0.
→      gene_id "NM_001194986"; transcript_id "NM_001194986";
chr1  hg19_refGene  exon     66081691     66081907     0.000000      +      .
→      gene_id "NM_002303"; transcript_id "NM_002303";
chr1  hg19_refGene  CDS      145334684    145334792    0.000000      +      2.
→      gene_id "NM_001039703"; transcript_id "NM_001039703";
chr1  hg19_refGene  exon     172017752    172017890    0.000000      +      .
→      gene_id "NM_001136127"; transcript_id "NM_001136127";
chr1  hg19_refGene  CDS      206589249    206589333    0.000000      +      2.
→      gene_id "NM_001170637"; transcript_id "NM_001170637";
chr1  hg19_refGene  exon     210573812    210574006    0.000000      +      .
→      gene_id "NM_001170580"; transcript_id "NM_001170580";
chr1  hg19_refGene  CDS      235850249    235850347    0.000000      -      0.
→      gene_id "NM_000081"; transcript_id "NM_000081";
chr1  hg19_refGene  CDS      235880012    235880078    0.000000      -      1.
→      gene_id "NM_000081"; transcript_id "NM_000081";
chr1  hg19_refGene  exon     3417741 3417872 0.000000      -      .      gene_id
→      "NM_001409"; transcript_id "NM_001409";
chr1  hg19_refGene  exon     10190773    10190871    0.000000      +      .
→      gene_id "NM_006048"; transcript_id "NM_006048";

$ head test.hg18.gtf
chr1  hg19_refGene  CDS      48039732     48039878     0.000000      -      0.
→      gene_id "NM_001194986"; transcript_id "NM_001194986";
chr1  hg19_refGene  exon     65854279     65854495     0.000000      +      .
→      gene_id "NM_002303"; transcript_id "NM_002303";
chr1  hg19_refGene  CDS      144046041    144046149    0.000000      +      2.
→      gene_id "NM_001039703"; transcript_id "NM_001039703";
chr1  hg19_refGene  exon     170284375    170284513    0.000000      +      .
→      gene_id "NM_001136127"; transcript_id "NM_001136127";
chr1  hg19_refGene  CDS      204655872    204655956    0.000000      +      2.
→      gene_id "NM_001170637"; transcript_id "NM_001170637";

```

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chr1	hg19_refGene	exon	208640435	208640629	0.000000	+	. _u
→	gene_id "NM_001170580"; transcript_id "NM_001170580";						
chr1	hg19_refGene	CDS	233916872	233916970	0.000000	-	0 _u
→	gene_id "NM_000081"; transcript_id "NM_000081";						
chr1	hg19_refGene	CDS	233946635	233946701	0.000000	-	1 _u
→	gene_id "NM_000081"; transcript_id "NM_000081";						
chr1	hg19_refGene	exon	3407601	3407732	0.000000	-	.
→	"NM_001409"; transcript_id "NM_001409";						
chr1	hg19_refGene	exon	10113360	10113458	0.000000	+	. _u
→	gene_id "NM_006048"; transcript_id "NM_006048";						

Note:

1. Each feature (exon, intron, UTR, etc) is processed separately and independently, and we do NOT check if features originally belonging to the same gene were converted into the same gene.
2. If a user wants to lift over gene annotation files, use BED12 format.
3. If no output file was specified, the output will be printed to screen (console). In this case, items that failed to convert are also printed out.

5.6 Convert VCF format files

VCF (variant call format) is a flexible and extendable line-oriented text format developed by the [1000 Genome Project](#). It is useful for representing single nucleotide variants, indels, copy number variants, and structural variants. Chromosomes, coordinates, and reference alleles are updated to a new assembly, and all the other fields are not changed.

Typing `CrossMap vcf -h` will print help message:

```
$ CrossMap vcf -h

usage: CrossMap vcf [-h] [--chromid {a,s,l}] [--no-comp-alleles] [--compress]
                    input.chain input.vcf refgenome.fa out_vcf

positional arguments:
  input.chain           Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)u
  →describes           pairwise alignments between two genomes. The input chain file canu
  →be a plain          text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.vcf            Input VCF (variant call format, https://samtools.github.io/hts-specs/VCFv4.2.pdf). The VCF file can be plain text file, compressedu
  →file with           extension of .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URLu
  →pointing to         accessible remote files (http://, https:// and ftp://). Compressedu
  →remote files        are not supported.
  refgenome.fa         Chromosome sequences of target assembly in FASTA
                      (https://en.wikipedia.org/wiki/FASTA\_format) format.
```

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```

out_vcf          Output VCF file.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}    The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
  ↪ "chr1",
                      "chrX"); "s" = "short style" (eg. "1", "X").
  --no-comp-alleles    If set, CrossMap does NOT check if the reference allele is
  ↪ different from the
                      alternate allele.
  --compress          If set, compress the output VCF file by calling the system "gzip".

```

Example: filter out variants [reference_allele == alternative_allele]:

```

$ CrossMap vcf GRCh37_to_GRCh38.chain.gz test02_hg19.vcf hg38.fa out.hg38.vcf
@ 2020-12-08 22:33:16: Read the chain file:  ../data/human/GRCh37_to_GRCh38.chain.gz
@ 2020-12-08 22:33:17: Filter out variants [reference_allele == alternative_allele] ...
@ 2020-12-08 22:33:17: Updating contig field ...
@ 2020-12-08 22:33:17: Lifting over ...
@ 2020-12-08 22:33:17: Total entries: 882
@ 2020-12-08 22:33:17: Failed to map: 2

```

Example: Keep variants [reference_allele == alternative_allele]. Turn on --no-comp-allele:

```

$ CrossMap vcf GRCh37_to_GRCh38.chain.gz test02_hg19.vcf hg38.fa out.hg38.vcf --no-comp-
  ↪ allele
@ 2020-12-08 22:36:51: Read the chain file:  ../data/human/GRCh37_to_GRCh38.chain.gz
@ 2020-12-08 22:36:51: Keep variants [reference_allele == alternative_allele] ...
@ 2020-12-08 22:36:51: Updating contig field ...
@ 2020-12-08 22:36:51: Lifting over ...
@ 2020-12-08 22:36:51: Total entries: 882
@ 2020-12-08 22:36:51: Failed to map: 1

```

Note:

1. Genome coordinates and reference alleles will be updated to target assembly.
 2. The reference genome is the genome sequences of target assembly.
 3. If the reference genome sequence file (../database/genome/hg18.fa) was not indexed, CrossMap will automatically index it (only the first time you run CrossMap).
 4. Output files: *output_file* and *output_file.unmap*.
 5. In the output VCF file, whether the chromosome IDs contain “chr” or not depends on the format of the input VCF file.
-

Interpretation of Failed tags:

- Fail(Multiple_hits) : This genomic location was mapped to two or more locations to the target assembly.
- Fail(REF==ALT) : After liftover, the reference allele is the same as the alternative allele (i.e. this is NOT an SNP/variant after liftover). In version 0.5.2, this checking can be turned off by setting ‘--no-comp-alleles’.
- Fail(Unmap) : Unable to map this location to the target assembly.

- Fail(KeyError) : Unable to find the contig ID (or chromosome ID) from the reference genome sequence (of the target assembly).

5.7 Convert MAF format files

MAF (mutation annotation format) files are tab-delimited files that contain somatic and/or germline mutation annotations. Please do not confuse with the [Multiple Alignment Format](#).

Typing `CrossMap maf -h` will print help message:

```
$ CrossMap maf -h

usage: CrossMap maf [-h] [--chromid {a,s,l}] input.chain input.maf refgenome.fa build_
↳name out_maf

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)↳
↳describes            pairwise alignments between two genomes. The input chain file can↳
↳be a plain           text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.maf           Input MAF (https://docs.gdc.cancer.gov/Data/File\_Formats/MAF\_Format/
↳) format             file. The MAF file can be plain text file, compressed file with↳
↳extension of         .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URL pointing to↳
↳accessible remote    files (http://, https:// and ftp://). Compressed remote files are↳
↳not supported.
  refgenome.fa        Chromosome sequences of target assembly in FASTA
                      (https://en.wikipedia.org/wiki/FASTA\_format) format.
  build_name          the name of the *target_assembly* (eg "GRCh38").
  out_maf             Output MAF file.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
↳"chr1",              "chrX"); "s" = "short style" (eg. "1", "X").
```

5.8 Convert GVCF format files

GVCF file format is described in [here](#).

Typing `CrossMap gvcf -h` will print help message:

```
$ CrossMap gvcf -h

usage: CrossMap gvcf [-h] [--chromid {a,s,l}] [--no-comp-alleles] [--compress]
                      input.chain input.gvcf refgenome.fa out_gvcf
```

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```
positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
↳ describes           pairwise alignments between two genomes. The input chain file can
↳ be a plain          text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.gvcf          Input gVCF (genomic variant call format, https://samtools.github.io/hts-specs/VCFv4.2.pdf). The gVCF file can be plain text file,
↳ hts-                compressed file with
↳ compressed file with extension of .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URL
↳ pointing to         accessible remote files (http://, https:// and ftp://). Compressed
↳ remote files        are not supported.
  refgenome.fa        Chromosome sequences of target assembly in FASTA
                      (https://en.wikipedia.org/wiki/FASTA\_format) format.
  out_gvcf            Output gVCF file.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style" (eg.
↳ "chr1",             "chrX"); "s" = "short style" (eg. "1", "X").
  --no-comp-alleles   If set, CrossMap does NOT check if the reference allele is
↳ different from the  alternate allele.
  --compress          If set, compress the output VCF file by calling the system "gzip".
```

Example (Convert GVCf file from hg19 to hg38):

```
$ CrossMap gvcf GRCh37_to_GRCh38.chain.gz test10_hg19.gvcf hg38.fa out.hg38.gvcf
@ 2020-12-08 22:19:44: Read the chain file:  ../data/human/GRCh37_to_GRCh38.chain.gz
@ 2020-12-08 22:19:44: Filter out variants [reference_allele == alternative_allele] ...
@ 2020-12-08 22:19:44: Updating contig field ...
@ 2020-12-08 22:19:44: Lifting over ...
@ 2020-12-08 22:19:44: Total variants: 10
@ 2020-12-08 22:19:44: Variants failed to map: 1
@ 2020-12-08 22:19:44: Total non-variant regions: 22
@ 2020-12-08 22:19:44: Non-variant regions failed to map: 0
```

5.9 Convert large genomic regions

For **large genomic regions** such as CNV blocks, the `CrossMap bed` will split each large region into smaller blocks that are 100% matched to the target assembly. `CrossMap region` will NOT split large regions, instead, it will calculate the **map ratio** (i.e. {bases mapped to target genome} / {total bases in query region}). If the **map ratio** is larger than the threshold specified by `-r`, the coordinates will be converted to the target genome, otherwise, it fails.

Typing `CrossMap region -h` will print help message:

```
usage: CrossMap region [-h] [--chromid {a,s,l}] [-r MIN_MAP_RATIO] input.chain input.bed
↳[out_bed]

positional arguments:
  input.chain          Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html)
↳describes            pairwise alignments between two genomes. The input chain file
↳can be a plain       text file or compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.
  input.bed           The input BED file. The first 3 columns must be "chrom", "start",
↳and "end".           The input BED file can be plain text file, compressed file with
↳extension of         .gz, .Z, .z, .bz, .bz2 and .bzip2, or even a URL pointing to
↳accessible           remote files (http://, https:// and ftp://). Compressed remote
↳files are not        supported.
  out_bed             Output BED file. if argument is missing, CrossMap will write BED
↳file to the          STDOUT.

optional arguments:
  -h, --help          show this help message and exit
  --chromid {a,s,l}   The style of chromosome IDs. "a" = "as-is"; "l" = "long style"
↳(eg. "chr1",        "chrX"); "s" = "short style" (eg. "1", "X").
  -r MIN_MAP_RATIO, --ratio MIN_MAP_RATIO
                      Minimum ratio of bases that must remap.
```

Example:

```
$CrossMap region GRCh37_to_GRCh38.chain.gz test11_hg19_region.bed

@ 2020-08-14 16:46:04: Read the chain file: ../data/human/GRCh37_to_GRCh38.chain.gz
chr1    0      25000000 ->    chr1    10000    2568561 map_ratio=0.9360
chr1    145394955 145807817 ->    chr1    145627235 146040039
↳map_ratio=0.9994
chr1    146527987 147394444 ->    chr1    147056425 147922330
↳map_ratio=0.9989
chr10   82045472  88931651  ->    chr10   80285716  87171894
↳map_ratio=1.0000
chr11   43940000  46020000  ->    chr11   43918450  45998449
↳map_ratio=1.0000
chr15   22805313  23094530  Fail    map_ratio=0.3607
chr15   22805313  28390339  ->    chr15   22598414  28145193
↳map_ratio=0.8967
chr15   31080645  32462776  ->    chr15   30788442  32170575
↳map_ratio=1.0000
chr15   72900171  78151253  ->    chr15   72607830  77858911
↳map_ratio=1.0000
chr15   83219735  85722039  ->    chr15   82550985  85178808
↳map_ratio=0.9800
```

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chr16	15511655	16293689	->	chr16	15417798	16199832	↵
↵map_ratio=1.0000							
chr16	21950135	22431889	->	chr16	21938814	22420568	↵
↵map_ratio=1.0000							
chr16	28823196	29046783	->	chr16	28811875	29035462	↵
↵map_ratio=1.0000							
chr16	29650840	30200773	->	chr16	29639519	30189452	↵
↵map_ratio=1.0000							
chr17	1247834	1303556	->	chr17	1344540	1400262	map_ratio=1.0000
chr17	2496923	2588909	->	chr17	2593629	2685615	map_ratio=1.0000
chr17	16812771	20211017	->	chr17	16909457	20307704	↵
↵map_ratio=1.0000							
chr17	29107491	30265075	->	chr17	30780473	31938056	↵
↵map_ratio=1.0000							
chr17	34815904	36217432	Unmap				
chr17	43705356	44164691	->	chr17	45627990	46087325	↵
↵map_ratio=1.0000							
chr2	50145643	51259674	->	chr2	49918505	51032536	↵
↵map_ratio=1.0000							
chr2	96742409	97677516	->	chr2	96076661	97011779	↵
↵map_ratio=1.0000							
chr2	111394040	112012649	->	chr2	110636463	111255072	↵
↵map_ratio=1.0000							
chr2	239716679	243199373	->	chr2	238808038	242183529	↵
↵map_ratio=0.9622							
chr22	19037332	21466726	Fail	map_ratio=0.8490			
chr22	21920127	23653646	->	chr22	21565838	23311459	↵
↵map_ratio=0.9996							
chr22	51113070	51171640	->	chr22	50674642	50733212	↵
↵map_ratio=1.0000							
chr3	195720167	197354826	->	chr3	195993296	197627955	↵
↵map_ratio=1.0000							
chr4	1552030	2091303	->	chr4	1550303	2089576	map_ratio=1.0000
chr5	175720924	177052594	->	chr5	176293921	177625593	↵
↵map_ratio=1.0000							
chr7	72744915	74142892	->	chr7	73330912	74728554	↵
↵map_ratio=0.9997							
chr8	8098990	11872558	->	chr8	8241468	12015049	map_ratio=1.0000
chr9	140513444	140730578	->	chr9	137618992	137836126	↵
↵map_ratio=1.0000							

Note:

1. Input BED file should have at least 3 columns (chrom, start, end). Additional columns will be kept as is.

5.10 View chain file

Typing `CrossMap viewchain -h` will print help message:

```
usage: CrossMap viewchain [-h] input.chain

positional arguments:
  input.chain  Chain file (https://genome.ucsc.edu/goldenPath/help/chain.html) describes
↳ pairwise   alignments between two genomes. The input chain file can be a plain text
↳ file or    compressed (.gz, .Z, .z, .bz, .bz2, .bzip2) file.

optional arguments:
  -h, --help  show this help message and exit
```

Example:

```
$CrossMap viewchain ../data/human/GRCh37_to_GRCh38.chain.gz >chain.tab
$head chain.tab
1 10000 177417 + 1 10000 177417 +
1 227417 267719 + 1 257666 297968 +
1 317719 471368 + 1 347968 501617 -
1 521368 1566075 + 1 585988 1630695 +
1 1566075 1569784 + 1 1630696 1634405 +
1 1569784 1570918 + 1 1634408 1635542 +
1 1570918 1570922 + 1 1635546 1635550 +
1 1570922 1574299 + 1 1635560 1638937 +
1 1574299 1583669 + 1 1638938 1648308 +
1 1583669 1583878 + 1 1648309 1648518 +
```

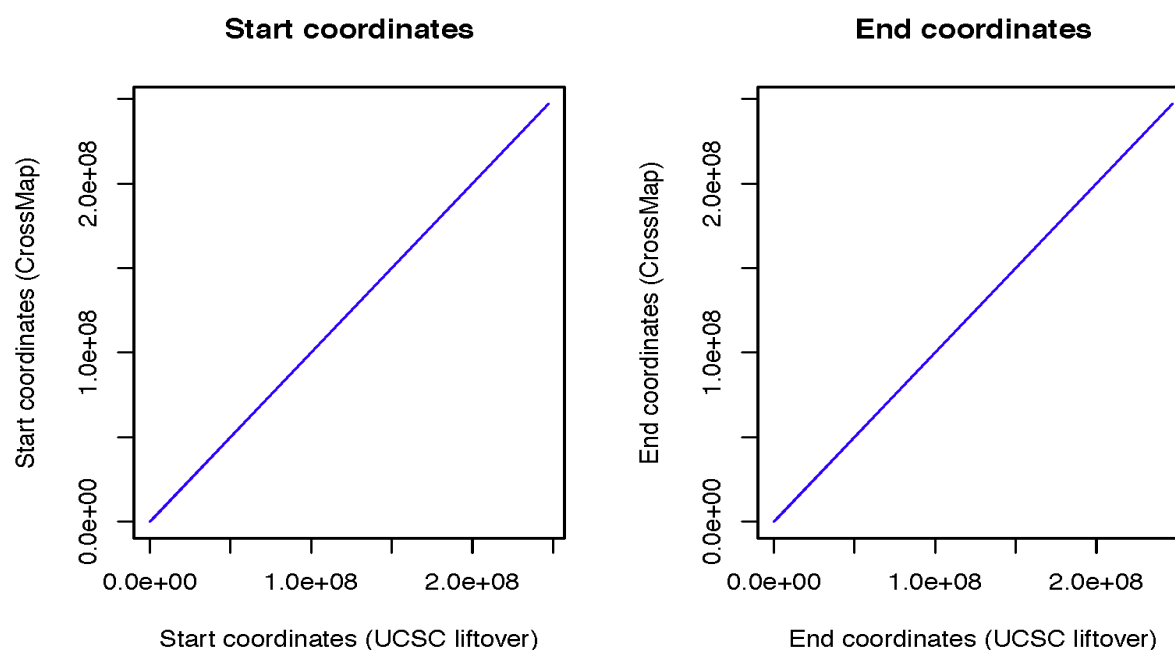

COMPARE TO UCSC LIFTOVER TOOL

To assess the accuracy of CrossMap, we randomly generated 10,000 genome intervals (download from [here](#)) with the fixed interval size of 200 bp from hg19. Then we converted them into hg18 using CrossMap and [UCSC liftover tool](#) with default configurations. We compare CrossMap to [UCSC liftover tool](#) because it is the most widely used tool to convert genome coordinates.

CrossMap failed to convert 613 intervals, and the UCSC liftover tool failed to convert 614 intervals. All failed intervals are exactly the same except for one region (chr2 90542908 90543108). UCSC failed to convert it because this region needs to be split twice:

Original (hg19)	Split (hg19)	Target (hg18)
chr2 90542908 90543108 -	chr2 90542908 90542933 -	chr2 89906445 89906470 -
chr2 90542908 90543108 -	chr2 90542933 90543001 -	chr2 87414583 87414651 -
chr2 90542908 90543108 -	chr2 90543010 90543108 -	chr2 87414276 87414374 -

For genome intervals that were successfully converted to hg18, the start and end coordinates are exactly the same between UCSC conversion and CrossMap conversion.



CITATION

Zhao, H., Sun, Z., Wang, J., Huang, H., Kocher, J.-P., & Wang, L. (2013). CrossMap: a versatile tool for coordinate conversion between genome assemblies. *Bioinformatics* (Oxford, England), btt730

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