CrossMap
Convert Genome Coordinates Between Assemblies

What is CrossMap ?

- CrossMap is a program for convenient conversion of genome coordinates (or annotation files) between *different assemblies* (such as Human hg18 (NCBI36) <> hg19 (GRCh37), Mouse mm9 (MGSCv37) <> mm10 (GRCm38)).
- It supports most commonly used file formats including SAM/BAM, Wiggle/BigWig, BED, GFF/GTF, VCF.
- CrossMap is designed to liftover genome coordinates between assemblies. It's *not* a program for aligning sequences to reference genome.
- We *do not* recommend using CrossMap to convert genome coordinates between species.

Why CrossMap ?

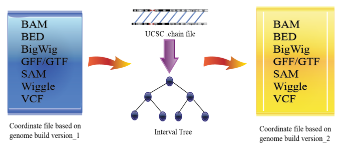
Full genome sequencing, especially mammalian (eg. human) genomes, requires extensive, continuous efforts. Therefore reference genome assemblies are subject to change and refinement from time to time. Generally, researchers need to convert results that have been analyzed according to old assemblies to newer versions or *vice versa*, to facilitate meta-analysis, direct comparison as well as data integration and visualization.

Several useful conversion tools have been developed:

- UCSC liftover tool only supports BED input.
- NCBI remap support BED, GFF, GTF, VCF, etc
- Galaxy (Based on UCSC liftover tool) supports BED, GFF, GTF input.
- Ensembl assembly converter supports BED, GFF, GTF, PSL input, but output is GFF only.
- pyliftover "only does conversion of point coordinates, that is, unlike liftOver, it does not convert ranges, nor does it provide any special facilities to work with BED files".

But none have the functionality to convert files in BAM/SAM or BigWig format. This is a significant gap in computational genomics tools, since these formats are the ones most widely used for representing high-throughput sequencing data such as RNA-seq, ChIP-seq, DNA-seq, etc.

How CrossMap works?


BAM
BED
BigWig
GFF/GTF
SAM
Wiggle
VCF
Coordinate file based on genome build version_1
UCSC chain file
Interval Tree
BAM
BED
BigWig
GFF/GTF
SAM
Wiggle
VCF
Coordinate file based on genome build version_2

Algorithm

CrossMap first determines the correspondence between genome assemblies from UCSC chain file (chain file describes the pair-wise alignments between two genomes). Genome intervals will be stored in interval tree data structure, which allows one to efficiently find all intervals that overlap with any given interval or point. Then CrossMap remaps each entry in BAM/SAM, BED, GFF/GTF, VCF file to the target assembly by querying the interval tree. Exon/intron structure in BED file; spliced alignments, paired alignments, insert size, header section, SAM flags in BAM/SAM file; reference alleles, indels in VCF file will be processed properly.

For Wiggle/BigWig format files, line-by-line computation will be very slow. To increase speed, CrossMap groups consecutive coordinates with the same coverage score into bins (i.e. genomic regions), then remaps those regions one-by-one to the target assembly by querying the interval tree. In other words, Wiggle/BigWig files will be converted into bedGraph format internally, which will be converted into BigWig format (if UCSC's 'wigToBigWig' executable exists and is callable).

Time complexity

Assume there are N lines in the chain file. CrossMap loads the chain file first and process the query file line by line. Thus the space complexity is O(N). For each query region (s,t), it takes O(logN) time to locate which chain(s) overlap with s and t. Then it takes O(logN) time to search the sorted ungapped alignments in this chain that overlap with s and t and calculate the converted values for s and t in the target assembly. So in total it takes O(logN) time to convert one query. The time complexity is O(logN*M) to convert M queries.

In practical, the time CrossMap takes increases linearly to the size of input file.

News

- 07/27/15: Release version 0.1.9. For VCF file conversion in v0.1.9:
  - CrossMap uses the indexed reference genome (target assembly) sequences rather than load the entire file into memory. Users could index their reference genome file using **samtools faidx** before running CrossMap, otherwise CrossMap will index it automatically the first time you run it.
  - In the output VCF file, whether the chromosome IDs contain "chr" or not depends on the input format.
- 05/15/15: Release version 0.1.8: Fixed the bug that CrossMap will output invalid VCF file when the input VCF file contains a INFO field with whitespace.
- 05/04/15: Release version 0.1.7: Address the problem that CrossMap does not convert strand in inversions when input file is BED6 or BED12 format.
- 11/06/14: Release version 0.1.6: Fixed "negative coordinates" bug.
- 08/05/14: Release version 0.1.5: Support compressed (*.gz, *.Z, *.z, *.bz, *.bz2, *.bzip2) wiggle file as input.
- 05/19/14: add chain files for hg38->hg19, hg19->hg38, hg18->hg38, hg19->GRCh37, GRCh37->hg19. In CrossMap v0.1.4, conversion results of BAM/SAM files can be directed to STDOUT to support piping.
- 12/12/13: CrossMap was accepted by Bioinformatics
- 10/23/13: CrossMap (0.1.3) was released

Download

- Source code CrossMap (recommended)
- Test datsets

Installation

Prerequisite:

1. gcc
2. python2.7.*
3. numpy
4. cython

Download CrossMap program from here:

```
$ tar zxf CrossMap-VERSION.tar.gz

$ cd CrossMap-VERSION

# install CrossMap to default location. In Linux/Unix, this location is like:
# /home/user/lib/python2.7/site-packages/
$ python setup.py install

# or you can install CrossMap to a specified location:
$ python setup.py install --root=/home/user/CrossMap

# setup PYTHONPATH. Skip this step if CrossMap was installed to default location.
$ export PYTHONPATH=/home/user/CrossMap/usr/local/lib/python2.7/site-packages:$PYTHONPAT

# Skip this step if CrossMap was installed to default location.
$ export PATH=/home/user/CrossMap/usr/local/bin:$PATH
```

NOTE:

1. Due to intensive computation, CrossMap is designed to run on Linux/Unix and Mac OS. Some modules may not work properly on Windows.
2. Mac users need to download and install Xcode command line tools.

Input and Output

CrossMap basically needs 2 input files. chain format file describing genom-wide pairwise alignments between assemblies and the file containing genome coordinates that you want to convert to different assembly. If input file is in VCF format, a reference genome sequence file(in FASTA format) is needed.

Chain file

Example of chain file:

```
chain 4900 chrY 58368225 + 25985403 25985638 chr5 151006098 - 43257292 43257528 1
 9       1       0
 10      0       5
 61      4       0
 16      0       4
 42      3       0
 16      0       8
 14      1       0
 3       7       0
 48

 chain 4900 chrY 58368225 + 25985406 25985566 chr5 151006098 - 43549808 43549970 2
 16      0       2
 60      4       0
 10      0       4
 70
```

UCSC prebuilt most commonly used chain files:

- Human (*Homo sapiens*)

- hg38ToHg19.over.chain.gz (Chain file needed to convert hg38 to hg19)
- hg19ToHg38.over.chain.gz (Chain file needed to convert hg19 to hg38)
- hg18ToHg38.over.chain.gz (Chain file needed to convert hg18 to hg38)
- hg19ToHg18.over.chain.gz (Chain file needed to convert hg19 to hg18)
- hg19ToHg17.over.chain.gz (Chain file needed to convert hg19 to hg17)
- hg18ToHg19.over.chain.gz (Chain file needed to convert hg18 to hg19)
- hg18ToHg17.over.chain.gz (Chain file needed to convert hg18 to hg17)
- hg17ToHg19.over.chain.gz (Chain file needed to convert hg17 to hg19)
- hg17ToHg18.over.chain.gz (Chain file needed to convert hg17 to hg18)
- GRCh37ToHg19.over.chain.gz (Chain file needed to convert GRCh37 to hg19)
- hg19ToGRCh37.over.chain.gz (Chain file needed to convert hg19 to GRCh37)

- Mouse (*Mus musculus*)
  - mm10ToMm9.over.chain.gz (Chain file needed to convert mm10 to mm9)
  - mm9ToMm10.over.chain.gz (Chain file needed to convert mm9 to mm10)
  - mm9ToMm8.over.chain.gz (Chain file needed to convert mm9 to mm8)

Chain file of other species can be downloaded from http://hgdownload.soe.ucsc.edu/downloads.html

User Input file

1. BAM or SAM format.
2. BED or BED-like format. BED file must has at least 3 columns ('chrom', 'start', 'end').
3. Wiggle format. "variableStep", "fixedStep" and "bedGraph" wiggle line are supported.
4. BigWig format.
5. GFF or GTF format.
6. VCF format.

NOTE: When converting **bedGraph** file, Treat it as **Wiggle** format rather than **BED** format.

Output file

Format of Output files depends on the input format

Input_format	Output_format
BED	BED (Genome coordinates will be updated to the target assembly)
BAM	BAM (Genome coordinates, header section, all SAM flags, insert size will be updated accordingly)
SAM	SAM (Genome coordinates, header section, all SAM flags, insert size will be updated accordingly)
Wiggle	bedGraph (if wigToBigWig executable does not exist)
Wiggle	BigWig (if wigToBigWig executable exists)
BigWig	bedGraph (if wigToBigWig executable does not exist)
BigWig	BigWig (if wigToBigWig executable exists)

GFF	GFF (Genome coordinates will be updated to the target assembly)
GTF	GTF (Genome coordinates will be updated to the target assembly)
VCF	VCF (Genome coordinates and reference alleles will be updated to the target assembly)

Usage

Run CrossMap.py without any arguments will print help message:

```
# run CrossMap without argument
$ python CrossMap.py
```

Screen output:

```
Program: CrossMap (v0.1.1)

Description:
  CrossMap is a program for convenient conversion of genome coordinates
  and genomeannotation files between assemblies (eg. lift from human
  hg18 to hg19 or vice versa).It support file in BAM, SAM, BED, Wiggle,
  BigWig, GFF, GTF, VCF, etc.

Usage: CrossMap.py <command> [options]

  bam  convert alignment file in BAM or SAM format.
  bed  convert genome cooridnate or annotation file in BED or BED-like format.
  bigwig       convert genome coordinate file in BigWig format.
  gff  convert genome cooridnate or annotation file in GFF or GTF format.
  vcf  convert genome coordinate file in VCF format.
  wig  convert genome coordinate file in Wiggle, or bedGraph format.
```

Run CrossMap.py with command keyword will print help message for that command:

```
$ python CrossMap.py bed
```

Screen output:

```
Usage:
  CrossMap.py bed input_chain_file input_bed_file [output_file]

Description:
  "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. BED file must
  have at least 3 columns (chrom, start, end) and no more than 12
  columns. If  no "output_file" was specified, output will be directed
  to screen (console). BED format:
  http://genome.ucsc.edu/FAQ/FAQformat.html#format1

Example:
  CrossMapy.py bed hg18ToHg19.over.chain.gz test.hg18.bed test.hg19.bed
  # write output to "test.hg19.bed"

Example:
```

```
CrossMapy.py bed hg18ToHg19.over.chain.gz test.hg18.bed
# write output to screen
```

Convert BED format files

A BED (Browser Extensible Data) file is a tab-delimited text file describing genome regions or gene annotations. It is the standard file format used by UCSC. 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 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 (eg. exon); 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 exact 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 3 columns ("chrom", "start", "end") of BED format file.
- BED6: The first 6 columns ("chrom", "start", "end", "name", "score", "strand") of BED format file.
- Other: Format has at least 3 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 "chrom (1st column)", "start (2nd column) ", "end (3rd column) " and "strand" (if any). All other columns will keep AS-IS.
2. Lines starting with '#', 'browser', 'track' will be skipped.
3. Lines will less than 3 columns will be skipped.
4. 2nd-column and 3-column must be integer, otherwise skipped.
5. "+" strand is assumed if no strand information was 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. "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 output_file was not specified, results will be printed to screen (console). In this case, the original bed entries (include items failed to convert) were also printed out.
9. If input region cannot be consecutively mapped target assembly, it will be split.

Example (run CrossMap with **no** *output_file* specified):

```
$ python CrossMap.py 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
chr1   142623351       142626523       ->      chr1    143912009       143915181
```

```
chr1   142633862       142633883       ->      chr1    143922520       143922541
chr1   142633884       142636152       ->      chr1    143922542       143924810
chr1   142636152       142636326       ->      chr1    143924813       143924987
chr1   142636339       142636391       ->      chr1    143925000       143925052
chr1   142636392       142637362       ->      chr1    143925052       143926022
chr1   142637373       142639738       ->      chr1    143926033       143928398
chr1   142639739       142639760       ->      chr1    143928399       143928420
chr1   142639761       142640145       ->      chr1    143928421       143928805
chr1   142640153       142641149       ->      chr1    143928813       143929809
```

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

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

$ cat test.hg19.bed3
chr1   143903503       143906352
chr1   143906355       143911970
chr1   143911971       143912008
chr1   143912009       143915181
chr1   143922520       143922541
chr1   143922542       143924810
chr1   143924813       143924987
chr1   143925000       143925052
chr1   143925052       143926022
chr1   143926033       143928398
chr1   143928399       143928420
chr1   143928421       143928805
chr1   143928813       143929809
```

Example (one input region was split because it cannot be consecutively mapped target assembly):

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

chr10  81346644        81349952        +       ->      chr10   81356692        81360000
chr10  81349952        81364937        +       ->      chr10   81360000        81374985
chr10  81364952        81365854        +       ->      chr10   81375000        81375902
chr10  81365875        81369946        +       ->      chr10   81375929        81380000
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:+)     c
chr10  81371412        81371432        +       (split.2:chr10:81371422:81371432:+)     c
```

Convert BAM/SAM format files

SAM (Sequence Alignment Map) format is a generic format for storing sequencing alignments, and BAM is binary and compressed version of SAM (Li et al., 2009). 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. The program version (of CrossMap) 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). Output format is determined from the input format and BAM output will be sorted and indexed automatically.

Typing command without any arguments will print help message:

```
$ python CrossMap.py bam
```

Screen output:

```
Usage: CrossMap.py bam input_chain_file input_bam_file output_file

Options:
  -m INSERT_SIZE        Average insert size of pair-end sequencing (bp).
                        [default=200.0]
  -s INSERT_SIZE_STDEV  Stanadard deviation of insert size. [default=30.0]
  -t 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.
                        [default=3.0]
```

Example (Convert BAM from hg19 to hg18):

```
$ python2.7 CrossMap.py bam hg19ToHg18.over.chain.gz test.hg19.bam test.hg18
@ 2013-11-15 14:08:01: Read hg19ToHg18.over.chain.gz ...
@ 2013-11-15 14:08:01: Liftover BAM file: test.hg19.bam ==> test.hg18.bam
@ 2013-11-15 14:08:17: Done!
@ 2013-11-15 14:08:17: Total entries: 164930
@ 2013-11-15 14:08:17: Failed to map: 5257
@ 2013-11-15 14:08:17: Sort "test.hg18.bam" ...
@ 2013-11-15 14:08:23: Index "test.hg18.sorted.bam" ...
```

# 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:chr4 LN:191154276
@SQ     SN:chr5 LN:180915260
@SQ     SN:chr6 LN:171115067
@SQ     SN:chr7 LN:159138663
@SQ     SN:chr8 LN:146364022
@SQ     SN:chr9 LN:141213431
@SQ     SN:chr10        LN:135534747
@SQ     SN:chr11        LN:135006516
@SQ     SN:chr12        LN:133851895
@SQ     SN:chr13        LN:115169878
@SQ     SN:chr14        LN:107349540
@SQ     SN:chr15        LN:102531392
@SQ     SN:chr16        LN:90354753
@SQ     SN:chr17        LN:81195210
@SQ     SN:chr18        LN:78077248
@SQ     SN:chr19        LN:59128983
@SQ     SN:chr20        LN:63025520
@SQ     SN:chr21        LN:48129895
@SQ     SN:chr22        LN:51304566
@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:Illumi
@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:chr11_random LN:215294
@SQ    SN:chr12        LN:132349534
@SQ    SN:chr13        LN:114142980
@SQ    SN:chr13_random LN:186858
@SQ    SN:chr14        LN:106368585
@SQ    SN:chr15        LN:100338915
@SQ    SN:chr15_random LN:784346
@SQ    SN:chr16        LN:88827254
@SQ    SN:chr17        LN:78774742
@SQ    SN:chr17_random LN:2617613
@SQ    SN:chr18        LN:76117153
@SQ    SN:chr18_random LN:4262
@SQ    SN:chr19        LN:63811651
@SQ    SN:chr19_random LN:301858
@SQ    SN:chr1_random  LN:1663265
@SQ    SN:chr2 LN:242951149
@SQ    SN:chr20        LN:62435964
@SQ    SN:chr21        LN:46944323
@SQ    SN:chr21_random LN:1679693
@SQ    SN:chr22        LN:49691432
@SQ    SN:chr22_random LN:257318
@SQ    SN:chr3 LN:199501827
@SQ    SN:chr3_random  LN:749256
@SQ    SN:chr4 LN:191273063
@SQ    SN:chr4_random  LN:842648
@SQ    SN:chr5 LN:180857866
@SQ    SN:chr6 LN:170899992
@SQ    SN:chr6_random  LN:1875562
@SQ    SN:chr7 LN:158821424
@SQ    SN:chr7_random  LN:549659
@SQ    SN:chr8 LN:146274826
@SQ    SN:chr8_random  LN:943810
@SQ    SN:chr9 LN:140273252
@SQ    SN:chr9_random  LN:1146434
@SQ    SN:chrM LN:16571
@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:Illumi
@PG    PN:bwa  ID:bwa  VN:0.6.2-r126
@PG    ID:CrossMap     VN:0.1.3
@CO    Liftover from original BAM/SAM file: test.hg19.bam
@CO    Liftover is based on the chain file: ../test/hg19ToHg18.over.chain.gz
```

NOTE:

1. Input is BAM or SAM format file. Output format depends on input format. (i.e BAM -> BAM, SAM -> SAM)

2. Alignments that are failed to convert will be saved in "*.unmap.bam*" or '*.unmap.sam*'.
3. If no output file specified, output will be directed to STDOUT (screen). (in this case, unmapped alignments will be saved to "input.unmap.bam" or "input.unmap.sam")
4. Header section will be updated to target assembly.
5. Genome coordinates and all SAM flags in alignment section will be updated to target assembly.
6. Optional fields in alignment section will not be updated in current version (v0.1.3).

Convert Wiggle/BigWig format files

Wiggle (WIG) format is useful for displaying continuous data such as GC content and reads intensity of high-throughput sequencing data. BigWig is a self-indexed binary-format Wiggle file, and has the advantage of supporting random access. This means only regions that need to be displayed are retrieved by genome browser, and it dramatically reduces the time needed for data transferring (Kent et al., 2010). 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 will always in bedGraph format. bedGraph format is similar to wiggle format and can be converted into BigWig format using UCSC wigToBigWig tool. We export files in bedGraph because it is usually much smaller than file in wiggle format, and more importantly, CrossMap internally transforms wiggle into bedGraph to increase running speed.

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.

Typing command without any arguments will print help message:

```
$ python2.7 CrossMap.py  wig
```

Screen output:

```
Usage:
  CrossMap.py wig input_chain_file input_wig_file output_prefix

Description:
  "input_chain_file" can be regular or compressed (*.gz, *.Z, *.z, *.bz, *.bz2,
  *.bzip2) file, local file or URL (http://, https://, ftp://) pointing to remote
  file.  Both "variableStep" and "fixedStep" wiggle lines are supported. Wiggle
  format: http://genome.ucsc.edu/goldenPath/help/wiggle.html

Example:
  CrossMapy.py wig hg18ToHg19.over.chain.gz test.hg18.wig test.hg19
```

NOTE:

1. To improve performance, this script calls GNU "sort" command internally. If "sort" command does not exist, CrossMap will exit.

Typing command without any arguments will print help message:

```
$ python2.7 CrossMap.py  bigwig
```

Screen output:

```
Usage:
  CrossMap.py bigwig input_chain_file input__bigwig_file output_prefix

Description:
  "input_chain_file" can be regular or compressed (*.gz, *.Z, *.z, *.bz, *.bz2,
  *.bzip2) file, local file or URL (http://, https://, ftp://) pointing to remote
  file. Bigwig format: http://genome.ucsc.edu/goldenPath/help/bigWig.html

Example:
  CrossMapy.py bigwig hg18ToHg19.over.chain.gz test.hg18.bw test.hg19
```

Example (Convert BigWig file from hg18 to hg19):

```
$ python CrossMap.py 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:

1. To improve performance, this script calls GNU "sort" command internally. If "sort" command does not exist, CrossMap will exit.
2. Output files: output_prefix.bw, output_prefix.bgr, output_prefix.sorted.bgr

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 output is determined from the input.

Typing command without any arguments will print help message:

```
$ python2.7 CrossMap.py  gff
```

Screen output:

```
Usage:
  CrossMap.py gff input_chain_file input_gff_file output_file

Description:
  "input_chain_file" can be regular or compressed (*.gz, *.Z, *.z, *.bz, *.bz2,
  *.bzip2) file, local file or URL (http://, https://, ftp://) pointing to remote
  file. input file must be in GFF or GTF format. GFF format:
  http://genome.ucsc.edu/FAQ/FAQformat.html#format3 GTF format:
  http://genome.ucsc.edu/FAQ/FAQformat.html#format4

Example:
  CrossMap.py gff  hg19ToHg18.over.chain.gz test.hg19.gtf test.hg18.gtf #write output to

Example:
   CrossMap.py gff  hg19ToHg18.over.chain.gz test.hg19.gtf  # write output to screen
```

Example (Convert GTF file from hg19 to hg18):

```
$ python CrossMap.py 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
chr1   hg19_refGene    exon    66081691        66081907        0.000000        +       .
chr1   hg19_refGene    CDS     145334684       145334792       0.000000        +       2
chr1   hg19_refGene    exon    172017752       172017890       0.000000        +       .
chr1   hg19_refGene    CDS     206589249       206589333       0.000000        +       2
chr1   hg19_refGene    exon    210573812       210574006       0.000000        +       .
chr1   hg19_refGene    CDS     235850249       235850347       0.000000        -       0
chr1   hg19_refGene    CDS     235880012       235880078       0.000000        -       1
chr1   hg19_refGene    exon    3417741 3417872 0.000000        -       .       gene_id "
chr1   hg19_refGene    exon    10190773        10190871        0.000000        +       .

$ head test.hg18.gtf
chr1   hg19_refGene    CDS     48039732        48039878        0.000000        -       0
chr1   hg19_refGene    exon    65854279        65854495        0.000000        +       .
chr1   hg19_refGene    CDS     144046041       144046149       0.000000        +       2
chr1   hg19_refGene    exon    170284375       170284513       0.000000        +       .
chr1   hg19_refGene    CDS     204655872       204655956       0.000000        +       2
chr1   hg19_refGene    exon    208640435       208640629       0.000000        +       .
chr1   hg19_refGene    CDS     233916872       233916970       0.000000        -       0
chr1   hg19_refGene    CDS     233946635       233946701       0.000000        -       1
chr1   hg19_refGene    exon    3407601 3407732 0.000000        -       .       gene_id "
chr1   hg19_refGene    exon    10113360        10113458        0.000000        +       .
```

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 user want to liftover gene annotation files, use BED12 format.
3. If no output file was specified, output will be printed to screen (console). In this case, items failed to convert are also printed out.

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 command without any arguments will print help message:

```
$ python2.7 CrossMap.py  gff
```

Screen output:

```
usage:
  CrossMap.py vcf input_chain_file input_VCF_file ref_genome_file output_file

Description:
  "input_chain_file" and "input_VCF_file" can be regular or compressed (*.gz, *.Z,
  *.z, *.bz, *.bz2, *.bzip2) file, local file or URL (http://, https://, ftp://)
  pointing to remote file. "ref_genome_file" is genome sequence file of 'target
  assembly' in FASTA foramt.
```

```
Example:
  CrossMap.py vcf hg19ToHg18.over.chain.gz test.hg19.vcf hg18.fa test.hg18.vcf
```

Example (Convert VCF file from hg19 to hg18):

```
$ python CrossMap.py vcf hg19ToHg18.over.chain.gz test.hg19.vcf ../database/genome/hg18.
@ 2015-07-27 10:14:23: Read chain_file:  ../data/hg19ToHg18.over.chain.gz
@ 2013-11-17 20:53:39: Creating index for ../database/genome/hg18.fa
@ 2015-07-27 10:14:50: Total entries: 497
@ 2015-07-27 10:14:50: Failed to map: 0

$ grep -v '#' test.hg19.vcf  |head -10
chr1   10933566        .       C       G       .       PASS    ADP=13;WT=0;HET=0;HOM=1;N
chr1   11187893        .       T       C       .       PASS    ADP=224;WT=0;HET=0;HOM=1;
chr1   11205058        .       C       T       .       PASS    ADP=625;WT=0;HET=0;HOM=1;
chr1   11292753        .       A       G       .       PASS    ADP=52;WT=0;HET=0;HOM=1;N
chr1   11318763        .       C       G       .       str10   ADP=88;WT=0;HET=0;HOM=1;N
chr1   11319587        .       A       G       .       PASS    ADP=70;WT=0;HET=0;HOM=1;N
chr1   16202995        .       C       T       .       PASS    ADP=463;WT=0;HET=1;HOM=0;
chr1   27088546        .       A       T       .       PASS    ADP=124;WT=0;HET=1;HOM=0;
chr1   27101390        .       T       C       .       str10   ADP=267;WT=0;HET=1;HOM=0;
chr1   34007097        .       T       C       .       PASS    ADP=10;WT=0;HET=1;HOM=0;N

$ grep -v '#' test.hg18.vcf  |head -10
1      10856153        .       C       G       .       PASS    ADP=13;WT=0;HET=0;HOM=1;N
1      11110480        .       T       C       .       PASS    ADP=224;WT=0;HET=0;HOM=1;
1      11127645        .       C       T       .       PASS    ADP=625;WT=0;HET=0;HOM=1;
1      11215340        .       A       G       .       PASS    ADP=52;WT=0;HET=0;HOM=1;N
1      11241350        .       C       G       .       str10   ADP=88;WT=0;HET=0;HOM=1;N
1      11242174        .       A       G       .       PASS    ADP=70;WT=0;HET=0;HOM=1;N
1      16075582        .       C       T       .       PASS    ADP=463;WT=0;HET=1;HOM=0;
1      26961133        .       A       T       .       PASS    ADP=124;WT=0;HET=1;HOM=0;
1      26973977        .       T       C       .       str10   ADP=267;WT=0;HET=1;HOM=0;
1      33779684        .       T       C       .       PASS    ADP=10;WT=0;HET=1;HOM=0;N

$ grep -v '#' test.hg18.vcf.unmap      #coordinates are still based on hg19
chr14  20084444        .       G       C       .       PASS    ADP=253;WT=0;HET=1;HOM=0;
chr14  20086290        .       T       C       .       PASS    ADP=441;WT=0;HET=1;HOM=0;
```

NOTE:

1. Genome coordinates and reference allele will be updated to target assembly.
2. Reference genome is genome sequence of target assembly.
3. If the reference genome sequence file (../database/genome/hg18.fa) was not indexed, CrossMap will automatically indexed 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.

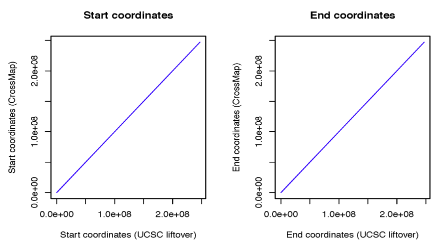
Compare to UCSC liftover tool

To access 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 UCSC liftover tool failed to convert 614 intervals. All failed intervals were exactly the same except one region (chr2 90542908 90543108). UCSC failed to convert it because this region needs to be split 2 times:

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 were exactly the same between UCSC conversion and CrossMap conversion.



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Contact

- Wang.Liguo AT mayo.edu