

# Invitae Bioinformatics Exercise B

## Problem Statement

The objective is to write software that translates transcript coordinates to genomic coordinates. For example consider the simple transcript TR1, which aligns to the a genome as follows:

COORD	0	5	10	15	20	25	30	35	40	45	50
GENOME: CHR1	ACTGTCATGTACGTTTAGCTAGCC--TAGCTAGGGACCTAGATAATTTAGCTAG										
TR1	GTCATGTA-----CTAGCCGGTA-----AGATAAT										
	0	5			10	15			20	24	

We can compactly express this alignment in the same way that we compactly represent a read alignment in the [SAM/BAM format](#): using a position and CIGAR string. In this case, the (0-based) position is CHR1:3, and the CIGAR string is 8M7D6M2I2M11D7M. For this exercise, you may assume that the transcript is always mapped from genomic 5' to 3'.

The objective is then to translate a (0-based) transcript coordinate to a (0 based) genome coordinate. For example the fifth base in TR1 (i.e. TR1:4) maps to genome coordinate CHR1:7. Similarly, TR1:13 maps to CHR1:23 and TR1:14 maps to an insertion immediately before CHR1:24.

## Problem Specification

The software (implemented in a language of your choice, with some preference towards python) should take the following inputs:

1. A four column (tab-separated) file containing the transcripts. The first column is the transcript name, and the remaining three columns indicate it's genomic mapping: chromosome name, 0-based starting position on the chromosome, and CIGAR string indicating the mapping.
2. A two column (tab-separated) file indicating a set of queries. The first column is a transcript name, and the second column is a 0-based transcript coordinate.

You may assume that the files are well-formatted, but any error handling is considered a plus. The output is a four column tab separated file with one row for each of the input queries. The first two columns are exactly the two columns from the second input file, and the remaining two columns are the chromosome name and chromosome coordinate, respectively. Example input/output is provided below.

Third-party libraries can used as much as desired except for solving the primary bioinformatics problem of translating coordinates. Correctness is naturally the most important feature of any solution. Following that, the implementation should demonstrate good software engineering practices with an eye towards efficiency and generality. Please explicitly document what you believe are key strengths and/or weaknesses of your implementation.

## Bells and Whistles

This exercise can be extended in a number of ways, if desired (this is absolutely not necessary, but it might be interesting to think about):

1. Handle transcripts mapping with reverse orientation, i.e. remove the limitation that transcripts map genomic 5' to 3' by allowing the transcript definition to include a binary variable for direction.
2. Consider mapping genomic coordinates onto transcript coordinates.
3. Consider mapping a transcript *range* onto a genomic range (or the reverse). A transcript CIGAR onto a genomic CIGAR (or the reverse)?
4. A real-world implementation of this code would need transcripts from external sources. Discuss where and how you might obtain these.

## Sample Input/Output

### Input file 1:

TR1	CHR1	3	8M7D6M2I2M11D7M
TR2	CHR2	10	20M

### Input file 2:

TR1	4
TR2	0
TR1	13
TR2	10

### Output file:

TR1	4	CHR1	7
TR2	0	CHR2	10
TR1	13	CHR1	23
TR2	10	CHR2	20