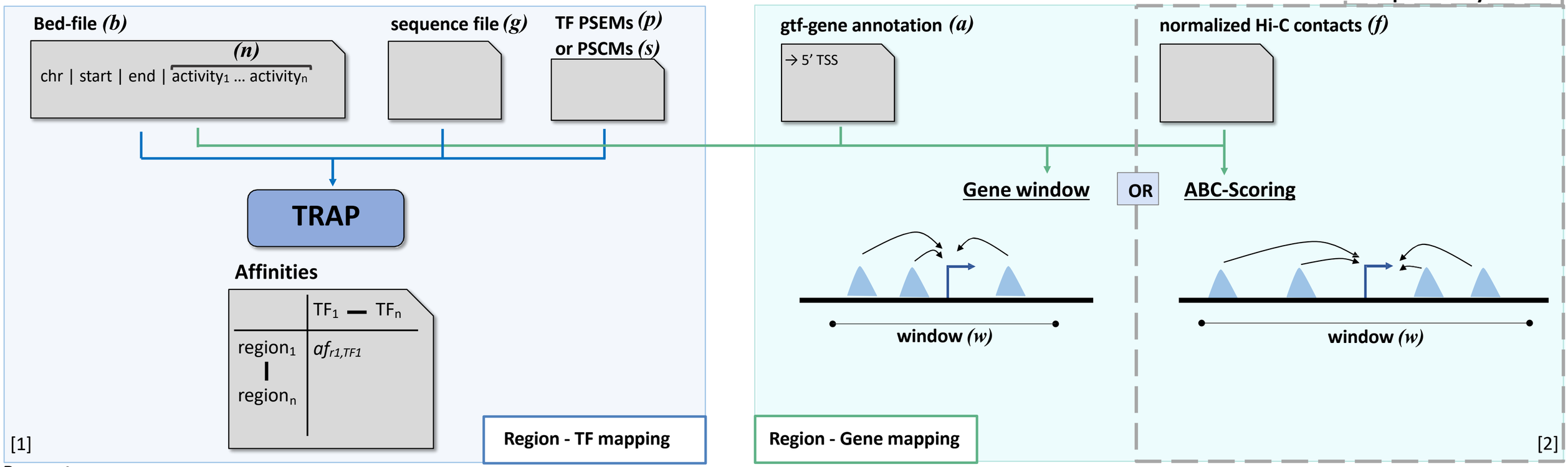
independently usable



Parameter

b - bed file, optionally with activity column(s) for cell types / metacells
a - gene annotation as gtf-file
g - fasta-file with the genome sequence
p - PSEMs of TFs <**OR**> ***s*** - PSCM as transfac and ***y*** - GC content
o - output prefix, creates a folder

optional:

w - window size centred at 5' TSS (default 50kb for 'Gene window' and 5MB for 'ABC-Scoring')
n - activity column(s), start counting at 1, e.g. for metacells
c - number of cores to use for computation
x - bed-file with regions to exclude
u - file with rows of gene IDs/symbols to limit the output (else all in gtf)

ABC-specific

i - 'all_tss' to average all TSS for ABC, or '5_tss' to only use 5'
q- use the adapted ABC-score (default True)
f - folder with normalized Hi-C contacts
k - bin-size of Hi-C files, required for ABC-Scoring
t - cut-off for ABC-scored interactions (default 0.02)
d - add pseudocount to Hi-C contacts (default True)
m -window size for -q adaptation (5MB, automatically ≥w)
r - ABC-Score file, if already calculated in advance
y - gc-content to calculcate PSEMs, default automatic from -b
e - scale for distance (default True) , only w/o ABC-mapping
z - write binary output (default False)

$$af_{g,tf} = \sum_{r \in R_g} \frac{af_{r,tf}}{ml_{tf}} \cdot scaler$$

$scaler$ depends on approach:

Gene window

$$A_r \cdot \underbrace{e^{-\frac{d_{r,g}}{d_0}}}_{(f)}$$

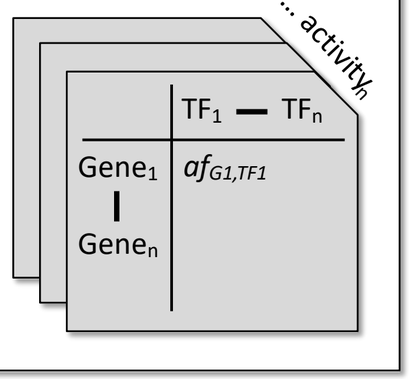
adapted ABC-scoring *(q)*

$$\begin{cases} A_r \cdot e^{-\frac{d_{r,g}}{d_0}}, & if\ d_{r,g} \leq 2500bp \\ A_{r,g}, & otherwise \end{cases}$$

ABC-scoring

$$\begin{cases} A_r \cdot e^{-\frac{d_{r,g}}{d_0}}, & if\ d_{r,g} \leq 2500bp \\ A_{r,g} \cdot \frac{C_{r,g}}{C_{max}}, & otherwise \end{cases}$$

Gene-TF matrices



$af_{g,tf}$: affinity score of TF *tf* to *g*
R_g: set of regions mapped to *g*
$af_{r,tf}$: affinity of *tf* in *r*
ml_{tf} : motif length of
A_r : activity of *r*
$A_{r,g}$: adapted activity of *r* to *g*
$d_{r,g}$: distance of *r* to *g*
d_0 : distance constant of 5000 bp
$C_{r,g}$: contact of *r* with *g*
C_{max} : maximum $C_{r,g}$

STARE

1 principle based on: Florian Schmidt, Fabian Kern, Peter Ebert, Nina Baumgarten, Marcel H Schulz, TEPIC 2—an extended framework for transcription factor binding prediction and integrative epigenomic analysis, *Bioinformatics*, Volume 35, Issue 9, 1 May 2019, Pages 1608–1609, https://doi.org/10.1093/bioinformatics/bty856; https://github.com/SchulzLab/TEPIC

2 principle based on: Fulco CP, Nasser J, Jones TR, Munson G, Bergman DT, Subramanian V, Grossman SR, Anyoha R, Doughty BR, Patwardhan TA, Nguyen TH, Kane M, Perez EM, Durand NC, Lareau CA, Stamenova EK, Aiden EL, Lander ES & Engreitz JM. Activity-by-contact model of enhancer–promoter regulation from thousands of CRISPR perturbations. Nat. Genet. 51, 1664–1669 (2019).
https://www.nature.com/articles/s41588-019-0538-0https://github.com/broadinstitute/ABC-Enhancer-Gene-Prediction