a
1
Pre-processing of data
Time-series data
Teff
Teff
Treg
Treg
0
20
40
340
360
Time (min)
STIMULATION
Data normalisation
Data filtering
Intersection of the transcripts
Donor-1
14712
transcripts
Common
transcripts
13601
Donor-2
14472
transcripts
2
System Identification:
All-2-one
All-2-one
$\frac{d[FOXP3](t)}{dt} = a_n[FOXP3](t) + b_n u_n(t)$
Inputs
Outputs
Transcript 1
Transcript 2
:
Transcript n
FOXP3 transcript 1
FOXP3 Transcript 2
Obtain fitness scores
$fitness = 100 * (1 - \frac{\sum_{k=1}^{N} \sqrt{(y_k - \hat{y}_k)^2}}{\sum_{k=1}^{N} \sqrt{(y_k - \bar{y}_k)^2}})$
Exclude inconsistent models with activation/repression discrepancy between donors
Donor-1
Donor-2
Tran-script i
(ACT)
FOXP3 tran-script 1
Tran-script i
(ACT)
FOXP3 tran-script 1
Tran-script j
(ACT)
FOXP3 tran-script 2
Tran-script j
(REP)
FOXP3 tran-script 2
3
Time delay and ranking
All-2-one with input time delays,
$\frac{d[FOXP3](t)}{dt} = a[FOXP3](t) + bu_1(t - \mu_{u_1})$
where, $\mu_{u_1} =$ 0, 20, 40, 60, 80, 100 min
Treg Donor-2 (normalised)
E.g.: 40 min delay
A
B
Output
Input
mRNA concentration
1
0
180
360
Time (min)
Select the highest fitness score among all delay cases
Rank input transcripts in descending order of their fitness score
b
Fitness score (from All-2-one)
60
40
20
0
2000
4000
6000
8000
Model number
60
50
0
200
c
Regulatory genes
RNF12
PDE4D
NRBF2
NCOA7
MAP1LC3B
FOXP3
Target gene