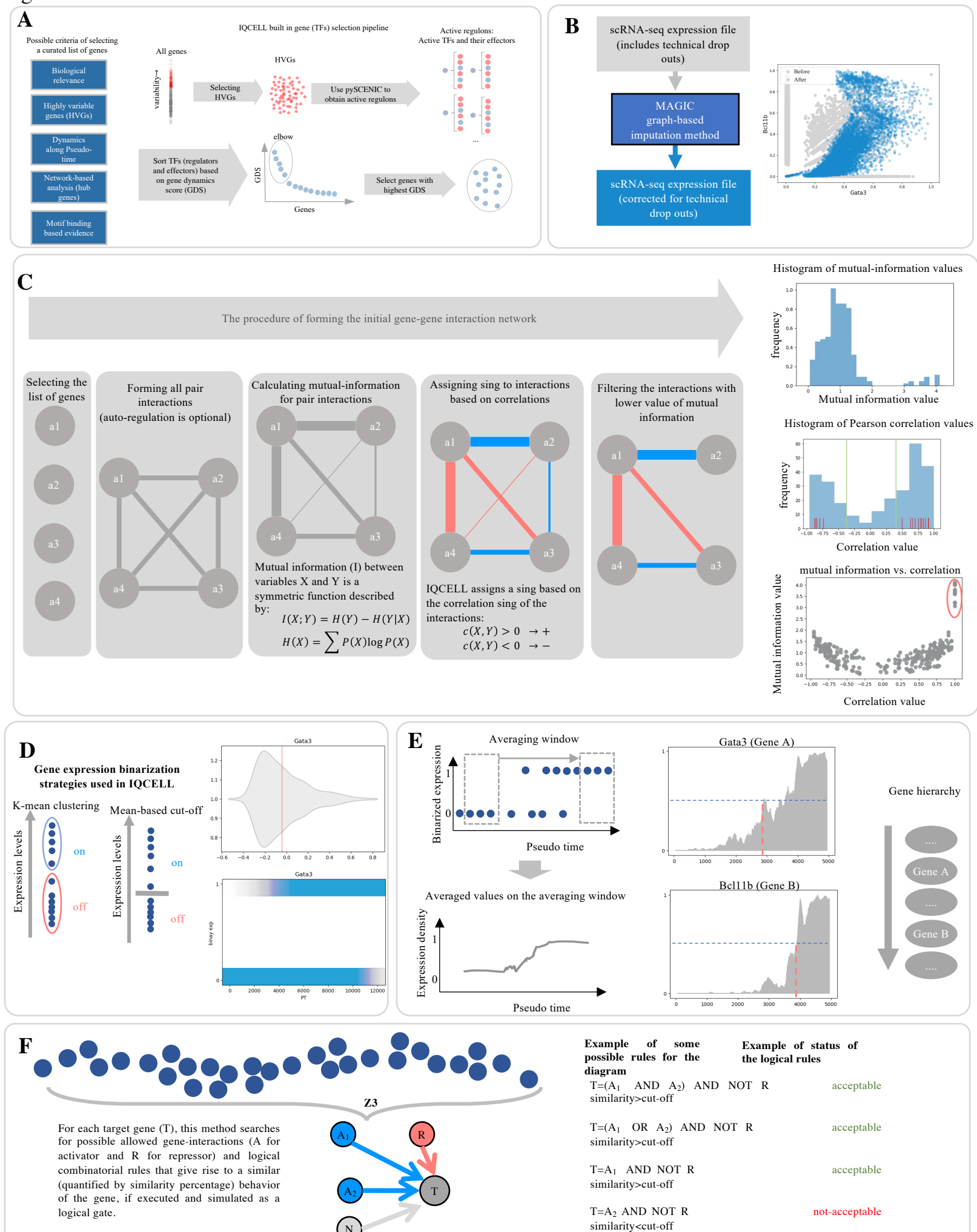
Fig. S1


A
Possible criteria of selecting a curated list of genes
Biological relevance
Highly variable genes (HVGs)
Dynamics along Pseudo-time
Network-based analysis (hub genes)
Motif binding based evidence
IQCELL built in gene (TFs) selection pipeline
All genes
variability
Selecting HVGs
HVGs
Use pySCENIC to obtain active regulons
Active regulons: Active TFs and their effectors
Sort TFs (regulators and effectors) based on gene dynamics score (GDS)
elbow
GDS
Genes
Select genes with highest GDS
B
scRNA-seq expression file (includes technical drop outs)
MAGIC graph-based imputation method
scRNA-seq expression file (corrected for technical drop outs)
Before
After
Bcl11b
Gata3
C
The procedure of forming the initial gene-gene interaction network
Selecting the list of genes
a1
a2
a3
a4
Forming all pair interactions (auto-regulation is optional)
Calculating mutual-information for pair interactions
Mutual information (I) between variables X and Y is a symmetric function described by:
$I(X;Y) = H(Y) - H(Y|X)$
$H(X) = \sum P(X)\log P(X)$
Assigning sing to interactions based on correlations
IQCELL assigns a sing based on the correlation sing of the interactions:
$c(X,Y) > 0 \rightarrow +$
$c(X,Y) < 0 \rightarrow -$
Filtering the interactions with lower value of mutual information
Histogram of mutual-information values
frequency
Mutual information value
Histogram of Pearson correlation values
Correlation value
mutual information vs. correlation
Mutual information value
Correlation value
D
Gene expression binarization strategies used in IQCELL
K-mean clustering
Mean-based cut-off
Expression levels
on
off
Gata3
binay exp
PT
E
Averaging window
Binarized expression
Pseudo time
Averaged values on the averaging window
Expression density
Gata3 (Gene A)
Bcl11b (Gene B)
Gene hierarchy
....
Gene A
Gene B
F
Z3
For each target gene (T), this method searches for possible allowed gene-interactions (A for activator and R for repressor) and logical combinatorial rules that give rise to a similar (quantified by similarity percentage) behavior of the gene, if executed and simulated as a logical gate.
A1
A2
R
T
N
Example of some possible rules for the diagram
Example of status of the logical rules
T=(A1 AND A2) AND NOT R similarity>cut-off acceptable
T=(A1 OR A2) AND NOT R similarity>cut-off acceptable
T=A1 AND NOT R similarity>cut-off acceptable
T=A2 AND NOT R similarity<cut-off not-acceptable