Cell Genomics, Volume *2*

Supplemental information

Uncovering novel mutational signatures

by *de novo* extraction with SigProfilerExtractor

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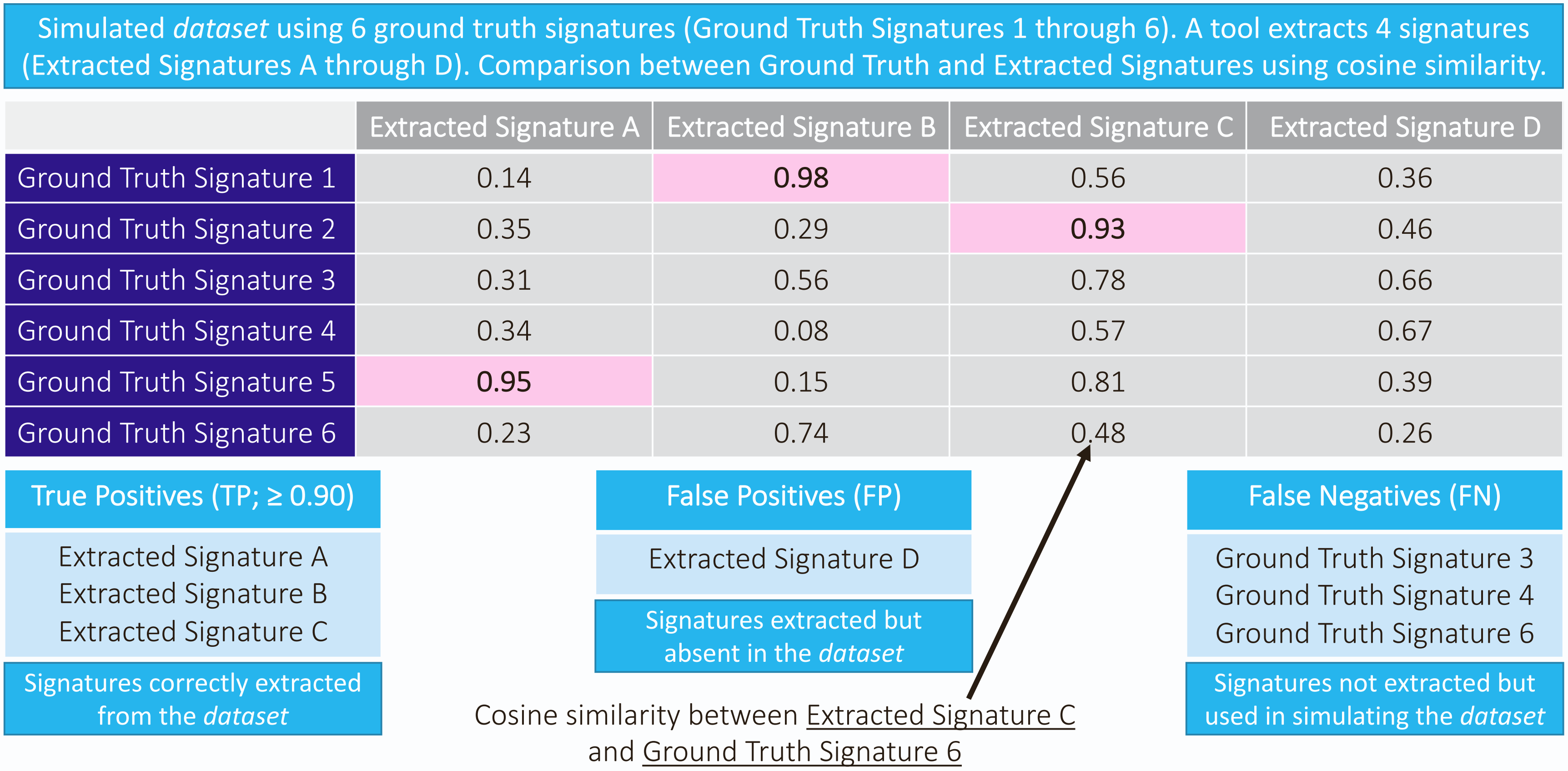
Supplementary Figures

Figure S1. Standard set of performance metrics used for benchmarking all bioinformatics tools, Related to Figures 2 and 3. An example demonstrating the derivation of *true positive* (TP), *false positive* (FP), or *false negative* (FN) signatures for a tool applied to a synthetic dataset generated using 6 ground-truth signatures (termed, Ground-Truth Signatures 1 through 6). The tool extracts 4 signatures (termed, Extracted Signatures A through D). In this example, an extracted signature is considered a true positive if it matches one of the ground-truth signatures with a cosine similarity threshold of at least 0.90.



Simulated *dataset* using 6 ground truth signatures (Ground Truth Signatures 1 through 6). A tool extracts 4 signatures (Extracted Signatures A through D). Comparison between Ground Truth and Extracted Signatures using cosine similarity.

	Extracted Signature A	Extracted Signature B	Extracted Signature C	Extracted Signature D
Ground Truth Signature 1	0.14	0.98	0.56	0.36
Ground Truth Signature 2	0.35	0.29	0.93	0.46
Ground Truth Signature 3	0.31	0.56	0.78	0.66
Ground Truth Signature 4	0.34	0.08	0.57	0.67
Ground Truth Signature 5	0.95	0.15	0.81	0.39
Ground Truth Signature 6	0.23	0.74	0.48	0.26

True Positives (TP; ≥ 0.90)

Extracted Signature A
Extracted Signature B
Extracted Signature C

Signatures correctly extracted from the *dataset*

False Positives (FP)

Extracted Signature D

Signatures extracted but absent in the *dataset*

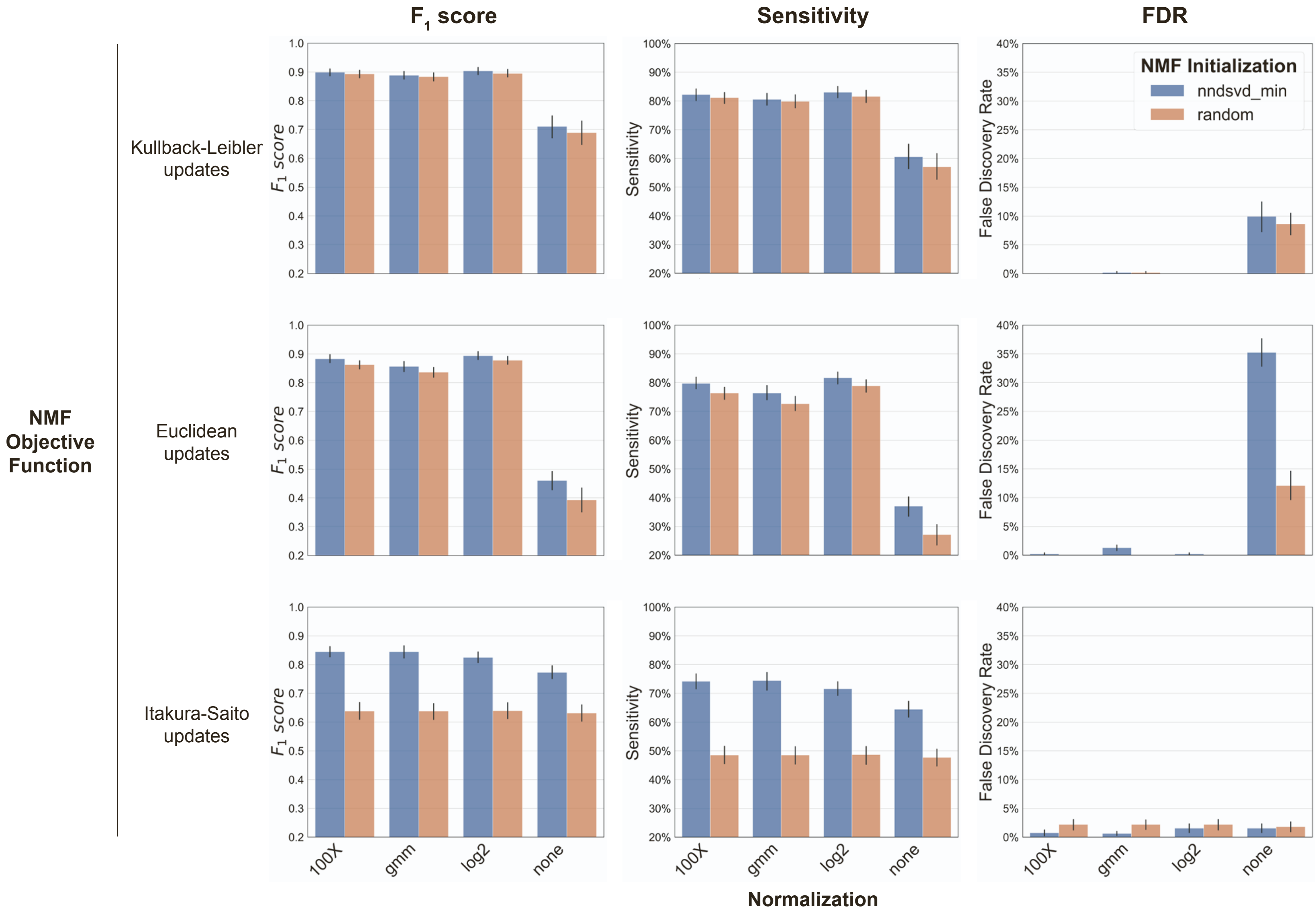
Cosine similarity between Extracted Signature C and Ground Truth Signature 6

False Negatives (FN)

Ground Truth Signature 3
Ground Truth Signature 4
Ground Truth Signature 6

Signatures not extracted but used in simulating the *dataset*

Figure S2. Comparison of the different options available in SigProfilerExtractor for matrix normalization, NMF initialization, and NMF objective function, Related to STAR Methods. Vertical axes reflect F_1 score (left plot), sensitivity (middle plot), and false discovery rate (right plot), respectively. Abbreviations: gmm: Gaussian mixture model; nndsvd_min: nonnegative double singular vector decomposition initialization where zeros are replaced by the minimum positive value.


F_1 score
Sensitivity
FDR
NMF Objective Function
Kullback-Leibler updates
Euclidean updates
Itakura-Saito updates
F_1 score
Sensitivity
False Discovery Rate
NMF Initialization
nndsvd_min
random
100X
gmm
log2
none
Normalization