

Aggregating GRNs via multiplex link prediction

Anonymous Author(s)

A Appendix

Standard deviation of AUPRC (%)														
LEAP	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PIDC	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Scribe	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GENIE3	0.01	0.02	0.02	0.06	0.03	0.03	0.02	0.01	0.01	0.02	0.05	0.03	0.02	0.02
GRNBoost2	0.01	0.07	0.05	0.18	0.09	0.09	0.13	0.01	0.04	0.01	0.06	0.09	0.09	0.09
FlowGRN	0.01	0.06	0.08	0.11	0.08	0.05	0.10	0.04	0.25	0.06	0.07	0.17	0.06	0.10
SINCERITIES	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	NE	0.00	NE
SCODE	0.01	0.02	0.03	0.01	0.02	0.01	0.01	0.00	0.01	0.02	0.01	0.01	0.01	0.02
GRISLI	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mean	0.01	0.04	0.03	0.11	0.04	0.04	0.07	0.01	0.07	0.01	0.04	0.07	0.05	0.08
COFFEE	0.01	0.04	0.04	0.15	0.06	0.03	0.02	0.01	0.04	0.02	0.06	0.08	0.03	0.08
MuxGRN	0.13	0.36	0.43	0.94	0.41	0.76	0.91	0.13	0.46	0.41	0.64	0.49	1.04	2.09
Standard deviation of the proportion (%) of newly recovered true edges														
Mean	0.10	0.06	0.06	0.20	0.06	0.24	0.30	0.08	0.06	0.06	0.11	0.07	0.07	0.14
COFFEE	0.77	0.30	0.31	1.84	0.38	0.58	0.87	0.57	0.33	0.21	0.74	0.29	0.41	0.30
MuxGRN	3.49	0.58	0.52	1.62	5.46	2.23	1.16	4.66	1.29	0.89	1.80	9.21	2.21	2.85
	hESC-500	hHep-500	mDC-500	mESC-500	mHSC-E-500	mHSC-GM-500	mHSC-L-500	hESC-1000	hHep-1000	mDC-1000	mESC-1000	mHSC-E-1000	mHSC-GM-1000	mHSC-L-1000

Fig. 2. Standard deviation of the AUPRC (%) (upper) and standard deviation of the portion (%) of newly discovered true positive edges (lower) of different GRN models on 14 BEELINE datasets out of 10 runs.

Table 1. Comparison between SOTA GRN models on their properties, inferred GRN types and methodologies. Model categories include Correlation (Corr), ODE, Regression (Reg), MI and Tree.

	Category	Signed?	Description
LEAP [10]	Corr	✗	A model that uses the maximum Pearson correlations at different time lags as the gene interaction strength
SCODE [4]	ODE	✓	A linear ODE model for the gene expression level
GRISLI [1]	ODE	✗	A model similar to SCODE but with sparsity constraint and less restrictions due to the stability selection algorithm
SINCERITIES [6]	Reg	✓	Models the gene distributional shift distances by linear regression to spot significant gene interactions
PIDC [2]	MI	✗	A model that decomposes partial information and quantifies the unique information between each pair of genes in all possible gene triplets.
Scribe [7]	MI	✗	Causality inferencing model on GRN that computes restricted directed information [8] and its variants [9]
GENIE3 [3]	Tree	✗	A tree model using random forests as predictors and feature importance as gene interaction strength
GRNBoost2 [5]	Tree	✗	A tree model using gradient boosting machines as predictors and feature importance as gene interaction strength
FlowGRN [11]	Tree	✗	A tree model using random forests as predictors and feature importance as gene interaction strength from cell trajectory reconstructed using conditional flow and score matching.

References

1. Aubin-Frankowski, P.C., Vert, J.P.: Gene regulation inference from single-cell rna-seq data with linear differential equations and velocity inference. *Bioinformatics* **36**(18), 4774–4780 (2020)
2. Chan, T.E., Stumpf, M.P., Babbie, A.C.: Gene Regulatory Network Inference from Single-Cell Data Using Multivariate Information Measures. *Cell Systems* **5**(3), 251–267 (2017)

3. Huynh-Thu, V.A., Irrthum, A., Wehenkel, L., Geurts, P.: Inferring regulatory networks from expression data using tree-based methods. *PLOS ONE* **5**(9), e12776 (2010)
4. Matsumoto, H., Kiryu, H., Furusawa, C., Ko, M.S., Ko, S.B., Gouda, N., Hayashi, T., Nikaido, I.: SCODE: an efficient regulatory network inference algorithm from single-cell RNA-Seq during differentiation. *Bioinformatics* **33**(15), 2314–2321 (2017)
5. Moerman, T., Aibar Santos, S., Bravo González-Blas, C., Simm, J., Moreau, Y., Aerts, J., Aerts, S.: GRNBoost2 and Arboreto: efficient and scalable inference of gene regulatory networks. *Bioinformatics* **35**(12), 2159–2161 (2019)
6. Papili Gao, N., Ud-Dean, S.M., Gandrillon, O., Gunawan, R.: SINCERITIES: inferring gene regulatory networks from time-stamped single cell transcriptional expression profiles. *Bioinformatics* **34**(2), 258–266 (2018)
7. Qiu, X., Rahimzamani, A., Wang, L., Ren, B., Mao, Q., Durham, T., McFaline-Figueroa, J.L., Saunders, L., Trapnell, C., Kannan, S.: Inferring causal gene regulatory networks from coupled single-cell expression dynamics using Scribe. *Cell Systems* **10**(3), 265–274 (2020)
8. Rahimzamani, A., Kannan, S.: Network inference using directed information: The deterministic limit. In: 2016 54th Annual Allerton Conference on Communication, Control, and Computing (Allerton). pp. 156–163. IEEE (2016)
9. Rahimzamani, A., Kannan, S.: Potential conditional mutual information: Estimators and properties. In: 2017 55th Annual Allerton Conference on Communication, Control, and Computing (Allerton). pp. 1228–1235. IEEE (2017)
10. Specht, A.T., Li, J.: LEAP: constructing gene co-expression networks for single-cell RNA-sequencing data using pseudotime ordering. *Bioinformatics* **33**(5), 764–766 (2017)
11. Tong, T.P., Pang, J.: FlowGRN: Scalable and dropout-robust gene regulatory network inference via flow matching-based trajectory reconstruction. In: 16th ACM International Conference on Bioinformatics, Computational Biology, and Health Informatics (BCB '25). ACM (2025)