

Fig. 1. Overview of the scNAE framework. STEP1: Gene expression profiles of each cell over the extraction time course. Then, expand the time point and calculate its differential value. STEP2: The reference GRN is rewired τ times. STEP3: Model and optimize scRNA-seq data based on ODE system. STEP4: Solve the regulatory relationship of displacement network under specific cell type and calculate the activity of reference network based on empirical test.

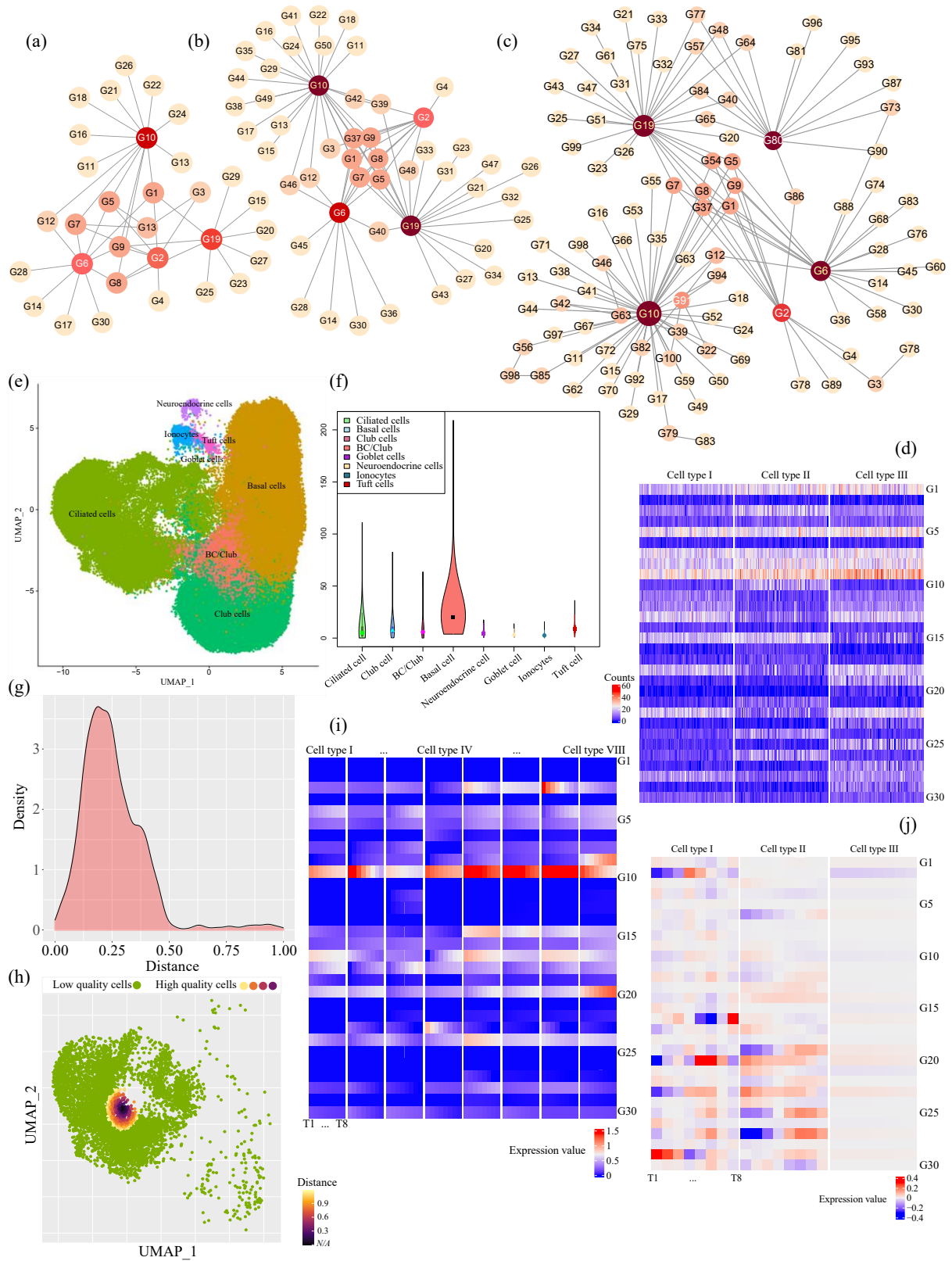


Fig. 2. (a)-(c) Simulation datasets with 30, 50 and 100 genes. (d) Simulation counts for 30 genes with 100 time-course cells per cell type. (e) Visualization of differentiated human bronchial epithelial cells infected by SARS-CoV-2. (f) Expression distribution of GSE166766 ('COVID-19 pathway') in each cell type. (g) The distance density distribution curve of Ciliated cells to the center of the class (normalized). (h) Ciliated cells closer to the class center are marked as high-quality cells, and this part of the data is extracted for downstream analysis. (i) Gene expression profile of SARS-CoV-2 infection after preprocessing (only some genes are shown). (j) Gene expression profile of Simu_30_3 after preprocessing

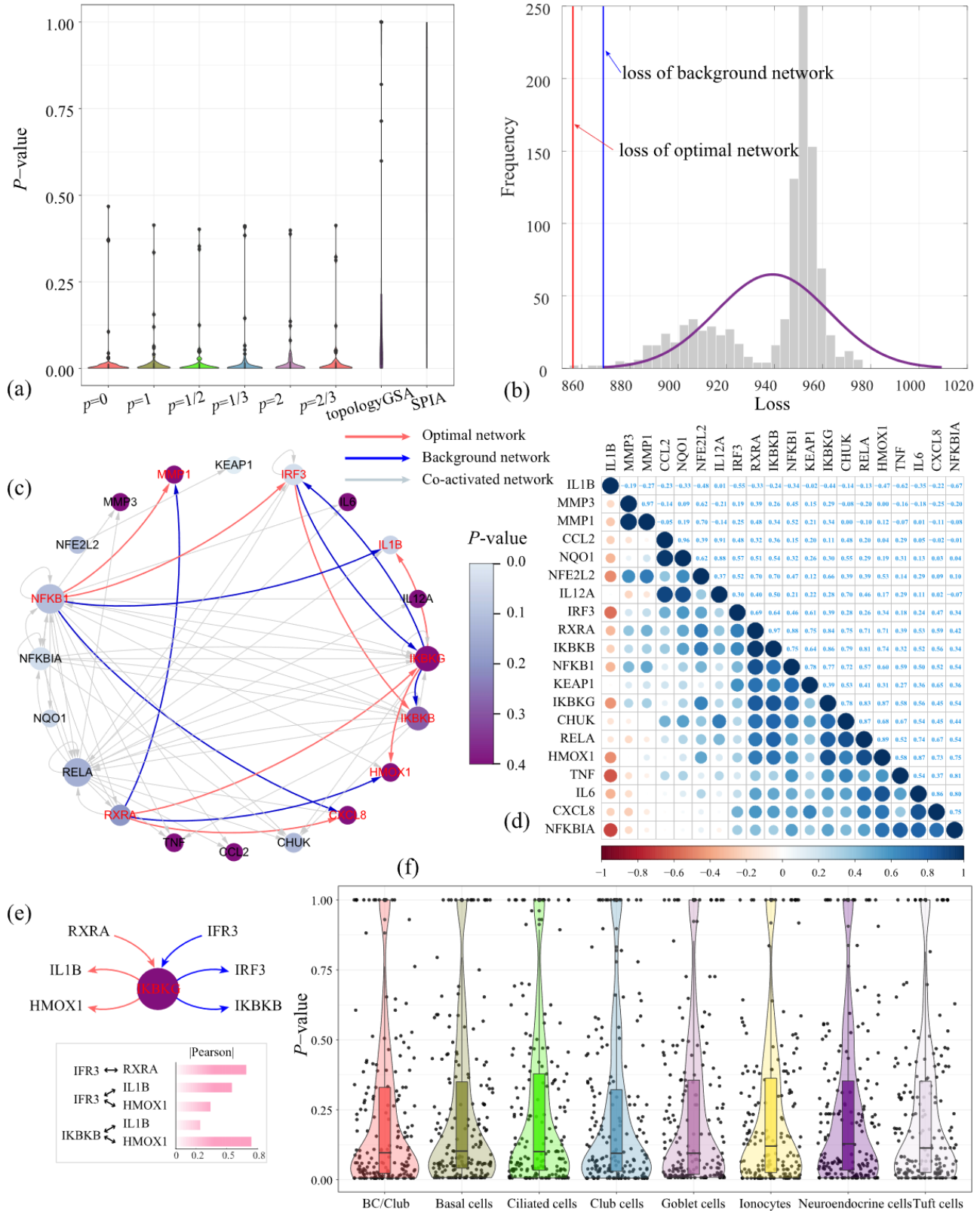


Fig. 3. Results in simulation data and SARS-CoV-2 data. (a) Comparison of P -value evaluation results between scNAE and other algorithms under different L_p -norm. (b) scNAE calculates all network loss values of COVID-19 pathway. (c) Activation network of pathway WP5113 in Goblet cells obtained by scNAE analysis (d) Pearson correlation coefficient between gene pairs in WP5113 (e) Gene IKKB corrected regulatory relationship after scNAE calculation (red represents the corrected regulatory relationship, blue represents the regulatory relationship in the knowledge base). (f) COVID-19 pathway evaluation under different cell types after SARS-CoV-2 infection.

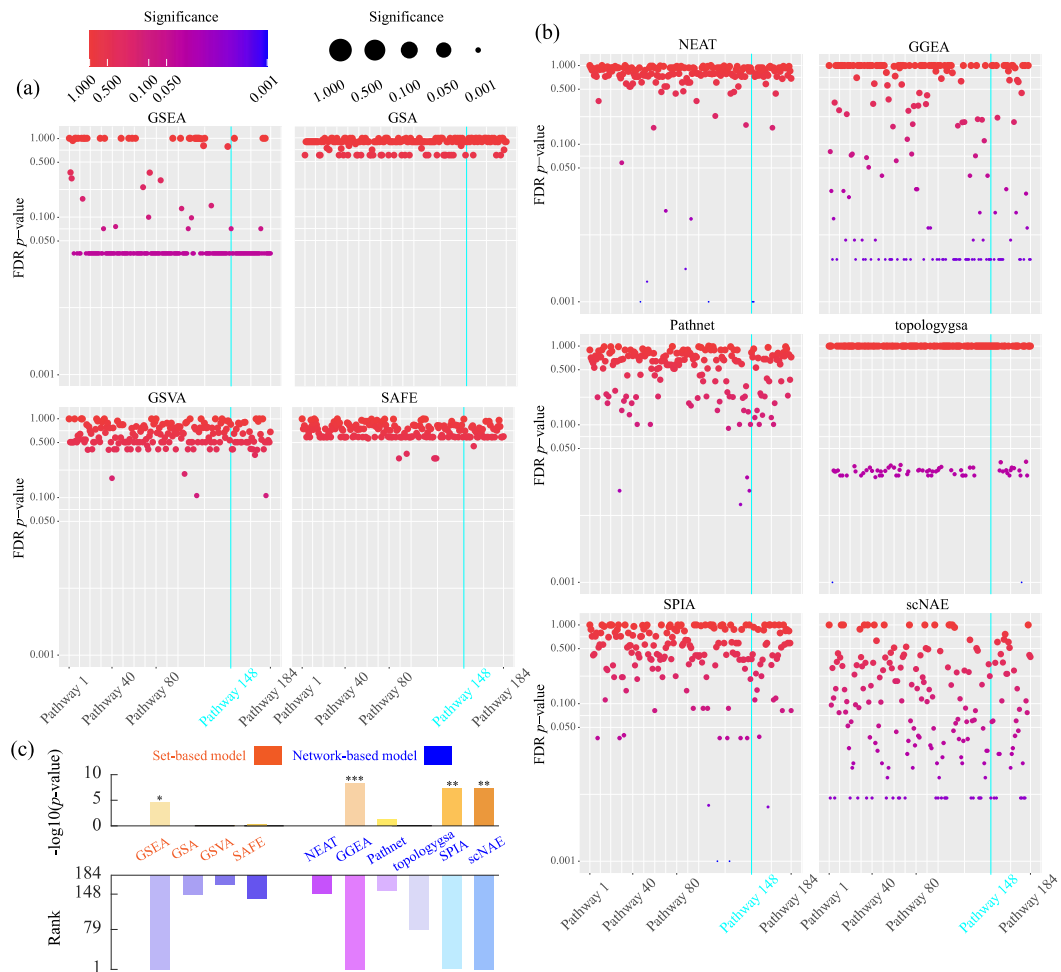


Fig. 4. Gene set enrichment analysis results of all methods on the KEGG pathway, in which the related pathway hsa05171 of SARS-CoV-2 infection is renumbered as Pathway148. (a) Set-based model. (b) Network-based model. (c) Rank and P -value of hsa05171 on all methods (“***” means $p\text{-value}<0.005$; “**” means $p\text{-value}<0.05$; “*” means $p\text{-value}<0.01$)