Supplementary Materials

I. Experimental settings

The experimental configuration was formulated using the PyTorch open-source machine learning framework, accessible via https://pytorch.org. Our training environment was established on a Linux operating system, leveraging a powerful 4090 GPU endowed with 24GB of memory. A modest learning rate of 0.001 was selected, and the topK parameter for the similarity network was set to 10. Employing a threshold (γ) of 3, we maintained a confidence level of 0.5. When selecting highly credible negative samples, we adhered to a topK value of 5. Additionally, for local smoothness, a distance threshold of 0.2 was utilized. The optimization process was entrusted to the Adam optimizer.

II. The introduction of different methods

For a thorough evaluation of LSNSCDA's performance, we compared it against eight alternative models specifically designed to handle various association prediction challenges in the field of bioinformatics. The following are the details of these eight approaches.

- MNGACDA [1]: This method predicts circRNA–drug sensitivity associations by constructing multimodal networks from multiple information sources. It then uses node-level attention graph auto-encoders to derive low-dimensional embeddings for prediction through an inner product decoder.
- MNCLCDA [2]: This framework predicts drug sensitivity and circRNA associations by utilizing drug structure, circRNA gene sequences, and GIP kernel similarities. It enhances robustness with a mixed neighbourhood graph convolutional network and graph-based contrastive learning, followed by a double Laplace-regularized least-squares method for prediction.
- GATECDA [3]: This model leverages graph attention auto-encoders and multiple databases to predict circRNA-drug sensitivity associations. It extracts low-dimensional representations, retaining key information from high-dimensional features and integrating neighborhood data effectively.
- DGATCCDA [4]: This deep learning method identifies circRNA-drug sensitivity associations by creating multimodal networks and using DeepWalk-aware graph attention networks. These networks combine global and local graph structure information, fusing features via layer attention for prediction.
- KATZHCDA [5]: This computational model predicts circRNA-disease associations using a heterogeneous network constructed from circRNA expression profiles, disease phenotype similarity, and Gaussian interaction profile kernel similarity. The KATZ measure is then applied for the final prediction.
- VGAE [6]: This framework uses variational graph auto-encoders for unsupervised learning on graph data, employing latent variables for interpretable representations. It uses a GCN encoder and an inner product decoder, achieving competitive link prediction results.
- VGAMF [7]: This model integrates miRNA and disease information into comprehensive similarity networks and uses variational graph auto-encoders for non-linear representations. It combines these with non-negative matrix factorization and a neural network to predict miRNA-disease associations.
- GCNMDA [8]: This framework predicts Microbe-Drug Associations using a heterogeneous network built from biological data and a GCN-based approach. A CRF layer ensures similar nodes have similar representations, and an attention mechanism improves neighborhood representation aggregation.

III. Figures and Tables

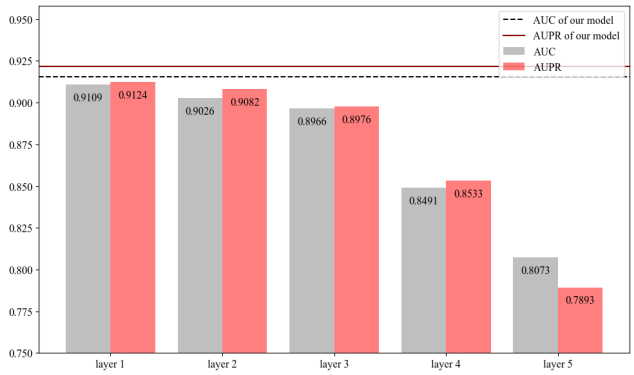

Fig. 1. Performance of Traditional Neural Network Models with Varying Layers

TABLE I
THE TOP 20 CIRCRNAS ASSOCIATED WITH THE DRUG FLUOROURACIL.

Rank	circRNA	Evidence	Rank	circRNA	Evidence
1	KRT19	CTRP	11	PTMS	GDSC
2	THBS1	GDSC	12	COL1A1	GDSC
3	ASPH	GDSC	13	COL6A2	GDSC
4	MGAT4B	CTRP	14	MUC16	non
5	COL18A1	GDSC	15	EFEMP1	CTRP
6	CRIM1	GDSC	16	DCBLD2	CTRP
7	CTTN	GDSC	17	MAL2	non
8	PEA15	GDSC	18	ANXA2	GDSC
9	LTBP3	GDSC	19	SPINT2	non
10	FBLN1	GDSC	20	AHNAK	CTRP

"Non" indicates a non-significant association. Entries labeled "GDSC" denote that the drug sensitivity data for the respective circRNA-drug association is obtained from the GDSC database. Similarly, entries labeled "CTRP" indicate that the drug sensitivity information is sourced from the CTRP database.

TABLE II
THE TOP 20 CIRCRNAS ASSOCIATED WITH DRUG IMATINIB.

Rank	circRNA	Evidence	Rank	circRNA	Evidence
1	THBS1	GDSC	11	DCBLD2	CTRP
2	KRT19	CTRP	12	COL6A2	CTRP
3	SPINT2	CTRP	13	CALD1	non
4	PEA15	CTRP	14	MUC1	non
5	COL1A1	non	15	POLR2A	GDSC
6	MUC16	non	16	MGAT4B	non
7	FBLN1	CTRP	17	LTBP3	CTRP
8	EFEMP1	CTRP	18	VIM	non
9	COL1A2	non	19	GJB3	CTRP
10	COL18A1	non	20	CPSF6	non

"Non" indicates a non-significant association. Entries labeled "GDSC" denote that the drug sensitivity data for the respective circRNA-drug association is obtained from the GDSC database. Similarly, entries labeled "CTRP" indicate that the drug sensitivity information is sourced from the CTRP database.

TABLE III
THE TOP 20 CIRCRNAS ASSOCIATED WITH DRUG ETOPOSIDE.

Rank	circRNA	Evidence	Rank	circRNA	Evidence
1	SPINT2	CTRP	11	KRT7	CTRP
2	THBS1	CTRP	12	ENO2	non
3	COL1A1	CTRP	13	DCBLD2	CTRP
4	MUC16	CTRP	14	ADPGK	non
5	VIM	GDSC	15	COL7A1	CTRP
6	EFEMP1	CTRP	16	LTBP1	non
7	COL1A2	non	17	SFPQ	CTRP
8	DBN1	non	18	PEA15	CTRP
9	EVPL	CTRP	19	CNKSR1	CTRP
10	MUC1	CTRP	20	MCAM	non

"Non" indicates a non-significant association. Entries labeled "GDSC" denote that the drug sensitivity data for the respective circRNA-drug association is obtained from the GDSC database. Similarly, entries labeled "CTRP" indicate that the drug sensitivity information is sourced from the CTRP database.

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