CoRAE: Concreate Relaxation Autoencoder for Differentiable Gene Selection and Pan-Cancer Classification

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Supplementary

- ***Supplementary-1.pdf*** contains a list of top-100 genes using all three methods, visualization of sample distributions, Figures of all five performance evaluation matrices, and annealing scheduling curve for lncRNA.
- ***Supplementary-2.xlsx*** contains data used to generate all the figures and tables in this paper.

1. Selected Genes

Table 1: Top-100 coding and non-coding genes selected using proposed and competing methods.

Method	mRNA type	Gene name
LASSO	mRNA	AMIGO2, ANXA8, ARHGAP6, ARHGEF6, ASB13, ATP8B2, B3GNT7, BAALC, BAMBI, BARX1, BMP7, CA12, CA9, CALML5, CCL25, CITED1, CPVL, CTSE, CYP2J2, DACT2, DAPP1, DHCR24, DHRS2, DNAJC12, EN1, FAM163A, FBXO41, GATA3, GATA4, GGT6, GINS1, GPSM2, HFE, HOXA9, HOXB13, HOXB7, HOXC10, HOXD8, IGFBP2, IRF5, IRX3, IRX5, ISL1, KAZALD1, KCNJ12, KIAA1161, KRT14, KRT23, KRT7, KRT80, KRT81, LIPE, LY6D, MGST1, MLC1, MLPH, MMP3, MT3, NDRG2, NEBL, NETO2, NKX2-1, NPM2, NR1H4, OLR1, PADI2, PAPSS2, PAQR5, PAX8, PCDH7, PCDHB9, PDLIM4, PITX1, PKNOX2, PRAME, PRKAR2B, PRLR, PTH2R, PVRL3, RAB31, RBMS3, RBPMS2, RXRG, S100P, SAMD5, SFTA2, SFTPB, SGCD, SH3BGRL2, SMC1B, SMPD3, SNCG, SOX17, SPNS2, STXBP6, TRNP1, TSHR, TTYH1, VAV3, ZNF280B
	lncRNA	AC000123.4, AC005082.12, AC005083.1, AC005152.3, AC008268.1, AC016735.2, AC093850.2, AC108142.1, AC109642.1, AC114730.3, AC115522.3, ADIRF-AS1, ALDH1L1-AS2, AP000251.3, AP000439.3, AP001065.15, AP001626.1, AP003774.1, BMPR1B-AS1, C5orf66-AS1, CITF22-92A6.1, CKMT2-AS1, CTA-363E6.6, CTA-384D8.31, CTC-327F10.4, CTD-2015G9.2, CTD-2015H6.3, CTD-2089N3.1, CTD-2314G24.2, CTD-2377D24.4, CTD-3032H12.2, CTD-3094K11.1, DNMBP-AS1, DYNLL1-AS1, GATA3-AS1, H19, HAND2-AS1, HNF1A-AS1, HOXB-AS4, HOXC13-AS, HOXD-AS2, LA16c-316G12.2, LHFPL3-AS1, LINC00152, LINC00518, LINC00884, LINC00885, LINC00887, LINC00925, LINC01158, LINC01235, LINC01268, LINC01410, LINC01540, LOXL1-AS1, MIR202HG, MIR205HG, MIR4435-1HG, MIR503HG, PIK3CD-AS2, PTCSC2, RBMS3-AS3, RP1-232P20.1, RP1-288H2.2, RP11-1017G21.5, RP11-1055B8.3, RP11-10A14.5, RP11-10C24.3, RP11-1149O23.2, RP11-1149O23.3, RP11-119F7.5, RP11-11N9.4, RP11-12M5.3, RP11-157J24.2, RP11-166D19.1, RP11-19E11.1, RP11-206M11.7, RP11-20F24.2, RP11-218E20.3, RP11-264I13.2, RP11-277P12.20, RP11-290H9.4, RP11-304L19.3, RP11-320N7.2, RP11-3P17.5, RP11-473M20.16, RP4-610C12.3, RP4-740C4.5, SATB2-AS1, SLCO4A1-AS1, SNHG14, SOX9-AS1, ST3GAL6-AS1, TINCR, TP73-AS1, VPS9D1-AS1, WDR86-AS1, ZFPM2-AS1, ZIM2-AS1, ZNF528-AS1
SVM-RFE	mRNA	ACTG2, AZGP1, BARX1, C1orf186, CA12, CALML3, CAMK2N1, CDCA7, CDH1, CDH16, CDKN2A, CEACAM5, CLDN3, CLDN4, CLDN6, CP, DDX3Y, DES, DLK1, DNER, DSG2, EEF1A2, EIF3CL, EMX2, EPCAM, ESRP1, FGFR4, FOXA1, FOXA2, FOXE1, GATA3, GATA4, GFAP, GJB1, GNL3L, GPX2, GRHL2, GRIK5, HNF1B, HNF4A, HOXA9, HOXB7, HOXC10, IFFO1, IRX2, KIF1A, KRT19, KRT5, KRT7, KRT8, LGALS4, LYPLAL1, MAL, MALAT1, MFAP2, MGST1, MLANA, MLPH, MMP12, MSLN, NACA2, NFIX, NKX2-1, NME2P1, NPM3, NUDT16P1, PABPC3, PAX8, PITX1, PNMAL1, POU3F3, PRAME, PTPRH, PTPRN2, RAB25, REC8, RNF128, RPL39L, RPL41, RPS4Y1, S100A1, S100A14, SALL1, SERPINA5, SFN, SFRP2, SFTPB, SLC34A2, SOX15, SOX17, SOX2, SYTL1, TBX5, TM4SF4, TSPAN1, UCHL1, USH1C, WDR72, WNK2, ZBTB7A

	lncRNA	AC005082.12, AC006042.6, AC007405.6, AC009299.3, AC016747.3, AC093850.2, AC133528.2, AFAP1-AS1, AL450992.2, AP000251.3, BBOX1-AS1, CASC9, CECR7, CRNDE, CTA-384D8.31, CTD-2015H6.3, CTD-2231H16.1, DNM3OS, EMX2OS, FAM83H-AS1, FENDRR, GATA2-AS1, H19, HNF1A-AS1, HOXA10-AS, HOXA11-AS, HOXD-AS2, LA16c-329F2.1, LINC00086, LINC00261, LINC00511, LINC00857, LINC00958, LINC01116, LINC01133, LINC01139, LINC01158, MAGI2-AS3, MALAT1, MEG3, MIR205HG, MIR99AHG, MNX1-AS1, NKX2-1-AS1, PIK3CD-AS2, PTCSC2, RP1-288H2.2, RP1-60O19.1, RP11-1149O23.3, RP11-11N9.4, RP11-132A1.4, RP11-13J10.1, RP11-164P12.4, RP11-166D19.1, RP11-223I10.1, RP11-264B14.2, RP11-276H19.2, RP11-284F21.7, RP11-304L19.1, RP11-304L19.3, RP11-329L6.2, RP11-350J20.12, RP11-357H14.17, RP11-373D23.2, RP11-392P7.6, RP11-395G23.3, RP11-3P17.5, RP11-449J21.5, RP11-44F21.5, RP11-465B22.8, RP11-465N4.4, RP11-47A8.5, RP11-530C5.1, RP11-532F12.5, RP11-567G11.1, RP11-680F8.1, RP11-739N20.2, RP11-760H22.2, RP11-977G19.5, RP3-404F18.5, RP3-406A7.7, RP3-416H24.1, RP4-639F20.1, SFTA1P, SLC38A3, SLCO4A1-AS1, SNHG18, SOX21-AS1, TBX5-AS1, TINCR, TRPM2-AS, TTTY14, TTTY15, U47924.27, UCA1, VPS9D1-AS1, XIST, ZFPM2-AS1, ZNF582-AS1, ZNF667-AS1
CoRAE	mRNA	ACYP2, ADAM23, AKAP8L, AKR1B10, ALDH1A3, ANO9, ANXA3, APOB, ASB16, B3GAT1, BAZ2B, BCL11B, BEGAIN, C12orf10, CBS, CCDC77, CCDC85B, CD109, CEP55, CHRNA4, CHST13, CHTF18, CLEC2D, CMTM1, CNTFR, COL8A2, COX10, CWC25, CXADR, CYFIP2, CYP4F3, DCDC2, DCLK2, DFFB, DLL3, DUSP14, ELP3, EPHB3, EPS8L1, FAM182B, FAM83B, FBXO43, FCHO1, FGF2, FLI1, FLT4, GJB3, GPR35, GPSM2, HABP4, HBEGF, HOXA11, IGJ, IL17RD, INMT, INPP5J, IRX6, ISG20, ITGA9, KIAA1549, KLK3, KLK5, KREMEN2, LHFPL2, MAPT, MED9, MGAT5B, MSX2, MYEF2, NCF1B, NME5, OLR1, PDK1, PHOSPHO2, PHYHIPL, PPP1R3E, PRRX2, RGMA, RGS11, RPS6KC1, S100PBP, SLC17A5, SLC34A2, SLC39A5, SPAG1, TAF2, TAGAP, TAGLN, TFF1, TLN2, TLR7, TMEM229B, TTBK2, TTLL3, ZBTB25, ZNF43, ZNF486, ZNF561, ZNF665, ZNF770
	lncRNA	ABHD11-AS1, AC012360.4, AC016831.7, AC079630.4, AC106786.1, AC139100.3, CTA-212D2.2, CTA-217C2.2, CTA-331P3.1, CTC-444N24.6, CTC-487M23.5, CTD-2014E2.6, CTD-2020K17.4, CTD-2135J3.3, CTD-2331H12.7, CTD-2527I21.14, CTD-2554C21.3, CTD-2555C10.3, CTD-2561B21.4, EIF3J-AS1, HS1BP3-IT1, IGBP1-AS1, IGFBP7-AS1, ITGB2-AS1, KB-1410C5.5, KCNMB2-AS1, LINC00471, LINC00543, LINC00592, LINC00630, LINC00668, LINC00958, LINC01207, LINC01484, LINC01507, MIAT, MIR210HG, MIR99AHG, NBAT1, PWAR6, RP1-102K2.8, RP1-269M15.3, RP1-288H2.2, RP11-1017G21.5, RP11-1055B8.3, RP11-108M12.3, RP11-110I1.11, RP11-110I1.12, RP11-111K18.2, RP11-111M22.5, RP11-146F11.1, RP11-158M2.3, RP11-1D12.2, RP11-20F24.2, RP11-21M24.2, RP11-227F19.5, RP11-234B24.2, RP11-273G15.2, RP11-276H7.2, RP11-298D21.3, RP11-35G9.3, RP11-381N20.2, RP11-397A16.1, RP11-402G3.5, RP11-403I13.5, RP11-406H21.2, RP11-429J17.7, RP11-452H21.2, RP11-505E24.3, RP11-507K2.3, RP11-526F3.1, RP11-537H15.3, RP11-547D24.1, RP11-554D14.6, RP11-554D15.1, RP11-627G23.1, RP11-655C2.3, RP11-731J8.2, RP11-736N17.8, RP11-750H9.7, RP11-767N6.7, RP11-806O11.1, RP11-807H17.1, RP11-867G23.1, RP11-8L8.2, RP13-726E6.2, RP3-395M20.9, RP3-507I15.2, RP4-555L14.4, RP4-564M11.2, RP4-740C4.5, RP5-1085F17.3, RP5-1184F4.5, SATB2-AS1, SNHG20, THUMPD3-AS1, TUSC8, U91324.1, VPS9D1-AS1, YEATS2-AS1

2. Data distribution

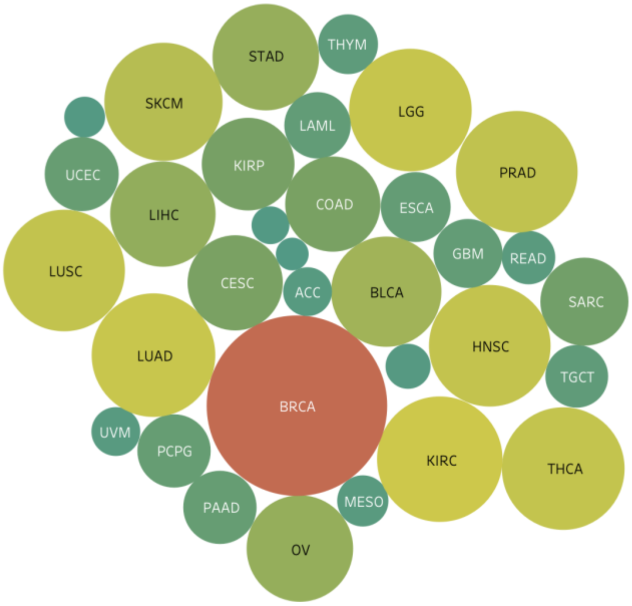
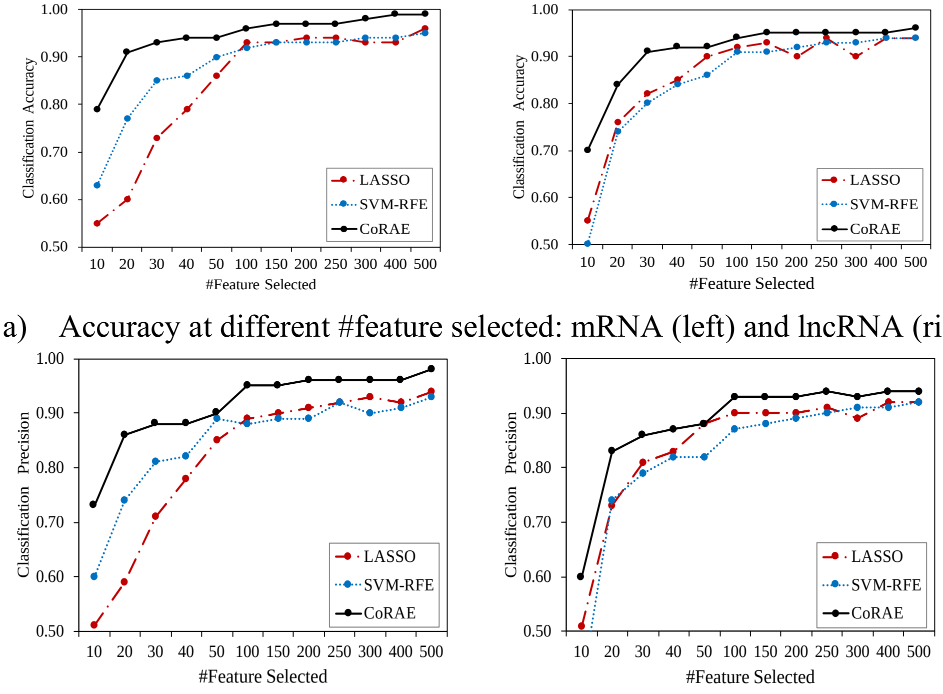


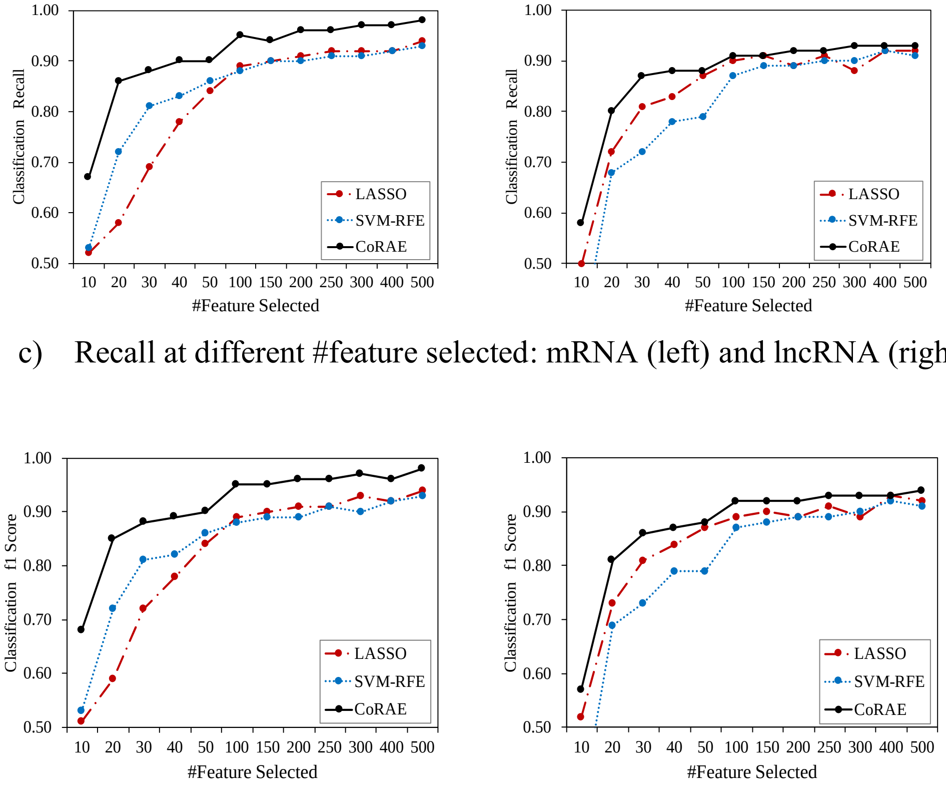
Fig 1: **Bubble chart of cancer samples of 33 cancer types.** Here, the size of bubbles refers the number of samples of a particular cancer type. For example, Breast cancer (BRCA) has highest number of sample whereas Adrenocortical Cancer (ACC) has lowest number of samples available.

3. Performance Evaluations



a) Accuracy at different #feature selected: mRNA (left) and lncRNA (right)

b) Precision at different #feature selected: mRNA (left) and lncRNA (right)



c) Recall at different #feature selected: mRNA (left) and lncRNA (right)

d) f1 score at different #feature selected: mRNA (left) and lncRNA (right)

Fig 2: **Classification performance using selected RNA features.** Comparison of CoRAE with other feature selection methods. Throughout the all values of *k* tested on both mRNA (left) and lncRNA (right) expressions. For all the performance metrics (a) Accuracy (b) Precision (c) Recall (d) f1 score.

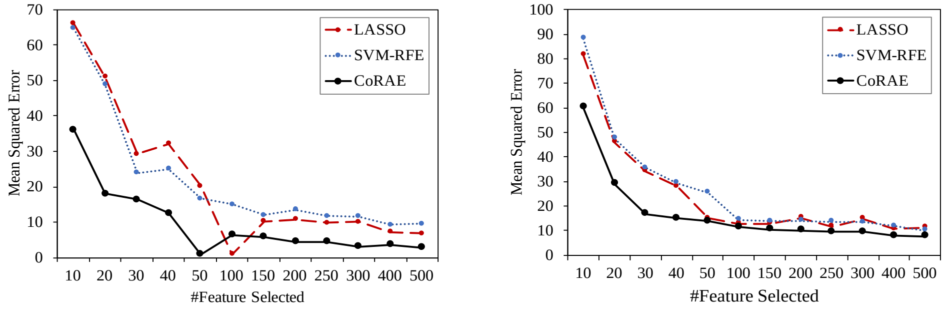


Fig 3: Reconstruction mean squared error using selected mRNA (left) and lncRNA (right)

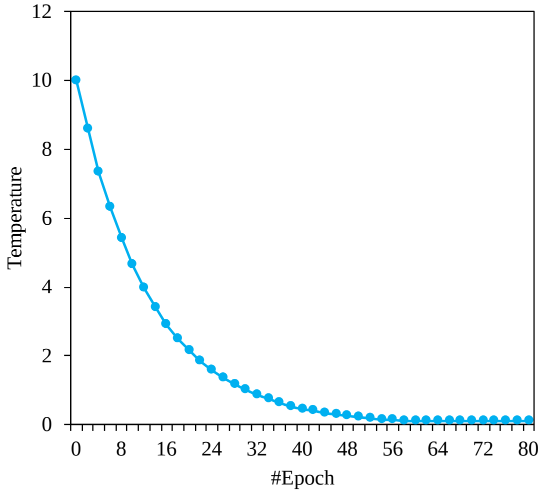


Fig 7: Annealing schedule of CoRAE for k = 100 using lncRNA

Table 2: Classification and Reconstruction performances for different number of selected mRNA and lncRNAs

		mRNA					**lncRNA**				
#Feature	**Method**	**Accuracy**	**Precision**	**Recall**	**F1**	**MSE**	**Accuracy**	**Precision**	**Recall**	**F1**	**MSE**
500	LASSO	0.96	0.94	0.94	0.94	6.79	0.94	0.92	0.92	0.92	11.19
	CoRAE	0.99	0.98	0.98	0.98	2.86	0.96	0.94	0.93	0.94	7.7
	SVM-RFE	0.95	0.93	0.93	0.93	9.47	0.94	0.92	0.91	0.91	10.01
400	LASSO	0.93	0.92	0.92	0.92	7.22	0.94	0.92	0.92	0.93	10.63
	CoRAE	0.99	0.96	0.97	0.96	3.7	0.95	0.94	0.93	0.93	7.95
	SVM-RFE	0.94	0.91	0.92	0.92	9.2	0.94	0.91	0.92	0.92	11.88
300	LASSO	0.93	0.93	0.92	0.93	10.05	0.9	0.89	0.88	0.89	14.87
	CoRAE	0.98	0.96	0.97	0.97	3.04	0.95	0.93	0.93	0.93	9.48
	SVM-RFE	0.94	0.9	0.91	0.9	11.56	0.93	0.91	0.9	0.9	13.38
250	LASSO	0.94	0.92	0.92	0.91	9.77	0.94	0.91	0.91	0.91	11.57
	CoRAE	0.98	0.97	0.97	0.97	4.03	0.95	0.94	0.92	0.93	9.41
	SVM-RFE	0.93	0.92	0.91	0.91	11.69	0.93	0.9	0.9	0.89	13.64
200	LASSO	0.94	0.91	0.91	0.91	10.73	0.9	0.9	0.89	0.89	15.2
	CoRAE	0.97	0.96	0.96	0.96	4.41	0.95	0.93	0.92	0.92	9.99
	SVM-RFE	0.93	0.89	0.9	0.89	13.56	0.92	0.89	0.89	0.89	14.01
150	LASSO	0.93	0.9	0.9	0.9	10.22	0.93	0.9	0.91	0.9	12.87
	CoRAE	0.97	0.95	0.94	0.95	5.8	0.95	0.93	0.91	0.92	10.41
	SVM-RFE	0.93	0.89	0.9	0.89	12	0.91	0.88	0.89	0.88	13.77
100	LASSO	0.93	0.89	0.89	0.89	10.4	0.92	0.9	0.9	0.89	12.83
	CoRAE	0.96	0.95	0.95	0.95	6.4	0.94	0.93	0.91	0.92	11.37

	SVM-RFE	0.92	0.88	0.88	0.88	15.04	0.91	0.87	0.87	0.87	14.36
50	LASSO	0.86	0.85	0.84	0.84	20.21	0.9	0.88	0.87	0.87	15.05
	CoRAE	0.94	0.9	0.9	0.9	11.64	0.92	0.88	0.88	0.88	13.82
	SVM-RFE	0.9	0.89	0.86	0.86	16.71	0.86	0.82	0.79	0.79	25.44
40	LASSO	0.79	0.78	0.78	0.78	32.06	0.85	0.83	0.83	0.84	28.04
	CoRAE	0.94	0.88	0.9	0.89	12.54	0.92	0.87	0.88	0.87	14.95
	SVM-RFE	0.86	0.82	0.83	0.82	24.99	0.84	0.82	0.78	0.79	29.42
30	LASSO	0.73	0.71	0.69	0.72	29.25	0.82	0.81	0.81	0.81	34.13
	CoRAE	0.93	0.88	0.88	0.88	16.36	0.91	0.86	0.87	0.86	16.73
	SVM-RFE	0.85	0.81	0.81	0.81	23.87	0.8	0.79	0.72	0.73	35.52
20	LASSO	0.6	0.59	0.58	0.59	51.01	0.76	0.73	0.72	0.73	45.99
	CoRAE	0.91	0.86	0.86	0.85	18.06	0.84	0.83	0.8	0.81	29
	SVM-RFE	0.77	0.74	0.72	0.72	48.78	0.74	0.74	0.68	0.69	47.64
10	LASSO	0.55	0.51	0.52	0.51	66.02	0.55	0.51	0.5	0.52	81.56
	CoRAE	0.79	0.73	0.67	0.68	36.07	0.7	0.6	0.58	0.57	60.11
	SVM-RFE	0.63	0.6	0.53	0.53	64.69	0.5	0.4	0.36	0.35	88.19