









Loss Function

- Generative Loss
- Latent Loss

$$\mathcal{L}\left(x,\hat{x}\right) + \sum_{j} KL\left(q_{j}\left(z|x\right) || p\left(z\right)\right)$$

										A p	ancan_so	caled_zer	oone_rnas	seq (1).tsv	v ~										
		ALUN302							ULTM4	СИПКО	SUEL	MUCIS	451	FAMIDIA	GUA		WUK/Z		STIN	TIGDO	CTUINTE	A.		SECOA14	
				TMPRSS2					FGFBP1		FGG	UGT1A9		MUC16	TMC5		C9orf15		PLP1	SERPINB				SDR16C5	KLK7
	C20orf11			CST1 ANXA8L2				C19orf33 F0XE1		CBLC SYT13	MMP1 LGALS4	FGA	IYD TP63	FOXA2 POF1B	C19orf2:		DES		ADH1B DUOX2	TFF3 TNNT1	PDZK1IP SLPI	1 A0P4	MUC15 COMP	DMBT1 SERPINA	
C10orf81												VTCN1	CDH16	MUC4	MMP13	CYorf15I	P. HP		SPRR3	PGC	CACNG4		CLDN10	EPCAM	EPN3
											EEF1A2		CALML5	Clorf11		S100A7		PROM2		DEFB1	TF CACING	C10orf9		HMGA2	EFINS
						PLA2G4F					PPP2R2C		TSIX		KIAA1324		SFRP2		FAM83E	KLK8	SERPINA		KRT4	50X10	
ALDH1L1							S100A2			C20orf56		FUT6	ALDOB		LRRC15				SLC4A4	BMP7		SLC39A5		C19orf7	77
	ELF3	VSIG2	CAPN8 I	PRSS3	CHGB	PCP4	SERPINA	3			KLHDC7A	CHST9	LM03	GCNT3	REG1A		SCNN1G	EPS8L3	EMX20S	ORM1	WNT7B	FUT3	MSMB	ST6GALN	
	C7	KIF12	HKDC1 (CPLX2	FAM3B	NKX2-1	GATA4	CCL21	KLK5	NLRP2	ANKS4B	FABP7	BEX1	ERBB4	RBP4	ATP13A4	C16orf89	9	FAM3D	CNTN1	BARX2	MLPH	EMX2	SPRR2A	XDH
			C2orf54 (C20orf15		HSD17B2		SLITRK6		F0XJ1	S0X21	CNTNAP2		GP2	ALB	CCDC64B		PTPRT	TRIM15	DNER	CRABP2	BNC1	
B4GALNT4							CYP24A1			PPAN-P2F				ZIC1			SLC6A15			DU0XA1	DU0XA2	MASP1	RNF128	ZIC2	
ABCA12		C2orf72						MAGEA6		GABRB3		PPP1R1A		FABP1	GREM1	SERPINB:		PRKY		CYP4F3	CDHR2		CCL20	AGT	LGI3
		SULT1C2						MAL				SERPINB4			HHLA2	ATP2B2			FAT2	CRABP1	ALDH3A1		CXCL13	TFAP2A	PAH
				SLC04C1 EPHA7							SBSN	SHISA9 RIMS4			MAPK4	PDZK1 NKAIN4	C14orf19		GPR115 LGR5		CHRDL1 LGALS7B	NMU	NAPSA SFTA3	MFAP5 CNTFR	
CRTAC1 SERPINB1				GAL3ST1				SLC15A1 UCA1		CEACAM7	C6orf223		S100A8 PRR15	INA	MYEOV DPT	POSTN		LPAR3 LYPD3		HOXA9	CXCL1	ARSE	PPP1R14		FBN3
						SULT2B1					S100A9		VSNL1	ADCY2	VGLL1	SCGB1D2		SLC01A2		PRSS21	IGSF9	PRLR	PTPRH PTPRH	SLC38A3	
				SEMA3E									PKHD1		AIM1L	EREG	CLCA4	SFTA2		LONRF2	SFRP1	CDH17	SLC6A11		
			CYP2B7P1									ACE2	C19orf4		TRPV6	L1CAM	ADH6		C2orf40		CAMK2B	PNCK	KNDC1	HOXA13	
TMPRSS3		CKMT1B					NCCRP1				MGC29506			TMPRSS1		CA4		KLK3	LIX1	CHRM1	PITX2		OGN	CLDN7	
PADI3	C3orf57	UGT1A10	GJB4 (GALNT5	ASTN1	ELFN2	PAX2	GABRA3	GFRA1	FABP6	ANXA13	Clorf210).	H0XB8	MUC2	SST	C12orf3	6	L0C3395		ODZ1	CHL1	GNG4	ACTG2	
CYP4F11 i		SOSTDC1							RASAL1				KCNJ3	TMEM125		HS6ST2		MARCO	ODZ2	GJB2	TMC4	AQP3	LBP	GPD1	
			METTL7B N						SLC26A9			HOXA10			Clorf64		APOH		DIRAS2		D4S234E		CDHR1	SORCS1	
						Clorf106			ABCA13		DPYSL5		GAL3ST3			C5orf38		PIP	CADPS	CD01	ZIC5	ATP6VØA		CLIC6	TOW
								COL2A1			HOXA11		TUBB2B		ACMSD		LRRN1		LY6K	HS6ST3		CDX2	SLC17A4		TBX5
	FAIM2 SLC30A2							AGXT2L1 KCNK3		MB		SERPINA4 WT1		CILP	GPR158	NTS	DKK1	SPP1	UBD REG4	DPP10	SLC1A2 TMEFF2	CPNE4 AKR7A3	TG DPP4	CACNA18 SH3GL2	
				GALNT14					GYLTL1B ACTC1			CLDN18	NKAIN1	WBSCR17	CPB1	SLC01B3	Clorf17	IRX1	SLC28A3		PMP2		MLXIPL		FPIN2
IL22RA1									PLEKHG4B		LRRC31		DUOX1		ATCAY	VSTM2L		VGF	CHI3L1		CBorf47		GOLT1A		
C12orf27									COL4A3			PRIMA1		HOXC9		SULT4A1			CDH1	ACPP		TMEM171			
				L0C84740		IGF2BP3				MYOM3	N (TBL	5-3BIV	TYP2	6		LRG1	TMSB4Y		CHI3L2	DBC1	LASS1	Clorf18		TMEM139) F5
	LAMB3	DSP	C2CD4A (GLYAT	ARL14	DSG1	ABCA8	DSCAML1	PNMA2	A0X1	1 RHDE	font 5	E A	A	WNT2		IGF2BP2	STK33	CA8	MY07B	KIF5C	GRIA4		TMEM59L	MME
	PIK3C2G	ZNF385B	MAG I	LUM	ENTPD3	MS4A1	TMEM30B			EN1	T VH1	PSP2	G	FAM C	SERPINB:	7	SERPINA:	11	GDF1	MAOB	ESPN	NPY1R	SLC16A1	2	
PNMAL1 I		LRRTM1					SLITRK2					ADAM23		RNF186	GDF15	AGTR1	ESR1	SLC22A3		CD79A	ETV4	PCDHA11		MAGEA4	NWD1
	SPAG17						HOXA11AS			TMEM184A		SCGB1A1			DPEP1	H0XC6	GALNT13		RELN	ADCY8		CYP2B6		KIF5A	
ELOVL2		KIAA0408		LOC10013				RANBP3L		GALNT9		TPSAB1			NELL1			COL1A1		NRCAM	PPARGC1			TGM3	
SMPDL3B			SLC2A2 [STYK1]						C15orf48 ITIH2		CREB3L3 CCL14-CC		C11orf4: GPR81		EDN2	SYT1 TMEM63C	HAPLN1	LOC38949	GAL	IL1F5 CCNA1	ARHGEF4 SHH	ASPG	TBC1D3G	TMEM130	FST
		ATP6V1B1								FGL1		KRTCAP3		NIPAL4 GPR109A		AFF3	UPK3B	DSG2	ROS1		TMPRSS6		FAM83C		EMX1
			NOVA1								EPHA10		PHACTR3			AK5	DMGDH		L0C4401		NRG3	SCARA5	ISL1	PTN	FLIVI
PLEKHG6			TMPRSS11					SLC13A5				PCP4L1		VWDE	NDP			LHFPL3			CNTN3	AP3B2		ADAMDEC	1
			MFSD6L I									HOXD10		KIAA202		AMY1A	KCNK2	ARHGAP3		IQCA1	VIPR2	LGALS2	FM02	PHF21B	
RIMBP2 I			L0C554202		ST6GAL2				SLC6A17		L0C44090		CRB3		TFCP2L1		RAB27B	SLC28A1			SLC5A12		FAM181B		
FAM189A1			ANXA10 [L0C38933		ZYG11A		STEAP4		STXBP5L		IGFBP1		SLC27A2			PCDHA12		
			PCDHA10 [GPC3	Clorf168			DNAH11		PCDH20		L0C28600		ARHGEF3		BAALC	SLC6A19			L0C6437		
	BAIAP2L2		ENTPD8			SLC47A1		L0C96610			MEGF10		ABCC2		CYP4F22		PGR	PDX1	CFB	GRIA1		ZNF488	HR	PLCXD3	
PHGR1 !		CBorf85				NOTUM HEPACAM2		MIOX CACNA2D1	PKN0X2		Clorf136	FAM135B	BPIL1	SIX2 HIF3A	KLHL14 SUSD4	TRIM58 SCN2A	MYT1	SERPIND: XAGE1D		LOC1458 CALB1	TNNT3	MFAP2 KRT75	KIAA119 C11orf9		
	COL3A1 FAM189A2					CYP2W1							C14orf7		SYT14	LRRN4	PTH2R		CYP4A11		GRIN2A		POU2F3		
ANKRD43		SNORD116							KIAA0125		NME5	XG	LIPC	PRSS12		TMEM35			PLA2G12		C10orf1		IGFL1	MT1H	
												SPOCK1		TCERG1L		L0C6453		CELF3	MEG3	CDH19	UGT3A1		IP6K3	RET	
			PPAPDC1A			C6orf132			PPP1R14D		HHIP	Clorf88		EN2	EFHD1	SLC14A1		AQP9	TRPA1		NECAB2	ADD2	RAB17	PCSK1	
EPHX3	C5orf23	DNASE1L3		TGM1	PDPN	RNF212	PTPN20B	PTGS2	GABRB2	PC0LCE2	PLAC8	SLC19A3	IGFL2	ALDH1A1	ELAVL2	S0X15	LPHN3	0SR2	EMID2	KNG1	DNAJC22		GIPC2	NUDT11	OMD
	SP5		KIAA1244		RPS6KA6			RUNDC3A			EPS8L1			SLC23A1	UNC5D	AKR1C3		L0C8485	5	EYA4	APOC2	LY6G6C	LEMD1	HPCAL4	
	ARHGDIG		STXBP6						SULT1E1		PLEKHB1		ANKS1B	RGL3	COL9A1	TRIM10		AN04	STX19		BCL2L14		HEPACAM		
	WNT10A		TTC22 I		SLC38A5			PCDH19			IRX3	F0XG1	YBX2	NPTX2	KBTBD12		C3		MSX2	VNN1		CTSL2	C20orf1		
GLT25D2			ADAMTS16		C6orf141			TUBBP5			PAEP	FSD1	DCLK1	NPNT	HOXB6	FAT3		L0C2545		KLF15	F7		GLYATL2		
ABCC6P1									C3orf15		FLNC	SH0X2	CXCL10	CKMT2	HAP1	TNNT2	TFF2		S100A7A		NRG1	EDIL3		C21orf6	
	ST6GALNA								DUSP26		ALDH1A2 GREB1L		COCH	FGFR3	TPRXL	HPX	KRTDAP		AQP7	CST2	TLX1	SYT5	RGMA	RNF182	GPX3
RNF183		B3GALT5 MRAP2	COL23A1 (FLJ45983 COL6A3			CASKIN1 LOC10027		C1QL4 ALOX12P2			ARHGAP8 SLITRK4		ARPP21	CDKL2		L0C25510 AL0X15		CSAG3 MAGEA2	RIPK4 TNNI1	LRRC19 IL1R2	FAM69C AGXT2	OCA2 PCYT1B	HACO
		JAKMIP2					L0C28339				SEC14L4		DDX25		GPR109B		TD02		PCDH9	BCM01	ASPA		CYP2J2	FER1L4	RRAD
				CTTNBP2					HORMAD1		COL9A3		SELE	LRAT	CTSG		BCL2L15			SLC22A1		MGAT5B	PDE8B	FCAMR	MAD
				CCDC160								FAM101A			HSD17B6		psiTPTE:		C6orf22		AGXT		CD164L2		
			TMEM151A			Clorf173		LRRC4C				Clorf95				TNFAIP6		ANKRD56			RBP5	COBL	PKP2	PRKAA2	NEBL



0.45780935528750694

0.22697550425028923

0.18142200432460073

0.08781947123050524

0.6714327378782355

0.5600658182831513

0.18798472187310325

0.8530350194552531

Feature 82 → Patient Sex

There are 17 genes with high activation in node 82
All genes are located on sex chromosomes
sex_node_plot.head(17)

Out[15]:

	encoding 82	encoding 85
EIF1AY	-0.543605	0.013644
UTY	-0.514367	0.019198
CYorf15A	-0.514013	0.016753
KDM5D	-0.499488	0.019061
DDX3Y	-0.497709	0.022053
TMSB4Y	-0.495302	-0.003714
USP9Y	-0.494874	0.022164
TTTY15	-0.487078	0.014047
NCRNA00185	-0.473645	-0.019878
CYorf15B	-0.472546	0.019967
ZFY	-0.453348	0.018549
RPS4Y1	-0.452888	0.016435
NLGN4Y	-0.371427	-0.013003
DAZ1	-0.369805	-0.008085
XIST	0.316281	-0.023227
TSIX	0.298300	-0.030515
PRKY	-0.294522	0.017516

Feature 66 and 53 → Primary and Metastatic SKCM tumours

Out[18]:		encoding 66	direction	Out[19]:		encoding 53	direction
	genes				genes		
	ROPN1	0.115224	positive		HCG22	0.084451	positive
	ROPN1B	0.108729	positive		RXRG	0.081329	positive
	ADIPOQ	0.107172	positive		MGAT4C	0.076966	positive
	SOX10	0.105733	positive		PLP1	0.076440	positive
	CIDEA	0.103107	positive		C10orf90	0.076005	positive

0.45780935528750694

0.22697550425028923

0.18142200432460073

0.08781947123050524

0.6714327378782355

0.5600658182831513

0.18798472187310325

0.8530350194552531

GO terms

geneset descrip	tion link	C 0	E	R	PValue	FDR	overlapGene	0ver	lapGene_	UserID	
GO:0030300	regulation of	intestinal o	holesterol	absorption	http://	amigo.	geneontology.or	g/amigo/	term/GO:	0030300	5
G0:1904729	regulation of	intestinal l	ipid absor	ption	http://	amigo.	geneontology.or	g/amigo/	term/GO:	1904729	5
GO:0006069	ethanol oxida	tion ht	tp://amigo	.geneontolo	gy.org/a	migo/t	erm/G0:0006069	7	3	0.073	1343283582
G0:1904478	regulation of	intestinal a	bsorption	http://	amigo.ge	neonto	logy.org/amigo/	term/GO:	1904478	7	3
GO:0032371	regulation of	sterol trans	port http	://amigo.ge	neontolo	gy.org	/amigo/term/GO:	0032371	20	4	0.20895
G0:0032374	regulation of	cholesterol	transport	http://	amigo.ge	neonto	logy.org/amigo/	term/GO:	0032374	20	4
G0:0016042	lipid catabol	ic process ht	tp://amigo	.geneontolo	gy.org/a	migo/t	erm/G0:0016042	96	7	1.002	9850746268
GO:0006067	ethanol metab	olic process	http	://amigo.ge	neontolo	gy.org	/amigo/term/GO:	0006067	8	3	0.08358
G0:0030299	intestinal ch	olesterol abs	orption	http://	amigo.ge	neonto	logy.org/amigo/	term/GO:	0030299	9	3
GO:0098856	intestinal li	pid absorptio	n http	://amigo.ge	neontolo	gy.org	/amigo/term/GO:	0098856	9	3	0.09402



5 Key Takeaways

• VAE's are generative models that allows for reconstruction of original input data as well as identification and recapturement of variations/patterns within the data.

• The weights in the decoder network are able to learn which genes contributed to a particular feature.

• Through the decoder network, we are able to understand that the VAE was able to construct features representing patient sex and another capturing SKCM tumours.

• The genes with the highest weight are the most expressed meaning they have a higher chance of being the cause of the state of a cancerous tumour.

• We are able to identify the functional processes of the highly expressed genes within a feature, using ORA. This can help researchers identify which particular gene products or pathways to target when curing for a disease.



Pro:

The papers presented in #NIPS2017

applications? Transfer learning potential?

- Potential for discovering genetic/biological patterns for certain conditions (strong enough conclusion?)
- Conditions (strong enough conclusion?)
 The manifolds of the VAE provide the potential for representing differing pathway activations, transitions between cancer states, or indicating particular tumors vulnerability to specific drugs; versatile
- This is a open source project and for code and dataset of this paper search /Greenelab/Tybalt
- Very simple VAE structure
 The model has two direct benefits of modeling cancer gene
 - expression data.
- Automatically engineer non-linear features

 Learning the reduced dimension manifold of cancer expression
 space
 - Side note: VAEs are different from deterministic autoencoders because of the added constraint of normally distributed feature activations per sample. This constraint not only regularizes the model, but also provides the interpretable manifold.

Cons:

- Is the genetic expression of gender found in this paper enough to validate the hypothesis on genetic expression of disorders?
- What are the evaluation/validation techniques are used by the authors (sounds like pattern matching from select examples)?

How would validation need to take place for more extensive

- research?

 Why and how normalization happened and how we can measure it
 - effects

 Predefined type of cancers in latent space!!! Very selective choices
- Measuring the relation of the depth of VAE to latent space size and interpretability of extracted features