

c*GMΔVÆs—q

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c*GMΔVÆs—q

a Master Thesis in Bioinformatics

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Reviewer: Professor Tim Conrad

Glossary

c*GMΔVÆ (maybe Conditional) Gaussian Mixture with Dirichlet prior Variational Auto Encoder

c*GMΔVÆs—q c*GMΔVÆ (for) s(ingle-cell-RNA-Se)q.

Topics to cover

- ▶ what was our initial subject of interest
- ▶ AEs are non-linear PCA basically
- ▶ VAEs
- ▶ other animals
- ▶ GMVAE and why I derived $c^*GM\Delta VAE$
- ▶ example use of $c^*GM\Delta VAE$ on synthetic conditional-categorical data
- ▶ examples on MNIST
- ▶ examples on scRNAseq

Autoencoders

A "vanilla" autoencoder is a neural networks that "learns" the identity (subject to dimensional restriction).

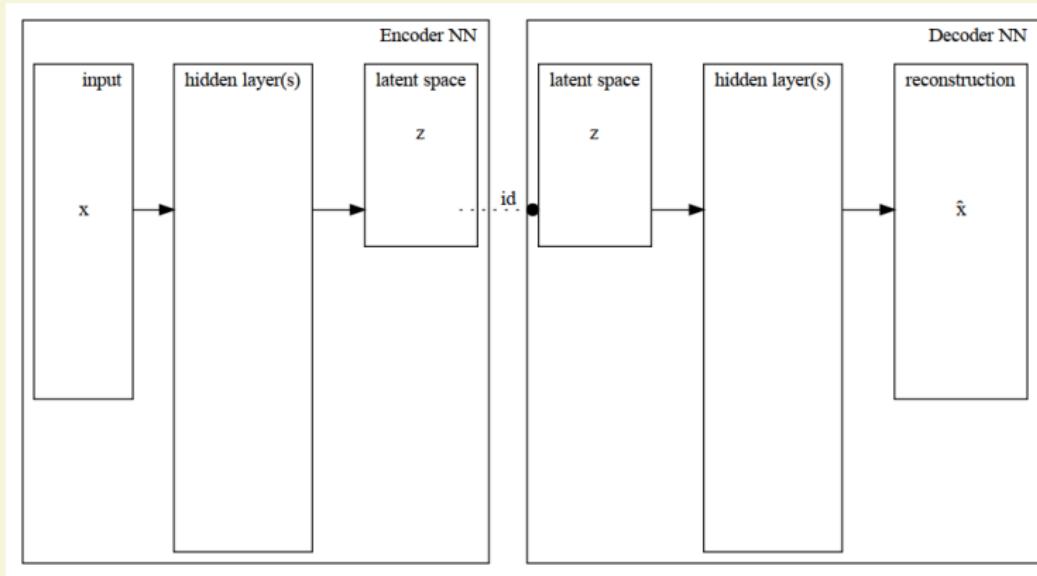


Figure: Autoencoder

Autoencoders and PCA

(On centered data[8])

PCA

$$\tilde{\mathbf{V}} = \operatorname{argmin}_{\mathbf{W}} \{ \| \mathbf{X} - \mathbf{X} \mathbf{W} \mathbf{W}^T \|_F^2 : \mathbf{W} \in \mathbb{R}^{n \times l}, \mathbf{W}^T \mathbf{W} = \mathbf{I}_l \} \quad (1)$$

Linear AE

$$\operatorname{argmin}_{\mathbf{E}, \mathbf{D}} \{ \| \mathbf{X} - \mathbf{X} \mathbf{E} \mathbf{D} \|_F^2 : \mathbf{E}, \mathbf{D}^T \in \mathbb{R}^{n \times l}, \} \quad (2)$$

$$\tilde{\mathbf{W}} \in \operatorname{argmin}_{\mathbf{W}} \{ \| \mathbf{X} - \mathbf{X} \mathbf{W} \mathbf{W}^\dagger \|_F^2 : \mathbf{W} \in \mathbb{R}^{n \times l}, \} \quad (3)$$

$$\operatorname{span}\{\tilde{\mathbf{W}}\} = \operatorname{span}\{\tilde{\mathbf{V}}\}$$

VAEs

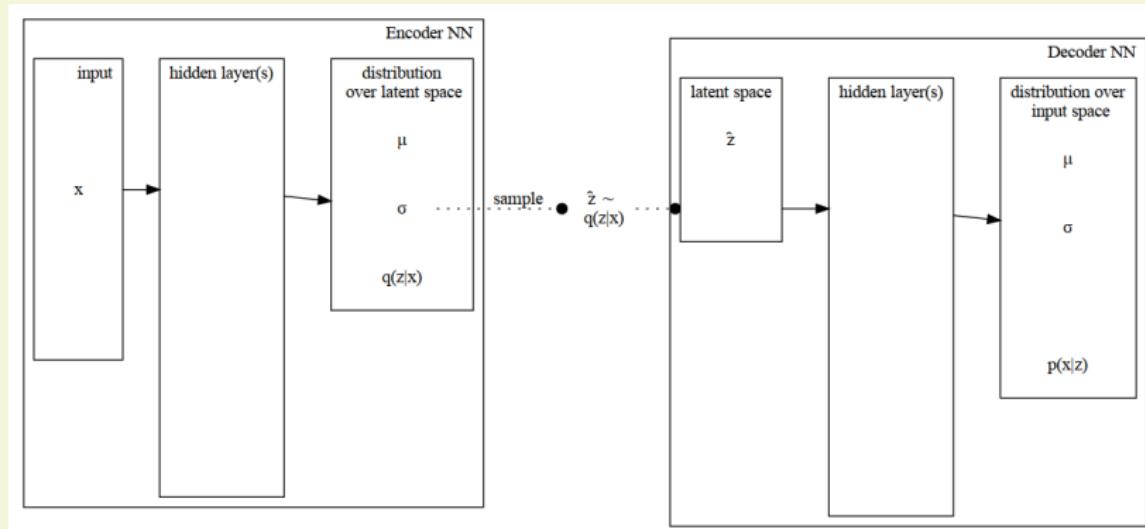


Figure: VAE

VAE: encoding

Instead of deterministic mapping, define distribution.

Define distribution on the latent space (\mathbf{z}) by mapping \mathbf{x} into the distribution parameters e.g. $\mu(\mathbf{x})$, $\Sigma(\mathbf{x})$ when we use Gaussian
 $q(\mathbf{z}|\mathbf{x}) = \mathcal{N}(\mathbf{z}|\mu, \Sigma)$.

VAE: decoding

sample from the latent space $\mathbf{z} \sim \mathcal{N}(\cdot|\mu, \Sigma)$

map \mathbf{z} to a distribution on the input space $p(\mathbf{x}|\mathbf{z})$

VAE: loss function

The *evidence lower bound (ELBO)* with respect to p, q is:

$$-\mathcal{L}(q, p, \mathbf{x}) \triangleq \int \log \frac{p(\mathbf{x}, \mathbf{z})}{q(\mathbf{z})} dq(\mathbf{z}) \quad (4)$$

$$-\mathcal{L}(q, p) \triangleq -\mathcal{L}(q, p, \mathbf{X}) = \frac{1}{N} \sum_1^N (-\mathcal{L}(q, p, \mathbf{x}_i)) \quad (5)$$

$$\approx \mathbf{E}_{\mathbf{x}}[-\mathcal{L}(q, p, \mathbf{x})] \quad (6)$$

We minimize the minus ELBO function:

VAE: log evidence

It can be shown that maximizing the ELBO is equivalent to maximinizing the "log evidence" $\log p(\mathbf{X})$

$$\begin{aligned}\frac{1}{N} \log p(\mathbf{X}) &= \frac{1}{N} \log \int p(\mathbf{X}, \mathbf{Z}) d\mathbf{Z} && \text{taking marginal} \\ &= \frac{1}{N} \log \int \frac{p(\mathbf{X}, \mathbf{Z})}{q(\mathbf{Z})} q(\mathbf{Z}) d\mathbf{Z} && \text{multiplying by 1 inside} \\ &= \frac{1}{N} \log \int \frac{p(\mathbf{X}, \mathbf{Z})}{q(\mathbf{Z})} dq(\mathbf{Z}) && \text{definition of } dq(\mathbf{Z}) \\ &\geq \frac{1}{N} \int \log \frac{p(\mathbf{X}, \mathbf{Z})}{q(\mathbf{Z})} dq(\mathbf{Z}) && \text{Jensen inequality} \tag{7} \\ &= \frac{1}{N} \int \sum_1^N \log \frac{p(\mathbf{x}_i, \mathbf{z}_i)}{q(\mathbf{z}_i)} dq(\mathbf{z}_i) && \text{using the iid property} \\ &= \frac{1}{N} \sum_1^N -\mathcal{L}(q, p, \mathbf{x}_i) && \text{definition of } \mathcal{L}(q, p, \mathbf{x}_i) \\ &= -\mathcal{L}(q, p, \mathbf{X}) \triangleq -\mathcal{L}(q, p) && \text{again definition of } \mathcal{L}(p, q) \quad \square\end{aligned}$$

Monte Carlo integration

As you can see we the loss function requires us to compute an integral, which usually cannot be done analytically.

Instead the integral is approximated by Monte Carlo integration.

sample $\mathbf{z}_i \sim q(\mathbf{z}|\mathbf{x})$ then :

$$\begin{aligned}\mathcal{L}(p, q, \mathbf{x}) &= \int -\log \frac{p(\mathbf{x}|\mathbf{z})p(\mathbf{z})}{q(\mathbf{z}|\mathbf{x})} dq(\mathbf{z}|\mathbf{x}) \\ &= \int -\log p(\mathbf{x}|\mathbf{z}) dq(\mathbf{z}|\mathbf{x}) + \int \log \frac{q(\mathbf{z}|\mathbf{x})}{p(\mathbf{z})} dq(\mathbf{z}|\mathbf{x}) \quad (8) \\ &\approx \frac{1}{k} \sum_{i=1}^k [-\log p(\mathbf{x}|\mathbf{z}_i) + \log \frac{q(\mathbf{z}_i|\mathbf{x})}{p(\mathbf{z}_i)}]\end{aligned}$$

VAE: compounding the latent distribution

More complicated distributions such as mixture distribution can be modelled by "unpacking" the latent \mathbf{z} and the observed \mathbf{x}

1. Define the set of observed random vectors $\mathbf{x}_1, \mathbf{x}_2, \dots, \mathbf{x}_k$, and the set of latent random vectors and stochastic parameters $\mathbf{z}_1, \dots, \mathbf{z}_l$.
2. Specify how to factor the generative model
 $p(\mathbf{x}_1, \dots, \mathbf{x}_k | \mathbf{z}_1, \dots, \mathbf{z}_l)$
3. Specify how to factor the inference model
 $q(\mathbf{z}_1 \dots \mathbf{z}_l | \mathbf{x}_1, \dots, \mathbf{x}_k)$
4. Choose appropriate priors $p(\mathbf{z}_i)$ and
5. Choose appropriate distribution families for the \mathbf{x}_i and \mathbf{z}_i , and choose priors $p(\mathbf{z}_i)$.

VAE: Graphical representation

Every distribution can be represented by a DAG. Nodes represent random variables (and also priors), and directed arrows represent conditional dependency.

VAE: base case

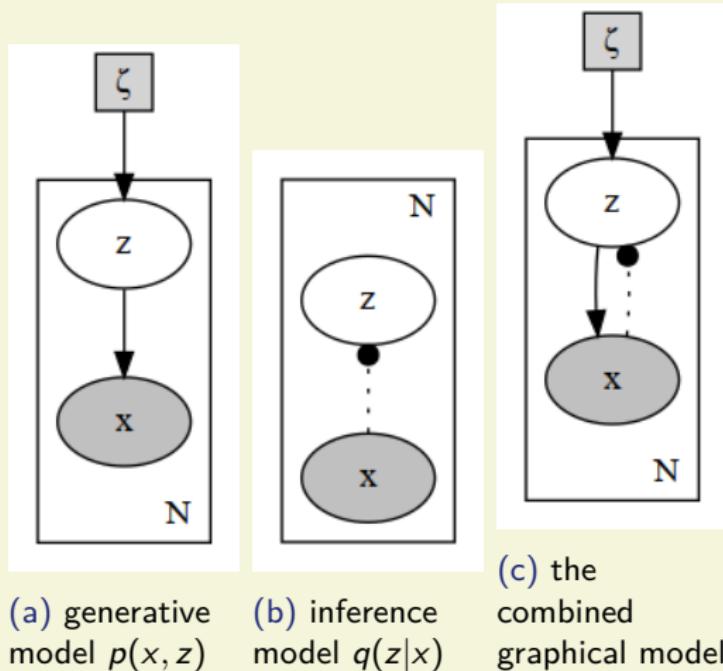
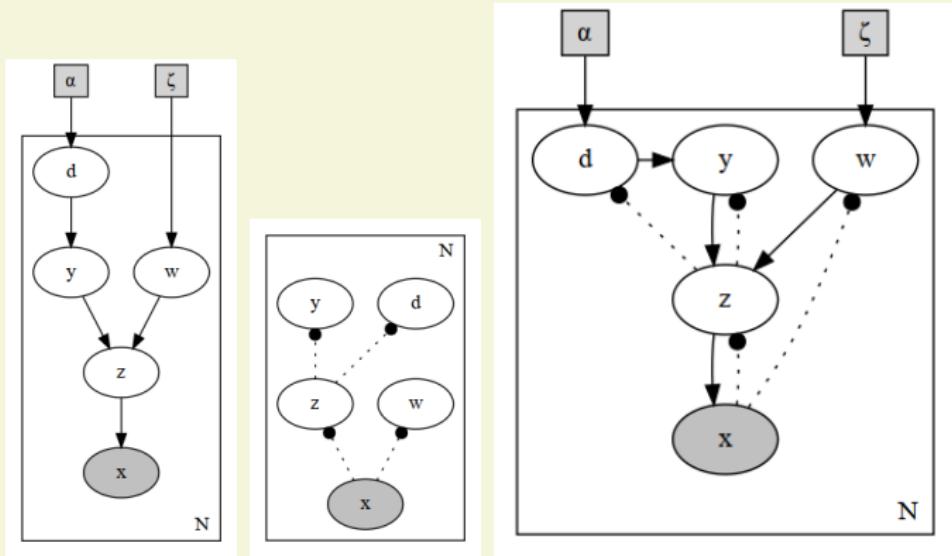


Figure: VAE graphical model

VAE: pathological case



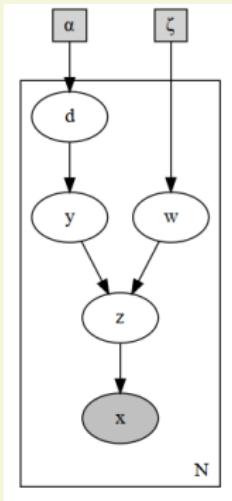
(a) generative
model $p(x, z)$

(b) inference
model $q(z|x)$

(c) the combined graphical
model

Figure: c*GMΔVAE graphical model

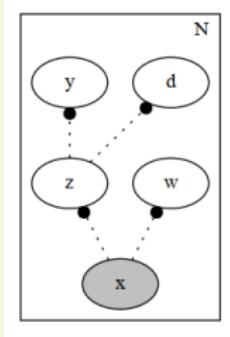
c*GMΔVÆ generative model



$$\begin{aligned} p(x, y, z, w, d) &= p(x|z)p(z|w, y)p(y|d)p(d)p(w) \\ p(w) &= \mathcal{N}(w|\mathbf{0}, \mathbf{1}) \\ p(d) &= \text{Dir}(d|\alpha) \\ p(y|d) &= \text{Cat}(y|d) \\ p(z|w, y) &= \mathcal{N}(z|\mu(w)_y, \sigma(w)_y) \\ p(x|z) &= \mathcal{N}(x|\mu(z), \sigma(z)) \end{aligned}$$

(9)

c*GMΔVÆ inference model



$$\begin{aligned} q(y, z, w, d|x) &= q(z|x)q(w|x)q(y|z)q(d|z) \\ q(z|x) &= \mathcal{N}(z|\mu_z(x), \sigma_z(x)) \\ q(w|x) &= \mathcal{N}(w|\mu_w(x), \sigma_w(x)) \quad (10) \\ q(y|z) &= \text{Cat}(y|f(z)) \\ q(d|z) &= \text{Dir}(d|g(z)) \end{aligned}$$

c*GMΔVÆ loss function

The loss function remains the -ELBO and we can break it into different terms:

$$\mathcal{L}(p, q, \mathbf{x}) = \int -\log \frac{p(\mathbf{x}, \mathbf{y}, \mathbf{z}, \mathbf{w}, \mathbf{d})}{q(\mathbf{z}, \mathbf{y}, \mathbf{w}, \mathbf{d}|\mathbf{x})} dq(\mathbf{z}, \mathbf{y}, \mathbf{w}, \mathbf{d}|\mathbf{x}) \quad (11)$$

$$= \int -\log \frac{p(\mathbf{x}|\mathbf{z})p(\mathbf{z}|\mathbf{w}, \mathbf{y})p(\mathbf{y}|\mathbf{d})p(\mathbf{w})p(\mathbf{d})}{q(\mathbf{z}|\mathbf{x})q(\mathbf{w}|\mathbf{x})q(\mathbf{y}|\mathbf{z})q(\mathbf{d}|\mathbf{z})} dq \quad (12)$$

$$= \int -\log p(\mathbf{x}|\mathbf{z})dq \quad (13)$$

$$+ \int \log \frac{q(\mathbf{z}|\mathbf{x})}{p(\mathbf{z}|\mathbf{w}, \mathbf{y})} dq \quad (14)$$

$$+ \int \log \frac{q(\mathbf{w}|\mathbf{x})}{p(\mathbf{w})} dq \quad (15)$$

$$+ \int \log \frac{q(\mathbf{y}|\mathbf{z})}{p(\mathbf{y}|\mathbf{d})} dq \quad (16)$$

$$+ \int \log \frac{q(\mathbf{d}|\mathbf{z})}{p(\mathbf{d})} dq \quad (17)$$

c*GMΔVÆ : supervised case

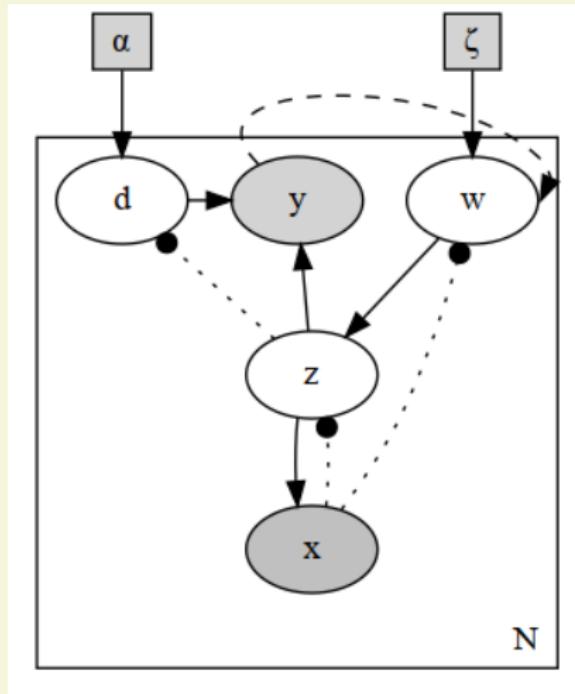
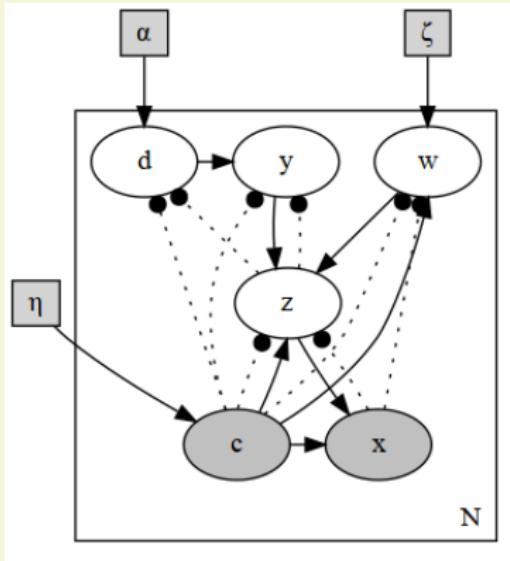
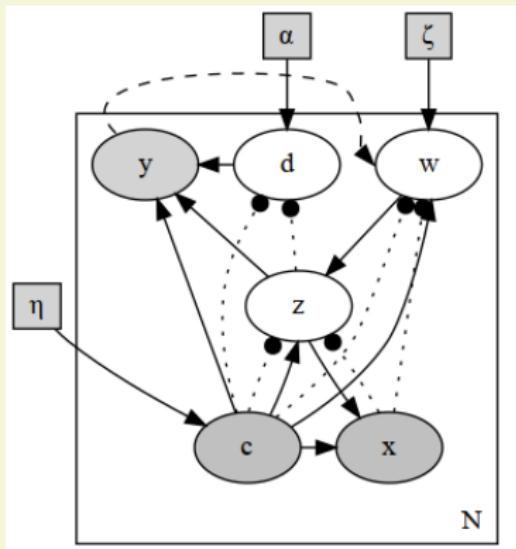


Figure: c*GMΔVÆ : the supervised case, where y is an observed variable.

the conditional flavor of $c^*GM\Delta VAE$

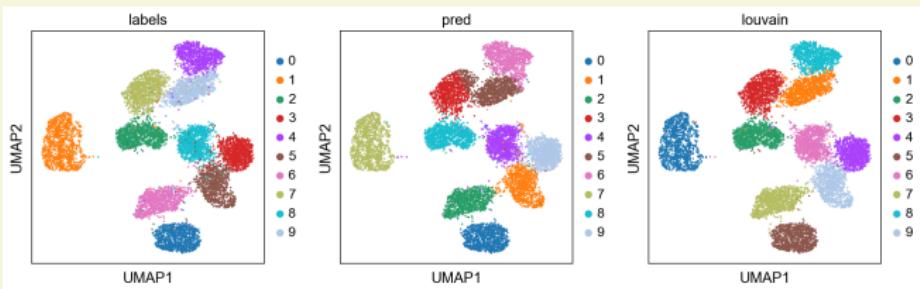


(a) $c^*GM\Delta VAE$ (cond.),
unsupervised case. Sorry for the
arrow clutter



(b) $c^*GM\Delta VAE$ (cond.), supervised
case

Tests on MNIST



(a) UMAP of the latent space

0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	7	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	7	9	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	9	4	1	2	3
0	5	6	7	8	7	4	1	2	3

Testing on synthetic conditional-categorical "blobs" dataset

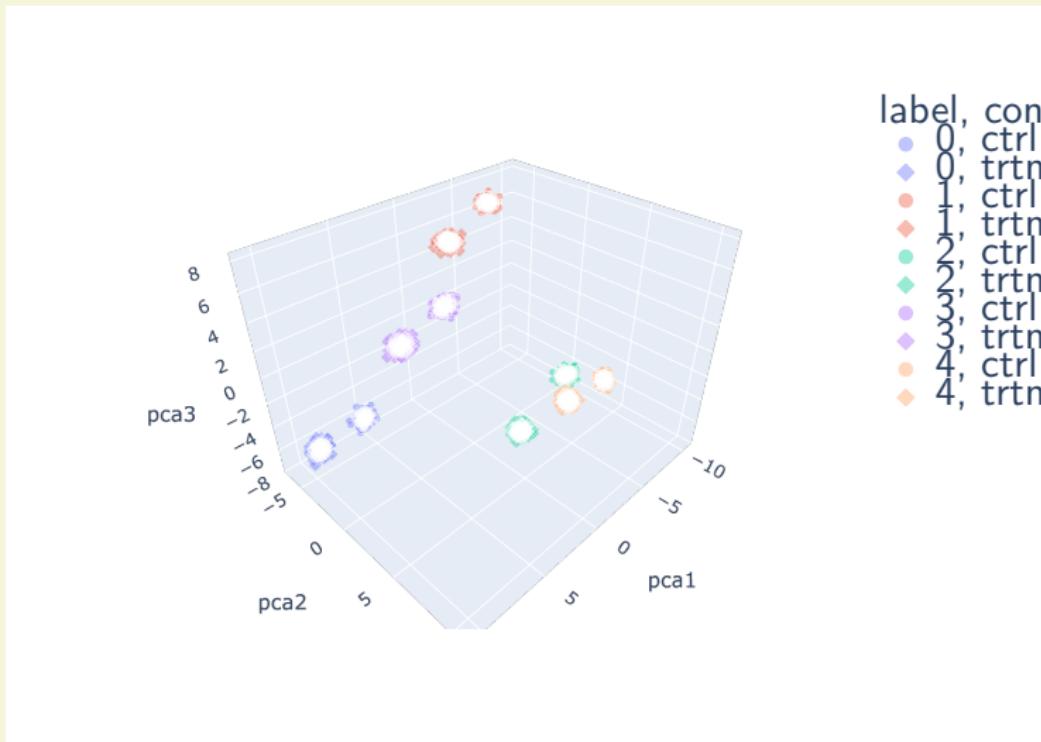


Figure: The toy dataset, showing a 3d plot of its 3 major PCA components.

w embedding

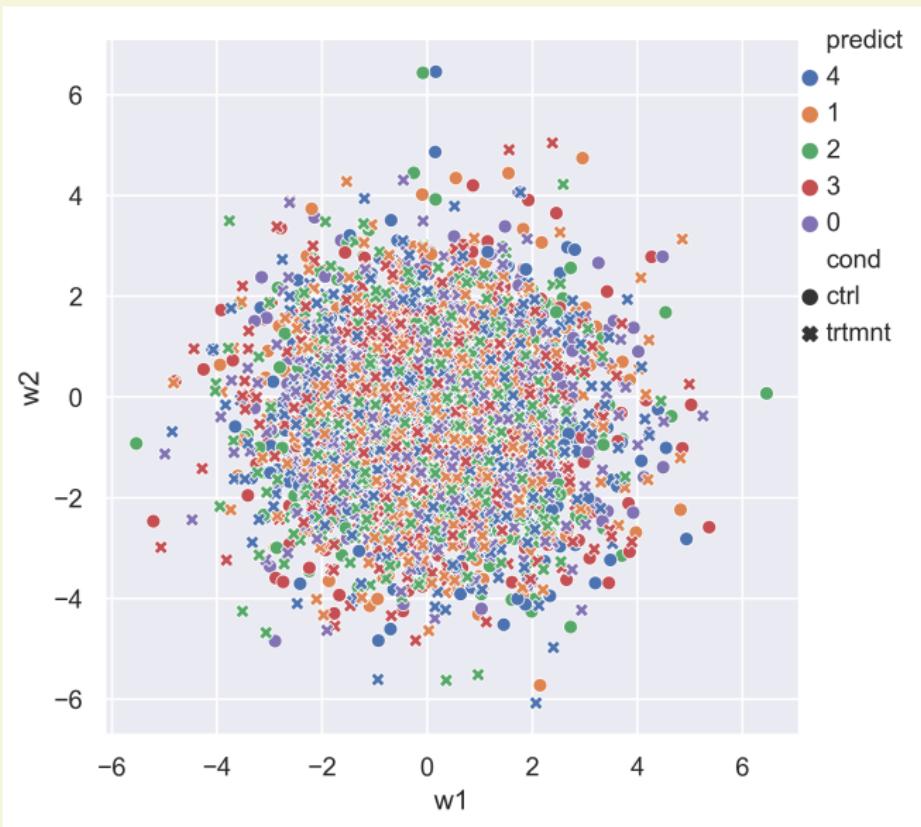


Figure: Random sampling from the encoded distribution of the w space.

z embedding

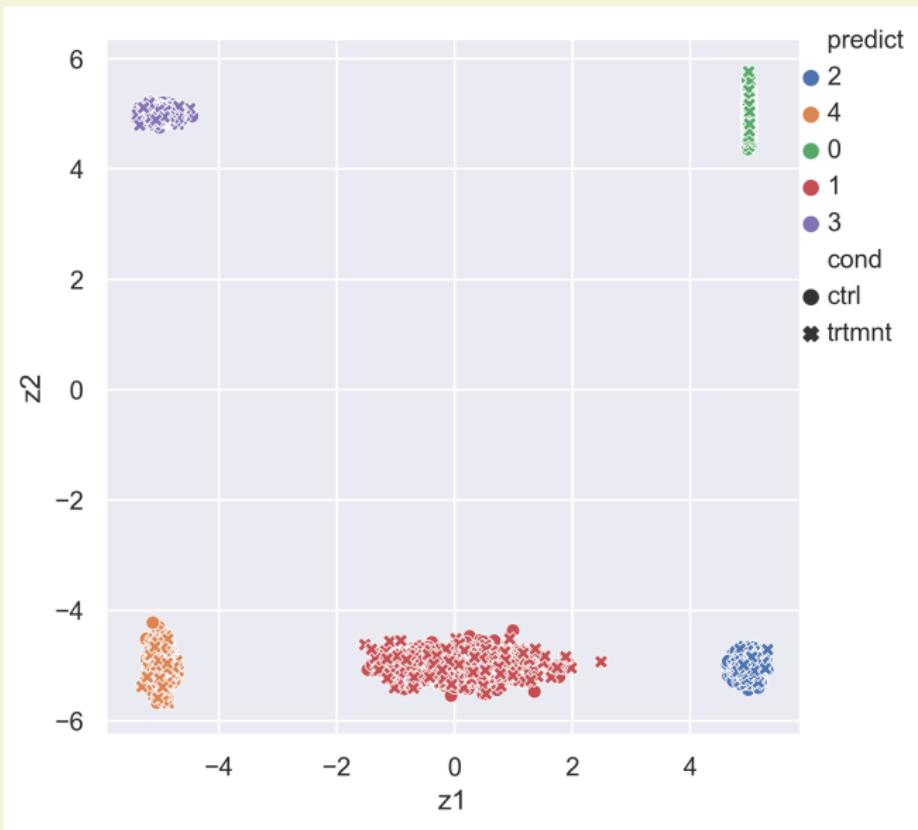


Figure: Sampling from encoded z space, fixed standard normal prior case.

Transfer learning

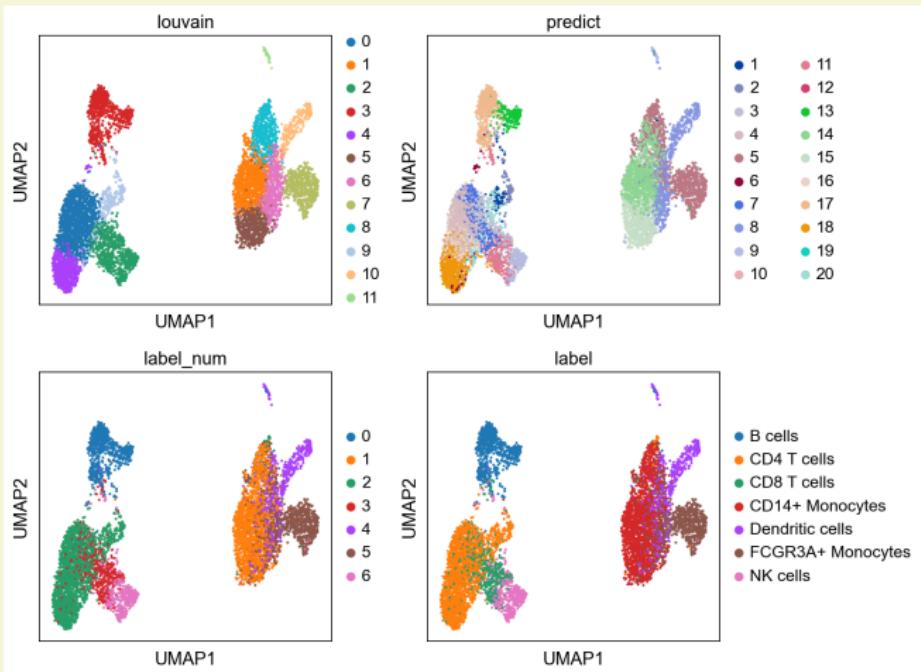


Figure: UMAP of PCA space of the Kang train data.

Transfer learning

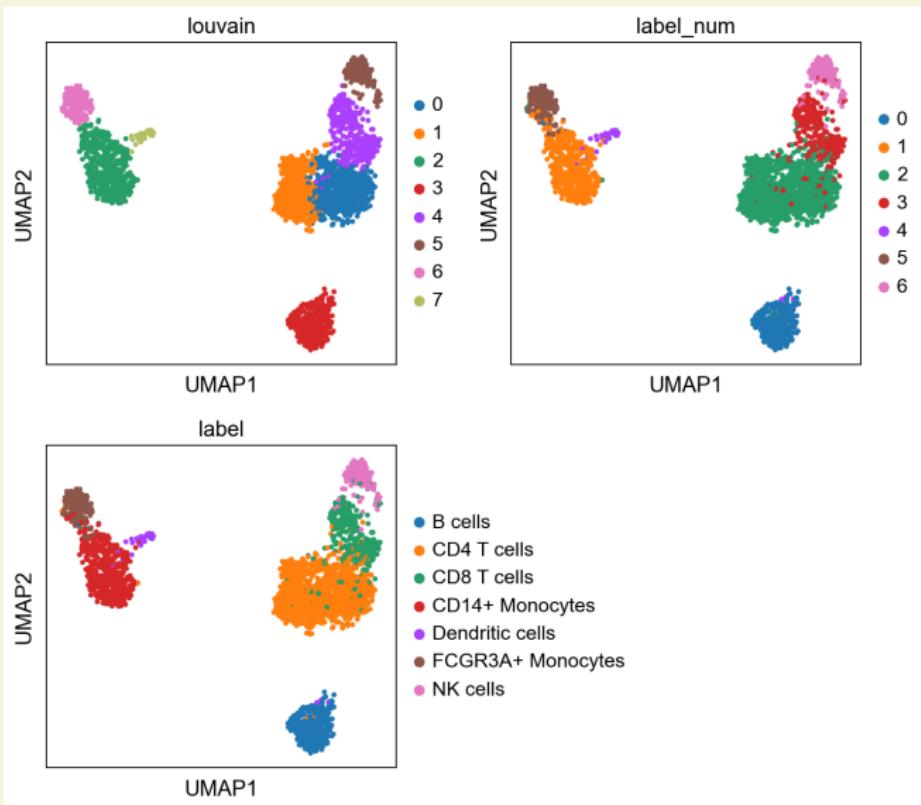


Figure: UMAP of the Zheng dataset.

Transfer learning

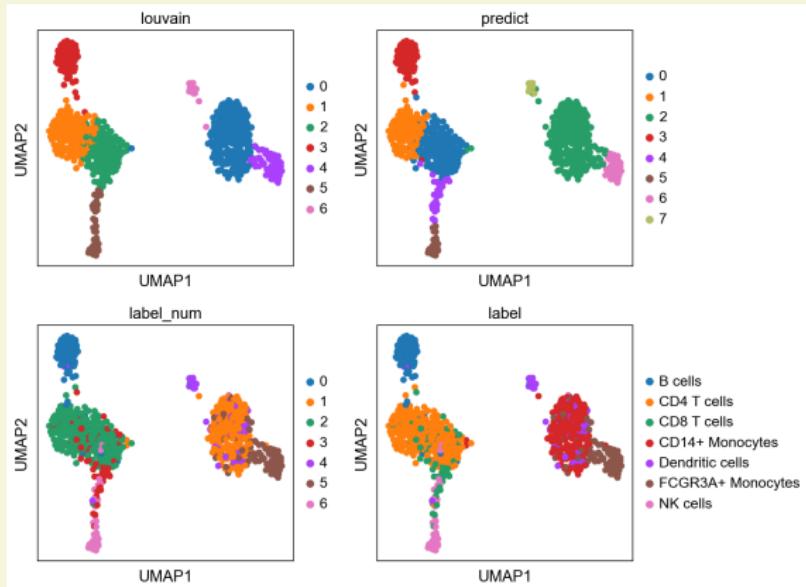


Figure: UMAP of the latent space of the Kang validation subset (the holdout).

converting treatment effect

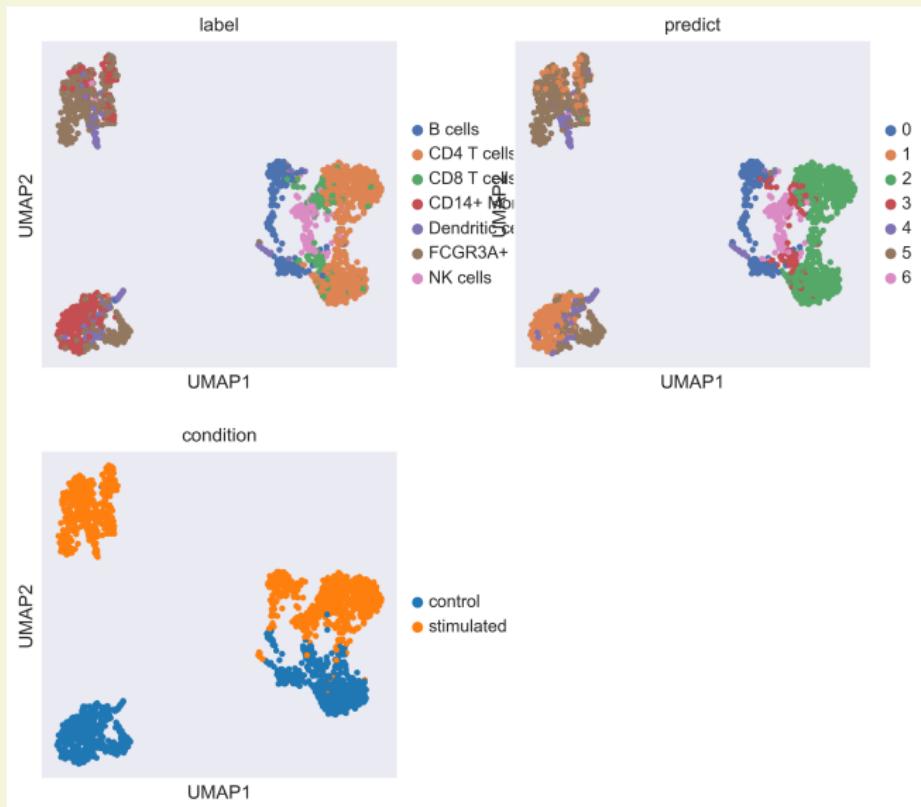


Figure: UMAP of the Kang validation dataset

converting treatment effect

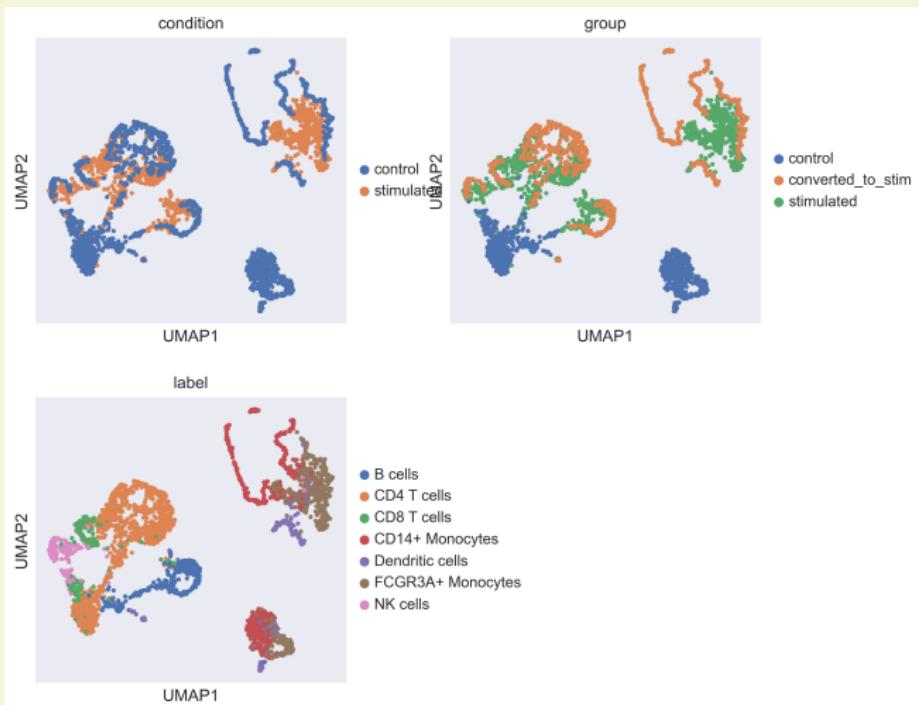
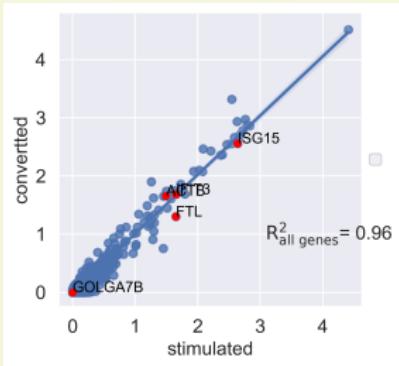
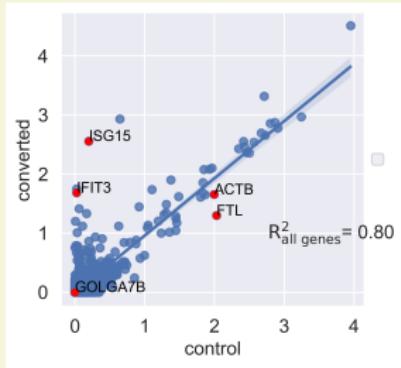
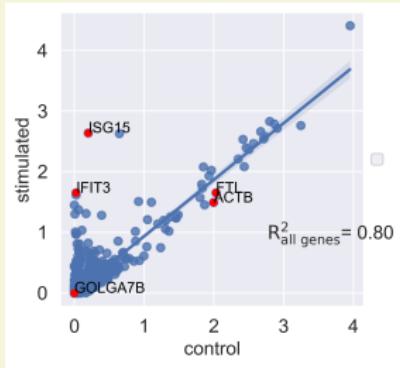


Figure: UMAP of the combined validation subset with its control group remapped into stimulated state.

converting treatment effect



Generating data

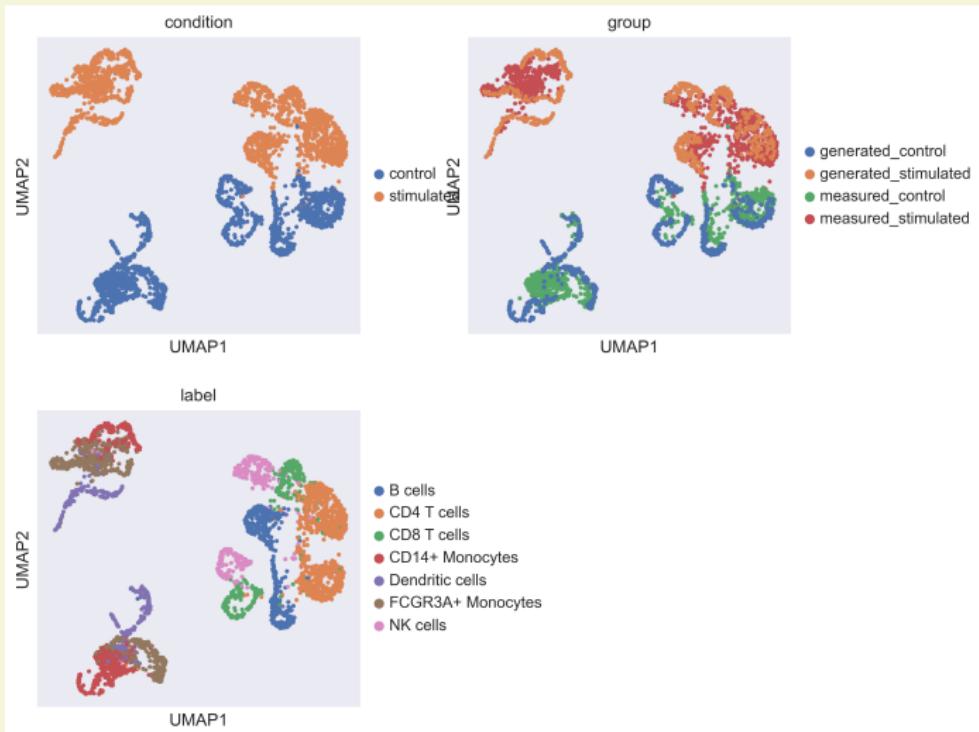


Figure: The Kang UMAP of real data combined with randomly generated data.

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