Dimension Reduction and Life Sciences

Panorama and Probabilistic View of some Recent Approaches

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Outline

Exploratory analysis of (modern) data sets

Assume a table with n individuals described by p features/variables

$$\mathbf{X}_{n\times p} = \begin{array}{|c|c|c|c|c|c|c|} \hline & & & & & & \\ \hline & & & x_{ij} & & & \\ \hline & & & & & & \\ \hline \end{array}$$

- genetics: variant j in genome i
- genomics: gene j in cell i
- ecology: species j in site j
- etc.

Challenges

- **Large** (n and p grows) and **high dimensional** (n grows but $\ll p$)
- **Redundancy** many variables may carry the same information
- **Discrete**: measures with counts are as common as with intensity

Dimension reduction: general goals

Find a **low-dimensional representation** that captures the "essence" (local and/or global structure, signal) of the original data

- **ML**: preprocessing, denoising, compression
- **Stat.**: descriptive/exploratory methods, visualization

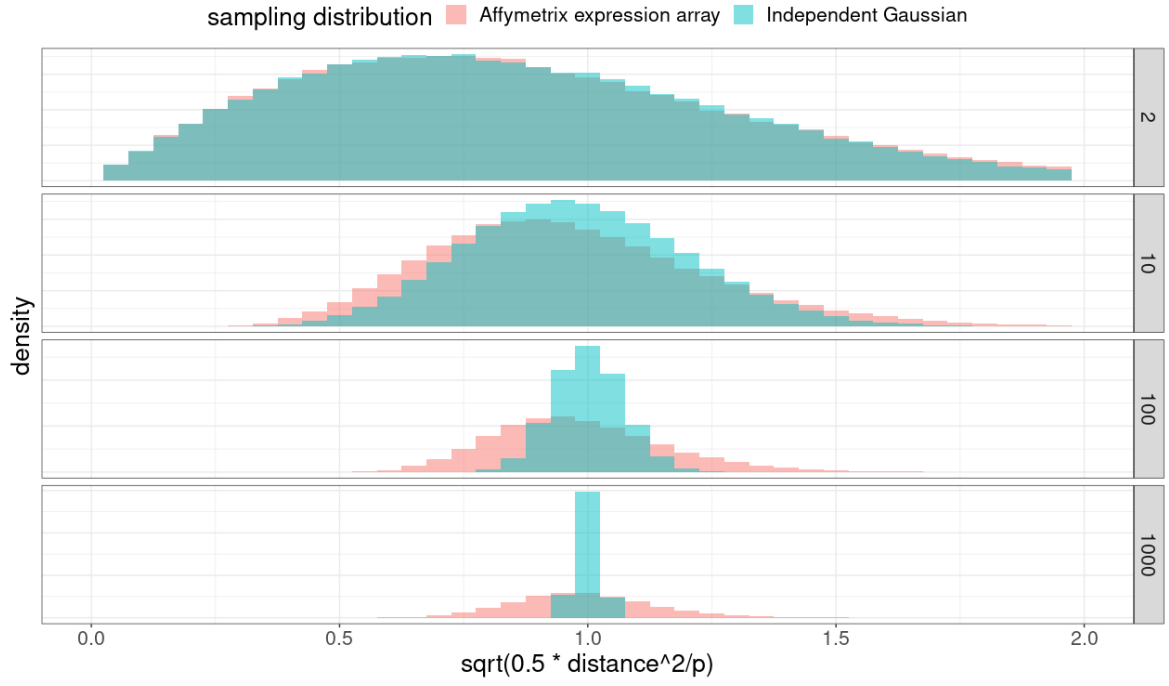
Dimensionality curse

Theorem (Folks theorem)

Let $\mathbf{x}_1, \ldots, \mathbf{x}_n$ be in the p-hypercube with i.i.d. coordinates. Then,

$$p^{-1/2} \left(\max \|\mathbf{x}_i - \mathbf{x}_{i'}\|_2 - \min \|\mathbf{x}_i - \mathbf{x}_{i'}\|_2 \right) = 0 + \mathcal{O}\left(\sqrt{\frac{\log n}{p}} \right)$$

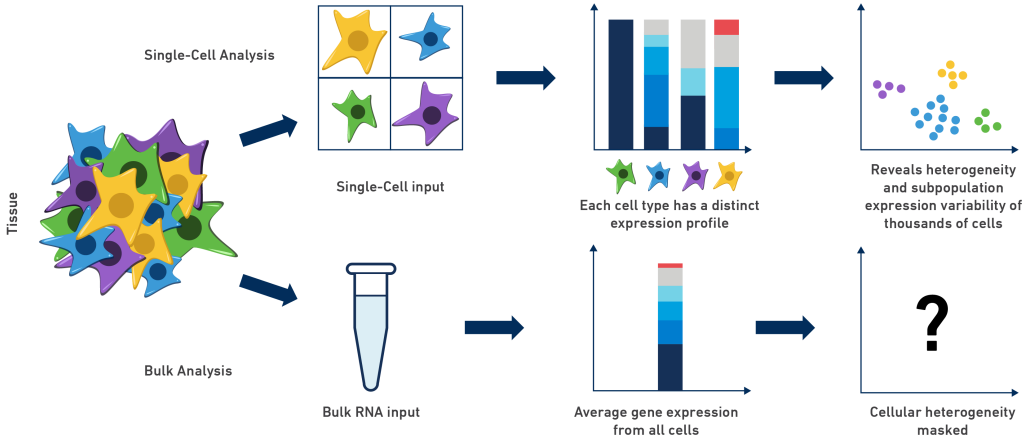
↝ *When p is large, all the points are almost equidistant*



↝ Hopefully, the data **are not really leaving in p** dimensions!

Example in genomics

Genome-wide cell biology with single-cell RNAseq data



Describe cell population ($n \to 10^6$) with high dimensional molecular features ($p \to 10^5$)

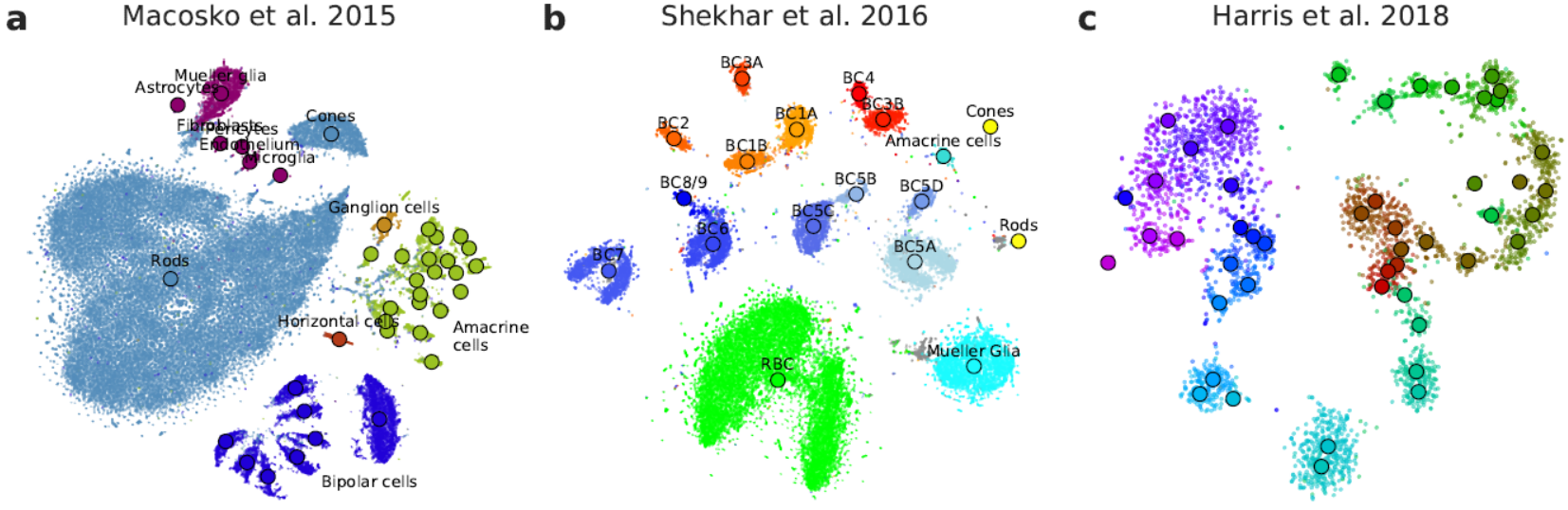
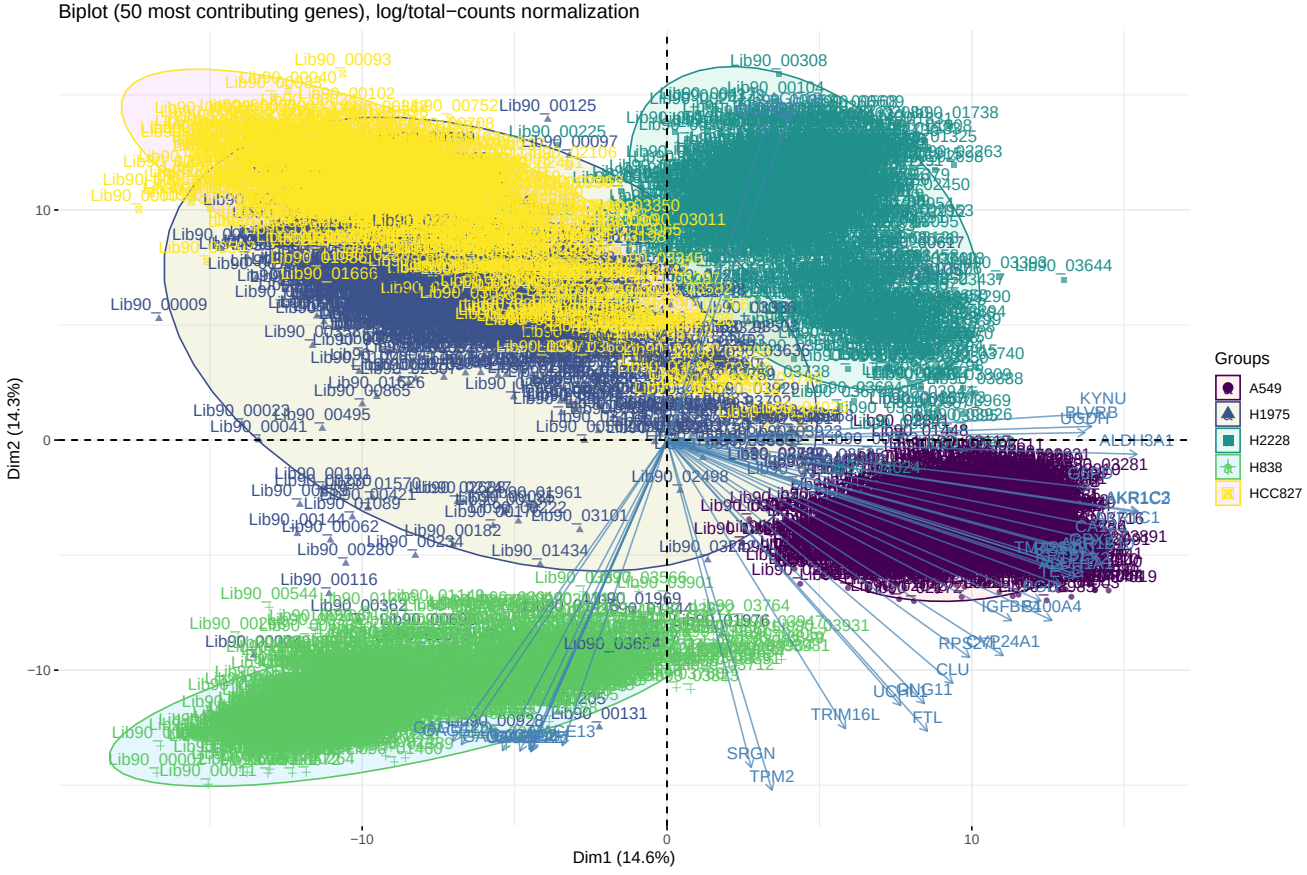


Figure 1: Successful t-SNE visualizations of sc-RNAseq data

Single-Cell data analysed with PCA

Toy single-cell RNA data set (https://github.com/LuyiTian/sc_mixology/)

The dataset `scRNA` contains the counts of the 500 most varying transcripts (tens of thousands) in the mixtures of 5 cell lines for a total of 3918 cells in human liver (obtained with standard 10x scRNAseq Chromium protocol).



Beyond PCA and linear methods

Robust but

- badly shaped for complex geometries (like multiscale properties)
- Fails with **Count** or **Skew** data (hidden Gaussian assumption)

Ideas

- Modify the model by playing with the **reconstruction error**
- Focus on **relationship preservation** to keep local characteristics

⇝ Gain in versatility with **probabilistic/model-based approaches**

Challenges

With, non-linear transformations...

- tradeoff between interpretability and **versatility**
- tradeoff between **high** or low computational resource

Outline

Principle

Find maps Φ and $\tilde{\Phi}$ in a given family (e.g, linear, constraint on parameters, etc.), minimizing an error between $\mathbf{x}$ and $\hat{\mathbf{x}} = \tilde{\Phi}(\Phi(\mathbf{x}))$, with $\Phi(\mathbf{x}) = \mathbf{z}$, e.g.

- **Distance** between $\mathbf{X}$ and $\hat{\mathbf{X}}$, e.g, sum of squares:

$$\epsilon^{\text{SSQ}}(\mathbf{X}, \hat{\mathbf{X}}) = \left\|\mathbf{X} - \hat{\mathbf{X}}\right\|_F^2 = \sum_{i=1}^{n} \left\|\mathbf{x}_i - \tilde{\Phi}(\Phi(\mathbf{x}_i))\right\|^2$$

- **Log-likelihood** of a parametric model p_θ, with $\hat{\mathbf{X}} = \mathbb{E}_{\hat{\theta}}(\cdot)$:

$$-\log p_\theta(\mathbf{X}) = -\sum_{i=1}^{n} \log p_\theta(\mathbf{X}_i)$$

PCA and Reconstruction error

Model

Let $\mathbf{V}_q$ be a $p \times q$ matrix whose columns are of q orthonormal vectors.

$$\Phi(\mathbf{x}) = \mathbf{V}_q^\top(\mathbf{x} - \boldsymbol{\mu}) = \mathbf{z}, \quad \hat{\mathbf{x}} = \tilde{\Phi}(\mathbf{z}) = \boldsymbol{\mu} + \mathbf{V}_q\mathbf{z}.$$

↝ Model with **Linear assumption + ortho-normality constraints**

Reconstruction error

$$\underset{\substack{\boldsymbol{\mu}\in\mathbb{R}^p \\ \mathbf{V}_q\in\mathcal{O}_{p,q}}}{\text{minimize}} \sum_{i=1}^{n} \left\|(\mathbf{x}_i - \boldsymbol{\mu}) - \mathbf{V}_q\mathbf{V}_q^\top(\mathbf{x}_i - \boldsymbol{\mu})\right\|^2 = \left(\underset{\substack{\mathbf{F}_q\in\mathcal{M}_{n,q} \\ \mathbf{V}_q\in\mathcal{O}_{p,q}}}{\text{minimize}} \left\|\mathbf{X}^c - \mathbf{F_q}\mathbf{V_q}^\top\right\|_F^2 \right)$$

Solution (explicit)

- $\boldsymbol{\mu}$ is the empirical mean, $\mathbf{V}_q$ eigenvectors of the empirical covariance
- In practice: SVD of the centered matrix $\mathbf{X}^c = \mathbf{U}_q\mathbf{D}_q\mathbf{V}_q^\top = \mathbf{F}_q\mathbf{V}_q^\top$

Other methods with same rational

Linear models with other constraints

$$(\hat{\boldsymbol{\mu}}, \hat{\mathbf{V}}, \hat{\mathbf{Z}}) = \arg\min \sum_{i=1}^{n} \left\| \mathbf{x}_i - \tilde{\Phi}(\Phi(\mathbf{x}_i)) \right\|^2, \quad \hat{\mathbf{x}} = \tilde{\Phi}(\mathbf{z}) = \boldsymbol{\mu} + \mathbf{V}_q \mathbf{z}$$

- **sparse PCA**: $\mathbf{V}_q$ sparse, possibly orthogonal
- **Dictionary learning**: $\mathbf{Z}$ sparse
- **Independent Component Anaysis** $(z^j, z^{j'})$ independent

Kernel-PCA: non linear transformation of the input $\Psi(\mathbf{x}_i)$, then PCA:

$$\Phi(\mathbf{x}) = \mathbf{V}_q^\top \Psi(\mathbf{x} - \boldsymbol{\mu}) = \mathbf{z}, \qquad \Psi : \mathbb{R}^p \to \mathbb{R}^n$$

Non Linear Matrix Factorization

Poisson likelihood for $\mathbf{X}_{ij}$ with intensity $\lambda_{ij}^q = (\mathbf{F}_q \mathbf{V}_q^\top)_{ij} \geq 0$:

$$\hat{\mathbf{X}}^{\text{poisson}} = \underset{\substack{\mathbf{F} \in \mathscr{M}(\mathbb{R}_+)_{n,q} \\ \mathbf{V} \in \mathscr{M}(\mathbb{R}_+)_{p,q}}}{\arg\max} \sum_{i,j} x_{ij} \log(\lambda_{ij}^q) - \lambda_{ij}^q.$$

Probabilistic Gaussian PCA (Tipping and Bishop 1999)

Generative model

pPCA is a special factor model with parameter $\theta = (\mathbf{C}, \sigma)$:

$$\begin{array}{rccc} \text{latent space} & \mathbf{Z}_i & \text{i.i.d.} & \mathbf{Z}_i \sim \mathcal{N}(\mathbf{0}_q, \mathbf{I}_q) \\ \text{observation space} & \mathbf{X}_i|\mathbf{Z}_i & \text{indep.} & \mathbf{X}|\mathbf{Z}_i \sim \mathcal{N}\left(\boldsymbol{\mu} + \mathbf{C}\mathbf{Z}, \sigma^2\mathbf{I}_n\right) \end{array}$$

By direct integration[1], the marginal distribution of the observation is

$$p_\theta(\mathbf{X}_i) = \int_{\mathbb{R}_q} p_\theta(\mathbf{X}_i|\mathbf{Z}_i)\, p(\mathbf{Z}_i) \mathrm{d}\mathbf{Z}_i = \mathcal{N}\left(\boldsymbol{\mu}, \boldsymbol{\Sigma}\right), \quad \boldsymbol{\Sigma} = \mathbf{C}\mathbf{C}^\top + \sigma^2\mathbf{I}_n$$

↝ rank-q decomposition of the covariance matrix + noise.

[1] easy since everything is Gaussian

Estimation

Criterion: negative log-likelihood

$$-\sum_{i=1}^{n} \log p_\theta(\mathbf{X}_i) = \log|\boldsymbol{\Sigma}| + \operatorname{tr}\left(\boldsymbol{\Sigma}^{-1}\hat{\boldsymbol{\Sigma}}\right), \quad \hat{\boldsymbol{\Sigma}} = \frac{1}{n}\sum_i (\mathbf{x}_i - \bar{\mathbf{x}})(\mathbf{x}_i - \bar{\mathbf{x}})^\top$$

Maximum likelihood estimator

$$\hat{\mathbf{C}}^{\text{mle}} = \mathbf{V}_q \left(\boldsymbol{\Lambda}_q - \hat{\sigma}^2 \mathbf{I}_n\right)^{1/2}, \quad \hat{\sigma}^2 = \frac{1}{p-q}\sum_{i=q+1}^{p} \lambda_i, \quad \hat{\boldsymbol{\Sigma}} = \mathbf{V}\boldsymbol{\Lambda}\mathbf{V}^\top$$

Latent position: posterior distribution

$$\mathbf{Z}_i \,|\, \mathbf{X}_i \sim \mathcal{N}\left(\mathbf{S}^{-1}\hat{\mathbf{C}}^\top(\mathbf{X}_i - \bar{\mathbf{x}}), \mathbf{S}^{-1}\hat{\sigma}^2\right), \quad \mathbf{S} = \left(\hat{\mathbf{C}}^\top\hat{\mathbf{C}} + \hat{\sigma}^2\mathbf{I}_q\right)$$

When $\sigma^2 \to 0$, $\mathbb{E}(\mathbf{Z}_i|\mathbf{X}_i) \equiv$ **orthogonal projection in the latent space**.

Estimation: alternative

Expectation-Maximization

With $\mathscr{H}(p) = -\mathbb{E}_p(\log(p))$ the entropy of p,

$$\log p_\theta(\mathbf{X}) = \mathbb{E}[\log p_\theta(\mathbf{X}, \mathbf{Z}) \,|\, \mathbf{X}; \theta)] + \mathscr{H}[p_\theta(\mathbf{Z} \,|\, \mathbf{X}; \theta)]$$

EM requires to evaluate (some moments of) $p_\theta(\mathbf{Z} \,|\, \mathbf{X}; \theta)$

- E-step: evaluate $Q(\theta|\theta') = \mathbb{E}(\log \ell(\mathbf{X}, \mathbf{W}; \theta)|\mathbf{X}; \theta')$
- M-step: update θ by maximizing $Q(\theta|\theta')$

EM for pPCA

- E-step: update the latente position means $\mathbb{E}(\mathbf{Z}|\mathbf{X})$
- M-step: update the model parameters $\mathbf{C}, \sigma^2$

On-going: Fast `JAX` implementation by Hugo Gangloff, mixture of pPCA with Pierre Barbillon and MsC intern Pierre Brand

PCA for counts: Poisson lognormal PCA

Generative Model (Chiquet, Mariadassou, and Robin 2018)

$$\begin{aligned} \text{latent space} \quad & \mathbf{Z}_i \quad \text{i.i.d.} \quad && \mathbf{Z}_i \sim \mathcal{N}(\mathbf{0}_q, \mathbf{I}_q) \\ \text{observation space} \quad & \mathbf{X}_i|\mathbf{Z}_i \quad \text{indep.} \quad && \mathbf{X}|\mathbf{Z}_i \sim \mathcal{P}\left(\exp\{\boldsymbol{\mu} + \mathbf{C}^\top \mathbf{Z}_i\}\right) \end{aligned}$$

Estimation: Issues

- The marginal distribution is hard to compute, even numerically

$$p_\theta(\mathbf{X}_i) = \int_{\mathbb{R}_p} \prod_{j=1}^{p} p_\theta(X_{ij}|Z_{ij})\, p_\theta(\mathbf{Z}_i) \mathrm{d}\mathbf{Z}_i$$

↝ no direct MLE possible

- Posterior distribution of $\mathbf{Z}_i$ has no close form

↝ no genuine application of EM possible

Variational inference (Chiquet, Mariadassou, and Robin 2021)

Variational approximation (Blei, Kucukelbir, and McAuliffe 2017)

- Use a proxy q_ψ of $p_\theta(\mathbf{Z} \,|\, \mathbf{X})$ minimizing a divergence in a class $\mathcal{Q}$

$$q_\psi(\mathbf{Z})^\star = \arg\min_{q \in \mathcal{Q}} D_{KL}\left(q(\mathbf{Z}), p(\mathbf{Z}|\mathbf{Y})\right), \quad D_{KL}(p,q) = \mathbb{E}_q\left[\log \frac{q(z)}{p(z)}\right].$$

- maximize the ELBO (Evidence Lower BOund)

$$J(\theta, \psi) = \log p_\theta(\mathbf{Y}) - KL[q_\psi(\mathbf{Z}) || p_\theta(\mathbf{Z}|\mathbf{Y})] = \mathbb{E}_\psi[\log p_\theta(\mathbf{Y}, \mathbf{Z})] + \mathscr{H}[q_\psi(\mathbf{Z})]$$

Variational EM for Poisson-lognormal PCA (PLN-PCA)

Consider $\mathcal{Q}$ the class of diagonal multivariate Gaussian distributions.
The ELBO $J(\theta, \psi)$ hat close-form and is bi-concave.

- E-step: solve in ψ for given θ
- M-step: solve in θ for given ψ

Model selection and Visualization for PLN-PCA

Selection of number of components (rank k)

Use likelihood lower bound in information criteia, e.g,

$$\hat{k} = \arg\max_k \text{vBIC}_k \quad \text{with } \text{vBIC}_k = J(\hat{\boldsymbol{\beta}}, \tilde{p}) - \frac{1}{2} p(d+k) \log(n)$$

Visualization: non-nested subspaces (≠ Gaussian PCA)

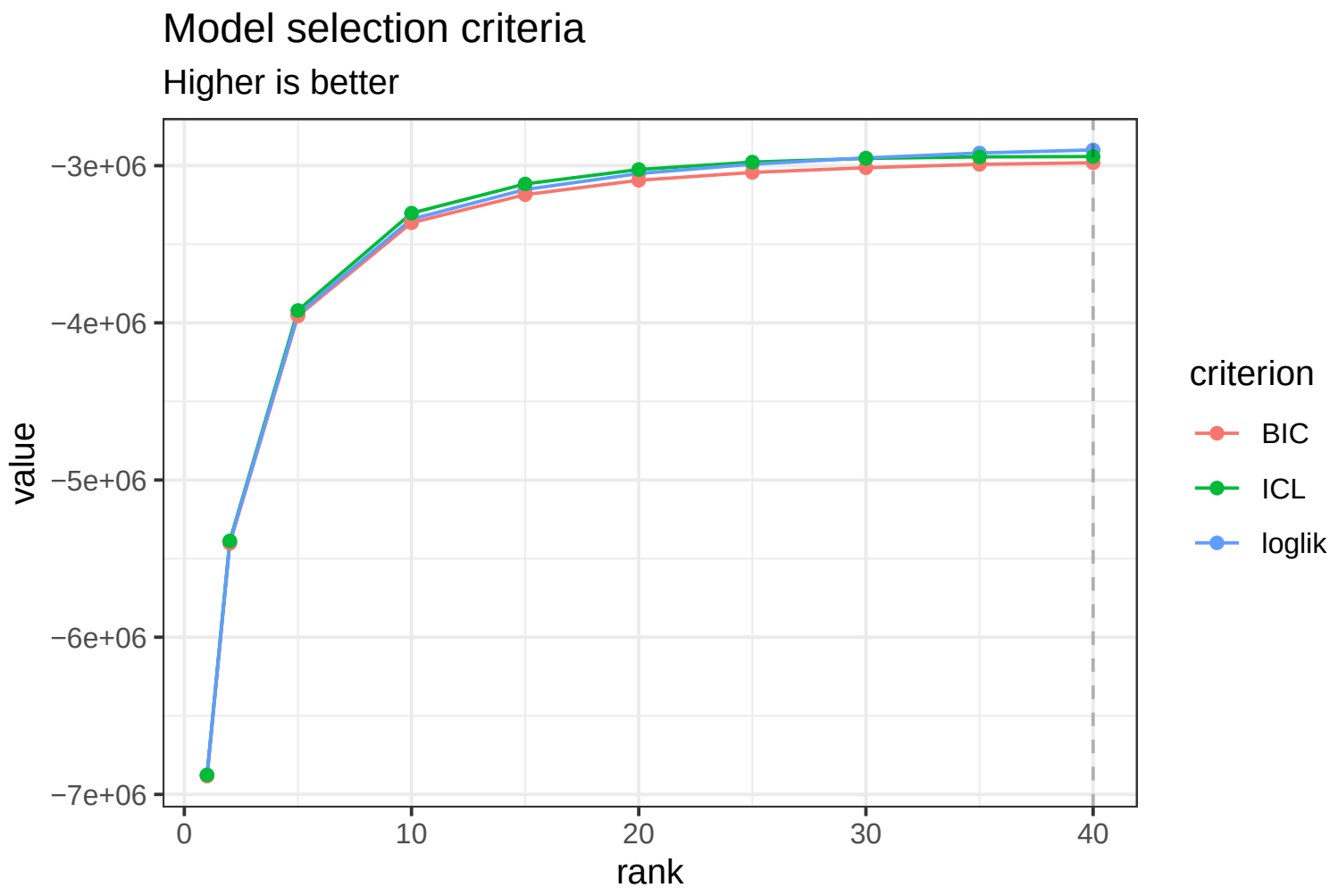
For the selected dimension $\hat{k}$, compute the estimated latent positions $\mathbb{E}_q(\mathbf{Z}_i)$ and perform PCA

Goodness of fit: deviance based criterion

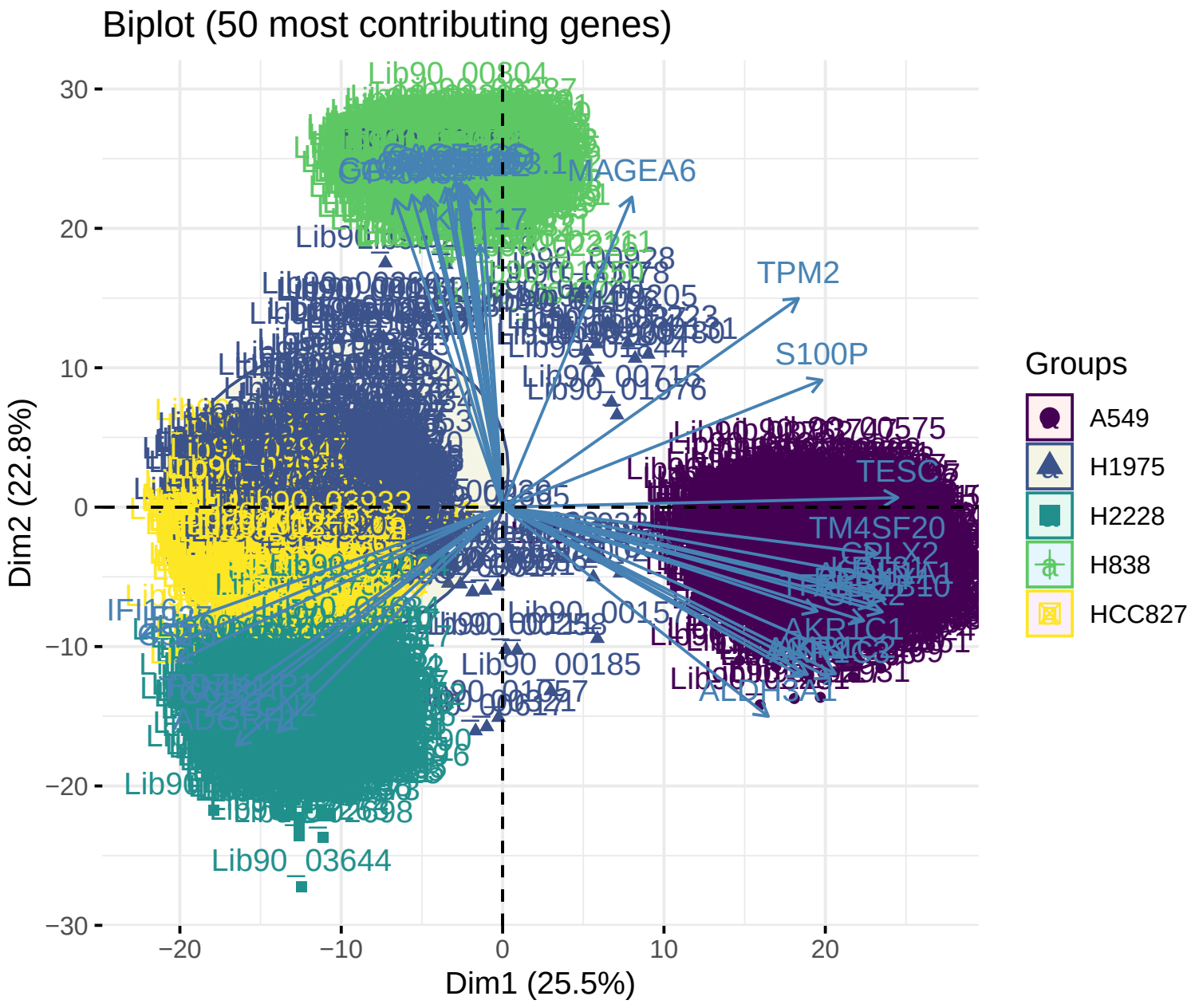
For $\ell_k = \log \mathbb{P}(\mathbf{X}; \lambda^{(k)})$ the Poisson likelihood,

$$R^2_k = \frac{\ell_k - \ell_0}{\ell_{\max} - \ell_0}, \quad \text{with } \lambda_{ij}^{(k)} = \exp\left(\mathbb{E}_q(Z_{ij}^{(k)})\right), \quad \lambda_{ij}^{\max} = Y_{ij}.$$

Poisson-lognormal PCA for the scRNA data set



Poisson-lognormal PCA for the scRNA data set



Mixture of PLN-PCA with Nicolas Jouvin

Gaussian mixture in the **common** latent q-dimensional subspace

$$\begin{aligned}
\mathbf{G}_i &\sim \mathcal{M}(1, \boldsymbol{\pi} = (\pi_1, \dots, \pi_K)) && \text{(clustering)} \\
\mathbf{Z}_i &\sim \mathcal{N}_q(\mathbf{0}, \mathbf{I}_q) && \text{(subspace)} \\
\mathbf{W}_i \mid \mathbf{G}_{ik} = 1 &\sim \mu_k + \sigma_k \mathbf{Z}_i && \text{(linear transform)} \\
\mathbf{X}_i \mid \mathbf{W}_i, \mathbf{G}_i &\sim \mathcal{P}(\exp(\mathbf{C}\mathbf{W}_i)) && \text{(emission)}
\end{aligned}$$

With parameters $\{\boldsymbol{\mu}_k, \boldsymbol{\mu}_k, \mathbf{C}, \boldsymbol{\pi}\}$: use variational inference.

More general models

- Add covariate effects
- Use diagonal variance (rather than spherical) $\sigma_k^2 \mathbf{I}_q \to \mathbf{D}_k$
- Use different $\mathbf{C}_k \rightsquigarrow$ no common projection

Variational Auto-Encoders (Kingma and Welling 2013)

Highly non-linear model

Find Φ and $\tilde{\Phi}$ with **two** neural-networks, controlling the error.

$$\epsilon(\mathbf{X}, \hat{\mathbf{X}}) = \sum_{i=1}^{n} \left\| \mathbf{x}_i - \tilde{\Phi}(\Phi(\mathbf{x}_i)) \right\|^2 + \text{regularization}(\Phi, \tilde{\Phi})$$

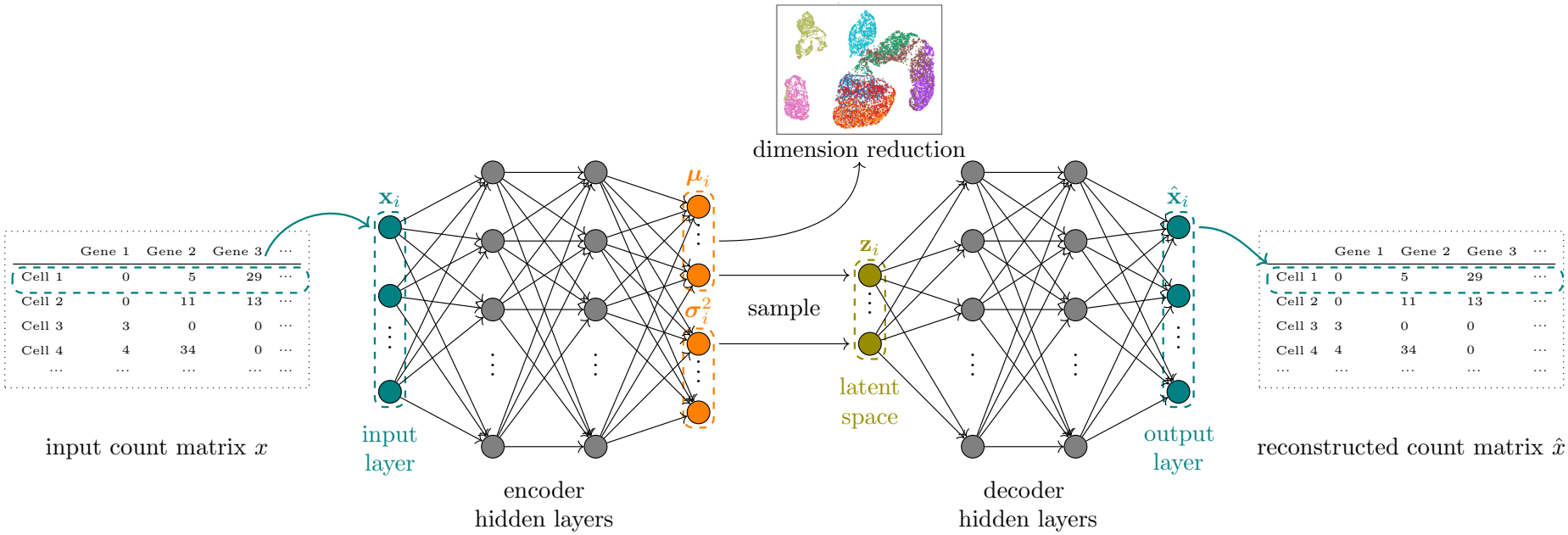


Figure 2: Figure by Hugo Gangloff

Variational Auto-Encoders

Decoder: Generative model

$$p_\theta(\mathbf{X}_i, \mathbf{Z}_i) = p_\theta(\mathbf{Z}_i) p_\theta(\mathbf{X}_i|\mathbf{Z}_i), \text{ with } \begin{cases} p_\theta(\mathbf{Z}_i) & = \mathcal{N}(0, \mathbf{I}_q), \\ p_\theta(\mathbf{X}_i|\mathbf{Z}_i) & \text{cond. likelihood.} \end{cases}$$

Encoder: Variational Inference model

The encoder approximate the posterior distribution with q_ψ, $\psi = \{\boldsymbol{\mu}_i, \boldsymbol{\sigma}^2\}$:

$$q_\psi(\mathbf{Z}_i|\mathbf{X}_i) = \mathcal{N}(\boldsymbol{\mu}_i, \boldsymbol{\sigma}_i^2 \mathbf{I}_q) \approx p_\theta(\mathbf{Z}_i|\mathbf{X}_i)$$

Optimization/training

Maximize a lower bound of the marginal $\log p_\theta(\mathbf{X})$ (a.k.a the ELBO):

$$\log p_\theta(\mathbf{X}_i) \geq \mathscr{E}_{\theta,\psi}(\mathbf{X}_i) = \mathbb{E}_{q_\psi(\mathbf{Z}_i|\mathbf{X}_i)} [\log p_\theta(\mathbf{X}_i|\mathbf{Z}_i)] - D_{KL}(q_\psi(\mathbf{Z}_i|\mathbf{X}_i)||p_\theta(\mathbf{Z}_i))$$

Variational Auto-Encoders

Likelihoods relevent for count data

- Data scaled to [0,1] + Continuous Bernoulli (CB) likelihood (Wang and Gu 2018)
- (Zero Inflated) Negative Binomial (ZINB) likelihood (Dony et al. 2020)
- **(Zero Inflated) Poisson likelihood** (tried this with Hugo Gangloff)

Let $\lambda \in (\mathbb{R}_*^+)^p$ and $\rho \in [0,1]^p$ be the outputs of the decoder,

$$p_\theta(\mathbf{x}|\mathbf{z}) = \prod_{j=1}^{p} \begin{cases} \rho_j + (1-\rho_j) p_\theta^{Poiss}(x_{m,n}|\lambda_n), & x_{ij} = 0, \\ (1-\rho_j) p_\theta^{Poiss}(x_{ij}|\lambda_n), & x_{ij} > 0. \end{cases}$$

Promising works and questions

- Grønbech et al. (2020): Gaussian Mixture VAE
- Seninge et al. (2021): Semi-supervised VA
- Us: Connexion with traditional variational inference
- Us: Use as block in wider model-based approches

Variational Auto-Encoders on scRNA data[2]

- encoder dimensions: [256, 128, 64]
- decoder dimensions: [64, 128, 256]
- ADAM with learning rate = 1e-3

Negative-Binomial distribution

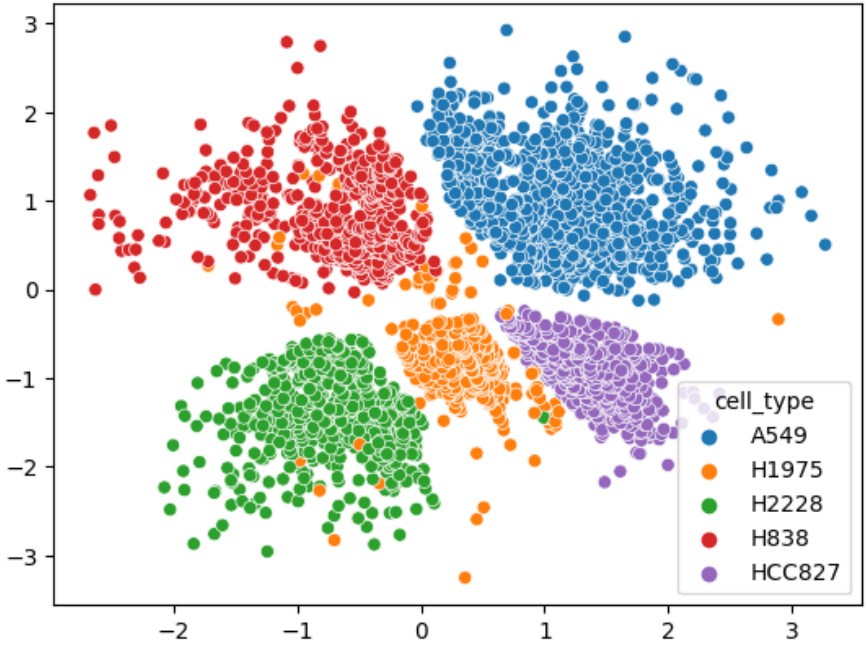


Figure 3: Negative Binomial

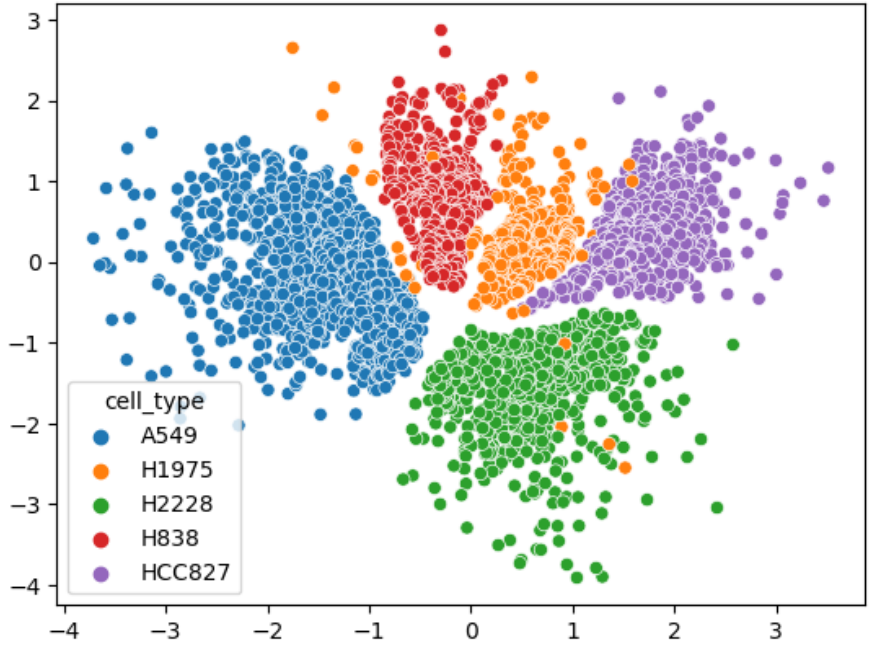


Figure 4: Zero-Inflated Negative Binomial

[2] based on code by Hugo Gangloff

Variational Auto-Encoders on scRNA data[3]

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- ADAM with learning rate = 1e-3

Poisson distribution

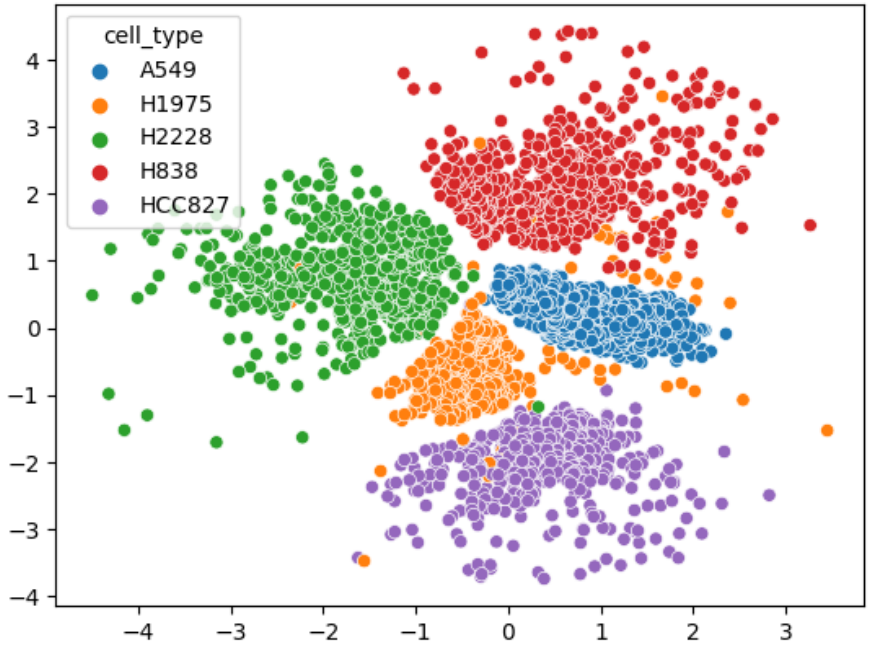


Figure 5: Poisson

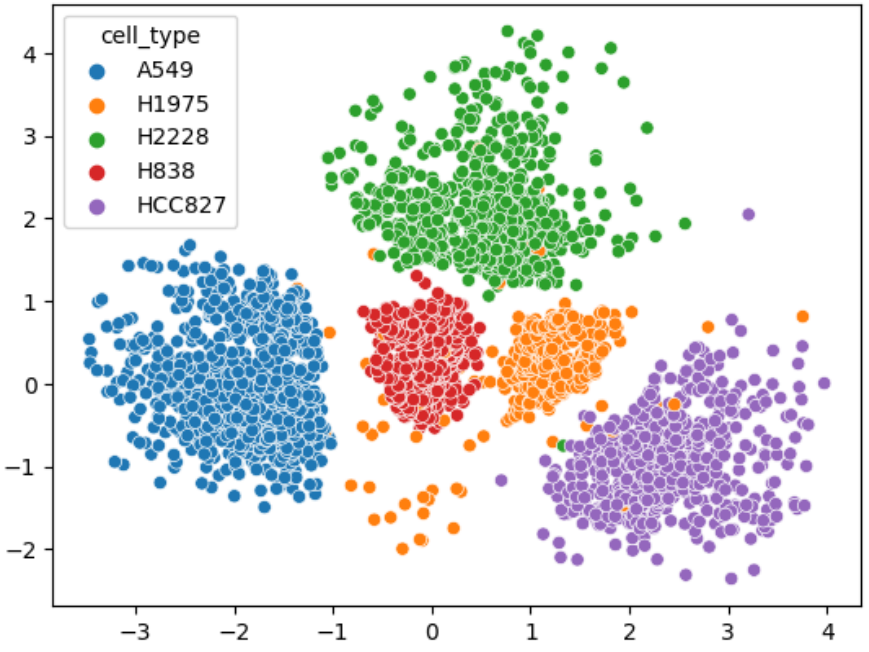


Figure 6: Zero-Inflated Poisson

[3] based on code by Hugo Gangloff

Outline

Principle

Consider an $n \times n$ (dis)similarity matrix associated to $\mathbf{x}_i \in \mathbb{R}^p$, measuring pairwise relations $\mathscr{R}(\bullet, \bullet')$, using one among

- distances,
- kernels,
- inner products,
- probability distributions.

Goal: find $\mathbf{z}_i \in \mathbb{R}^q$ while preserving the (dis)similarities in the latent space

Preserve local properties

Find a map Φ from $\mathbb{R}^p \to \mathbb{R}^q$ such that

$$\mathscr{R}(\mathbf{x}_i, \mathbf{x}_{i'}) \sim \mathscr{R}'(\mathbf{z}_i, \mathbf{z}_{i'})$$

↝ preserve $\mathscr{R}$ both in high and low dimensional spaces to catch complex geometries

Multidimensional scaling

a.k.a Principale Coordinates Analysis

Classical Multidimensional Scalings

Preserve similarities in terms **inner product**:

$$\text{Stress}^{cMDS}(\mathbf{z}_i) = \sum_{i \neq i'} \left((\mathbf{x}_i - \boldsymbol{\mu})^\top (\mathbf{x}_i - \boldsymbol{\mu}) - \mathbf{z}_i^\top \mathbf{z}_{i'} \right)^2,$$

Metric Multidimensional Scalings

Remarking that cMDS amount to preserve dissimilarities in terms of Euclidean distance, use

$$\text{Stress}(\mathbf{z}_1, \ldots, \mathbf{z}_n) = \sum_{i \neq i'} \left(d_{ii'} - \|\mathbf{z}_i - \mathbf{z}_{i'}\| \right)^2,$$

↝ Generalize to other dissimilarities/distances or stress functions

Some Embedding methods

Isomap (Balasubramanian and Schwartz 2002)

- Build a k-nearest neighbor graph with adjacency matrix $\mathbf{W}$
- Weight edges by $W_{ii'} = \|\mathbf{x}_i - \mathbf{x}_{i'}\|$
- Compute the shortest path distance
- Embeds the distance with MDS.

Laplacian Eigenmaps (Belkin and Niyogi 2003)

- Build a k-nearest neighbor graph with adjacency matrix $\mathbf{W}$
- Weight edges with Gaussian kernel $W_{ii'} = \exp(\|\mathbf{x}_i - \mathbf{x}_{i'}\|^2/\sigma^2)$
- Compute the graph Laplacian $\mathbf{L} = \mathbf{D} - \mathbf{W}$ with $\mathbf{D}$ diagonal with degrees
- Embeddings are obtained with the first eigenvectors associated to positive eigenvalues of $\mathbf{L}$.

Classical embeddings on scRNA data set[4]

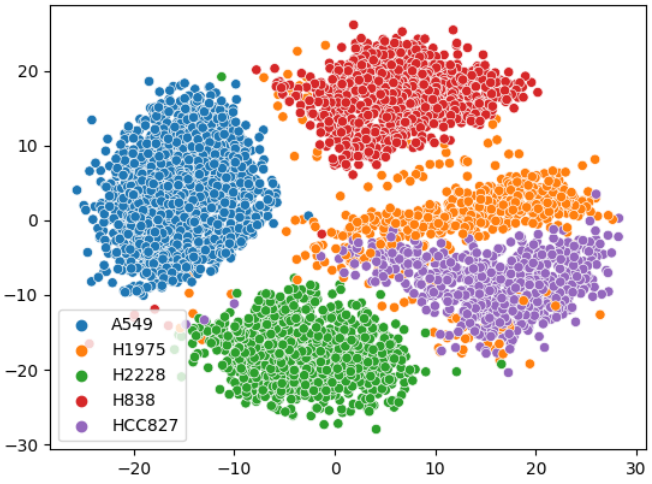


Figure 7: Multidimensional Scaling

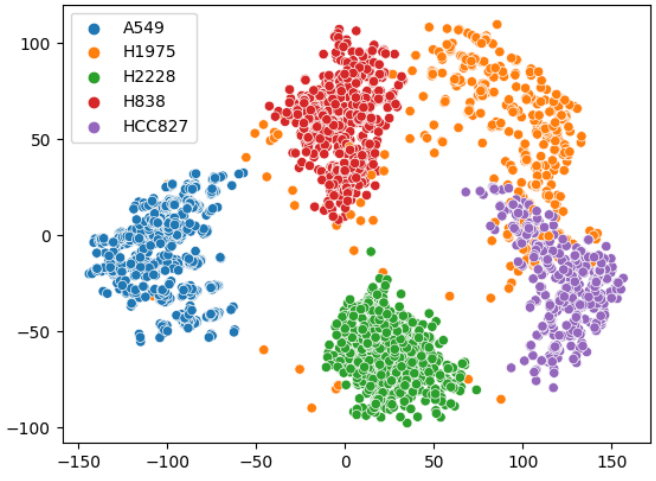


Figure 8: Isomap

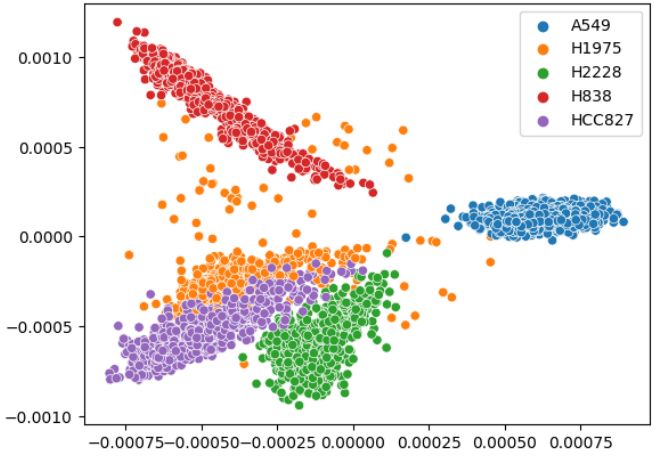


Figure 9: Laplacian Eigenmap

[4] using `sklearn.manifold`

Stochastic Neighbor Embedding (SNE) (Hinton and Roweis 2002)

High dimensional space

Let $(\mathbf{x}_1, \dots, \mathbf{x}_n)$ be the original points in $\mathbb{R}^p$, and measure similarities by

$$p_{ij} = (p_{j|i} + p_{i|j})/2n, \quad \text{with } p_{j|i} = \frac{\exp(-\|\mathbf{x}_j - \mathbf{x}_i\|^2/2\sigma_i^2)}{\sum_{k \neq i} \exp(-\|\mathbf{x}_k - \mathbf{x}_i\|^2/2\sigma_i^2)}$$

- preserves relations with **close neighbors**
- σ_i adjusts to local densities (neighborhood of i)

Perplexity

A smoothed effective number of neighbors:

$$Perp(p_i) = 2^{H(p_i)}, \qquad H(p_i) = -\sum_{j=1}^{n} p_{j|i} \log_2 p_{j|i}$$

↝ σ_i found by binary search to match a user-defined perplexity for p_i

tSNE and Student / Cauchy kernels (Maaten and Hinton 2008)

Similarities in the low dimension space

Let $(\mathbf{z}_1, \ldots, \mathbf{z}_n)$ be the points in the the low-dimensional space $\mathbb{R}^{q=2}$

$$\textbf{(SNE)} \quad q_{i|j} = \frac{\exp(-\|\mathbf{z}_i - \mathbf{z}_j\|^2)}{\sum_{k \neq i} \exp(-\|\mathbf{z}_k - \mathbf{z}_j\|^2)}$$

$$\textbf{(t - SNE)} \quad q_{i|j} = \frac{(1 + \|\mathbf{z}_i - \mathbf{z}_j\|^2)^{-1}}{\sum_{k \neq i} (1 + \|\mathbf{z}_i - \mathbf{z}_k\|^2)^{-1}}$$

↝ t-SNE robustifies Gaussian kernel by using Student(1) (Cauchy) kernels

Optimization

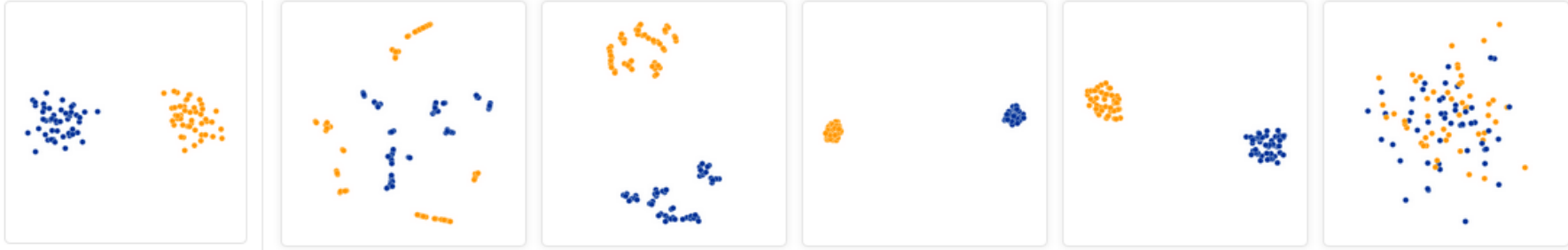
Criterion – Kullback-Leibler between p and q : $C(\mathbf{z}) = \sum_{ij} KL(p_{ij}, q_{ij})$

Algorithm – adaptive stochastic gradient initialized by $\mathcal{N}(0, \epsilon I_q)$

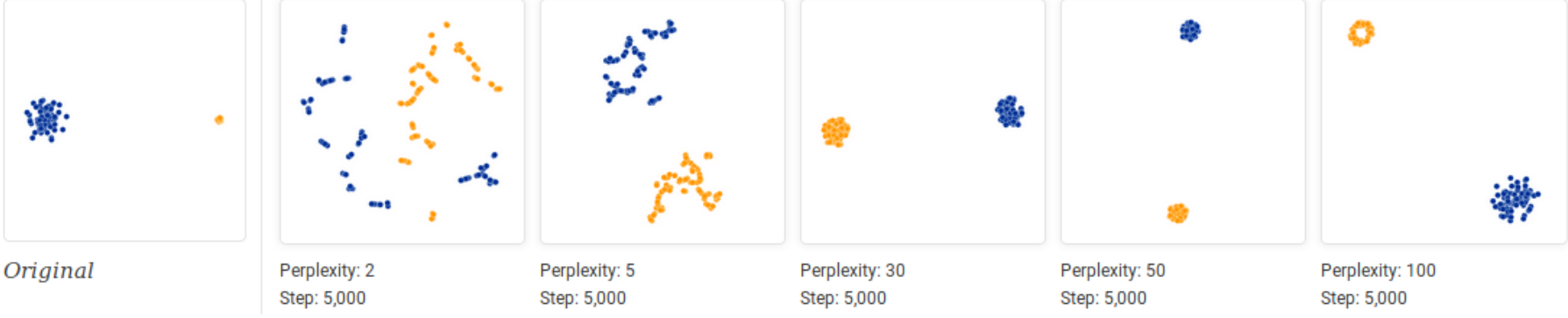
Initiatization – reduce original data with PCA then initialized by $\mathcal{N}(0, \epsilon I_q)$

Empirical properties of tSNE (1)

Effect of Hyperparameters : Perplexity



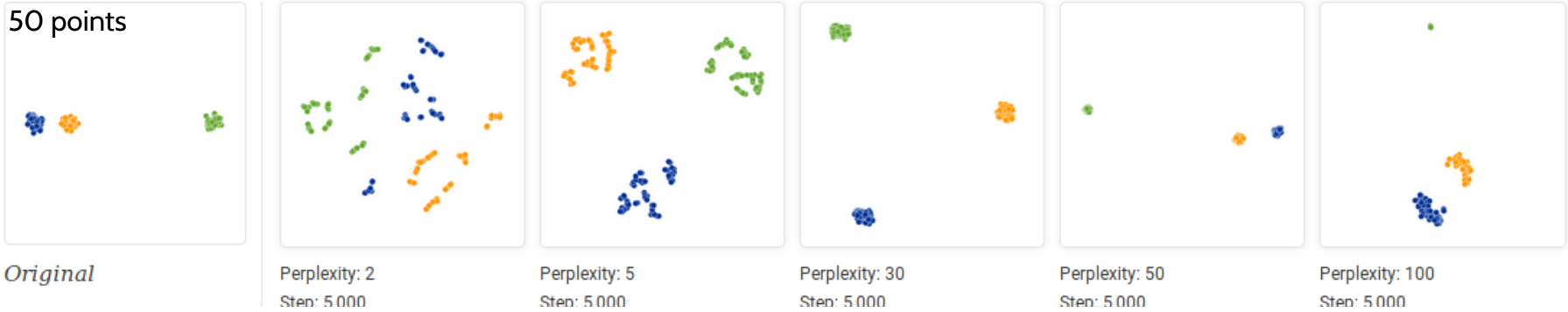
tSNE does not account for heteroscedasticity

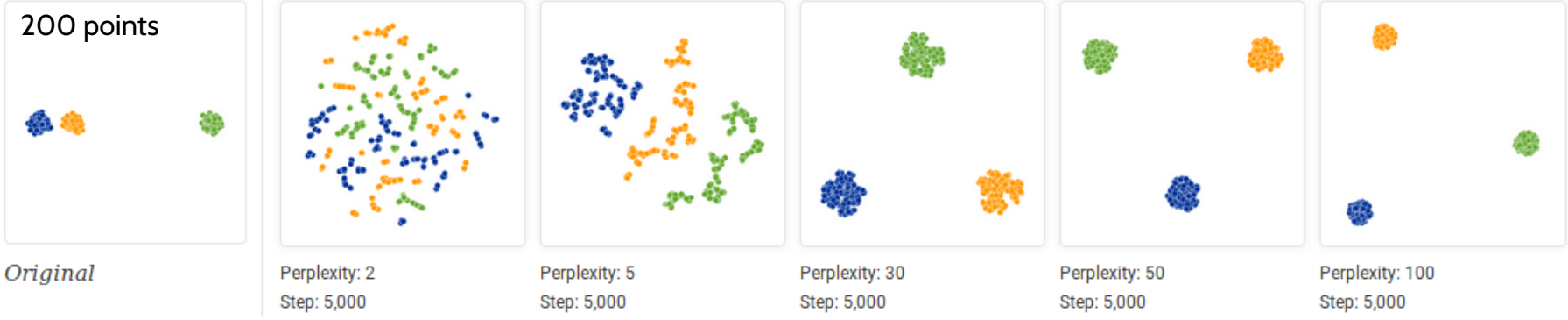


https://distill.pub/2016/misread-tsne/

Empirical properties of tSNE (2)

tSNE does not account for between-cluster distance





What about random noise ?

Empirical properties of tSNE (3)

Catching Complex Geometries

tSNE and UMAP scRNA data[5]

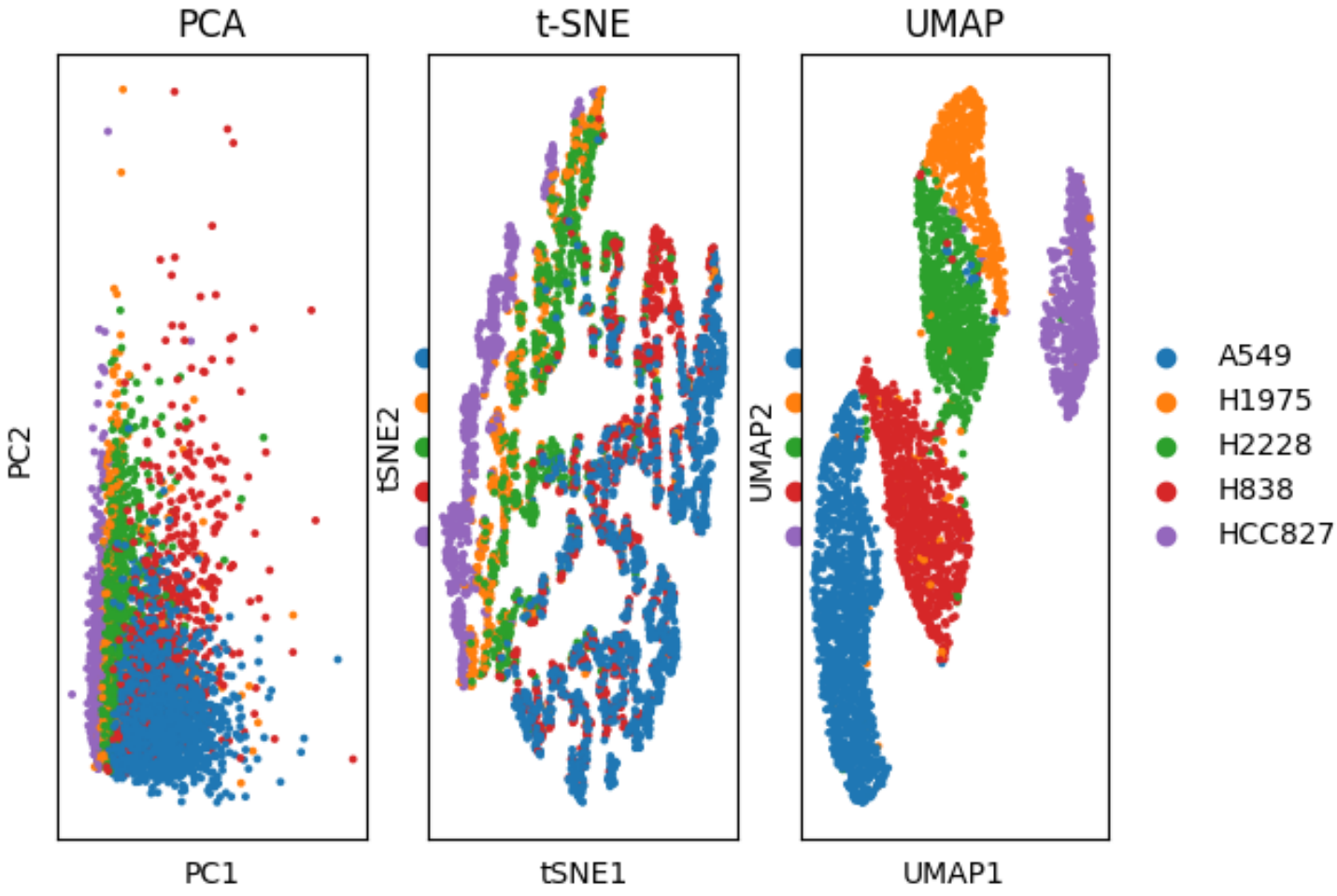


Figure 10: tSNE + UMAP on raw data

[5] using the Python module `scanpy`

tSNE and UMAP scRNA data[6]

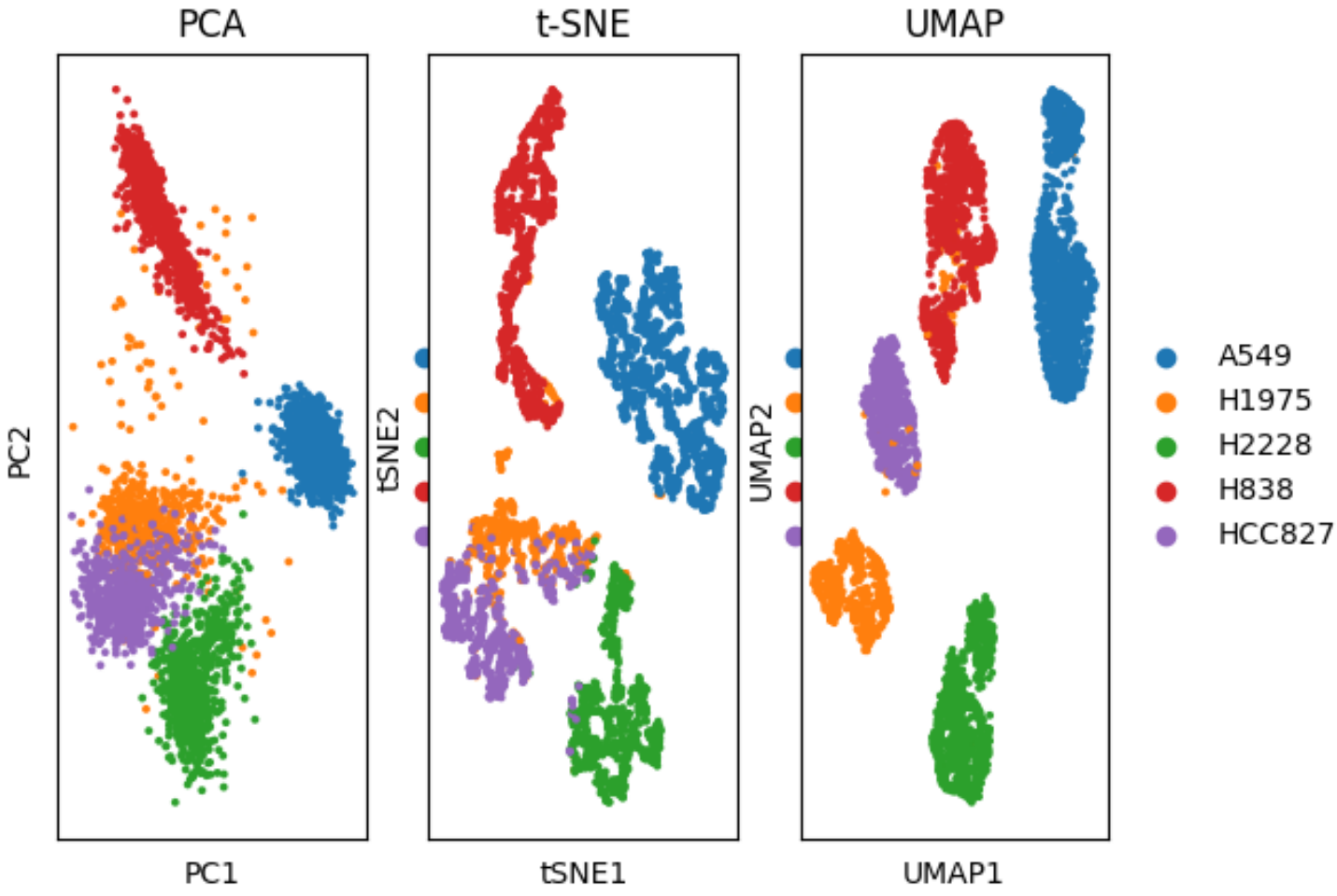


Figure 11: tSNE + UMAP on log-transformed data

[6] using the Python module `scanpy`

Probabilistic Neighborhood Embedding (Van Assel et al. 2022)

Hidden Graph to structure observations

Consider W the adjacency matrix of a hidden random graph[7]
The graph Laplacian operator is the map L such that

$$L(\mathbf{W})_{ij} = \begin{cases} -W_{ij} & \text{if } i \neq j \\ \sum_{k \in [n]} W_{ik} & \text{otherwise .} \end{cases}$$

$L = L(\mathbf{W})$ has the following property:

$$\forall X \in \mathbb{R}^{n \times p}, \quad \sum_{i,j} W_{ij} \|X_i - X_j\|^2 = \operatorname{tr}(X^T L X).$$

[7] we start with one connected component

Conditional distribution of X on a graph W_X

Consider a Matrix Normal model with row and column dependencies

$$X \mid W_X \sim \mathscr{M}\mathscr{N}\left(0, L_X^{-1}, \Sigma^{-1}\right),$$

The conditional density relates to the Gaussian kernel

$$k(X_i - X_j) = \exp\left(-\frac{1}{2}\|X_i - X_j\|_\Sigma^2\right),$$

which can be generalized to translation invariant kernels:

$$\mathbb{P}(X \mid W_X) \propto \prod_{(i,j)\in[n]^2} k(\mathbf{X}_i - \mathbf{X}_j)^{W_{X,ij}} .$$

Conditional distribution of Z on a graph W_Z

Consider that the low-dimensional representation is also structured according to a graph

$$Z \mid W_Z \sim \mathcal{MN}\left(0, L_Z^{-1}, I_q\right),$$

with the Gaussian kernel for Z

$$k(Z_i - Z_j) = \exp\left(-\frac{1}{2}\|Z_i - Z_j\|_{I_q}^2\right),$$

The Conditional distribution of $Z \mid W_Z$ is

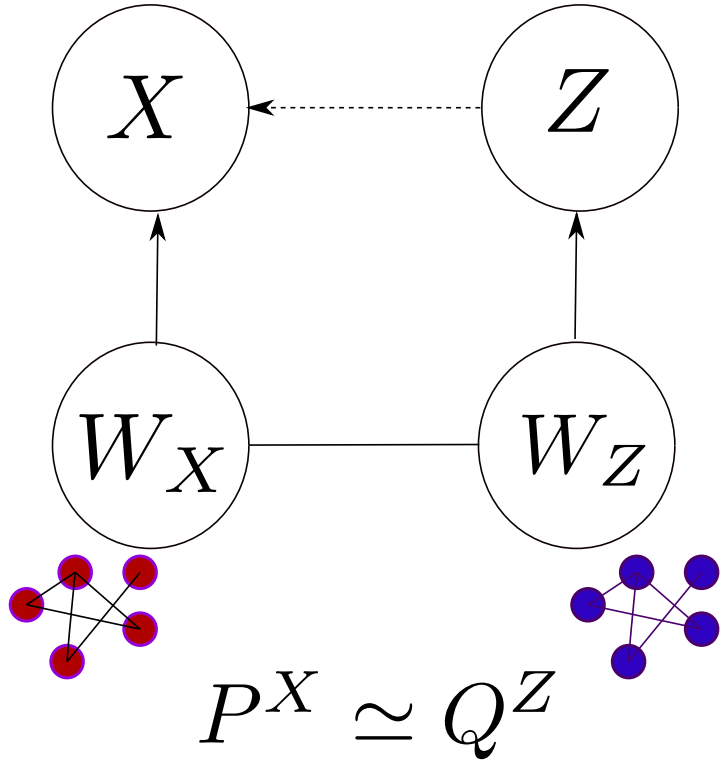
$$\mathbb{P}(Z \mid W_Z) \propto \prod_{(i,j)\in[n]^2} k(Z_i - Z_j)^{W_{Z,ij}}$$

Embedding with Graph Coupling

Couple the 2 hidden graphs W_X and W_Z in a probabilistic way by matching their posterior distributions:

$$\mathbf{P}^X = \mathbb{P}(W_X \mid X)$$
$$\mathbf{Q}^Z = \mathbb{P}(W_Z \mid X; Z)$$

$\rightsquigarrow$ Z becomes a parameter to be estimated



Probabilistic Coupling

Graph Coupling with Z as a parameter

Consider the cross entropy between posteriors

$$\mathscr{H}\left(\mathbf{P}^X, \mathbf{Q}^Z\right) = -\mathbb{E}_{W_X \sim \mathbf{P}^X}\Big(\log \mathbb{P}(W_Z = W_X \mid X; Z)\Big)$$

Find the best low-dimensional representation such that the two graphs match

$$Z(X) = \arg\min_Z \left\{ \mathscr{H}\left(\mathbf{P}^X, \mathbf{Q}^Z\right) \right\}$$

Connection with the KL between posteriors

$$\mathrm{KL}\left(\mathbf{P}^X, \mathbf{Q}^Z\right) = \mathscr{H}\left(\mathbf{P}^X, \mathbf{Q}^Z\right) - \mathscr{H}\left(\mathbf{P}^X, \mathbf{P}^X\right)$$

Conjugate priors and posteriors for hidden graphs

Consider a prior distribution for the hidden graph in the general form

$$\mathbb{P}_{\mathscr{P}}(\mathbf{W};\boldsymbol{\pi}) \propto \underbrace{\cancel{\mathscr{C}_k(W)^\alpha}}_{\alpha=0} \Omega_{\mathscr{P}}(\mathbf{W}) \prod_{(i,j)\in[n]^2} \pi_{ij}^{W_{ij}}$$

For the following priors family, we derive the posterior $\mathbb{P}_{\mathscr{P}}(\mathbf{W} \mid X;\boldsymbol{\pi},k)$

$\mathscr{P}$		$\Omega_{\mathscr{P}}(\mathbf{W})$	Prior for W	
$\mathscr{B}$	Bernoulli	$\prod_{ij} \mathbf{1}_{W_{ij}\leq 1}$	$\mathscr{B}\left(\frac{\pi_{ij}}{1+\pi_{ij}}\right)$	$\mathscr{B}\left(\frac{\pi_{ij}k_{ij}}{1+\pi_{ij}k_{ij}}\right)$
$\mathscr{D}$	Unitary Fixed degree	$\prod_i \mathbf{1}_{W_{i+}=1}$	$\mathscr{M}\left(1, \frac{\pi_i}{\pi_{i+}}\right)$	$\mathscr{M}\left(1, \frac{[\pi k]_i}{[\pi k]_{i+}}\right)$
$\mathscr{E}$	Fixed Number of edges	$\prod_{ij}(W_{ij}!)^{-1}$	$\mathscr{M}\left(n, \frac{\pi}{\pi_{++}}\right)$	$\mathscr{M}\left(n, \frac{\pi k}{[\pi k]_{++}}\right)$

$\pi_{ij}k_{ij} = \pi_{ij}k(X_i - X_j)$ is the posterior strength of edges (normalized or not)

Mixing Prior distributions for coupling

Priors for W_X, W_Z induce posteriors $\mathbf{P}^{\mathscr{P}_X}, \mathbf{Q}^{\mathscr{P}_Z}$ matched with cross entropy $\mathscr{H}\left(\mathbf{P}^{\mathscr{P}_X}, \mathbf{Q}^{\mathscr{P}_Z}\right)$

Model-based Neighbor Embedding

Choosing $\mathscr{P}_X = \mathscr{P}_Z = \mathscr{D}$ lead us to $\mathscr{H}_{D,D} = -\sum_{i \neq j} P_{ij}^D \log Q_{ij}^D$ and

$$P_{ij}^D = \frac{\pi_{ij} k(X_i - X_j)}{\sum_{\ell=1}^n \pi_{i\ell} k(X_i - X_\ell)}, \quad Q_{ij}^D = \frac{\pi_{ij} k(Z_i - Z_j)}{\sum_{\ell=1}^n \pi_{i\ell} k(Z_i - Z_\ell)}.$$

We defined the generative model for SNE!. Similarly,

Algorithm	Input Similarity	Latent Similarity	Loss Function
SNE	$P_{ij}^D = \frac{k_x(\mathbf{X}_i - \mathbf{X}_j)}{\sum_\ell k_x(\mathbf{X}_i - \mathbf{X}_\ell)}$	$Q_{ij}^D = \frac{k_z(\mathbf{Z}_i - \mathbf{Z}_j)}{\sum_\ell k_z(\mathbf{Z}_i - \mathbf{Z}_\ell)}$	$-\sum_{i \neq j} P_{ij}^D \log Q_{ij}^D$
Sym-SNE	$\overline{P}_{ij}^D = P_{ij}^D + P_{ji}^D$	$Q_{ij}^E = \frac{k_z(\mathbf{Z}_i - \mathbf{Z}_j)}{\sum_{\ell,t} k_z(\mathbf{Z}_\ell - \mathbf{Z}_t)}$	$-\sum_{i<j} \overline{P}_{ij}^D \log Q_{ij}^E$
LargeVis	$\overline{P}_{ij}^D = P_{ij}^D + P_{ji}^D$	$Q_{ij}^B = \frac{k_z(\mathbf{Z}_i - \mathbf{Z}_j)}{1 + k_z(\mathbf{Z}_i - \mathbf{Z}_j)}$	$-\sum_{i<j} \overline{P}_{ij}^D \log Q_{ij}^B + \left(2 - \overline{P}_{ij}^D\right) \log(1 - Q_{ij}^B)$
UMAP	$\widetilde{P}_{ij}^B = P_{ij}^B + P_{ji}^B - P_{ij}^B P_{ji}^B$	$Q_{ij}^B = \frac{k_z(\mathbf{Z}_i - \mathbf{Z}_j)}{1 + k_z(\mathbf{Z}_i - \mathbf{Z}_j)}$	$-\sum_{i<j} \widetilde{P}_{ij}^B \log Q_{ij}^B + \left(1 - \widetilde{P}_{ij}^B\right) \log(1 - Q_{ij}^B)$

Conclusion

Thank you for your attention

Co-authors on this topic

- Poisson log-normal PCA: Stéphane Robin, Mahendra Maridassou, Bastien Batardière, Nicolas Jouvin
- Probabilistic t-SNE: Hugues van Assel, Franck Picard, Thibault Espinasse, Eddie Aamari

Some code

- `R`/`C++` package `PLNmodels` is on https://cran.r-project.org/
- `Python`/`Pytorch` package `pyplnmodels` is on https://pypi.org/
- Github repos of this presentation is available at https://github.com/jchiquet/dimred_intro

Advertissing

https://computo.sfds.asso.fr/, an open diamond academic journal promoting reproducibility

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