

# 1

## scVI

### Model

The output of a scRNAseq experiment is a matrix of counts with  $N$  rows (the number of cells) and  $G$  columns (the number of genes), where each entry  $x_{ng}$  is an integer representing how many transcripts of gene  $g$  were seen in cell  $n$ . scVI is a generative hierarchical Bayesian model for scRNAseq data with conditional distributions parametrized by neural networks for each gene.<sup>1</sup> There are technical variables to account for different batches ( $s_n$ ) and for library size ( $l_n$ , which can be interpreted as cell size or sequencing depth). Thus the number of networks being trained is  $2 \cdot G \cdot K$ , where  $K$  is the total number of batches (datasets).

Conditional distribution  $p(x_{ng} | z_n, l_n, s_n)$  is a zero-inflated negative binomial distribution (ZINB) to model the kinetics of stochastic gene expression with some entries replaced by zeros. It can also be modelled using Negative binomial or Zero-inflated negative binomial using the `gene_likelihood` argument.

The neural networks  $f_w^g$  and  $f_h^g$  use dropout regularization and batch normalization to model gene expression while accounting for library sizes and batch effects respectively. Each network typically has 3 fully connected-layers, with 128-256 nodes each. The activation functions are ReLU, exponential, or linear.  $f_w$  has a final softmax layer to represent normalized expected frequencies of gene expression as in. Weights for some layers are shared between  $f_w$  and  $f_h$ .

<sup>1</sup> Lopez et al., "Deep Generative Modeling for Single-Cell Transcriptomics," *Nature Methods* 15, no. 12 (2018): 1053–58.

### Inference

Detail the inference objective

### Training

Any details that aren't clear in manuscripts but are important for training.

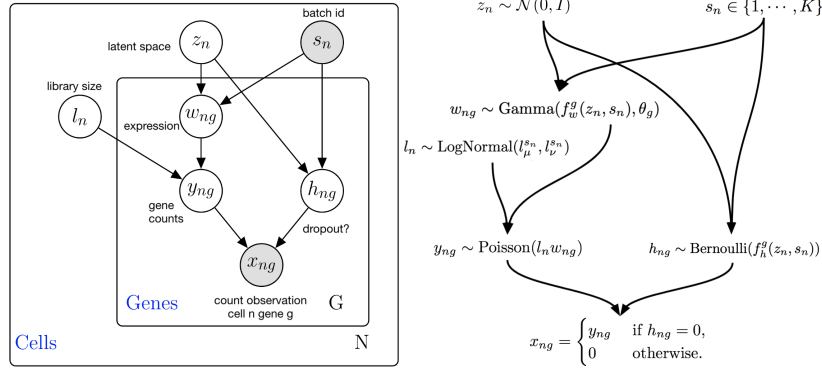


Figure 1: Fancy plot

## Tasks

Here we put the mathematical description of tasks.

## Math to code

Table for each variable, what it's variable name is in the code

## References

Lopez, Romain, Jeffrey Regier, Michael B Cole, Michael I Jordan, and Nir Yosef. "Deep Generative Modeling for Single-Cell Transcriptomics." *Nature Methods* 15, no. 12 (2018): 1053–58.