## 1

## scVI

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 where seen in cell n. scVI is a generative hierarchical Bayesian model for scRNAseq data with conditional distributions parametrized by neural networks for each gene. 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 the 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 nomalization 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  $f_h$ .

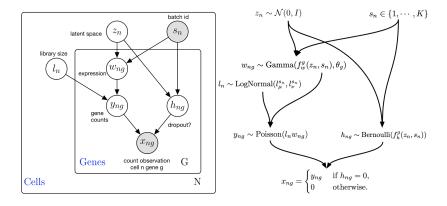


Figure 1: Fancy plot

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

## 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.