
Bayesian Clustering and Topic Discovery: Adventures with Gene Expression Data

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1. Introduction

Tumors cell lines are composed of different sub-populations of cells which often exhibit shared patterns of gene expression. Biologists are interested in two key questions: given gene expressions values, (1) can we identify cell clusterings, and (2) can we identify clusters of biologically-related genes? Our goal with this project was to answer both these two questions using Bayesian methods.

In brief, we explored the use of three Bayesian clustering methods (a vanilla mixture, integrated topic-mixture, and non-parametric models) to address the first question, and two topic models (vanilla and a dynamic-topic LDA) to address the second.

1.1. Description of Data

Using a contemporary gene sequencing machine, we obtained samples of single-cell RNA-sequencing data (scRNA-seq) taken from tumors in mice. Our data consisted of the expression values of 22,712 genes for each of 4645 cells. In total, the dataset amounted to 0.86 GB, presenting significant computational challenges when attempting posterior estimation. Apart from a few computational tricks (online inference, multi-core parallelization), for most methods, we pruned non-informative genes from the dataset, ranking based on the deviation in value across cells¹. We eschewed dimensionality reduction techniques such as PCA because of loss of its direct feature interpretability. The complete dataset, as well our preprocessed and pruned versions, are available at (Yang & Koppula).

1.2. Prior work

Prior research has explored the use of various computational techniques to analyze gene expression data.

¹We recognize that this can bias towards noisy genes. We favor this method because it is simple and easy to implement, and a practice used in literature (Ling, 2012)

Most commonly, Spearman and Pearson correlation metrics are frequently used infer sets of genes that cluster together (Xie, 2015; Borenszstein, 2017). Other techniques, including PCA followed by linear regression, has been used for expression-based cell clustering (Stegle, 2016). Yu et al. propose a unsupervised classifier ensemble as another approach to cell clustering (Yu, 2016).

More Bayesian approaches have also been tried in prior work from the Pe'er lab. (Prabhakaran, 2016) uses a Heirarchical Dirichlet Mixture Model to learn cell clusterings. (Azizi, 2017) builds on this to jointly learn optimal normalization pre-processing of the data. Bayesian networks have also been used in an attempt to learn gene dependencies from expression data (Pe'er, 2000).

1.3. Structure of Report

We first discuss our experiments using Bayesian topic models to discover related sets of genes in a 'topic': LDA in Section 2 and Dynamic Time Models in Section 4. We discuss our experiments in clustering: Dirichlet Mixtures in Section 3, Integrated Topic-Clustering in Section 5, and non-parametric models in Section 6. Finally, we conclude our paper with our obversations from across all studies.

2. Latent Dirichlet Allocation

2.1. Model Description

Algorithm 2 describes the generative process for LDA.

Algorithm 1 Latent Dirichlet Allocation

Input: data x_i , size m
repeat
 Initialize $noChange = true$.
 for $i = 1$ **to** $m - 1$ **do**
 if $x_i > x_{i+1}$ **then**
 Swap x_i and x_{i+1}
 $noChange = false$
 end if
 end for
until $noChange$ is $true$

Algorithm 2 Mixture Model

Input: data x_i , size m
repeat
 Initialize $noChange = true$.
 for $i = 1$ **to** $m - 1$ **do**
 if $x_i > x_{i+1}$ **then**
 Swap x_i and x_{i+1}
 $noChange = false$
 end if
 end for
until $noChange$ is $true$

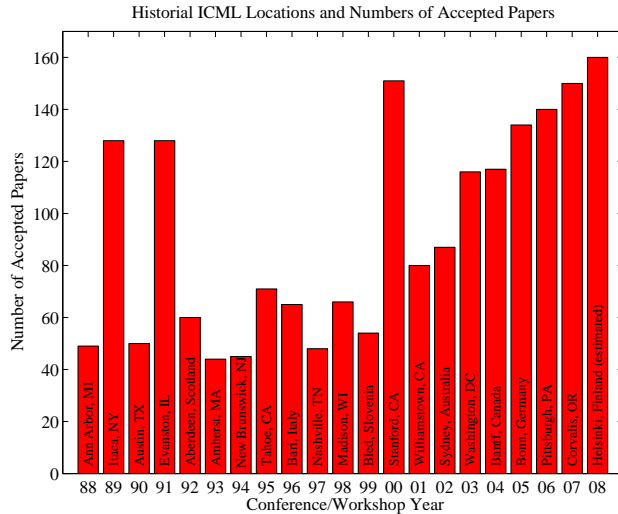


Figure 1. This is a demo figure.

2.2. Implementation

2.3. Experiments

3. Dirichlet Mixture Model

3.1. Model Description

Algorithm 2 describes the generative process for the mixture model.

3.2. Implementation

3.3. Experiments

4. Dynamic Time Model

4.1. Model Description

4.2. Implementation

4.3. Experiments

5. Integrated Topic-Clustering Model

5.1. Model Description

5.2. Implementation

5.3. Experiments

6. Non-parametric Models: IBP and HDP

6.1. Model Description

6.2. Implementation

6.3. Experiments

References

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7. Appendix

7.1. Latent Dirichlet Allocation