Gaining Biological Intuition from Feature Importances

02-620 Machine Learning for Scientists Project

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Introduction

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- Examples
 - Deep Neural Networks
 - Convolutional NNs (image task)

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- Helps researchers and doctors understand genetic drivers of disease

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 - Random Forest
 - SVM
 - Naive Bayes

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Methods

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Transcriptomic Data



Figure 1: Transcriptomics Workflow

use recount2 counts for TCGA (cancer,) and GTEx (normal, 373) lung samples

Transcriptomic Data

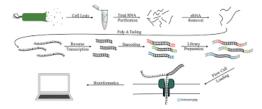


Figure 1: Transcriptomics Workflow

- use recount2 counts for TCGA (cancer,) and GTEx (normal, 373) lung samples
- ► **Features:** gene-level transcript counts for ~ 20,000 coding genes

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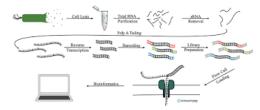


Figure 1: Transcriptomics Workflow

- use recount2 counts for TCGA (cancer,) and GTEx (normal, 373) lung samples
- **Features:** gene-level transcript counts for $\sim 20,000$ coding genes
- Labels: binary, cancer/not cancer

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- chose classifiers that
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- Importance of feature (gene) g
 - Naive Bayes: P(g|y) for y=1 (cancer)
 - **SVM:** contribution of g to separating y = 0, y = 1
 - Random Forest: variability explained by g

Importance Analysis

extract feature (gene) importances from each model in predicting cancer

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- compare most important genes and GO terms found by each model
- train classifier on chosen genes and compare to all genes

Results

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prediction accuracy on the test set (n=289)

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Random Forest: 0.993

Top 5 Most Important Genes

SVM

► Eukaryotic Translation Elongation FACTOR 1/2

Naive Bayes

Random Forest

SVM

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- surfactant protein C, associated with lung disease

Naive Bayes

Random Forest

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all mitochondrial proteins

Random Forest

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all mitochondrial proteins

Random Forest

surfactant protein 2

SVM

- Eukaryotic Translation Elongation FACTOR 1/2
- surfactant protein C, associated with lung disease

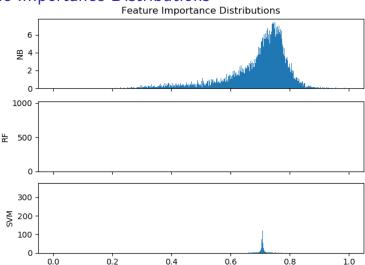
Naive Bayes

all mitochondrial proteins

Random Forest

- surfactant protein 2
- SLC11A1, associated with turbeculosis

Gene Importance Distributions



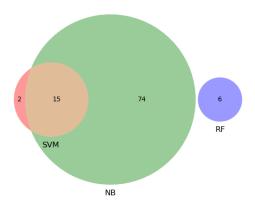
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GO Analysis of Important Genes

► Gene Ontology (GO) groups genes by function/mechanism

GO Term Overlaps

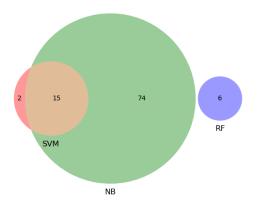


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GO Analysis of Important Genes

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GO Term Overlaps



GO terms the most important genes across all methods?

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Model Re-training

compare model trained on top 10, 50, 250, 500 and all genes separately

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- compare model trained on top 10, 50, 250, 500 and all genes separately
- where do precision and recall start to drop off?

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Results

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Interpretable Deep Learning

Seninge et al. propose a VAE Enchange by Gene Annotations

Results

Conclusion

- ► Even methods applied to the same problem with the same data can learn different things
- Underlying structure of a model is important to which features are learned
- There may be equally useful orthogonal ways to approach treating lung cancer

- Seninge et al. propose a VAE Enchange by Gene Annotations
- Rybakov et al. propose a similar method, like PCA along Reactome elements

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Results

- Underlying structure of a model is important to which features are learned
- There may be equally useful orthogonal ways to approach treating lung cancer

- Seninge et al. propose a VAE Enchange by Gene Annotations
- Rybakov et al. propose a similar method, like PCA along Reactome elements
- Associate latent variables with Biological Abstractions (gene sets)