Analysis of SAGE Results with Combined Learning Techniques

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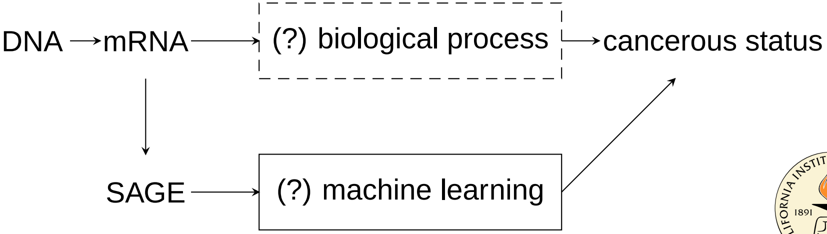
Outline

1. Difficulty in SAGE
2. Classification Techniques
3. Feature Selection Techniques
4. Error Estimation Techniques
5. Experimental Results
6. Conclusion

Problem Formulation

- SAGE: serial analysis of gene expressions
- the larger dataset: 90 samples (libraries) x_i, each with 27679 features (counts of SAGE tags) $(x_i)_d$
- labels y_i: 59 cancerous samples, and 31 normal ones
- **can we predict the cancerous status of the sample based on the features given?**



DNA → mRNA → (?) biological process → cancerous status

mRNA → SAGE → (?) machine learning → cancerous status

Difficulty of the Problem

- **how to build a classifier for the black box?**
  - many possibilities: linear models, decision trees, classifier ensembles, etc.
  - 27679 features with any models above can usually cover all possible labeling on 90 samples
    – fitting perfectly on 90 samples is as poor as fitting a random labeling
- **should all features be used in the black box?**
  - not all features are useful (Alves et al. 2005)
  - some features may even be misleading
- **how to compare different models?**
  - performance needs to be estimated with unseen samples
  - each sample is a precious one out of 90

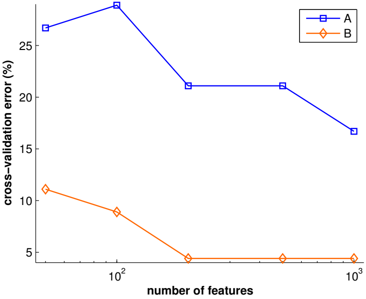
“Easiness” of the Problem

- 27679 features give each sample much information
- procedure: feature selection, then train with 89 samples, and test on the other
    - A: feature selection with 89 samples
    - B: feature selection with 90 samples
- B gets a test sample in data “preprocessing.”

how much does an extra sample in the “preprocessing” stage affect the prediction performance?

"Easiness" of the Problem

- procedure: feature selection, then train with 89, test on the other
  - A: feature selection with 89 samples
  - B: feature selection with 90 samples
- B is significantly biased towards the single sample



1. any piece of information can affect the result dramatically
2. careful NOT to look at any test information

Our Approach of Analysis

- combination of classification, feature selection, and error estimation techniques
- use different combinations to show the relative usefulness of different techniques
- systematic and repeatable on similar datasets
- careful use of unseen samples
- robust conclusion with multiple combinations and error estimations

Classification Techniques

- techniques that avoid overfitting
- models that seem promising
- four classification algorithms
    - AdaBoost-Stump
    - SVM-Linear
    - SVM-Gaussian
    - SVM-Stump
      – a novel and promising paradigm through **infinite ensemble learning** (Lin and Li, ECML 2005)

Adaptive Boosting with Decision Stumps

- model:

$$\hat{g}(x) = \operatorname{sign}\left(\sum_{t=1}^{T} w_t s_t(x)\right)$$

- a finite ensemble of weak rules
- each s_t is a decision stump (thresholding rule on a SAGE tag) – e.g. if the count of the tag 200 greater than 10, then cancerous
- each w_t: a nonnegative weight for s_t
- prediction: each s_t tells whether the sample is cancerous, and $\hat{g}$ reports the majority of weighted votes
- automatically selects $\leq T$ important tags and ignore others in prediction

Support Vector Machine with Linear Kernel

- model:

$$\hat{g}(x) = \mathrm{sign}\left(\sum_{d=1}^{D} w_d (x)_d + b\right)$$

- a hyperplane in $\mathbb{R}^D$
  – e.g. if the weighted sum of all counts is greater than 10, then cancerous
- a large-margin hyperplane: clear separation between cancerous and normal samples
- each w_d: sensitivity for change of $(x)_d$
  – measure of the importance of tag d

Support Vector Machine with Gaussian Kernel

- model:

$$\hat{g}(x) = \text{sign}\left(\sum_{i=1}^{N} y_i \lambda_i \exp(-\gamma(x - x_i)^2)\right)$$

- a nonlinear classifier, similar to a radial basis function network
- large-margin hyperplane in an infinite dimensional space
- pros: powerful model, often good prediction performance
- cons: time-consuming to choose parameter γ, hard to interpret

Support Vector Machine with Stump Kernel

- model:

$$\hat{g}(x) = \text{sign}\left(\sum_{d=1}^{D}\sum_{q\in\pm 1}\left(\int w_{q,d}(\alpha)s_{q,d,\alpha}(x)\,d\alpha\right)+b\right)$$

- large-margin infinite ensemble of decision stumps: novel and promising
- pros: powerful model, often good performance
- superior power to AdaBoost-Stump due to infinity
- superior power to SVM-Linear due to nonlinearity
- faster parameter selection than SVM-Gauss
- model: partially interpreted
  – $w_{q,d}$ can estimate the importance of tag d

Relative Comparison of Classification Techniques

- all four have some degree of regularization: avoid overfitting
- the first three were used in some gene/cancer related tasks
- SVM-Stump is closely related to AdaBoost-Stump
- pros and cons:

	AdaBoost -Stump	SVM -Linear	SVM -Gauss	SVM -Stump
model power(*)	–	–	↑	↑
interpretability	↑	↑	↓	–
speed	↑	–	↓	–

(*) it is hard to compare AdaBoost-Stump to SVM-Linear in power

Feature Selection with Ranking

Algorithm

1. rank (order) the features by their importance
2. select only the top M features

- a simple strategy
- relies on a good ranking algorithm
- three simple ranking algorithms:
  - Ranking with Fisher Score
  - Ranking with Linear Weight
  - Ranking with Stump Weight
- the first two have been used in similar tasks

Feature Ranking Techniques

- Rank with Fisher Score (RFS):
  how well can we use only $(x_i)_d$ to predict y_i?
- Rank with Linear Weight (RLW):
  what is the importance w_d of $(x)_d$ in the hyperplane

$$\sum w_d (x)_d + b$$

  found by SVM-Linear?
- Rank with Stump Weight (RSW):
  what is the amount of decision stumps $\sum_q \int w_{q,d}^2(\alpha)\, d\alpha$ needed for feature d in the ensemble

$$\sum_{d=1}^{D} \sum_{q \in \pm 1} \left(\int w_{q,d}(\alpha) s_{q,d,\alpha}(x)\, d\alpha \right) + b$$

  found by SVM-Stump?

Error Estimation Techniques

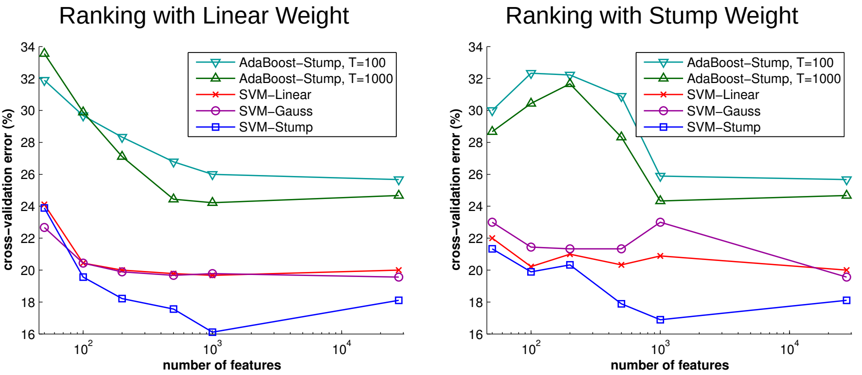
- v-fold cross-validation: economic use of samples
- training folds: $v - 1$ of the v folds
- test fold: the other folds is reserved unseen
- estimate: average error on the reduced test fold
- v-fold CV is a random process: can be repeated many times
- our setting: 10 fold $\times 10$, 5 fold $\times 20$, or 90 fold $\times 1$
- 90 fold: also called leave-one-out

Experiment Settings

Experiment Setting

1. Cross-validation splitting to training folds/test fold
2. Feature ranking on training folds
3. Feature selection by ranking (50, 100, 200, 500, 1000, 27679)
4. Classification on the reduced training folds
5. Test on the reduced test fold

Comparison of Classification Techniques



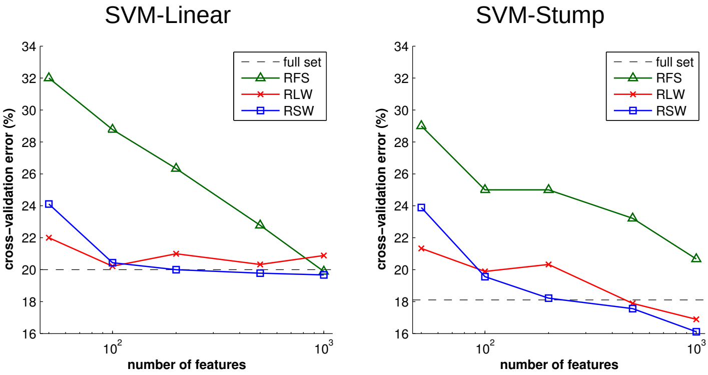
- results with 10 fold CV $\times 10$
- AdaBoost-Stump is not good
- SVM-Gauss is slightly worse than SVM-Linear
- SVM-Stump is slightly better than SVM-Linear

Comparison of Classification Techniques

SVM-Linear and SVM-Stump are the better choices

	AdaBoost -Stump	SVM -Linear	SVM -Gauss	SVM -Stump
model power	–	–	↑	↑
interpretability	↑	↑	↓	–
speed	↑	–	↓	–
performance	↓	↑	↑	↑

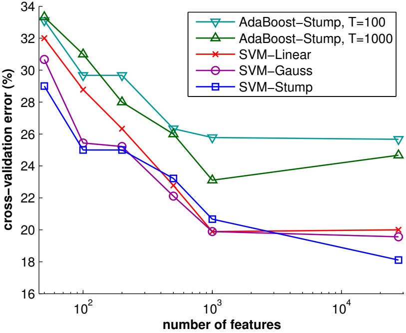
Comparison of Feature Selection Techniques



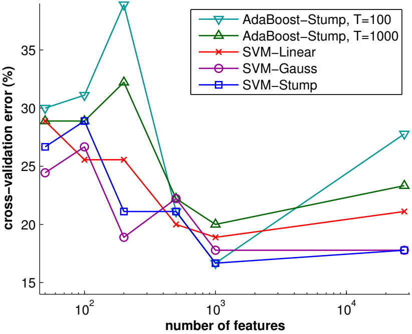
- results with 10 fold CV ×10
- Ranking with F-Score is not good
- Ranking with Stump Weight is slightly better than with Linear Weight

Comparison of Error Estimation Techniques

Ranking with F-Score (10 fold × 10)

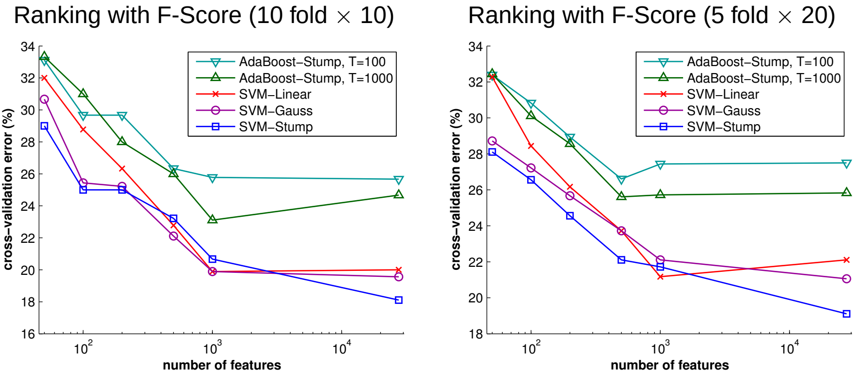


Ranking with F-Score (90 fold)



- leave-one-out does not give stable and explainable results

Comparison of Error Estimation Techniques



- similar conclusions from 5 fold and 10 fold CV
- 10-fold uses more samples for training
  – better choice considering the importance of samples

Conclusion

- **carefully analyzed the difficult SAGE dataset**
  - legitimate information only
  - robust conclusion through multiple testing
- classification: SVM-Linear and SVM-Stump are both promising
- feature selection: RLW and RSW are both good
  – possible to achieve better performance than full set
- error estimation: 10-fold CV seems to be a better choice and leave-one-out is bad
- how can we possibly distinguish between the linear model and the stump ensemble model?
  - are there more samples to verify the findings?
  - which model selects more biologically meaningful features?
  - which model is biologically more plausible?