Sparse Coding for Feature Selection on Genome-wide Association Data

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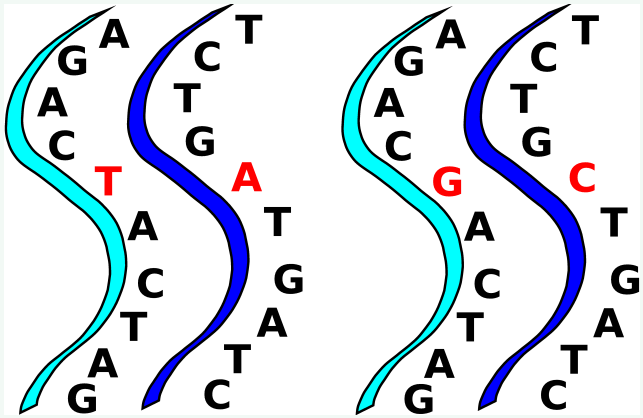
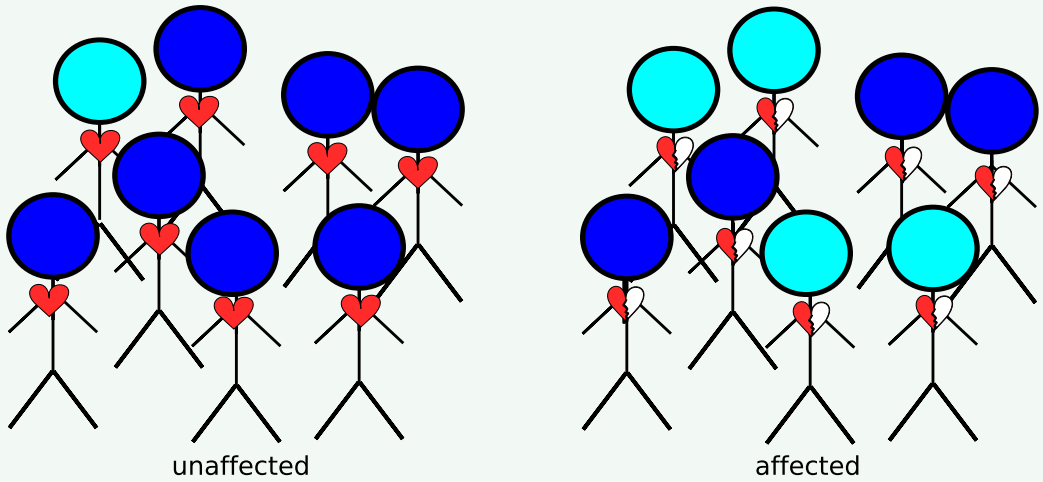
Genome Data

Single Nucleotide Polymorphism (SNP)

- Different bases at one locus in the genome
- Occur in at least 1% of the population
- Three possible genotypes (-1, 0, 1)
- Used as genetic markers



Genome-wide Association (GWA) studies



- Large numbers of SNPs
- Identify genetic loci
- Reveal genetic mechanisms
- Risk prediction

What makes it difficult?

- High-dimensional data (hundred thousand SNPs)
- Few data points (a few thousand)
- Discrete data (1,-1,0)
- Noisy data

Hypothesis

What do we expect?

- Disease effect through interaction
- No uniform pattern among all cases
- Disease pattern consisting of SNPs without individual effects
- Disease-unspecific patterns

Standard Approaches

- Single association test (p-values) [1]
- Support Vector Machine (SVM) [2]
- Principal Component Analysis (PCA) [3]

[1] Sekar Kathiresan, N Engl J Med,1240-1249, 2008
[2] Zhi Wei, PLoS Genetics,5(10):e1000678+,2009
[3] Peristera Pashou, PLoS genetics, 3(9) 1672-1686,2007

Standard Approaches

Association test

- Chi-squared distribution
- Feature selection by the p-values

SVM

- Linear hard-margin SVM
- Feature selection by the influence on the margin

Principal Component Analysis

Aim: cover as much of the variability of the data as possible

- Separate analysis for cases and controls
- M principal components

$$V^{class} = (\mathbf{v}_1^{class}, \ldots, \mathbf{v}_M^{class}) \tag{1}$$

- Feature selection by:

$$r_j = |\max_i |(\mathbf{v}_i^1)_j| - \max_i |(\mathbf{v}_i^{-1})_j|| \tag{2}$$

Sparse Coding

Aim: represent data $X = (\mathbf{x}_1, \ldots, \mathbf{x}_N)$, $x_i \in \mathbb{R}^D$, as a sparse linear combination of a dictionary C and coefficient vectors a_i, $\|\mathbf{a}\|_0 \leq k$.

$$\mathbf{x}_i = C\mathbf{a}_i$$

Sparse Coding

Goal: Minimize the reconstruction error: $\frac{1}{L}\sum_{i=1}^{L}\|\mathbf{x}_i - C\mathbf{a}_i\|_2^2$

- Problem 1: find optimal C
  –> Solution: Bag of Pursuits and Neural Gas [1]

- Problem 2: for given C find optimal a_i
  –> Solution: Bag of Pursuits [2]

$$\mathbf{x}_i^{\text{opt}} = C\mathbf{a}_i \text{ with } \mathbf{a}_i = \arg\min_{\mathbf{a}} \|\mathbf{x}_i - C\mathbf{a}\| \,, \|\mathbf{a}\|_0 \leq k$$

[1] K. Labusch, E. Barth, T. Martinetz, Proc. COMPSTAT, 327-336,2010
[2] K. Labusch, T. Martinetz, Proc. ESANN, 241-246, 2010

Sparse Coding

- separate analysis for cases and controls

$$C^{class} = (\mathbf{c}_1^{class}, \ldots, \mathbf{c}_M^{class})$$

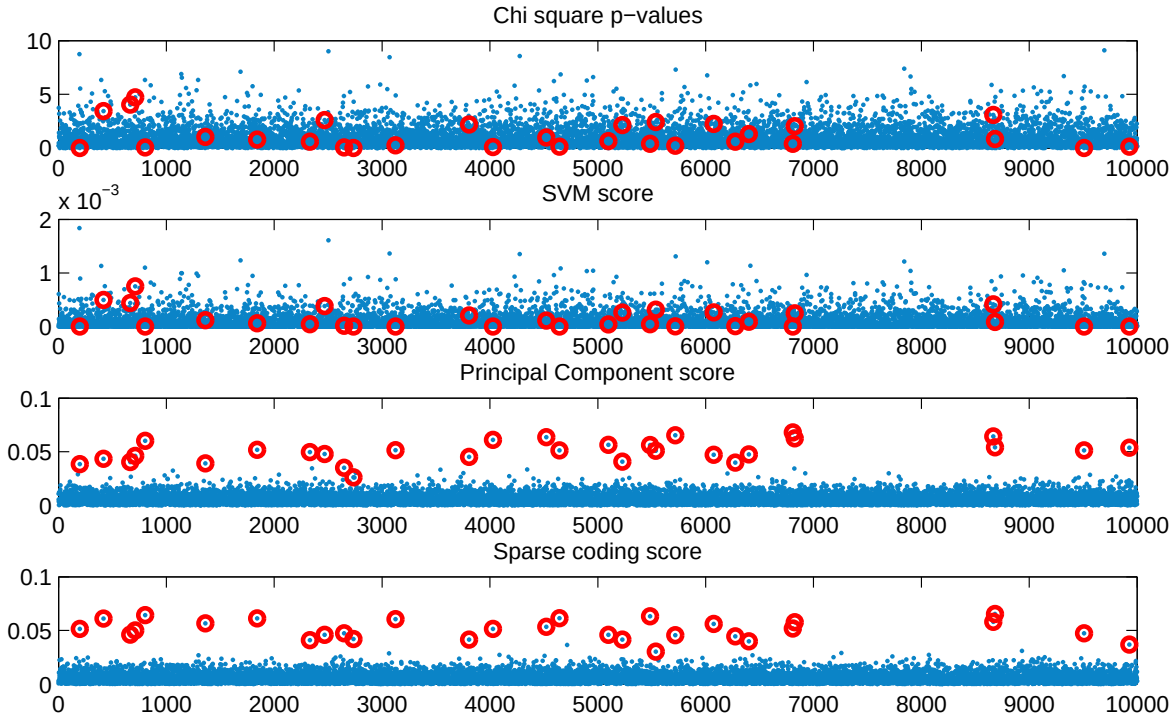
- feature selection by:

$$r_j = |\max_i |(\mathbf{c}_i^1)_j| - \max_i |(\mathbf{c}_i^{-1})_j||$$

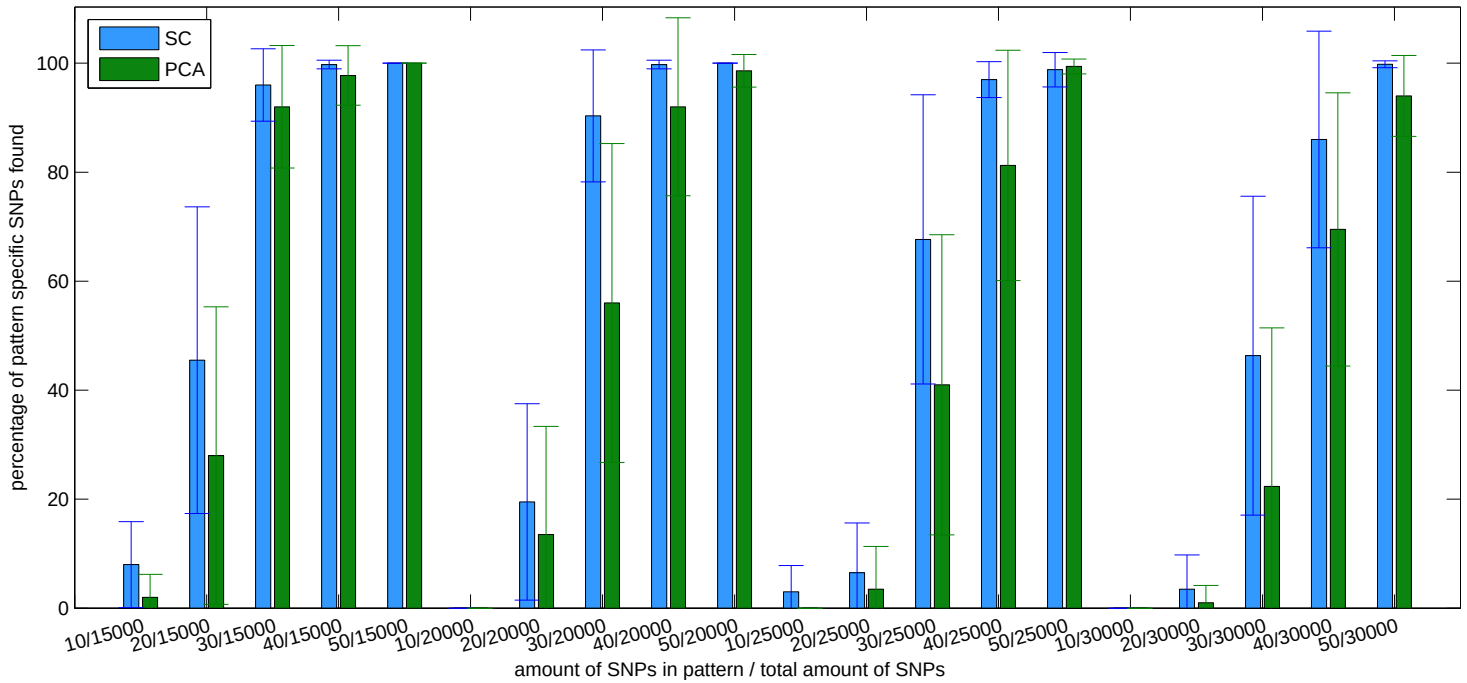
Simulated Data

- 2 types of Data sets
  - 1 disease pattern 1 unspecific pattern
  - 1 disease pattern 5 unspecific patterns
- Pattern size: SNPs: $10, 20, ..., 50$, individuals: 100
- SNPs: $15000, 20000, ..., 30000$
- Individuals: 500 cases and 500 controls

Comparing feature selection approaches

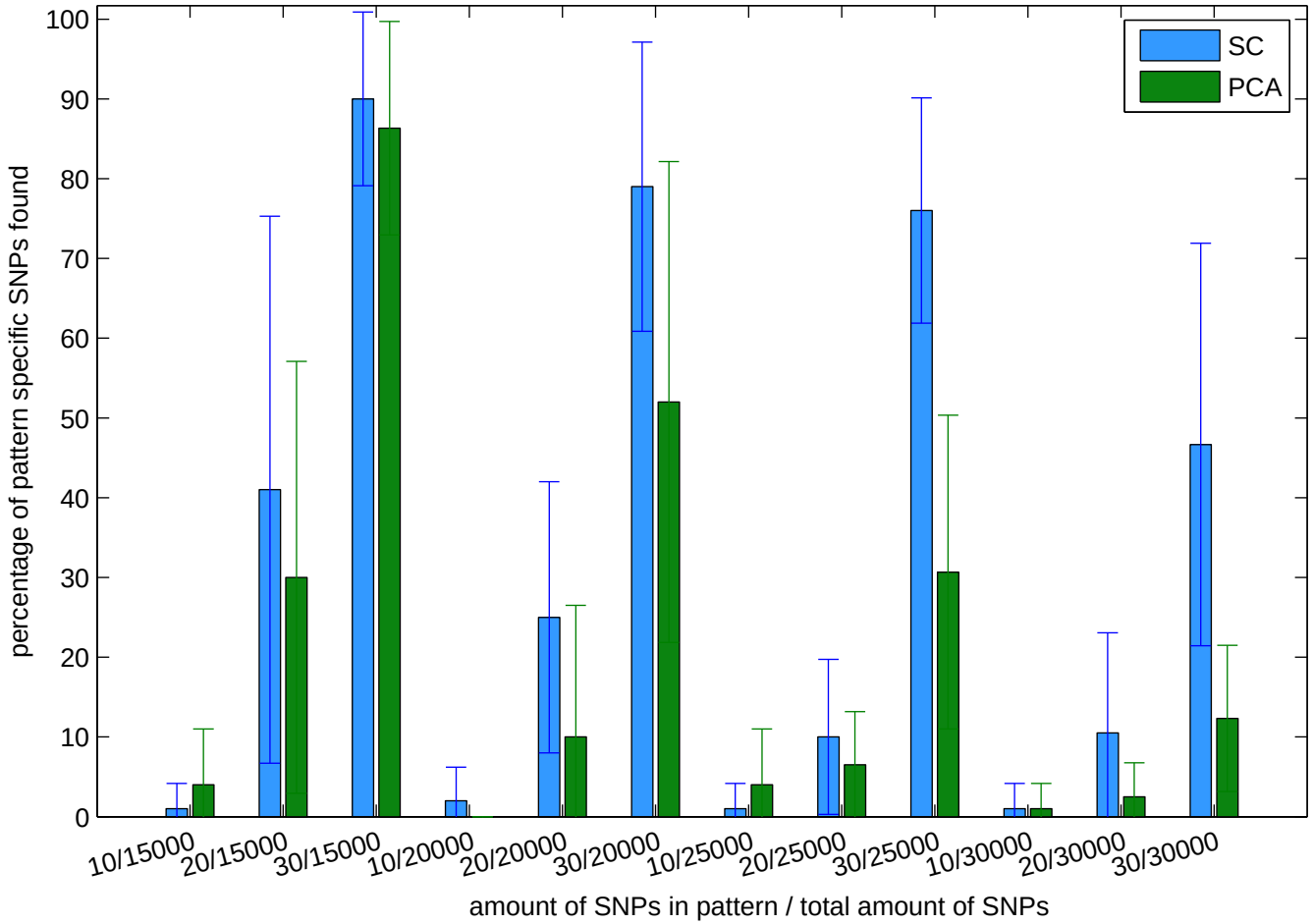


Sparse Coding versus PCA



1 disease-specific pattern, 1 unspecific pattern

Sparse Coding versus PCA



1 disease-specific pattern, 5 unspecific patterns

Conclusion

- p-values or SVM are not suitable for feature selection
- PCA and Sparse Coding suitable for the task
- Sparse Coding more robust to noise pattern
- Sparse Coding promising for real data

Thank you for your attention