# Bayesian variable selection with a focus on the analysis of genomic data - Part II

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Bayes 2013

# Challenges in High-dimensional Data

- **"High-dimensionality"**: growing data dimension along with the sample size, where $p_n > n$
- Important attributes of statistical procedures:
  - accuracy of inference
  - computational tractability
- **Challenges** in high-dimensional data
  - What is the sensible *threshold of dimensionality* to apply a statistical procedure?
  - Characterization of *optimality attributes*
  - Development of *reliable inferential tools*
  - *"Low assumptions in high dimensions"*

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# High Dimensions $\sim$ Strong Assumptions

- What is the convenient dimensionality of the parametrization?
- A crucial assumption is the one of sparsity
  - *parametrization using only a few coefficients*
  - *often in line with biological intuition*
- *Sparsity central to the implementation of variable selection!*
- **Bayesian variable selection**: natural incorporation of the prior knowledge on the pattern of sparsity

# Computational Aspects

- Penalized likelihood methods: (LASSO, SCAD...)
  - *easy for convex penalties*
  - *non-convex penalties*

    (Fan and Li (2009), Hunter and Li (2005))
- Bayesian shrinkage methods: (Bayesian LASSO...)
  - *MCMC with block updates*
  - *MAP estimation using EM algorithm*

    (Griffin and Brown (2005), Rockova and Lesaffre (2013))
- Bayesian variable selection: (spike and slab, SSVS)
  - *MCMC*

    (George and McCulloch (1993); Hans et al. (2010))
  - *EM algorithm for posterior model mode detection*

    (Rockova and George (2012))

# SSVS Setup

- Assume $\boldsymbol{Y} \sim \mathrm{N}_n(\alpha + \boldsymbol{X}\beta, \sigma^2 \mathrm{I}_n)$, interest in $p > n$
- Binary variable selection indicators $\gamma = (\gamma_1, \ldots, \gamma_p)'$, where $\gamma_i = 0$ if $\beta_i$ is "small" and $\gamma_i = 1$ if $\beta_i$ is "large"
- Conjugate "spike and slab" prior on regression coefficients

$$\pi(\beta_i \mid \sigma, \gamma) = \mathrm{N}(0, \sigma^2[(1-\gamma_i)v_0 + \gamma_i v_1]),$$

$\gamma_i = 0$: Spike variance $\sigma^2 v_0$ small
$\gamma_i = 1$: Slab variance $\sigma^2 v_1$ large

- Prior distribution for the variance $\pi(\sigma^2 \mid \gamma) = \mathrm{IG}(\nu/2, \nu\lambda/2)$
- Uniform improper prior on the intercept $\alpha \rightsquigarrow$ margined out

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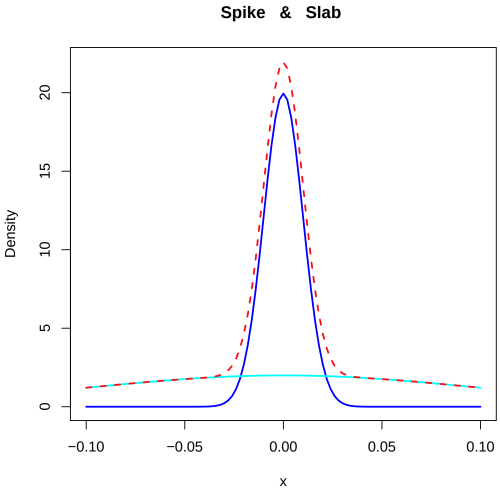
# SSVS Setup

Spike and slab prior for $v_0 = 0.01, v_1 = 0.1$



# Stochastic Model Search

- Favored selection criteria based on $\pi(\gamma | \boldsymbol{Y})$
  (a) *Highest posterior probability model*

$$\text{argmax}_{\gamma} \pi(\gamma \mid \boldsymbol{Y})$$

  (b) *Median probability model*: select variables with

$$\text{P}(\gamma_i = 1 \mid \boldsymbol{Y}) > 0.5$$

- MCMC stochastic search algorithms attempt to find these
  - *SSVS* (George and McCulloch (1993))
  - *ESS* (Botollo and Richardson (2010))
  - *SSS* (Hans et al. (2010))
- Slow and inefficient, especially when $p$ is large.
- Is there a better way?

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# Deterministic Model Search

Rockova and George (2012) propose an EM model search algorithm

(1) "$\pi(\gamma \mid \boldsymbol{Y}) \leftrightarrow \pi(\beta \mid \boldsymbol{Y})$"

- $\rightsquigarrow$ High posterior modes of $\pi(\gamma \mid \boldsymbol{Y})$ can be located by thresholding small coefficient estimates of associated high posterior modes of $\pi(\beta \mid \boldsymbol{Y})$
- $\rightsquigarrow$ Modes of the posterior $\pi(\beta \mid \boldsymbol{Y})$ can be found deterministically

(2) *"Spike-and-slab Regularization Diagram"*

- $\rightsquigarrow$ Obtain modal estimates for a sequence of mixture priors with increasing $v_0 > 0$
- $\rightsquigarrow$ Depicts evolution and gradual sparsification of selected subsets

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SSVS $\rightarrow$ EMVS

# Key Ingredients

(1) *Conjugacy*

- $\rightsquigarrow$ Allows analytical simplifications for the EM algorithm
- $\rightsquigarrow$ Enables computation of posterior model probabilities

(2) *Use of both* $v_0 > 0$ *and* $v_0 = 0$

- $\rightsquigarrow$ $v_0 > 0$: Feasible closed form EM algorithm
- $\rightsquigarrow$ $v_0 > 0$: Spike distribution absorbs small coefficients
- $\rightsquigarrow$ $v_0 = 0$: Correct posterior for candidate model evaluation

(3) $\pi(\gamma|\boldsymbol{\theta})$ *Flexibility*

- $\rightsquigarrow$ Allows incorporation of covariate pattern information

# EMVS Algorithm

GOAL To locate posterior mode

$$\text{argmax}_{\boldsymbol{\beta},\boldsymbol{\theta},\sigma} \log \pi(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma^2 \mid \boldsymbol{y}) \tag{1}$$

IDEA Solve this via EM by treating $\gamma$ as “missing data" and focusing on

$$\log \pi(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma^2, \gamma \mid \boldsymbol{y})$$

## *E-step*

Compute conditional expectation of “log complete data posterior":

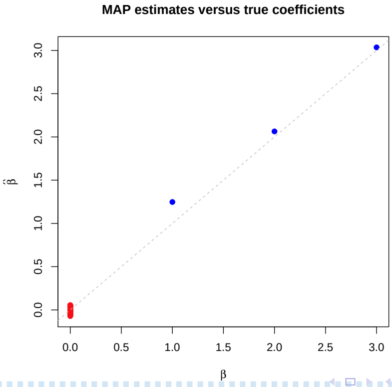
$$Q\left(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) = \mathsf{E}_{\gamma|\cdot}\left[\log \pi(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma, \gamma|\boldsymbol{y}) \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}, \boldsymbol{y}\right]$$

## *M-step*

Maximize $Q\left(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right)$ to get $(\boldsymbol{\beta}^{(k+1)}, \boldsymbol{\theta}^{(k+1)}, \sigma^{(k+1)})$

# Simple Implementation

- Assume $n = 100, p = 1\,000, \beta = (1, 2, 3, 0, \ldots, 0)'$
- Rows in $\boldsymbol{X}$ sampled from $\mathrm{N}_p(\mathbf{0}, \Sigma)$, where $\Sigma = (0.6^{|i-j|})_{i,j=1}^{p}$
- $\boldsymbol{Y} = \boldsymbol{X}\beta + \varepsilon$, where $\varepsilon \sim \mathrm{N}_n(\mathbf{0}, \sigma^2\,\mathrm{I}_p)$ and $\sigma^2 = 3$
- For now fixed $v_0 = 1$ and $v_1 = 1\,000$, $\theta \sim \mathrm{Beta}(1, 1)$



# Simple Implementation

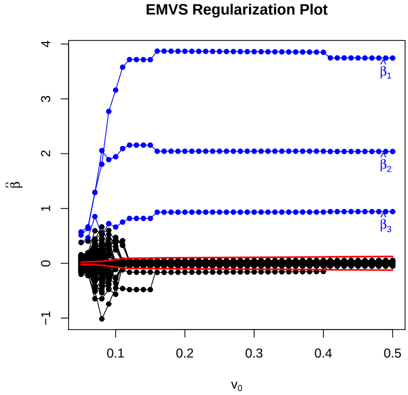
- Subset selection for fixed $v_0$:
  (a) *Based on conditional inclusion probabilities*
  Select $X_i$ when $\mathrm{P}(\gamma_i = 1|\widehat{\boldsymbol{\beta}}, \widehat{\sigma}, \widehat{\boldsymbol{\theta}}) > 0.5$
  (b) *Based on modal estimates* $\widehat{\boldsymbol{\beta}}$ (equivalent to (a))
  Select $X_i$ when $|\widehat{\beta}_i| > \mu_{v_0,v_1,\widehat{\sigma}} = \widehat{\sigma}\sqrt{2v_0 \log(\omega_i\, c)\, c^2/(c^2-1)}$
  with $c^2 = v_1/v_0$ and $\omega_i = [1 - \mathrm{P}(\gamma_i = 1 \mid \widehat{\boldsymbol{\theta}})]/\mathrm{P}(\gamma_i = 1 \mid \widehat{\boldsymbol{\theta}})$
- We can consider a grid $V$ of values $v_0$ and $\forall v_0 \in V$ determine an active set $\mathcal{S}_{v_0} = \{1 \leq i \leq p : |\widehat{\beta}_i| > \mu_{v_0,v_1,\widehat{\sigma}}\}$
- For each active set we evaluate $\gamma$ using

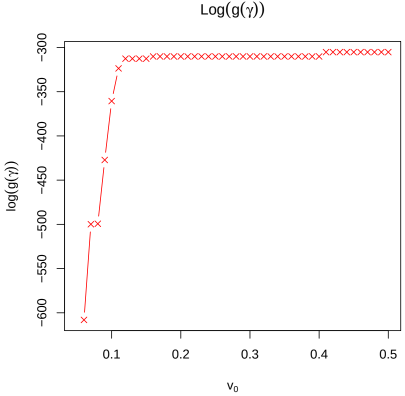
$$g_{v_0}(\gamma) = C\, p(\gamma|\boldsymbol{Y})$$

assuming that $v_0 = 0$ (correct submodel evaluation)

# Simple Implementation Continued

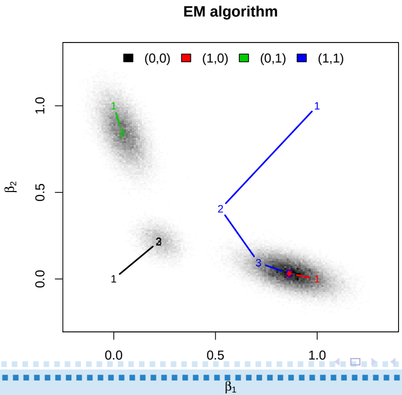
- [Regularization plot](#) for a grid of values $v_0$
- Starting values $\beta^{(0)} = \mathbf{1}_p, \sigma^{(0)} = 1$ and $\theta^{(0)} = 0.5$
- Increasing $v_0$ absorbs smaller coefficients



# Multimodality Issues

- EM algorithm guarantees monotonical convergence towards at least a local maximum
- Prone to entrapment around local modes
- Posterior from conjugate model with two correlated predictors, $\beta = (1, 0)'$, $v_1 = 1\,000$ and $v_0 = 0.005$, $\widehat{\beta}_{MLE} = (0.52, 0.4)'$



# Deterministic Annealing

- Maximize a tempered version of the objective function: for $0 < t < 1$

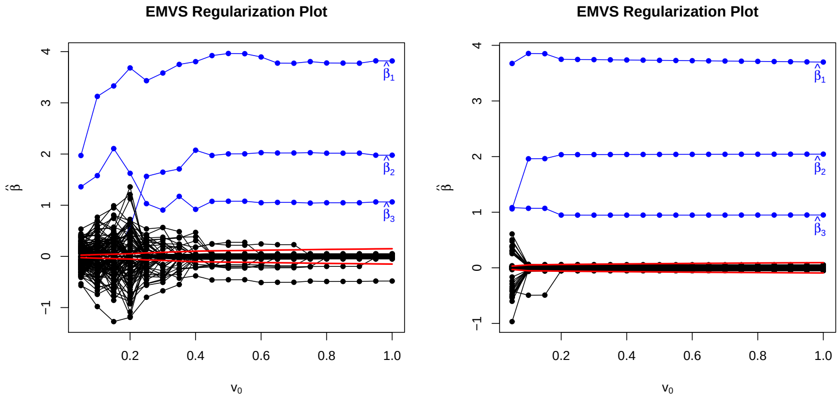
$$H_t(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma) = \frac{1}{t} \log \sum_{\gamma} \pi(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma, \gamma \mid \boldsymbol{y})^t \tag{2}$$

- Temperature $1/t$ regulates the degree of separation between multiple modes
- Small values $t$ smooth the function to have only one mode
- Consider temperature ladder $1/t_1 < 1/t_2 < \cdots < 1/t_T$
- Solutions at lower temperature can be used as starting points for computation at higher temperature

# Simple Implementation Continued

- [Regularization plot] for a grid of values $v_0$, $v_1 = 1\,000$
- Randomly generated starting values $\beta^{(0)} \sim \mathrm{N}_p(\mathbf{0}, \mathrm{I})$

Temperature 1 | Temperature 10



# Structured Model Priors

⇝ Variable selection indicators assigned prior distribution $\pi(\gamma \mid \boldsymbol{\theta})$

(a) *Beta-binomial prior* (George and McCulloch (1993))

$$\pi(\gamma \mid \theta) = \theta^{\sum \gamma_i}(1-\theta)^{p-\sum \gamma_i} \quad \text{with} \quad \theta \sim B(a, b)$$

(b) *Logistic regression product prior* (Stingo et al. (2010))

$$\pi(\gamma \mid \boldsymbol{\theta}) = \prod_{i=1}^{p} \left( \frac{\exp(\boldsymbol{Z}_i'\boldsymbol{\theta})}{1+\exp(\boldsymbol{Z}_i'\boldsymbol{\theta})} \right)^{\gamma_i} \left( \frac{1}{1+\exp(\boldsymbol{Z}_i'\boldsymbol{\theta})} \right)^{1-\gamma_i}$$

(c) *Markov random field prior* (Li and Zhang (2010))

$$\pi(\gamma \mid \boldsymbol{\theta}) = \exp\left[\boldsymbol{\theta}_1'\gamma + \gamma'\boldsymbol{\theta}_2\gamma - \psi(\boldsymbol{\theta}_1, \boldsymbol{\theta}_2)\right]$$

# Simulated Example with Structured Covariates

- Assume $p = 99$ covariates cluster within three non-overlapping groups: $\boldsymbol{Z} = [\boldsymbol{z}_1, \boldsymbol{z}_2, \boldsymbol{z}_3]$, where $z_{ij} = \mathbb{I}_{[33\,(i-1)+1;\,33\,i]}(j)$
- Within group correlation 0.8, between group correlation 0
- Responses $\boldsymbol{Y} \sim \mathrm{N}(\boldsymbol{X}\beta, \sigma^2 \mathrm{I}_n)$ with $\beta = 2 \times \mathbb{I}_{[1;33]}(i)$, $n = 100$ and $\sigma^2 = 5$
- EMVS with *(a) Beta-binomial prior, (b) logistic regression prior, (c) MRF prior*

  Settings for model exploration

  - $v_0 \in \{0.01 + k \times 0.5 : 0 \leq k \leq 10\}$
  - $v_1$ assigned prior (6) with $a = 0.5$ and $b = 250$

  Settings for model evaluation

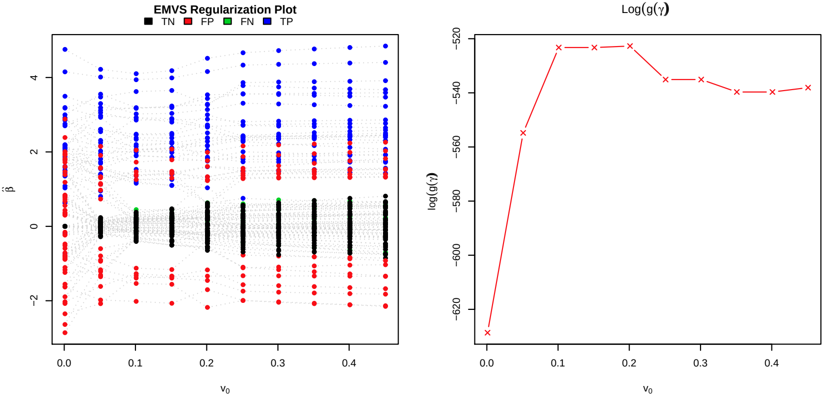
  - $v_1$ fixed to 1 000
  - Uniform beta-binomial for the $g$-function

# Simulated Example with Structured Covariates

(a) Beta-binomial prior, where $\theta \sim \mathrm{B}(1, 1)$

Best visited model:

25 *true positives* together with 11 *false negatives* and 8 *false positives*

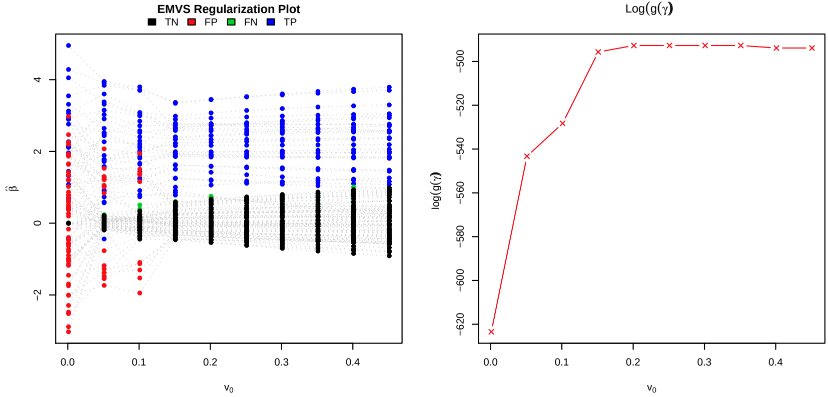


# Simulated Example with Structured Covariates

(b) Logistic regression prior $\boldsymbol{\theta} \sim \pi(\boldsymbol{\theta})$ in (3) with $a = b = 1$

Best visited model:

28 *true positives* together with 5 *false negatives* and 0 *false positives*

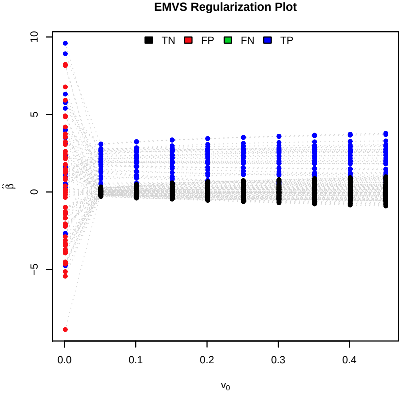


# Simulated Example with Structured Covariates

(c) MRF prior, $\theta$ fixed to the phase transition point, $\boldsymbol{\theta}_2 = (\mathbf{1}_{33\times 33} - \mathrm{I}_{33}) \otimes \mathrm{I}_3$

Best visited model:

33 *true positives* together with 0 *false negatives* and 0 *false positives*

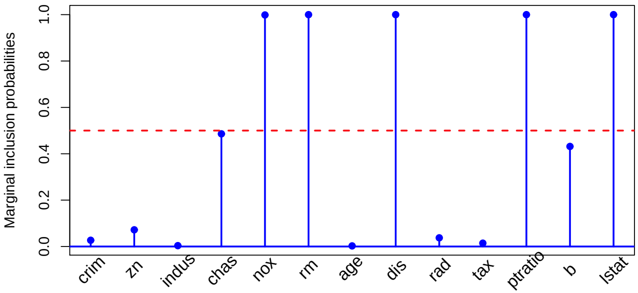


# Boston Housing Data: Application "$p < n$"

Predicting median price of homes in Boston on the basis of 13 predictors, $n = 506$

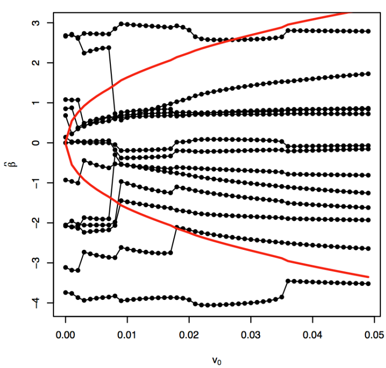
(1) Conjugate SSVS Gibbs sampler (CPU 21s)
$v_0 = 0.01, v_1 = 1\,000, \theta \sim B(1, 1)$, 10 000 iterations
Median probability model includes $\{5, 6, 8, 11, 13\}$

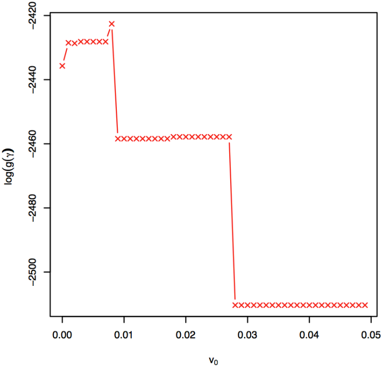
(2) Exhaustive evaluation of posterior model probabilities (CPU 6s)
$v_0 = 0, v_1 = 1\,000$ and $\theta \sim B(1, 1)$



# Boston Housing Data: Application "$p < n$"

(3) EMVS algorithm (CPU 0.53s)
$v_1 = 1\,000$, $v_0 \in \{10^{-6} + k \times 0.001; 1 \leq k \leq 50\}$, $\theta \sim B(1,1)$
$\beta^{(0)} \sim \mathrm{N}_{13}(\mathbf{0}, 10 \times \mathrm{I}_{13})$, best model contains $\{5, 6, 8, 11, 13\}$



# Detecting DNA Binding Motifs Using EMVS

- Spellman (1998) describe a yeast experiment to identify TF binding sites associated with cell cycle
- 800 genes found to have a periodic expression pattern across 2 cell cycles
- Another 800 that do not show any differential pattern across time selected as a reference
- Response vector $\boldsymbol{Y} = (Y_1, \ldots, Y_{1\,600})'$ summarizes expression of 1 600 genes over time

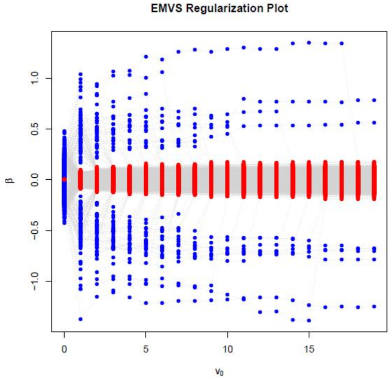
? *Can we explain the gene expression pattern by the occurrence of shared regulatory motifs?*

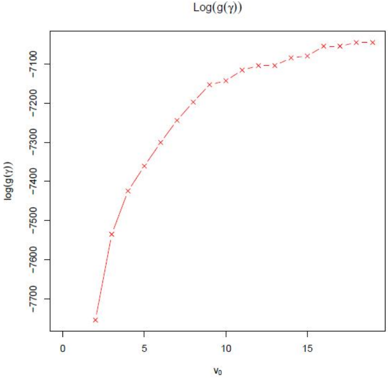
# Detecting DNA Binding Motifs Using EMVS

- Promoter regions of each genes screened for DNA motifs
- Motif $\equiv$ word of length 7 consisting of letters$\{A, G, T, C\}$ (altogether $4^7/2 = 8\,192$ motifs)
- Regression matrix $\boldsymbol{X}_{1\,600 \times 8\,192}$ contains counts of occurrences of each motif in the promoter region of each gene
- The motifs lie on a network with similar motifs being the neighbors
- For instance, *ACCTGTC* and *TCCTGTC* differ by only one letter $\rightsquigarrow$ they are connected on a graph
- Similar motifs assumed to attract the same TFs $\rightsquigarrow$ influence gene expression in a similar way

# (a) Beta-binomial Model

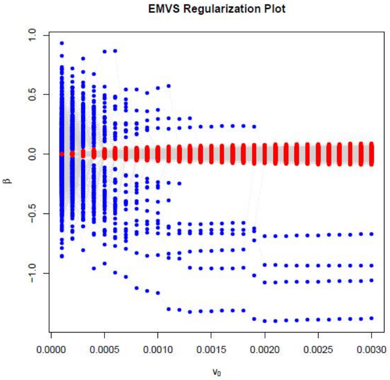
- $v_0 \in \{0.001 + k \times 1 : 0 \leq k \leq 20\}$
- $v_1$: random in EM with $a_{v_1} = 0.5$, $b_{v_1} = 250$, fixed to 1 000 in $g_0(\cdot)$
- $\beta^{(0)}$ according to (5) with $v_0 = 1$ and $v_1 = 1\,000$

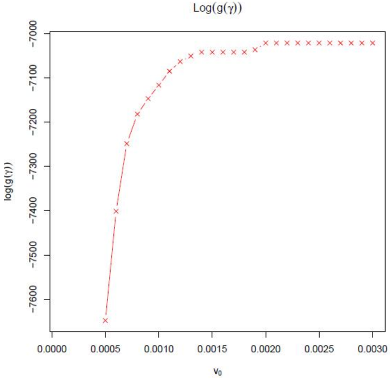


# (b) MRF Model

- $v_0 \in \{10^{-5} + k \times 10^{-5} : 0 \leq k \leq 30\}$
- $v_1$ and $\beta^0$ as in (a)
- Prior $\pi(\theta)$ located in the phase transition region



# Results

| 18 Selected Motifs | | 7 Selected Motifs | | |
|---|---|---|---|---|
| (a) | (b) | (a) | (b) | Known |
| *GACGCGT*[1] | *GACGCGT*[1] | *GACGCGT*[1] | *GACGCGT*[1] | × |
| *TACGCGT*[1] | *TACGCGT*[1] | | *TACGCGT*[1] | × |
| *TTCGCGT*[1] | *TTCGCGT*[1] | *TTCGCGT*[1] | *TTCGCGT*[1] | × |
| | *TTACGCG*[2] | | | |
| *TTTCGCG*[2] | *TTTCGCG*[2] | *TTTCGCG*[2] | *TTTCGCG*[2] | × |
| | *TGACGCG*[2] | | | |
| *TTAGCAG* | | | | |
| *ACGCGTT* | *ACGCGTT* | *ACGCGTT* | *ACGCGTT* | |
| *CCGCTTG* | *CCGCTTG* | | | |
| *CCGTCCT* | *CCGTCCT* | | | |
| *CGCGTTT* | *CGCGTTT* | *CGCGTTT* | *CGCGTTT* | |
| *CGTCCCT* | *CGTCCCT* | | | |
| *CTGATGG* | *CTGATGG* | | | |
| *GAATTAT* | *GAATTAT* | | | |
| *GACAGGT* | | | | |
| *GCCATTT* | *GCCATTT* | | | |
| | *GCGTTTT* | | | |
| *GGACGAT* | *GGACGAT* | *GGACGAT* | | × |
| *GTCCTCT* | | | | |
| *TACACAG* | *TACACAG* | | | × |
| *TTTATCG* | *TTTATCG* | *TTTATCG* | *TTTATCG* | |

Known motifs found in the SCPD (Sacharomyces Cerevisiae Pomoter Database)

# Summary

- We develop a rapid deterministic method based on EM algorithm as an alternative to stochastic model search
- Regularization diagram combined with rigorous model evaluation enable simultaneous exploration and evaluation of candidate models
- EMVS framework encompasses situations with structured covariates
- Heavy-tailed slab distributions can be considered to alleviate over-shrinkage
- Extensions to multivariate/factor analytic models possible (Rockova and Lesaffre (2013))

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Thank you!

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# EMVS Algorithm: a Closer Look

Objective function:

$$Q\left(\boldsymbol{\beta},\boldsymbol{\theta},\sigma \mid \boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)}\right) = C(\gamma) + Q_1\left(\boldsymbol{\beta},\sigma \mid \boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)}\right) + Q_2\left(\boldsymbol{\theta} \mid \boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)}\right),$$

where

$$Q_1\left(\boldsymbol{\beta},\sigma|\boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)}\right) = -\frac{(\boldsymbol{Y}-\boldsymbol{X}\beta)'(\boldsymbol{Y}-\boldsymbol{X}\beta)}{2\sigma^2} - \frac{n+p+\nu}{2}\log(\sigma^2) - \frac{\nu\lambda}{2\sigma^2} - \frac{1}{2\sigma^2}\sum_{i=1}^{p}\beta_i^2\,\mathrm{E}_{\gamma|\cdot}\left[\frac{1}{v_0(1-\gamma_i)+v_1\gamma_i}\right],$$

$$Q_2\left(\boldsymbol{\theta}|\boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)}\right) = \mathrm{E}_{\gamma|\cdot}\log\pi(\gamma|\boldsymbol{\theta}) + \log\pi(\boldsymbol{\theta}),$$

and $\mathrm{E}_{\gamma|\cdot}(\cdot)$ denotes the conditional expectation $\mathrm{E}_{\gamma|\boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)},\boldsymbol{y}}(\cdot)$

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# EMVS Algorithm (Beta-binomial Case)

Objective function:

$$Q\left(\boldsymbol{\beta}, \boldsymbol{\theta}, \sigma \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) = C(\gamma) + Q_1\left(\boldsymbol{\beta}, \sigma \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) + Q_2\left(\boldsymbol{\theta} \mid \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right),$$

where

$$Q_1\left(\boldsymbol{\beta}, \sigma | \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) = -\frac{(\boldsymbol{Y} - \boldsymbol{X}\beta)'(\boldsymbol{Y} - \boldsymbol{X}\beta)}{2\sigma^2} - \frac{n+p+\nu}{2}\log(\sigma^2) - \frac{\nu\lambda}{2\sigma^2} - \frac{1}{2\sigma^2}\sum_{i=1}^{p}\beta_i^2 \, \mathrm{E}_{\gamma|\cdot}\left[\frac{1}{v_0(1-\gamma_i) + v_1\gamma_i}\right],$$

$$Q_2\left(\boldsymbol{\theta} | \boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) = \sum_{i=1}^{p}\log\left(\frac{\theta}{1-\theta}\right)\mathrm{E}_{\gamma|\cdot}\gamma_i + (a-1)\log\theta + (b+p-1)\log(1-\theta),$$

and $\mathrm{E}_{\gamma|\cdot}(\cdot)$ denotes the conditional expectation $\mathrm{E}_{\gamma|\boldsymbol{\beta}^{(k)},\boldsymbol{\theta}^{(k)},\sigma^{(k)},\boldsymbol{y}}(\cdot)$.

# E-step (Beta-binomial Case)

Variables $\gamma$ depend on the data $\boldsymbol{Y}$ only through the current estimates $\beta^{(k)}$.

We have:

$$(1) \quad \mathrm{E}_{\gamma|\cdot}\gamma_i = \mathrm{P}(\gamma_i = 1|\boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y}) = \mathrm{P}(\gamma_i = 1|\boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}) = p_i^\star,$$

where

$$p_i^\star = \frac{\pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 1)\mathrm{P}(\gamma_i = 1 \mid \theta^{(k)})}{\pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 1)\mathrm{P}(\gamma_i = 1 \mid \theta^{(k)}) + \pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 0)\mathrm{P}(\gamma_i = 0 \mid \theta^{(k)})}$$

are the mixing proportions when fitting a Gaussian mixture model via EM.

$$(2) \quad \mathrm{E}_{\gamma|\cdot}\left[\frac{1}{v_0(1-\gamma_i) + v_1\gamma_i}\right] = \frac{\mathrm{E}_{\gamma|\cdot}(1-\gamma_i)}{v_0} + \frac{\mathrm{E}_{\gamma|\cdot}\gamma_i}{v_1} = \frac{1-p_i^\star}{v_0} + \frac{p_i^\star}{v_1} = d_i^\star$$

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# M-step (Beta-binomial Case)

(1) Update $\beta^{(k+1)}$ Closed form ridge regression solution

$$\beta^{(k+1)} = (\boldsymbol{X}'\boldsymbol{X} + \boldsymbol{D}^{\star})^{-1}\boldsymbol{X}'\boldsymbol{Y}, \quad D^{\star} = \mathrm{diag}\{d_1^{\star}, \ldots, d_p^{\star}\}$$

$\rightsquigarrow$ For $p > n$, use Woodbury-Sherman formula to get

$$\beta^{(k+1)} = \left[\boldsymbol{D}^{\star-1} - \boldsymbol{D}^{\star-1}\boldsymbol{X}'\left(\mathrm{I}_{n\times n} + \boldsymbol{X}\boldsymbol{D}^{\star-1}\boldsymbol{X}'\right)^{-1}\boldsymbol{X}\boldsymbol{D}^{\star-1}\right]\boldsymbol{X}'\boldsymbol{y}$$

(2) Update $\sigma^{(k+1)}$ Closed form

$$\sigma^{(k+1)} = \sqrt{\frac{|\boldsymbol{Y} - \boldsymbol{X}\beta^{(k+1)}|_{l_2} + |\boldsymbol{D}^{\star 1/2}\beta^{(k+1)}|_{l_2} + \eta\lambda}{n + p + \eta}}.$$

(2) Update $\theta^{(k+1)}$ Closed form

$$\theta^{(k+1)} = \frac{\sum_{i=1}^{p} p_i^* + a - 1}{a + b + p - 2}$$

# EMVS for Structured Priors

(a) *Logistic regression product prior*

$$Q_2\left(\boldsymbol{\theta}|\boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}\right) = \sum_{i=1}^{p}\{\boldsymbol{Z}_i'\boldsymbol{\theta}\, \mathrm{E}_{\gamma|\cdot}\gamma_i - \log[1+\exp(\boldsymbol{Z}_i'\boldsymbol{\theta})]\} + \sum_{j=1}^{q}\log\pi(\theta_j),$$

Beta distribution on the inverse logistic transformation of $\theta_j$

$$\pi(\theta_j) = \frac{1}{B(a,b)}\left[\frac{\exp(\theta_j)}{1+\exp(\theta_j)}\right]^a\left[\frac{1}{1+\exp(\theta_j)}\right]^b \tag{3}$$

(b) *MRF prior with $\boldsymbol{\theta}_1 = \theta(1,\dots,1)'$*, where $\theta \sim \pi(\theta)$ in (3)

$$Q_2(\theta\,|\,\boldsymbol{\beta}^{(k)}, \boldsymbol{\theta}^{(k)}, \sigma^{(k)}) = \theta\left(\sum_{i=1}^{p}\mathrm{E}_{\gamma|\cdot}\gamma_i + a\right) + \psi(\theta, \boldsymbol{\theta}_2) - (a+b)\log[1+\exp(\theta)].$$

- $\leadsto$ $\mathrm{E}_{\gamma|\cdot}\gamma_i$ complicated due to dependence between $\gamma_i'$s
- $\leadsto$ $\psi(\theta, \boldsymbol{\theta}_2)$ not in closed form

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# EMVS for Structured Priors

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- $\rightsquigarrow$ $\mathrm{E}_{\boldsymbol{\gamma}|\cdot}\gamma_i$ complicated due to dependence between $\gamma_i's$
- $\rightsquigarrow$ $\psi(\theta,\boldsymbol{\theta}_2)$ not in closed form

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# Approximated E-step (MRF Prior)

Conditional posterior distribution $\pi(\gamma \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y})$ proportional to

$$\exp\left[\left(\frac{1}{2}\log\left(v_0/v_1\right)\mathbf{1}' - \frac{v_0 - v_1}{2\sigma^{(k)2}v_1 v_0}\boldsymbol{\beta}^{(k)'}\mathrm{diag}\{\beta_i^{(k)}\}_{i=1}^{p} + \theta^{(k)}\mathbf{1}'\right)\gamma + \gamma'\boldsymbol{\theta}_2\gamma\right].$$

Markov random field distribution $\mathrm{MRF}(\boldsymbol{\theta}^{\star}, \boldsymbol{\theta}_2)$

- $\rightsquigarrow$ Expectation $\mathrm{E}(\gamma \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y}) = \frac{\partial\psi(\boldsymbol{\theta},\boldsymbol{\theta}_2)}{\partial\boldsymbol{\theta}}|_{\boldsymbol{\theta}=\boldsymbol{\theta}^{\star}}$ not analytically tractable
- $\rightsquigarrow$ Mean field approximation $\rightsquigarrow$ iteratively solving

$$\widehat{\mu}_i = \frac{\exp(\theta_i^{\star} + \sum_{j\neq i}\theta_{ij}\widehat{\mu}_j)}{1 + \exp(\theta_i^{\star} + \sum_{j\neq i}\theta_{ij}\widehat{\mu}_j)}, \quad 1 \leq i \leq p$$

- $\rightsquigarrow$ We obtain approximations to the mixing proportions

$$\widehat{\mu}_i = \mathrm{P}(\gamma_i = 1 \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y})$$

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# Approximated E-step (MRF Prior)

Conditional posterior distribution $\pi(\gamma \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y})$ proportional to

$$\exp\left[\left(\frac{1}{2}\log\left(v_0/v_1\right)\mathbf{1}' - \frac{v_0 - v_1}{2\sigma^{(k)2} v_1 v_0}\boldsymbol{\beta}^{(k)'}\mathrm{diag}\{\beta_i^{(k)}\}_{i=1}^{p} + \theta^{(k)}\mathbf{1}'\right)\gamma + \gamma'\boldsymbol{\theta}_2\gamma\right].$$

Markov random field distribution $\mathrm{MRF}(\boldsymbol{\theta}^{\star}, \boldsymbol{\theta}_2)$

- ⇝ Expectation $\mathrm{E}(\gamma \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y}) = \frac{\partial\psi(\boldsymbol{\theta},\boldsymbol{\theta}_2)}{\partial\boldsymbol{\theta}}|_{\boldsymbol{\theta}=\boldsymbol{\theta}^{\star}}$ not analytically tractable
- ⇝ Mean field approximation ⇝ iteratively solving

$$\widehat{\mu}_i = \frac{\exp(\theta_i^{\star} + \sum_{j\neq i}\theta_{ij}\widehat{\mu}_j)}{1 + \exp(\theta_i^{\star} + \sum_{j\neq i}\theta_{ij}\widehat{\mu}_j)}, \quad 1 \leq i \leq p$$

- ⇝ We obtain approximations to the mixing proportions

$$\widehat{\mu}_i = \mathrm{P}(\gamma_i = 1 \mid \boldsymbol{\beta}^{(k)}, \theta^{(k)}, \sigma^{(k)}, \boldsymbol{y})$$

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# Approximated M-step (MRF Prior)

- Updates for $\beta$ and $\sigma$ the same as before
- Update $\theta$

$$\theta^{(k+1)} = \text{argmax}_{\theta \in \mathbb{R}} \left\{ \theta \left( \sum_{i=1}^{p} \widehat{\mu}_i^\star + a \right) + \psi(\theta, \boldsymbol{\theta}_2) - (a+b) \log[1 + \exp(\theta)] \right\}.$$

Mean field approximation to the partition function $\psi(\theta, \boldsymbol{\theta}_2)$

$$\psi(\theta, \boldsymbol{\theta}_2) \approx \theta \sum_{i=1}^{p} \mu_i + \boldsymbol{\mu}' \boldsymbol{\theta}_2 \boldsymbol{\mu} - \psi^\star(\boldsymbol{\mu}), \qquad (4)$$

where $\mu_i = \mathrm{E}_{\theta, \boldsymbol{\theta}_2}(\gamma_i)$ and $\psi^\star(\cdot)$ denotes the conjugate dual function

$$\psi^\star(\boldsymbol{\mu}) = \sum_{i=1}^{p} [\mu_i \log \mu_i + (1 - \mu_i) \log(1 - \mu_i)]$$

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# Deterministic Annealing EM (DAEM)

DAEM algorithm to maximize (2)

(1) Logistic/beta-binomial prior:

Mixing proportions replaced by

$$p^{\star}_{i,t} = \frac{\pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 1)^t \mathrm{P}(\gamma_i = 1 \mid \boldsymbol{b}^{(k)})^t}{\pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 1)^t \mathrm{P}(\gamma_i = 1 \mid \boldsymbol{b}^{(k)})^t + \pi(\beta_i^{(k)} \mid \sigma^{(k)}, \gamma_i = 0)^t \mathrm{P}(\gamma_i = 0 \mid \boldsymbol{b}^{(k)})^t},$$

$\rightsquigarrow$ Limiting behavior $p^{\star}_{i,t} \to 0.5$ as $t \to 0$ suggests a starting vector

$$\widehat{\boldsymbol{\beta}}_{t=0} = \left[\boldsymbol{X}'\boldsymbol{X} + \frac{v_0 + v_1}{2 v_0 v_1} \boldsymbol{I}_p\right]^{-1} \boldsymbol{X}'\boldsymbol{y} \tag{5}$$

(2) MRF prior:

MF approximation to evaluate expectation of $\mathrm{MRF}(t\,\theta^{\star}, t\,\boldsymbol{\theta}_2)$

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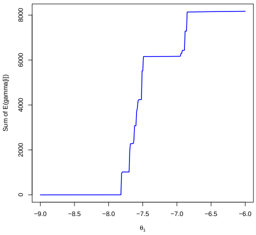
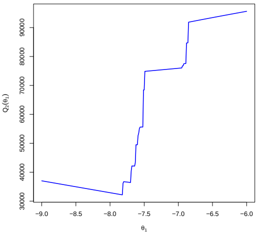
# Phase Transition

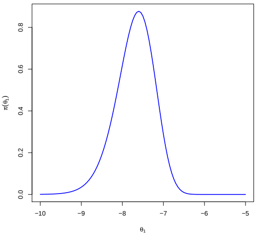
$\sum_{i=1}^{p} \mathrm{E}_{\theta,\boldsymbol{\theta}_2}\gamma_i$




$Q_2^{MRF}(\theta)$




$\pi(\theta)$

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# Heavy-tailed Alternative

- Gaussian slab density may overshrink $\rightsquigarrow$ put prior on $v_1$ to induce heavier tails
- Prior suggested in the "g-prior" context (Cui and George (2008), Maruyama and George (2011))

$$p(v_1) = \frac{v_1^b (1+v_1)^{-a-b-2}}{\mathrm{B}(a+1, b+1)} \mathrm{I}_{(0,\infty)}(v_1) \qquad (6)$$

- Implied marginal prior distribution

$$\pi(\beta_i | v_0, \sigma, \gamma) = (1-\gamma_i)\mathrm{N}(0, \sigma^2 v_0) + \gamma_i \widetilde{\pi}_{a,b,\sigma}(\beta_i),$$

where

$$\widetilde{\pi}_{a,b,\sigma}(\beta_i) \propto \frac{\exp\left(\frac{\beta_i^2}{4\sigma^2}\right)}{\sqrt{2\pi\sigma^2}} \left(\frac{\beta_i^2}{2\sigma^2}\right)^{\frac{b}{2}-\frac{1}{4}} W_{-a-\frac{b}{2}-\frac{5}{4}, -\frac{b}{2}-\frac{1}{4}} \left(\frac{\beta_i^2}{2\sigma^2}\right)$$

# Heavy-tailed Alternative

- Integrating out $v_1$ complicates the tractability of the M-step
- We treat $v_1$ as an additional unknown parameter
- Assuming prior (6) we update $v_1$ at the $k$-th iteration according to

$$v_1^{(k+1)} = \text{argmax}_{v_1} \left\{ -\frac{|\boldsymbol{P}^{\star 1/2}\boldsymbol{\beta}|_{l_2}}{2\sigma^{(k+1)}} \frac{1}{v_1} + \left( b - \sum_{i=1}^{p} \frac{p_i^\star}{2} \right) \log(v_1) - (a+b+2)\log(1+v_1) \right\},$$

where $\boldsymbol{P}^\star = \mathrm{diag}\{p_1^\star, \ldots, p_p^\star\}$

- EM algorithm remains unchanged, just with updates based on the current value $v_1^{(k)}$