Bayesian Group Lasso for Analyzing Contingency Tables

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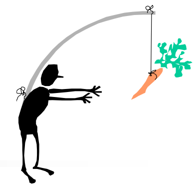
Talk Outline

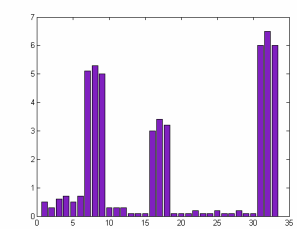
- Motivation
- Introduction
- Feature Selection
- Contingency Tables
- Application - Breast Cancer
- Results
- Summary

Motivation

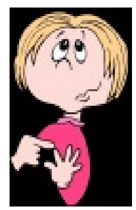


- Applications involving
  - Feature selection – Finding bio-markers.

  - Categorical variables - leading to sparsity in groups.



  - Count data – Frequently encountered in medical applications.



- Meaningful Variance estimates

Introduction

- Consider a standard linear regression problem

$$y_i = \boldsymbol{x}_i^t \boldsymbol{\beta} + \varepsilon_i \quad s.t.\ g(\boldsymbol{\beta}) \leq \kappa.$$

- A Bayesian version:

$$\underbrace{p(\boldsymbol{\beta}, \boldsymbol{\theta} | y, X)}_{\text{Posterior}} \propto \underbrace{p(y | X, \boldsymbol{\beta}, \boldsymbol{\theta})}_{\text{Likelihood}} \underbrace{p(\boldsymbol{\beta} | \boldsymbol{\theta})}_{\text{Prior}} p(\boldsymbol{\theta})$$

Feature Selection

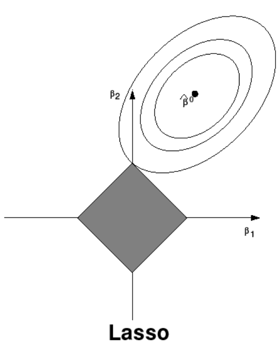
Feature Selection

Lasso

$$\|\boldsymbol{y} - X\boldsymbol{\beta}\|_2^2 \quad \text{subject to} \quad \|\boldsymbol{\beta}\|_1 \leq \kappa.$$

Prior (Park & Casella, 2008):

$$p(\boldsymbol{\beta}|0, k^{-1}) = \prod_{i=1}^{D} \frac{k}{2} exp(-k|\beta_i|)$$

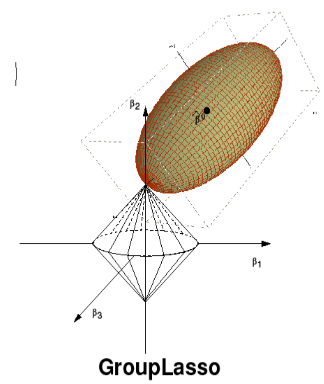


Group-Lasso

$$\text{minimize } l(\boldsymbol{\beta}) \quad \text{s.t.} \quad \sum_{g=1}^{G} \|\boldsymbol{\beta}_g\|_2 \leq \kappa.$$

Prior:

$$\prod_{g=1}^{G} \text{M-Laplace}(\boldsymbol{\beta}_g|\mathbf{0}, c^{-1}) \propto c^{p_g/2} \exp(-c\|\boldsymbol{\beta}_g\|_2),$$



Prior – Hierarchical model

- Hierarchical model

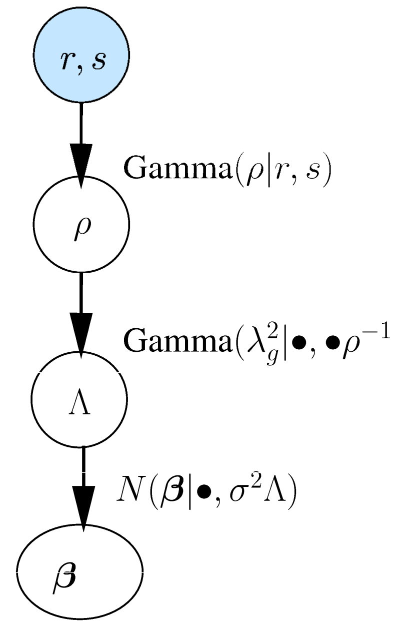
$$p(\boldsymbol{\beta}_g|\rho) = \int_0^\infty N(\boldsymbol{\beta}_g|0, \sigma^2\lambda_g^2 I)p(\lambda_g^2|\rho)\, d\lambda_g^2$$

- Normal-Gamma model:

$$p(\boldsymbol{\beta}_g|\rho) = \int_0^\infty N(\boldsymbol{\beta}_g|0, \sigma^2\lambda_g^2)\text{Gamma}(\lambda_g^2|\tfrac{p_g+1}{2}, \tfrac{2}{a_g})\, d\lambda_g^2$$

$$\propto \text{M-Laplace}(\boldsymbol{\beta}_g|\mathbf{0}, (a_g/\sigma^2)^{-\frac{1}{2}}).$$

where $a_g = p_g\rho$ and $b_g = ||\boldsymbol{\beta}_g||_2^2/\sigma^2$ (for each group g) , using the generalized inverse gaussian distribution.



Generalized linear models

- Stochastic component:
  - Z distributed based on mean θ.

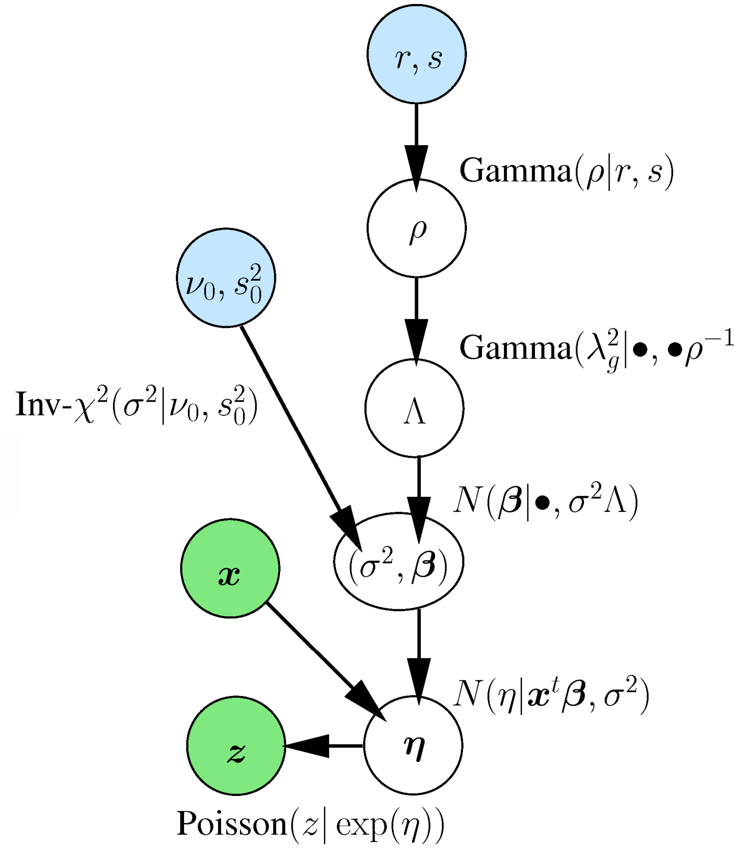
$$Z \sim f(\theta)$$

- Random Effect:

$$\eta_i = \boldsymbol{x}_i^t \boldsymbol{\beta} + \epsilon_i, \quad \epsilon_i \sim N(0, \sigma^2)$$

- Link Function:

$$g(\theta) = \eta$$



Contingency tables for count data

Contingency Tables

- Contingency tables
  - Count data
  - Categorical variables

Example

		BioMarkerX High	BioMarkerX Low	
BioMarkerY	High	4	10	14
	Low	50	25	75
		54	35	89

- Poisson for Modeling:
  - Random counts, fixed time period.

$$z_i|\theta_i \sim \text{Poisson}(\theta_i) = \frac{\theta_i^{z_i} e^{-\theta_i}}{z_i!},$$

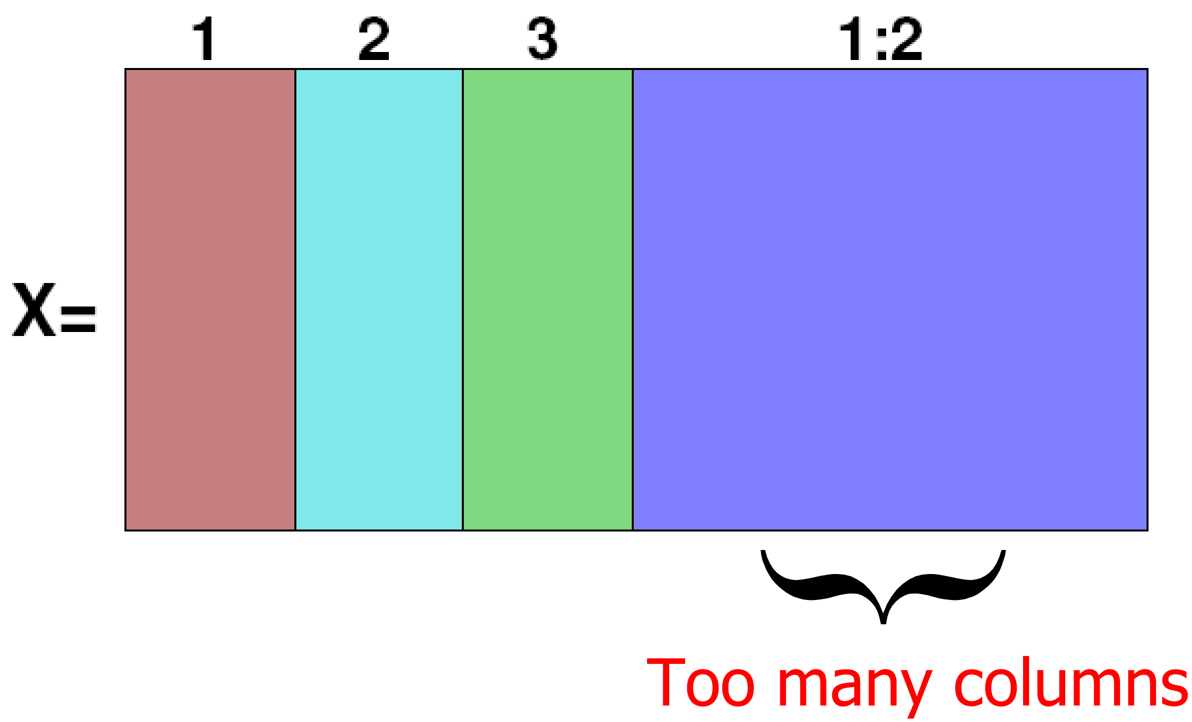
with the Poisson mean $\theta_i = e^{\eta_i}$, and $\eta_i \sim N(\boldsymbol{x}_i^t \boldsymbol{\beta}, \sigma^2)$.

  - Example – a clinical study of fixed time period.

What is X?

Dummy Coding - Example

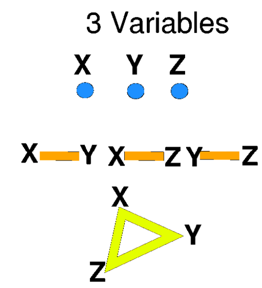
1	1	0	0	0
2	0	1	0	0
3	0	0	1	0
4	0	0	0	1



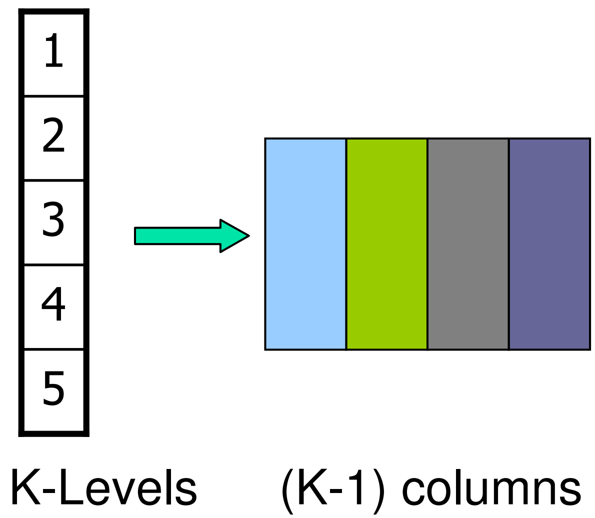
Construction of X

- Higher order interaction terms.

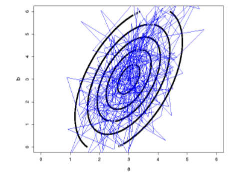
$$X = [\underbrace{X^{C_1}, \dots, X^{C_d}}_{\text{main effects}}, \underbrace{X^{C_1:C_2}, \dots, X^{C_{d-1}:C_d}}_{\text{1st order interactions}}, \dots, \underbrace{X^{C_1:\cdots:C_{Q+1}}, \dots, X^{C_{d-Q}:\cdots:C_d}}_{\text{highest order interactions}}].$$



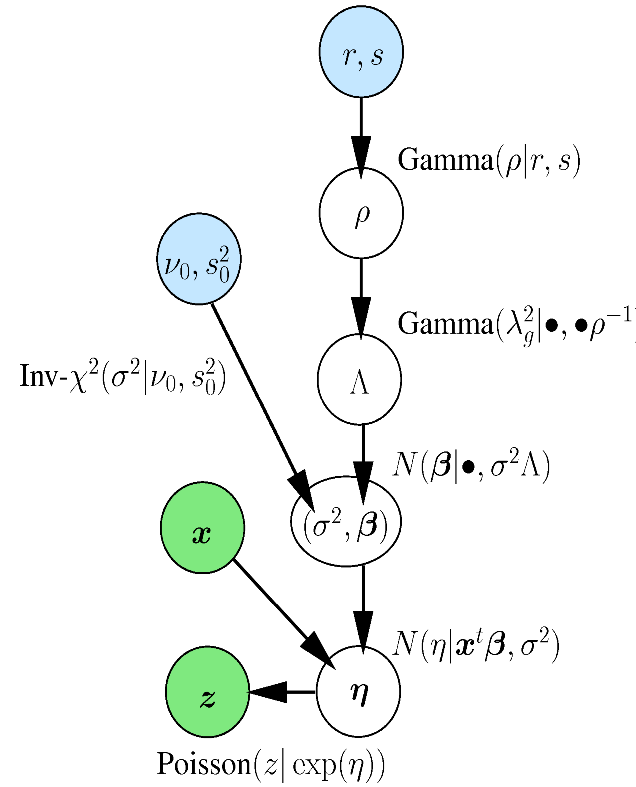
- Polynomial Contrast Codes
  - Used for ordered variables.
  - Avoids over-parameterization.
  - Orthogonal in nature – results in an orthogonal design matrix
    - ($X^TX = I$).



Inference:



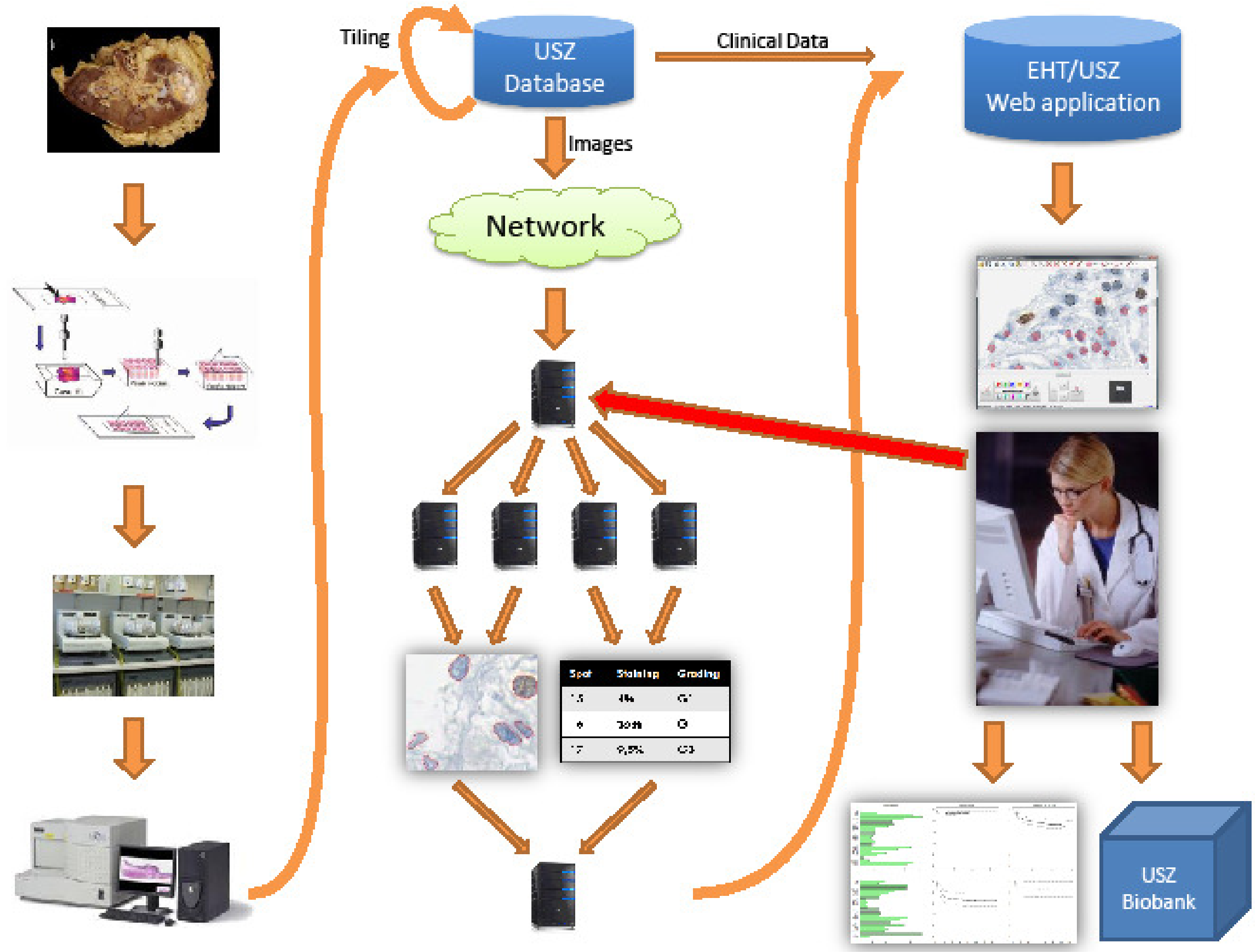
- Gibbs Sampling:
  - Highly efficient (no matrix inversion).
- Standard posterior conditionals.
- Sampling the η variable:
  - Adaptive Rejection sampling.
  - Laplace approximation:



$$p(\eta_i|\boldsymbol{\beta}, \sigma^2, X, \boldsymbol{z}) \propto \exp\left[\sum_i \eta_i z_i - \exp(\eta_i) - \frac{1}{2\sigma^2}(\boldsymbol{x}_i^t \boldsymbol{\beta} - \eta_i)^2\right].$$

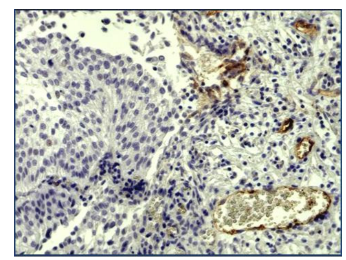
Experiments

Computational Pathology

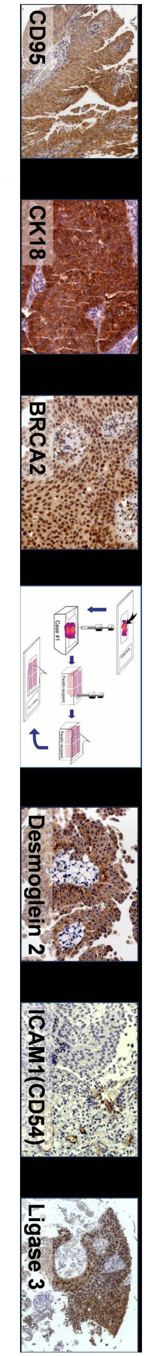


Application – Breast Cancer

- Breast Cancer – Leading cause for tumor-related death of women, particularly in Western countries.
  - Finding biomarkers for prediction and prognosis is important.
- Immunohistochemistry:
  - Labeling proteins in tissue sections using antibody-antigen interaction.
  - Cost effective, used on a routine basis.

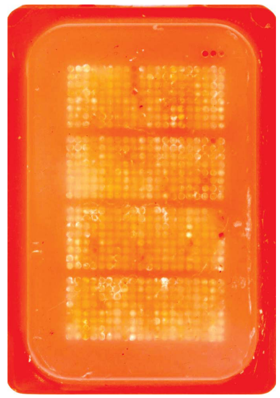


- Tissue Microarray Technology:
  - TMA: allows simultaneous in situ analysis of 1000 primary tumors.
  - Promises to significantly accelerate studies seeking for biomarkers.

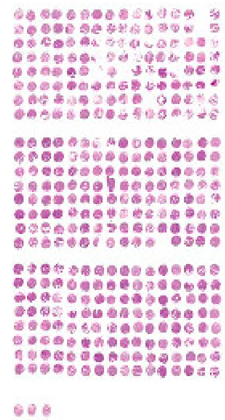


Tissue Microarrays

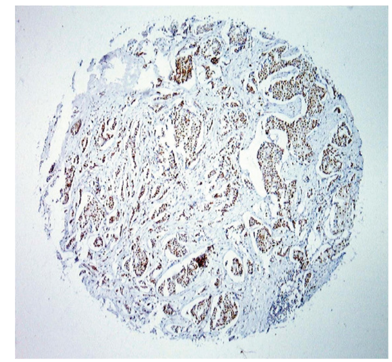
Primary samples are taken from cancerous breast tissue.



Tissue cylinders of size 0.6mm are arrayed in a paraffin block.



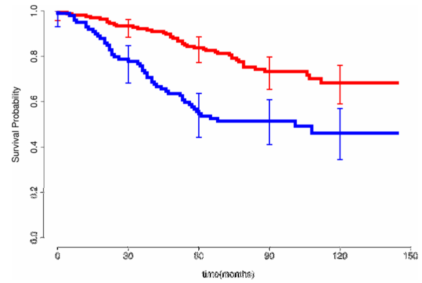
Slices of 0.6µm are cut off and are stained.

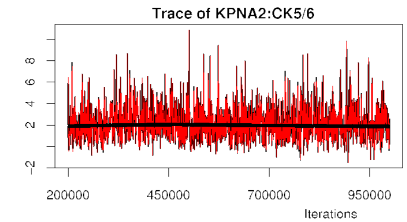


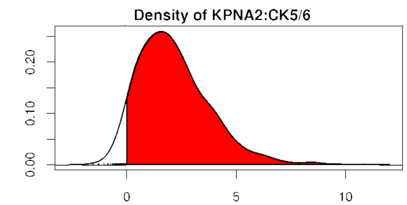
TMA spot from a single patient with breast cancer stained with the YB-1 antigen.

Results – Significant Interactions

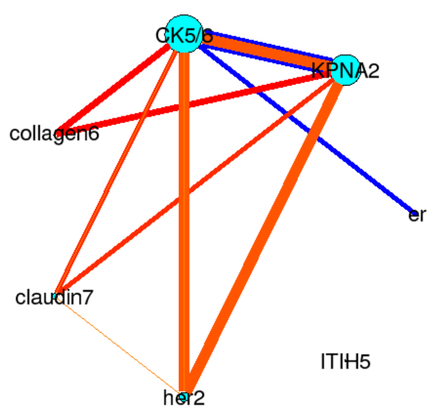
- Two patient groups – Find difference:
  - Low/High risk groups.
- Intensity levels for 7 proteins, with higher-order interactions up to order 2.



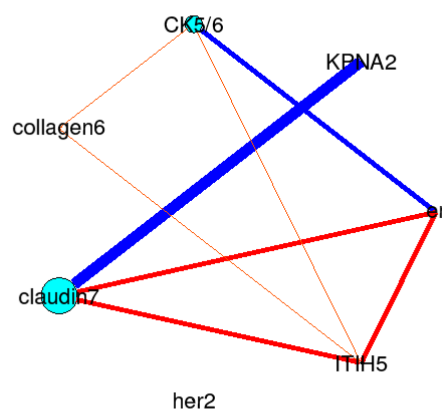


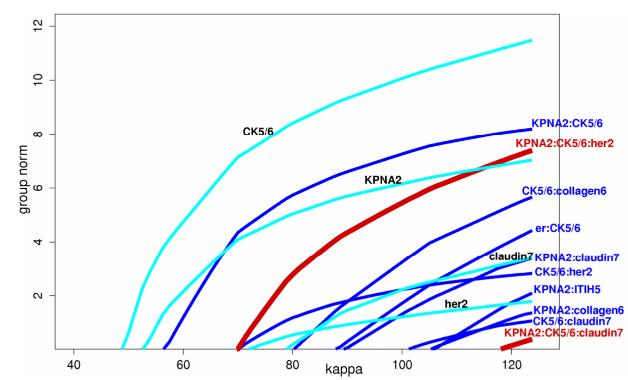


Low Risk Group



High Risk Group





Summary

- Bayesian Group-Lasso to deal with
  - Count data – Poisson Model
  - Feature selection with categorical variables
- Detection of novel *compound* bio-markers in the breast cancer dataset.
- Advantages:
  - Average over solutions, meaningful variance estimates.
  - Higher-order interactions.
- Future work:
  - Extending to other types of data (Weibull, Beta, Dirichlet).
  - Going beyond Group-Lasso – Applying more sparse constraints, based on [Caron & Doucet, 2008]).
  - Clustering.

Thank you for your attention.