Gaussian Graphical models and Dependency networks

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Plan for this section

- Overview of network inference (Sep 18th)
- Directed probabilistic graphical models Bayesian networks (Sep 18th, Sep 20th)
- Gaussian graphical models (Sep 25th)
- Dependency networks (Sep 25, 27th)
- Integrating prior information for network inference (Oct 2nd, 4th)

Goals for today

- Graphical Gaussian Models (GGMs)
- Different algorithms for learning GGMs
  - Graphical Lasso
  - Neighborhood selection
- Dependency networks
- GENIE3
- Evaluation of expression-based network inference methods

Recall the different types of probabilistic graphs

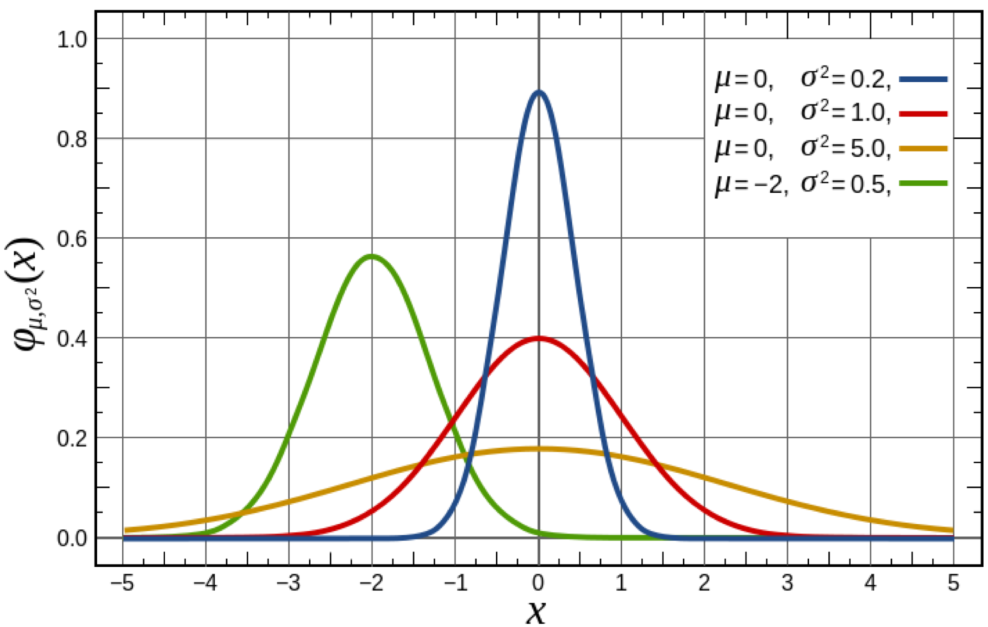
- In each graph type we can assert different conditional independencies
- Correlation networks
- Markov networks
  - Gaussian Graphical models
- Dependency networks
- Bayesian networks

Recall the univariate Gaussian distribution

- Gaussian distribution

$$f(x) = \frac{1}{\sqrt{2\pi\sigma^2}}\exp(-\frac{(x-\mu)^2}{2\sigma^2})$$

The Gaussian distribution is defined by two parameters:
Mean: μ
Standard deviation: σ



A multi-variate Gaussian Distribution

- Extends the univariate distribution to higher dimensions (p in our case)

$$P(\mathbf{x}|\boldsymbol{\mu}, \boldsymbol{\Sigma}) = \frac{1}{(2\pi)^{\frac{p}{2}} |\Sigma|^{\frac{1}{2}}} \exp\left(-\frac{1}{2}(\mathbf{x}-\boldsymbol{\mu})^T \Sigma^{-1} (\mathbf{x}-\boldsymbol{\mu})\right)$$

- As in the univariate case, we have two parameters
  - Mean: a p-dimensional vector $\boldsymbol{\mu}$
  - Co-variance: a $\mathrm{p} \mathrm{X} \mathrm{p}$ dimensional matrix $\boldsymbol{\Sigma}$
    - Each entry of the matrix specifies the variance of co-variance between any two dimensions

A two-dimensional Gaussian distribution

- The mean $\boldsymbol{\mu} = [\mu_1, \mu_2]$

Probability density of a Gaussian with

$$\boldsymbol{\mu} = [0, 0]$$

$$\boldsymbol{\Sigma} = \begin{bmatrix} 0.25 & 0.3 \\ 0.3 & 1 \end{bmatrix}$$

- The covariance matrix

Co-variance

$$\boldsymbol{\Sigma} = \begin{bmatrix} \sigma_{11}, \sigma_{12} \\ \sigma_{21}, \sigma_{22} \end{bmatrix}$$

Variance

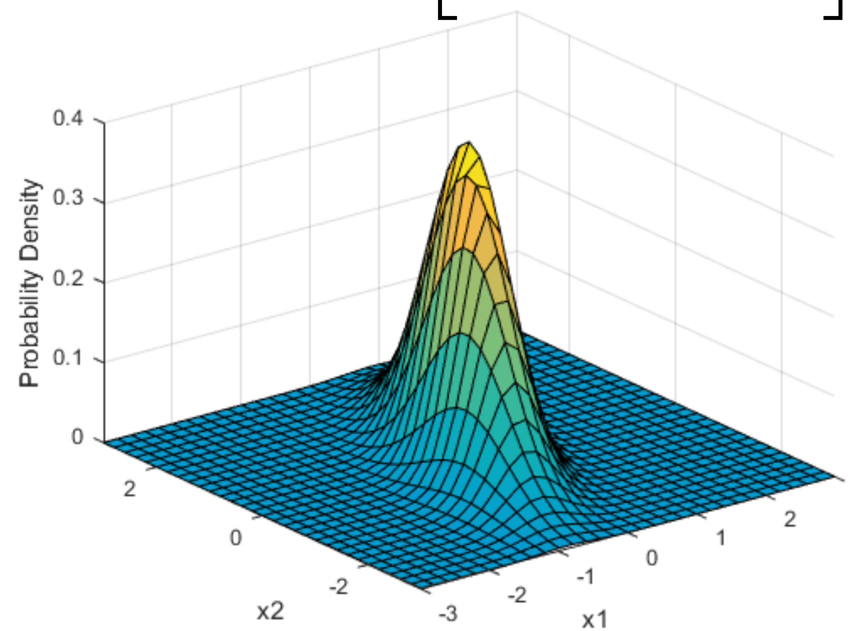
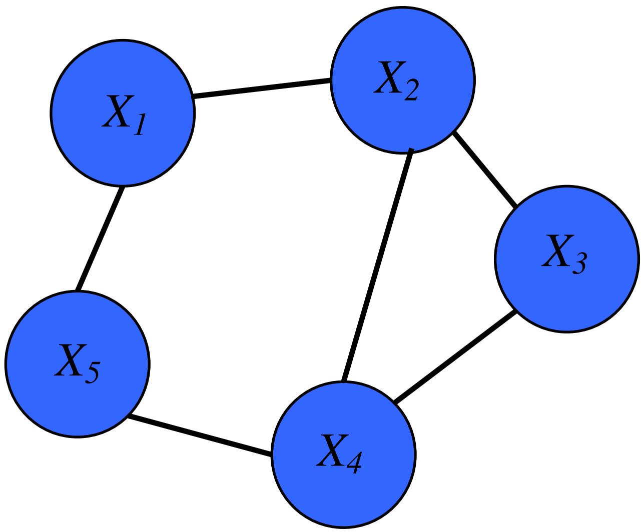


Image from Mathworks.com

Graphical Gaussian Models (GGMs)

- An undirected probabilistic graphical model
- Graph structure encode conditional independencies among variables
- The GGM assumes that X is drawn from a p-variate Gaussian distribution with mean $\boldsymbol{\mu}$ and co-variance $\boldsymbol{\Sigma}$
- The graph structure specifies the zero pattern in the $\boldsymbol{\Sigma}^{-1} = \Theta$
  - Zero entries in the inverse imply absence of an edge in the graph

Absence of edges and the zero-pattern of the precision matrix



$$\mathbf{\Theta} = \begin{bmatrix} \theta_{11} & \theta_{12} & 0 & 0 & \theta_{15} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} & 0 \\ 0 & \theta_{32} & \theta_{33} & \theta_{34} & 0 \\ 0 & \theta_{42} & \theta_{43} & \theta_{44} & \theta_{45} \\ \theta_{51} & 0 & 0 & \theta_{54} & \theta_{55} \end{bmatrix}$$

For example:

$$X_1 \perp X_4 | X_2, X_5$$

$$X_1 \perp X_3 | X_2, X_5$$

Matrix trace and determinant properties

- Trace of a pXp square matrix M is the sum of the diagonal elements

$$Tr(M) = \sum_{i}^{p} M_{ii}$$

- Trace of two matrices

$$Tr(MN) = Tr(NM)$$

- For a scalar a

$$Tr(a) = a$$

- Trace is additive

$$Tr(A + B) = Tr(A) + Tr(B)$$

- Determinant of inverse

$$\det(A^{-1}) = \frac{1}{\det(A)}$$

Joint probability of a sample from a GGM

- It is easier to work with the log

$$\log P(\mathbf{x}|\mu,\mathbf{\Sigma}) = \log\left(\frac{1}{(2\pi)^{\frac{p}{2}}|\Sigma|^{\frac{1}{2}}}\right) - \left(\frac{1}{2}(\mathbf{x}-\mu)^T\Sigma^{-1}(\mathbf{x}-\mu)\right)$$

$$\begin{aligned}\log P(\mathbf{x}|\mu,\mathbf{\Sigma}) &= -\frac{1}{2}\log\left((2\pi)^p|\Sigma|\right) - \left(\frac{1}{2}(\mathbf{x}-\mu)^T\Sigma^{-1}(\mathbf{x}-\mu)\right)\\ &\propto -\frac{1}{2}\log|\Sigma| - \left(\frac{1}{2}(\mathbf{x}-\mu)^T\Sigma^{-1}(\mathbf{x}-\mu)\right)\\ &= \frac{1}{2}\log|\Theta| - \left(\frac{1}{2}Tr((\mathbf{x}-\mu)^T\Sigma^{-1}(\mathbf{x}-\mu))\right)\end{aligned}$$

Joint probability of a sample from a GGM (contd)

- The previous term can be re-written as

$$= \frac{1}{2}\log|\Theta| - \left(\frac{1}{2}Tr((\mathbf{x}-\mu)^T\Theta(\mathbf{x}-\mu))\right)$$

Trace trick: Tr(MN)=Tr(NM)

$$= \frac{1}{2}\log|\Theta| - \left(\frac{1}{2}Tr(\Theta(\mathbf{x}-\mu)(\mathbf{x}-\mu)^T)\right)$$

$$= \frac{1}{2}\log|\Theta| - \left(\frac{1}{2}\left(\sum_{i=1}^{p}\theta_{ii}(x_i-\mu_i)^2\right) + \underbrace{\sum_{i\neq j}\theta_{ij}(x_i-\mu_i)(x_j-\mu_j)}_{\text{This term is 0, when there is no contribution from the pair } x_i,\, x_j}\right)$$

Data likelihood from a GGM

- Data likelihood of a dataset $\mathrm{D}=\{\boldsymbol{x}_1,\ldots,\boldsymbol{x}_N\}$ with N different samples from a GGM is

$$= \frac{1}{N}\sum_{j=1}^{N} \log P(\mathbf{x}_j|\mu, \boldsymbol{\Sigma})$$

- After some linear algebra is proportional to

$$= \log\ |\boldsymbol{\Theta}| - Tr(\mathbf{S}\boldsymbol{\Theta})$$

- where

$$\mathbf{S} = \frac{1}{N}\sum_{i=1}^{N}(\mathbf{x}_i - \mu)(\mathbf{x}_i - \mu)^{\mathsf{T}}$$

This formulation is nice because now we can think of entries of Θ as regression weights that we need to maximize the above objective

Learning a Graphical Gaussian Model

- Learning the structure of a GGM entails estimating which entries in the inverse of the covariance matrix are non-zero
- These correspond to the direct dependencies among two random variables

Learning a GGM

- Graphical Lasso
  - Exact approach
  - Friedman, Hastie and Tibshirani 2008
- Neighborhood selection
  - Approximate approach
  - Meinshausen and Buhlmann 2006

Linear regression with *p* predictors

- Suppose we have N samples of input output pairs
$$\{(\mathbf{x}_1, y_1), \cdots, (\mathbf{x}_N, y_N)\}$$
- Where $\mathbf{x}_i = (x_{i1}, \cdots, x_{ip})$ is p-dimensional
- That is we have p different features/predictors
- A linear regression model with p features is

$$y_i = \underbrace{\beta_0}_{\text{intercept}} + \sum_{j=1}^{p} x_{ij} \underbrace{\beta_j}_{\text{Regression coefficients}} + \epsilon_i$$

- Learning the linear regression model requires us to find the parameters than minimizes prediction error

Linear regression with *p* predictors

- Learning a regression model requires us find the regression weights that minimize the prediction error

$$\text{minimize}_{\beta_0,\beta_j}\left[\frac{1}{2N}\sum_{i=1}^{N}(y_i-\beta_0-\sum_{j=1}^{p}x_{ij}\beta_j)^2\right]$$

Residual sum of squared errors (RSS)

- To find the $\beta = \{\beta_0, \beta_1, \cdots, \beta_p\}$ we would need to the RSS with respect to each parameters, set the derivative to 0 and solve

OLS estimate

$$\widehat{\beta}_j = \frac{\sum_{i=1}^{N}(y_i-\beta_0)x_{ij}}{\sum_{i=1}^{N}x_{ij}^2}$$

Regularized regression

- The least squares solution is often not satisfactory
  - Prediction accuracy has high variance: small variations in the training set can result in very different answers
  - Interpretation is not easy: ideally, we would like to have a good predictive model, and that is interpretable
- The regularized regression framework can be generally described as follows:

Regularization term

$$\text{minimize}_{\beta_0,\beta_i} \left[\frac{1}{2N} \sum_{i=1}^{N} (y_i - \beta_0 - \sum_{j=1}^{p} x_{ij}\beta_j)^2 \right] + \lambda f(\beta)$$

Depending upon *f* we may have different types of regularized regression frameworks

Regularized regression

- $f(\beta)$ takes the form of some norm of β
- L1 norm used in LASSO regression

$$\sum_{j=1}^{p} |\beta_j|$$

- L2 norm used in Ridge regression

$$\sum_{j=1}^{p} \beta_j^2$$

Ridge regression

- The simplest type of regularized regression is called ridge regression
- This has the effect of smoothing out the regression weights

$$\text{minimize}_{\beta_0,\beta_j} \left[\frac{1}{2N} \sum_{i=1}^{N} (y_i - \beta_0 - \sum_{j=1}^{p} x_{ij}\beta_j)^2 \right] + \lambda \sum_{j=1}^{p} \beta_j^2$$

- It is often convenient to center the output (mean=0) and standardize the predictors (mean=0, variance =1)

$$\text{minimize}_{\beta_j} \left[\frac{1}{2N} \sum_{i=1}^{N} (y_i - \sum_{j=1}^{p} x_{ij}\beta_j)^2 \right] + \lambda \sum_{j=1}^{p} \beta_j^2$$

LASSO regression

- The ridge regression handles the case of variance, and suitable when there are correlated predictors
- But does not give an interpretable model
- The LASSO regression model was developed to learn a sparse model

$$\text{minimize}_{\beta_0,\beta_j}\left[\frac{1}{2N}\sum_{i=1}^{N}(y_i-\beta_0-\sum_{j=1}^{p}x_{ij}\beta_j)^2\right]+\lambda\sum_{j=1}^{p}|\beta_j|$$

- Or after standardization:

$$\text{minimize}_{\beta_j}\left[\frac{1}{2N}\sum_{i=1}^{N}(y_i-\sum_{j=1}^{p}x_{ij}\beta_j)^2\right]+\lambda\sum_{j=1}^{p}|\beta_j|$$

Cyclic coordinate descent to learn LASSO regression weights

- To estimate the regression weights in LASSO, we cycle through each regression weight, setting it to its optimal value while keeping the others constant
- That is we re-write the objective as

$$\left[\frac{1}{2N}\sum_{i=1}^{N}(y_i - \sum_{k\neq j} x_{ik}\beta_k - x_{ij}\beta_j)^2\right] + \lambda\sum_{k\neq j}|\beta_k| + \lambda|\beta_j|$$

- We derive with respect to β_j at a time, and set it to its optimal value.

Learning the regression weights in LASSO

- Due to the absolute value in the objective function, the derivative is not defined at 0
- That is derivative of $|b|$ at $b = 0$ is not defined
- To address this, we need to consider the possible scenarios of the regression weight

Learning the regression weights in Lasso

- To handle the discontinuity in the L1 norm, we consider the possible scenarios of sign of

$$\beta_j = \begin{cases} \frac{1}{N}\sum_{i=1}^{N} \mathbf{r}_i x_{ij} - \lambda, \text{ if } \beta_j > 0 \\ \frac{1}{N}\sum_{i=1}^{N} \mathbf{r}_i x_{ij} + \lambda, \text{ if } \beta_j < 0 \\ 0, \text{ otherwise} \end{cases}$$

- Here $\mathbf{r}_i = y_i - \sum_{k \neq j} x_{ik}\beta_k$
- Notice that the regularization term controls the extent to which β_j is pushed to 0.

Learning a GGM

- Graphical Lasso
  - Exact approach
  - Friedman, Hastie and Tibshirani 2008
- Neighborhood selection
  - Approximate approach
  - Meinshausen and Buhlmann 2006

Graphical LASSO

- Recall the Gaussian likelihood

$$= \log\ |\mathbf{\Theta}| - Tr(\mathbf{S}\mathbf{\Theta})$$

- Deriving with respect to Θ we get a form that allows for a LASSO-like algorithm
- The algorithm itself uses LASSO to solve a regression problem per variable.

Graphical LASSO

- Recall the Gaussian likelihood

$$= \log |\mathbf{\Theta}| - Tr(\mathbf{S\Theta}) = \log \det(\mathbf{\Theta}) - Tr(\mathbf{S\Theta})$$

- Learning the GGM requires us to solve the following optimization problem

$$\widehat{\Theta} = \arg\max_{\mathbf{\Theta}} \log \det(\mathbf{\Theta}) - Tr(\mathbf{\Theta S})$$

- But this in general is not going to work because of small sample size

$$\widehat{\Theta} = \arg\max_{\mathbf{\Theta}} \log \det(\mathbf{\Theta}) - Tr(\mathbf{\Theta S}) - \lambda ||\mathbf{\Theta}||_1$$

- This is the idea behind the Graphical LASSO algorithm

Friedman, Hastie, Tibshirani 2008

Graphical LASSO algorithm

- Deriving with respect to Θ we get

$$\mathbf{\Theta}^{-1} - \mathbf{S} - \lambda\Psi$$

- The algorithm itself uses a blockwise coordinate descent algorithm, each time considering one row and column

$$\mathbf{\Theta} = \begin{bmatrix} \mathbf{\Theta}_{11} & \theta_{12} \\ \theta_{12} & \theta_{22} \end{bmatrix} \mathbf{S} = \begin{bmatrix} \mathbf{S_{11}} & s_{12} \\ s_{12} & s_{22} \end{bmatrix}$$

Keep this fixed

Graphical LASSO contd

- Using partitioned inverse

$$\begin{bmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{C} & \mathbf{D} \end{bmatrix}^{-1} = \begin{bmatrix} (\mathbf{A}-\mathbf{B}\mathbf{D}^{-1}\mathbf{C})^{-1} & -(\mathbf{A}-\mathbf{B}\mathbf{D}^{-1}\mathbf{C})^{-1}\mathbf{B}\mathbf{D}^{-1} \\ -\mathbf{D}^{-1}\mathbf{C}(\mathbf{A}-\mathbf{B}\mathbf{D}^{-1}\mathbf{C})^{-1} & \mathbf{D}^{-1}+\mathbf{D}^{-1}\mathbf{C}(\mathbf{A}-\mathbf{B}\mathbf{D}^{-1}\mathbf{C})^{-1}\mathbf{B}\mathbf{D}^{-1} \end{bmatrix}.$$

$$\begin{bmatrix} \mathbf{\Theta}_{11} & \theta_{12} \\ \theta_{12} & \theta_{22} \end{bmatrix}^{-1} = \begin{bmatrix} \mathbf{W}_{11} & -\mathbf{W}_{11}\theta_{12}/\theta_{22} \\ w_{12} & w_{22} \end{bmatrix}$$

- Plugging this in

$$\mathbf{\Theta}^{-1} - \mathbf{S} - \lambda\Psi$$

- For each row/column we get

$$\mathbf{W}_{11}\beta - s_{12} + \lambda\psi_{12} = 0,$$

$$\text{where } \beta = -\theta_{12}/\theta_{22}$$

Graphical LASSO contd

- This specific function looks similar to the derivative of a LASSO objective

LASSO objective
$$\frac{1}{2N}(y - \mathbf{Z}\beta)^{\mathsf{T}}(y - \mathbf{Z}\beta) + \lambda||\beta||_1$$

Derivative
$$\frac{1}{N}\mathbf{Z}^{\mathsf{T}}\mathbf{Z}\beta - \frac{1}{N}\mathbf{Z}^{\mathsf{T}}y + \lambda\mathrm{sign}(\beta) = 0$$

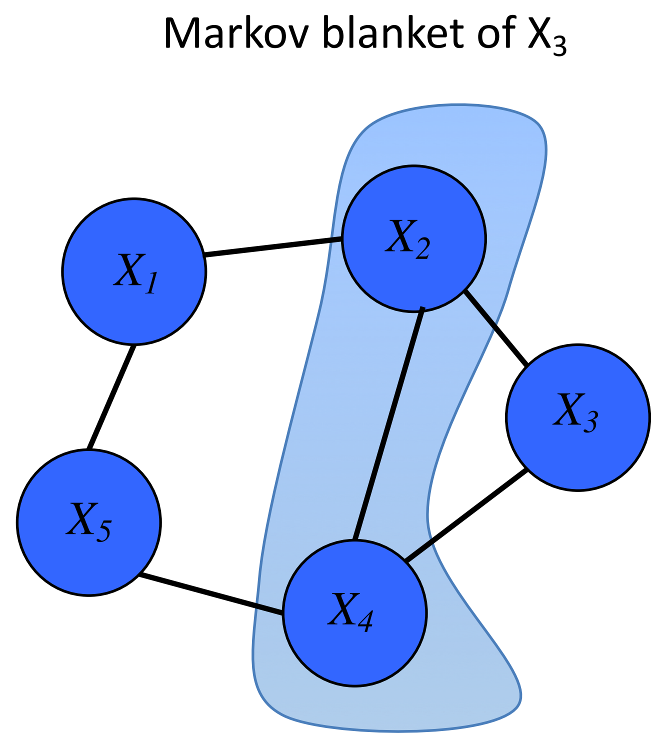
$$\mathbf{W}_{11}\beta - s_{12} + \lambda\psi_{12} = 0,$$
$$\text{where } \beta = -\theta_{12}/\theta_{22}$$

Graphical LASSO

- Let W be the current estimate of the inverse
- Repeat for each j^{th} row and column
  - Partition W into the two parts,
    - w_{12}: associated the j^{th} row and column, and
    - $\mathbf{W_{11}}$: for the rest
  - Solve the LASSO regression problem for the j^{th} to estimate β
  - Update $w_{12} = \boldsymbol{W}_{11}\beta$

Neighborhood selection

- Proposed by Meinshausen and Buhlmann 2006
- Markov blanket: The immediate neighborhood of a random variable
- Key idea: Find the Markov blanket or immediate neighbor set of each random variable



Neighborhood selection

- Here also we solve a set of regression problems for each random variable X_s

$$\frac{1}{2N}\sum_{i=1}^{N}(x_{is}-\sum_{j\neq s}x_{ij}\beta_{sj})^2+\lambda||\beta_s||_1$$

- The Markov blanket/neighborhood are those variables that have a non-zero coefficient
- Combine the neighborhood estimates using an AND or OR rule to create an undirected graph

Comparison between the two algorithms

- Neighborhood selection is fast compared to Graphical LASSO
- Neighborhood selection requires a "correction" to learn a valid structure, but this is not needed in Graphical LASSO