High-dimensional Bayesian inference of Graphical Models with Application to Brain Connectivity

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Bayesian Statistics in the Big Data Era

CIRM

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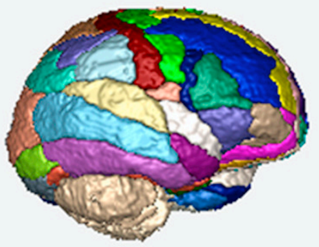
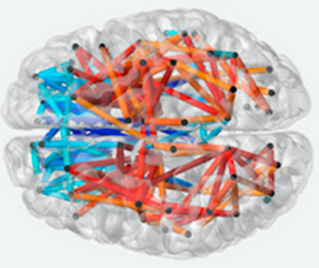
Graphcial inference for brain connectivity

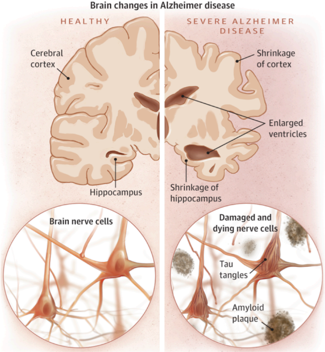
- Brain is complex system
- Treating neuro-deseases (e.g. Alzheimer) requires brain connectivity estimatoin
- Using graph theory to estimate brain connectivity
- Node is area of interest
- Link is connection between two area of brain

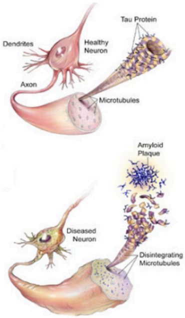




Brain connectivity and Alzheimer disease

- The most common neurodegenerative disease
- Can be assessed by various neuroimaging methods, MRI & PET



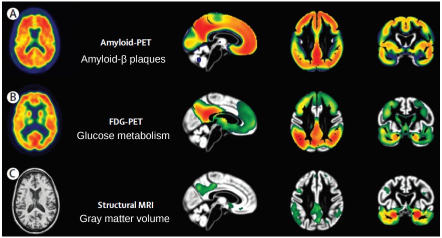


Dyrba, M., Mohammadi, A. & et al. (2017), Comparison of different hypotheses regarding the spread of Alzheimer's disease using Markov random fields and multimodal imaging, *Journal of Alzheimer Disease*

Dyrba, M., Mohammadi, R. & et al. (2018) "Assessing inter-modal and inter-regional dependencies in prodromal Alzheimer's disease using multimodal MRI/PET and Gaussian graphical models", *arXiv:1804.00049*

Data and Aim

	control	stage 1	stage 2	AD
Sample size	179	269	134	85
Age	73.8	71.4	72.4	75.6
Education	16.6	15.9	16.5	15.7
Delayed recall	7.5	5.9	3.3	0.7



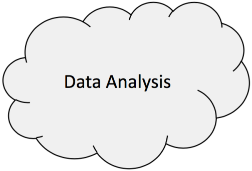
- 100 areas of brain
- 3 measurements

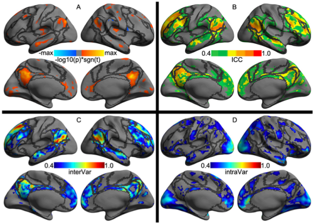
Aim

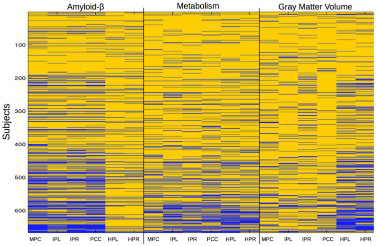
- Early detection of Alzheimer disease via graphical models
- Estimate brain connectivity for whole brain areas for each group

Dyrba, M., Mohammadi, A. & et al. (2018) "Assessing inter-modal and inter-regional dependencies in prodromal Alzheimer's disease using multimodal MRI/PET and Gaussian graphical models", *arXiv:1804.00049*

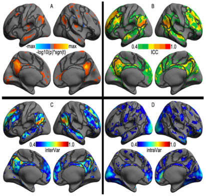
Data collection

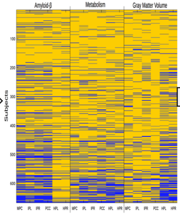






Graphcial inference for brain connectivity

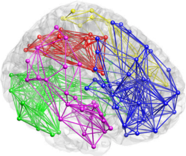




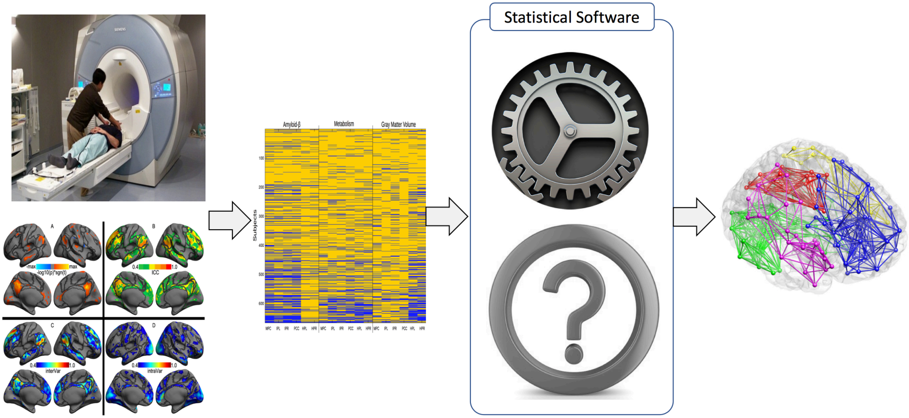
Statistical Software

User-friendly R package:

- **BDgraph**
- **ssgraph**

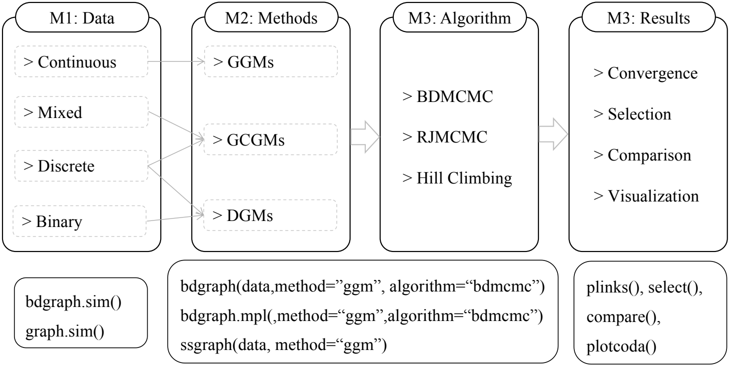


Graphcial inference for brain connectivity



Software for graph estimation

- **BDgraph** & **ssgraph**: Multi-core R package

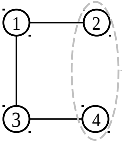


downloads 14K/month

Mohammadi, A. & Wit, E. (2017) BDgraph: An R Package for Bayesian Structure Learning in Graphical Models, *Journal of Statistical Software*, accepted

Mohammadi, A. & Dobra, A. (2017) “The R Package BDgraph for Bayesian Structure Learning in Graphical Models”, *ISBA Bulletin*

Graphical models and conditional independence



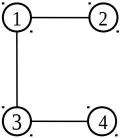
$X_2 \perp X_4 | X_1, X_3$
$X_1 \perp X_4 | X_2, X_3$
$X_2 \perp X_3 | X_1, X_4$

Gaussian graphical model: Graph $G = (V, E)$ as

$$X_1, \ldots, X_n \overset{iid}{\sim} \mathcal{N}_p(0, \Sigma), \qquad K = \Sigma^{-1} \text{ is positive definite based on G}$$

Graph, conditional independence and K:

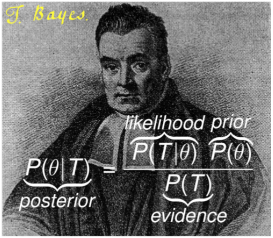
$$X_i \perp X_j \mid X_{V \setminus \{i,j\}} \quad \Leftrightarrow \quad k_{ij} = 0$$



$$K = \begin{bmatrix} k_{11} & k_{12} & k_{13} & 0 \\ & k_{22} & 0 & 0 \\ & & k_{33} & k_{34} \\ & & & k_{44} \end{bmatrix}$$

Bayesian structure learning in graphical models

$$Pr(G|data) = \frac{Pr(data|G)Pr(G)}{\sum_{G \in \mathcal{G}} Pr(data|G)Pr(G)}$$



Main problem

- Calculating posterior is not visible: graph-space $= 2^{p(p-1)/2}$
- Key is to detect **high posterior probability** regimes

Solutions: Search algorithm

- Reversible-jump MCMC: Green (1995, 1999), Dobra et al (2011)
- Shotgun stochastic search: Jones et al (2005)
- Birth-death MCMC: Mohammadi and Wit (2015)

Our solution: Birth-death MCMC

- BD-MCMC is continuous time Markov process
- Based on special birth-death process (Preston, 1976)
- Stationary distribution is joint posterior distribution of graph and parameters

Advantages of BD-MCMC

- In BD-MCMC move between models are always accepted
- BD-MCMC converges more faster than RJ-MCMC

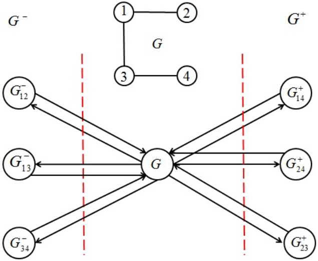
Mohammadi, A. & E. Wit (2015), Bayesian Structure Learning in Sparse Gaussian Graphical Models, *Bayesian Analysis*

BD-MCMC algorithm for GGMs

Theorem (Mohammadi and Wit, 2015)

Our birth-death MCMC algorithm has stationary distribution $Pr(G, K|\mathbf{x})$, if for each $e = (i, j)$

$$\beta_e(G) Pr(G, K|\mathbf{x}) = \delta_e(G^{-e}) Pr(G^{-e}, K^{-e}|\mathbf{x})$$

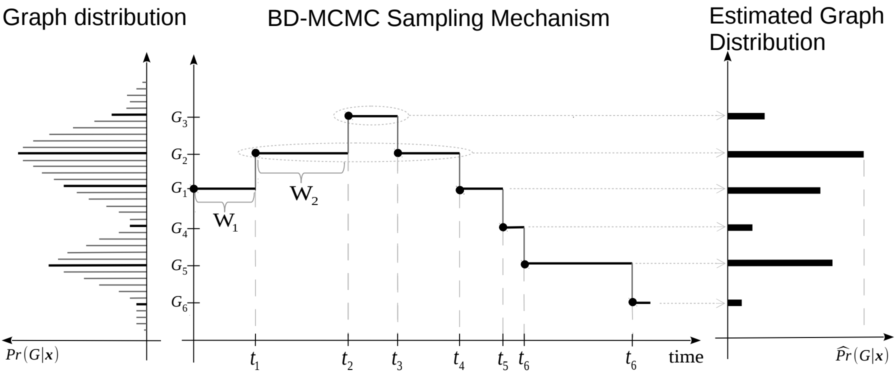


Preston (1976): Backward Kolmogorov

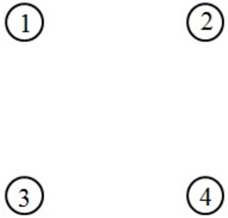
If balance conditions are hold, process converges to unique stationary distribution.

BD-MCMC search algorithm

- BD-MCMC is continuous time Markov birth-death process (Preston, 1976)
- Search in graph space: add/remove edge at birth/death event
- Stationary distribution is joint posterior of graph and parameters



Simple case of BD-MCMC



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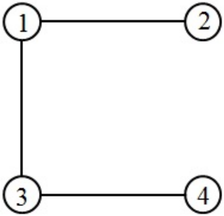

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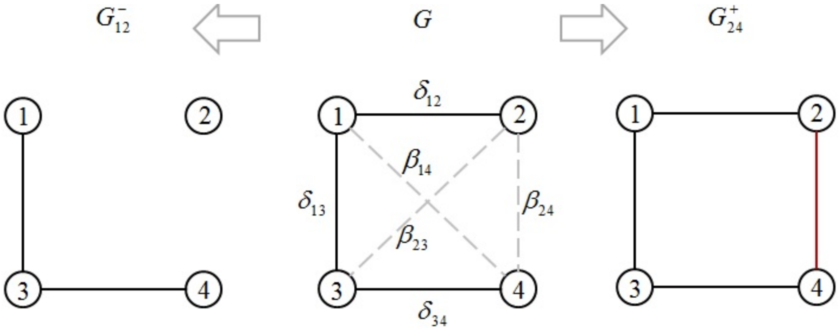

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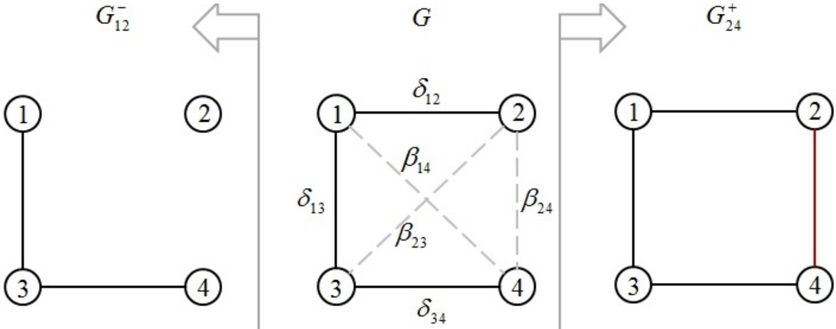


$$K_{12}^{-} = \begin{bmatrix} k_{11} & 0 & k_{13} & 0 \\ & k_{22} & 0 & 0 \\ & & k_{33} & k_{34} \\ & & & k_{44} \end{bmatrix} \quad K = \begin{bmatrix} k_{11} & k_{12} & k_{13} & 0 \\ & k_{22} & 0 & 0 \\ & & k_{33} & k_{34} \\ & & & k_{44} \end{bmatrix} \quad K_{24}^{+} = \begin{bmatrix} k_{11} & k_{12} & k_{13} & 0 \\ & k_{22} & 0 & k_{24} \\ & & k_{33} & k_{34} \\ & & & k_{44} \end{bmatrix}$$

BD-MCMC algorithm in GGMs

Step 1. Sampling from graph

1.1. Calculate birth and death rates

$$B_e(K) = \min\left\{ \frac{P(G^{+e}, K^{+e}|x)}{P(G, K|x)}, 1 \right\}$$

$$D_e(K) = \min\left\{ \frac{P(G^{-e}, K^{-e}|x)}{P(G, K|x)}, 1 \right\}$$

1.2. Calculate waiting time,

1.3. Simulate type of jump, birth or death

$$Pr(\text{birth of edge } e) \propto B_e(K)$$

$$Pr(\text{death of edge } e) \propto D_e(K)$$

Step 2. Sampling from new precision matrix: K^{+e} or K^{-e}

Bayesian framework in GGMs

Likelihood

$$Pr(\mathbf{x}|K, G) \propto |K|^{n/2} \exp\left\{-\frac{1}{2}\mathrm{tr}(KS)\right\}, \qquad \text{where } S = \mathbf{x}'\mathbf{x}$$

Prior for graph

- Discrete Uniform
- Truncated Poisson according to number of links

Prior for precision matrix

- G-Wishart: $W_G(b, D)$

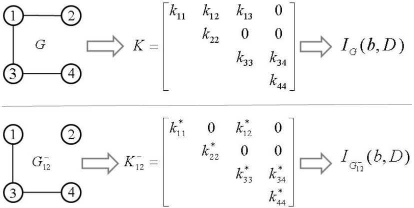
$$p(K|G) \propto |K|^{(b-2)/2} \exp\left\{-\frac{1}{2} tr(DK)\right\}$$

$$I_G(b, D) = \int_{\mathbb{P}_G} |K|^{(b-2)/2} \exp\left\{-\frac{1}{2} tr(DK)\right\} dK$$

Computational challenge

$$
\begin{aligned}
D_e(K) &= \frac{p(G^{-e}, K^{-e}|x)}{p(G, K|x)} \\
&= \boxed{\frac{I_G(b, D)}{I_{G^{-e}}(b, D)}} \left(\frac{|K^{-e}|}{|K|}\right)^{(b^*-2)/2} \exp\left\{-\frac{1}{2}\mathrm{tr}(D^*(K^{-e} - K))\right\}
\end{aligned}
$$

Normalizing constant of G-Wishart



Computational challenge

Exact form of Normalizing constant of G-Wishart

$$
\begin{aligned}
I_G(\delta, D) = \pi^{|I|/2}\, \Gamma_{|B|}\big(\delta + \tfrac{1}{2}(|B|+1)\big)|D_{BB}|^{-(\delta+\frac{1}{2}(|B|+1))} \\
\cdot \big(\det \partial_{I_1,I_2}(D, T_{AA})\big)^{-1/2} \\
\cdot \sum_{\substack{0\le j_{rs}<\infty \\ 1\le r\le s\le |I|}} \cdots \sum \big(\det \partial_{I_1,I_2}(D, U_{AA})\big)^{-j_{..}} \\
\cdot \Bigg(\prod_{1\le r\le s\le |I|} \frac{(1+\delta_{rs})^{j_{rs}}}{j_{rs}!}\, D^{j_{rs}}_{I_1(r),I_2(r)}\, D^{j_{rs}}_{I_1(s),I_2(s)} \\
\cdot \big(\mathrm{Cof}_{rs}\, \partial_{I_1,I_2}(D, U_{AA})\big)^{j_{rs}}\Bigg) \\
\cdot I_{G_A}\big(\delta + \tfrac{1}{2}|I| + j_{..}, U_{AA}\big)\Big|_{U_{AA}=T_{AA}}\Big|_{T_{AA}=D_{AA}}
\end{aligned}
$$

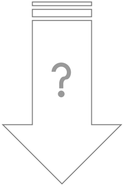
- Is it possible to implement it in model search algorithm?

Uhler, C., Lenkoski, A. & Richards, D. (2018) Exact formulas for the normalizing constants of Wishart distributions for graphical models, *Ann. Statist.*

Computational challenge

- Double Metropolis–Hasting (Murray & Ghahramani 2011)
- Our solution:

$$\frac{I_{G-e}(b, I_p)}{I_G(b, I_p)} = \frac{1}{2\sqrt{\pi}} \frac{\Gamma(b/2)}{\Gamma((b+1)/2)} \frac{\mathbb{E}\Big(\exp -\frac{1}{2}(\sum_{(i,j)\in \bar{E}} \psi_{ij}^2 + \psi_e^2)\Big)}{\mathbb{E}(\exp -\frac{1}{2}\sum_{(i,j)\in \bar{E}} \psi_{ij}^2)}.$$

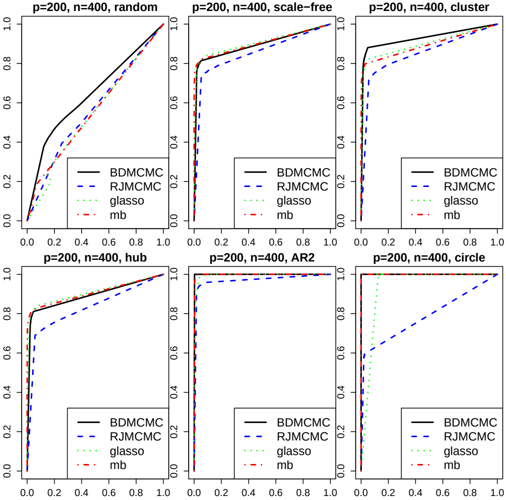


$$\frac{I_{G-e}(b, I_p)}{I_G(b, I_p)} \approx \frac{1}{2\sqrt{\pi}} \frac{\Gamma(\frac{b+d}{2})}{\Gamma(\frac{b+d+1}{2})}$$

Mohammadi, R., Massam, H., & Letac, G. (2017), The ratio of normalizing constants for Bayesian graphical Gaussian model selection, *arXiv:1706.04416*

Simulation study

ROC plot for 6 different graph Structures in GGMs with p=200, n=400



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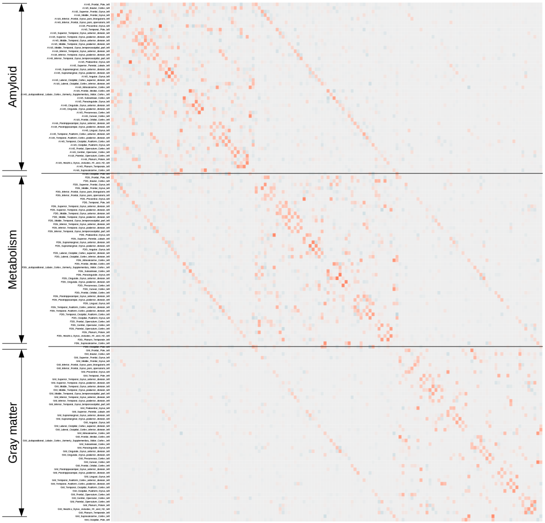
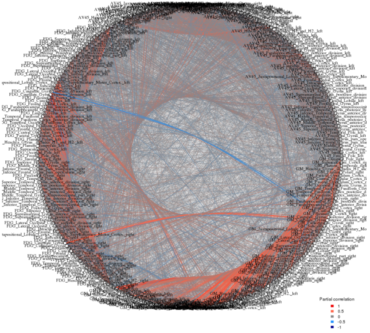
Results for brain connectivity

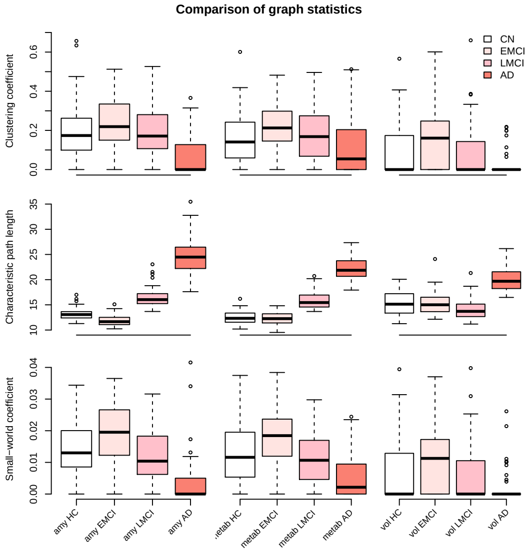




Connections > 3000
How can we interpret connectivity network?

Dyrba, M., Mohammadi, A. & et al. (2018) "Assessing inter-modal and inter-regional dependencies in prodromal Alzheimer's disease using multimodal MRI/PET and Gaussian graphical models", *arXiv:1804.00049*

Results for brain connectivity



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Extension to high-dimensional graphical models

Using Multivariate Birth-Death processes

- Instead of add/delete one link per time, add/delete multiple links

Using Pseudo-likelihood estimation

- replacing our likelihood with pseudo-likelihood:

$$Pr(G|x) = \frac{1}{Pr(x)} Pr(G) Pr(x|G)$$

$$Pr(x|G) = \int_{\theta_G} Pr(x, \theta_G | G)$$

$$Pr(x, \theta_G | G) \propto \sum_{i=1}^{p} Pr(x_i | x_V, \theta_G)$$

Dobra, A., & Mohammadi, R. (2018), Loglinear model selection and human mobility, *The Annals of Applied Statistics*

Wrap-up

Summary

- Develop Bayesian statistical methods for network analysis of high-dimensional data
- Compile methods into R-packages: BDgraph and ssgraph
- Applied our method to Alzheimer disease

Extension

- Applying to high-dimensional graphical models (Using Pseudo-likelihood estimation)

References

- Mohammadi, A. & E. Wit (2015), Bayesian Structure Learning in Sparse Gaussian Graphical Models, *Bayesian Analysis*
- Mohammadi, A. and E. Wit (2016), BDgraph: An R Package for Bayesian Structure Learning in Graphical Models, *Journal of Statistical Software*, accepted
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