

Graphical Models (Bayes Nets) for Medical Applications

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Outline

Bayesian Networks for Data Visualization and Biomarker Selection

- Liver diseases in obesity

- Weight Loss Prediction

Bayesian Networks for Data Visualization and Biomarker Selection

Liver diseases in obesity

Weight Loss Prediction

Motivation

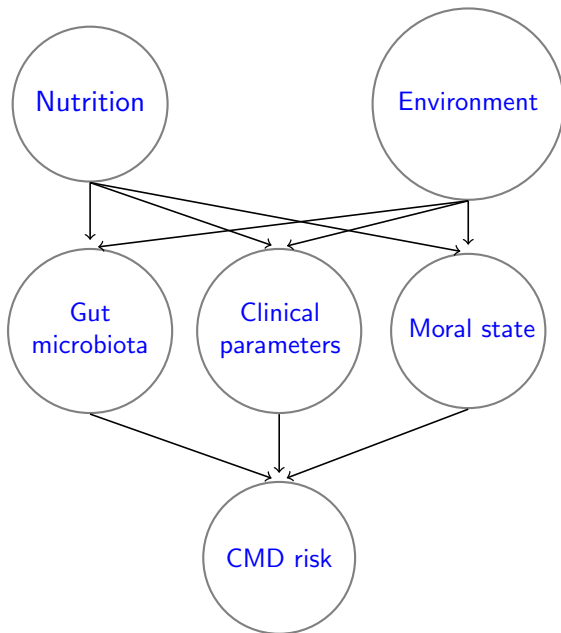
Graphical models(Bayesian Networks)

- ▶ Compact representation for expressing joint or conditional probability distributions
- ▶ Efficient framework for inference and learning

In the biological science

- ▶ Cellular networks
- ▶ Modeling protein signaling pathways
- ▶ **Systems biology, data integration**
- ▶ Classification (structured)
- ▶ Genetic data analysis

Motivation Example: Data Integration



Graphical Models: Directed and Undirected

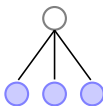
Graphical models

- ▶ are a marriage between probability theory and graph theory
- ▶ deal with uncertainty and complexity
- ▶ exploit interdependencies in data

▶ Undirected Graphical Models

- ▶ Markov random field

- ▶ Logistic regression



Graphical Models: Directed and Undirected

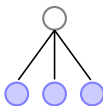
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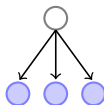
- ▶ Markov random field

- ▶ Logistic regression



▶ Directed Graphical Models

- ▶ **Bayesian Networks** (Hidden Markov Models, Kalman Filter)
- ▶ Clear “causality” in models (A “causes” B)
- ▶ Easier to learn (than undirected models)



- ▶ Naive Bayes

Bayesian Networks: Generalities

- ▶ Directed Acyclic Graph (efficient inference and learning)
- ▶ Variables are nodes
- ▶ Relations between nodes are edges
- ▶ Relationship between variables — conditional probability distributions
- ▶ Prior probabilities

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Bayesian Networks

- ▶ do not necessarily imply a commitment to Bayesian statistics
- ▶ It is common to use frequentists methods to estimate the parameters
- ▶ Use Bayes' rule for probabilistic inference

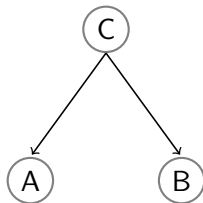
Conditional Independence

The simplest conditional independence relationship encoded in BN:
a node is independent of its ancestors given its parent:

$$p(x) = \prod_{i=1}^N p(x_i | x_{\text{pa}_i}).$$

Example

$$p(a, b, c) = p(c)p(a|c)p(b|c)$$



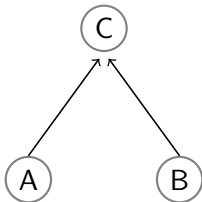
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Bayesian Networks: Learning

- ▶ Bayesian Networks are used to model a joint probability distribution.
- ▶ A set of model parameters θ may be learned for the data in such a way that maximizes the likelihood that the data came from this distribution
- ▶ Given a set of observed data $\mathcal{D} = \{x_i\}_{i=1}^N$, the likelihood

$$L(\theta) = p(\mathcal{D}|\theta) = \prod_{i=1}^N p(x_i|\theta).$$

Bayesian Networks: Inference

Inference is straightforward:

$$p(a|b)$$

is calculated as a product of relevant conditional probabilities using Bayes' rule:

$$p(a|b) = \frac{p(b|a)p(a)}{p(b)}.$$

Direct computation is **very expensive** \implies **exploit the structure of the graph**:

- ▶ Max-sum algorithm
- ▶ Sum-product algorithm

Bayesian Networks: Approximated Training

Many models of interest are **too big**, and the exact training is **not tractable**.

- ▶ Variational methods
- ▶ Sampling (Monte-Carlo) methods
- ▶ Loopy belief propagation
- ▶ Bounded cutset conditioning
- ▶ Parametric approximation methods

Structure Learning

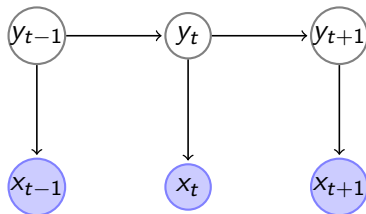
Structure	Observability	Method
Known	Full	Maximum Likelihood Estimation
Known	Partial	Expectation-Maximization Algorithm
Unknown	Full	Search through model space
Unknown	Partial	Expectation-Maximization + search through model space

Dynamic Bayesian Networks

Bayesian Networks can be used to model **times series**: the variables are **indexed by time and replicated** in the Bayesian Networks.

Special cases of Dynamic Bayesian Networks

- Hidden Markov Models



- Cyclic Bayesian Networks (apply loopy belief propagation)

Liver diseases in obesity : Non-alcoholic-fatty liver disease (NASH)

- ▶ NASH is a comorbidity associated largely with obesity which represents a risk factor for cardiovascular outcomes.
- ▶ How to extract metabolic signatures associated with NASH in very well phenotyped morbidly obese patients?
- ▶ Lipidomics analysis in systemic blood demonstrated an increased concentration of several Glycerophosphocholines (PC), Glycerophosphoethanolamines (PE), Glycerophosphoinositols (PI), Glycerophosphoglycerols (PG), Lyso-Glycerophosphocholines (LPC), and Ceramides (Cer) in NASH subjects.

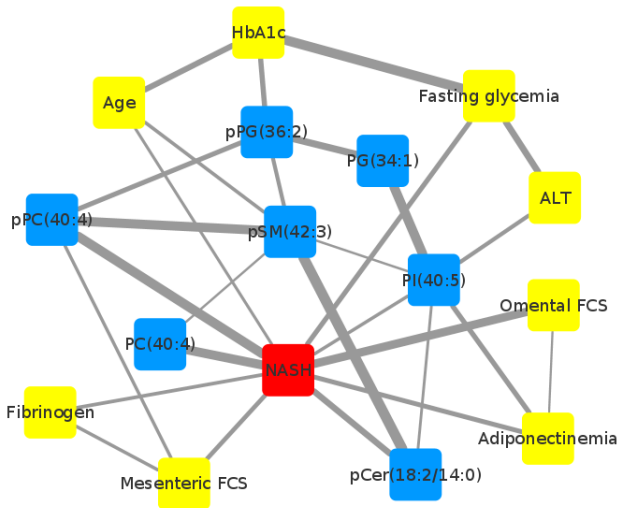
Liver diseases in obesity : Non-alcoholic-fatty liver disease (NASH)

The **objective**: to identify a signature of NASH that combines lipidomic profile of portal blood, systemic blood, as well as clinical parameters.

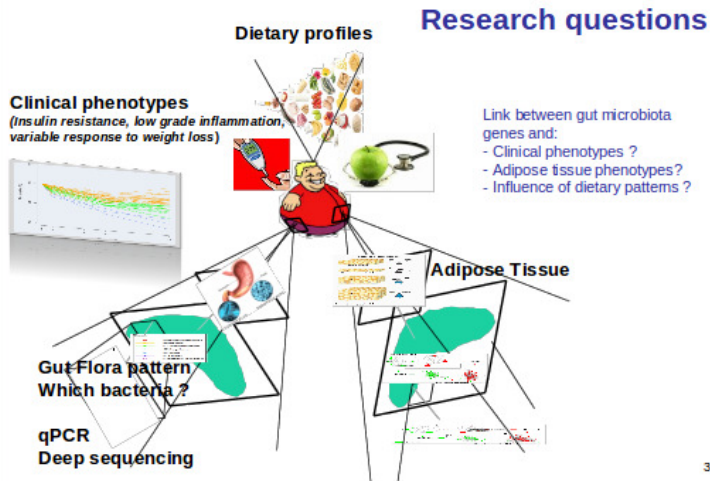
A **statistical machine learning** method to extract a signature:

- ▶ apply a SVM (support vector machine) to reduce the dimensions
- ▶ run a Bayesian network to reveal dependencies between the variables

Liver diseases in obesity : Non-alcoholic-fatty liver disease (NASH)



Weight Loss Prediction



Weight Loss Prediction

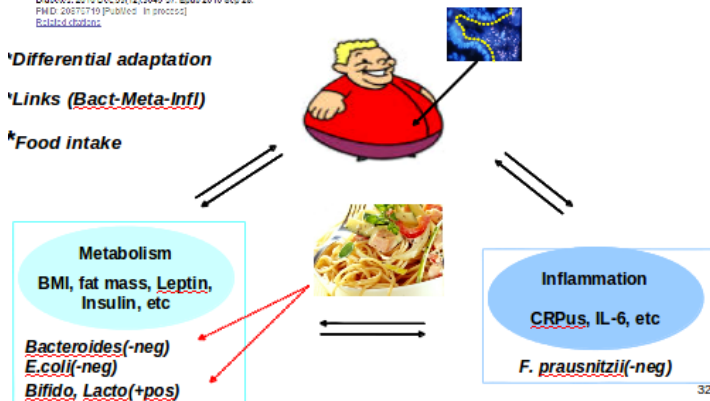
Gut microbiota differentially adapts after GBP

- ✓ [Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low-grade inflammation markers](#)
- Furet JP, Kong LC, Tap J, Porcari C, Gasdevant A, Bonifant JL, Manol D, Corthier G, Doré J, Heneghan C, Rizkalla S, Clément K. *Diabetes*. 2010 Dec 9;123(12):3049-57. Epub 2010 Sep 28. PMID: 20875719 [Published: In process] [Related citations](#)

'Differential adaptation

'Links (Bact-Meta-Infl)

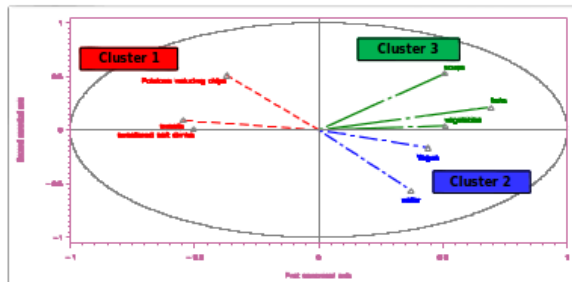
***Food intake**



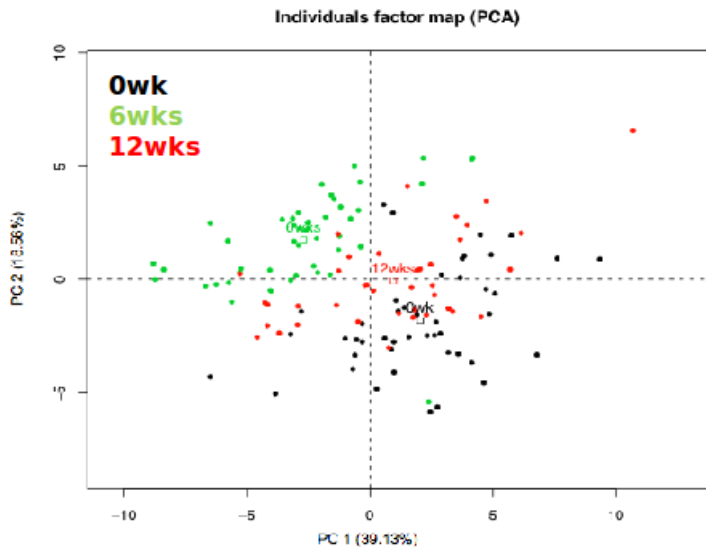
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J.P. Furet et al., Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low-grade inflammation markers. *Diabetes*, 2010

Weight Loss Prediction



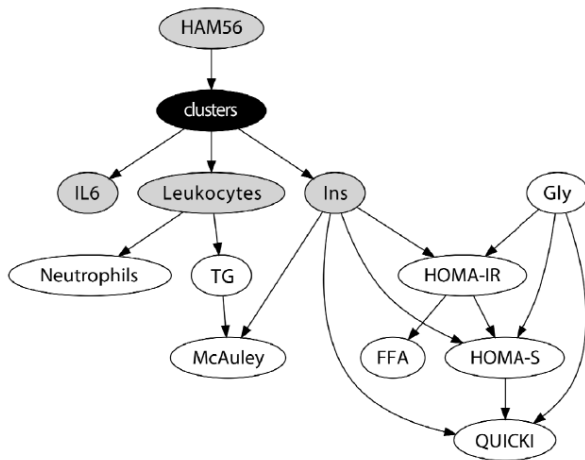
Weight Loss Prediction



Weight Loss Prediction

- ▶ Can gut microbiota, food items taken by the patients, and metabolic and inflammatory parameters predict the weight variation and metabolic outcomes?
- ▶ A Bayesian network approach was applied to find the best predictors of weight loss induced by energy restricted diet and obesity surgery intervention [L. Kong et al., 2013].
- ▶ A relatively small number of significant bioclinical variables has been chosen in this model.

Weight Loss Prediction



L. Kont et al., Insulin resistance and inflammation predict kinetic body weight changes in response to dietary weight loss and maintenance in overweight and obese subjects: using a Bayesian network approach. AJCN, 2013

Conclusions & Perspectives

► Conclusions

- Many systems biology applications have already taken advantage of statistical machine learning
- Some frameworks are relatively well studied
- Some approaches are very efficient

► Perspectives

- Data integration
- Optimization in large-scale models
- Compare various graphical models
- Graphical models of arbitrary structure

References

- ▶ Cotillard, A. et al. Dietary intervention impact on gut microbial gene richness. Nature doi:10.1038/nature12480, 2013.
- ▶ Le Chatelier, E. et al. Richness of human gut microbiome correlates with metabolic markers. Nature <http://dx.doi.org/10.1038/nature12506>, 2011
- ▶ Kong, L. et al. Insulin resistance and inflammation predict kinetic body weight changes in response to dietary weight loss and maintenance in overweight and obese subjects by using a Bayesian network approach. Am J Clin Nutr 2013; 98:110.
- ▶ T. Hastie, R. Tibshirani, J. Friedman. Elements of statistical learning. Springer, 2009
- ▶ A number of books on R for applied statistics/bioinformatics/systems biology