Bayesian nonparametric methods for clustering
Part 2: Outcome-guided analysis

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Summary of Part 1:

Nonparametric clustering

- ○ Heterogeneous population with unknown clusters
- ○ Cluster number estimated from the data
- ○ Unconstrained number of clusters

Characterized by

- ○ One or several variables (Gaussian, skew t-distributions...)

Bayesian framework

- ○ Dirichlet process prior
- ○ MCMC estimation

Introduction of Part 2:

Nonparametric clustering

- Heterogeneous population with unknown clusters
- Cluster number estimated from the data
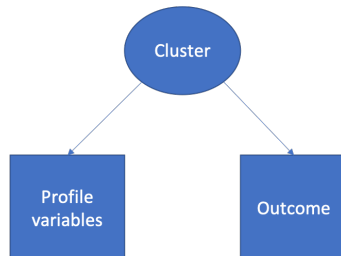- Unconstrained number of clusters

Characterized by

- One or several variables (Gaussian, skew t-distributions...)
- An outcome used as noisy surrogate for clusters (Bair, 2013)

Bayesian framework

- Dirichlet process prior
- MCMC estimation

Outcome-guided clustering

$\rightarrow$ Subgroups with specific outcome distributions and variable profiles

$\rightarrow$ Independence between profile variables and outcome conditionally on the clusters

Motivational example - Dementia study

Dementia

Syndrome (chronic or progressive nature)

Deterioration in cognitive functions

Impairment of the social and occupational functioning.

Precision medicine

Improve disease prevention and treatment

Refine patient characterisation

Predict disease risk and treatment effect at the individual level

Profile regression: methodology

Notations:

Y_i vector of individual outcome measurements
$W_i = (w_{i1}, ..., w_{iP})^\top$ individual vector of profile variables
c_i allocation variable

Likelihood:

$$L(\theta|Y, W) = \prod_{i=1}^{N} \sum_{g}^{\infty} P(c_i = g|\theta^c) \, f(W_i|c_i = g; \theta_g^W) \, f(Y_i|c_i = g; \theta_g^Y)$$

Independence assumption between W and Y given the cluster allocations.

Profile regression: membership probability

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Y_i vector of individual outcome measurements
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Likelihood:

$$L(\theta|Y, W) = \prod_{i=1}^{N} \sum_{g}^{\infty} \underbrace{P(c_i = g|\theta^c)}_{\text{Membership prob.}} f(W_i|c_i = g; \theta_g^W) \, f(Y_i|c_i = g; \theta_g^Y)$$

Independence assumption between W and Y given the cluster allocations.

Sub-model: Dirichlet Process mixture model

$\mathcal{A} = \sum_{g=1}^{G} \pi_g \, \delta_{\theta_g}$ 　　　　　　 $\boldsymbol{\pi}|\alpha \sim Dirichlet(\alpha/G, ..., \alpha/G)$

　　　　　　　　　　　　　　　 $c_i|\boldsymbol{\pi} \sim Multinom(\boldsymbol{\pi})$

α : Concentration parameter 　　　 $\theta_{c_i}|\mathcal{A}_0 \sim \mathcal{A}_0$

$\mathcal{A}_0$: Base distribution 　　　　　 $Y_i, W_i|c_i \sim f(\cdot; \theta_{c_i})$

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Independence assumption between W and Y given the cluster allocations.

Sub-model: Dirichlet Process mixture model

$\mathcal{A} = \sum_{g=1}^{+\infty} \pi_g \, \delta_{\theta_g}$ $\qquad\qquad$ $\pi|\alpha \sim GEM(\alpha)$

$\qquad\qquad\qquad\qquad\qquad$ $c_i|\pi \sim Multinom(\pi)$

α : Concentration parameter $\qquad$ $\theta_{c_i}|\mathcal{A}_0 \sim \mathcal{A}_0$

$\mathcal{A}_0$: Base distribution $\qquad\qquad$ $Y_i, W_i|c_i \sim f(\cdot; \theta_{c_i})$

Profile regression: profile variables

Notations:

Y_i vector of individual outcome measurements
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c_i allocation variable

Likelihood:

$$L(\theta|Y, W) = \prod_{i=1}^{N} \sum_{g}^{\infty} P(c_i = g|\theta^c) \underbrace{f(W_i|c_i = g; \theta_g^W)}_{\text{Profile variables}} f(Y_i|c_i = g; \theta_g^Y)$$

Independence assumption between W and Y given the cluster allocations.

Sub-model for profile variables: given $c_i = g$,

Discrete case: $\quad W_i^{(1)} \sim Multinom(\phi_{\mathbf{g}})$
Continuous case: $W_i^{(2)} \sim \mathcal{N}_P(\mu_{\mathbf{g}}; V_g)$

Profile regression: outcome

Notations:

Y_i vector of individual outcome measurements
$W_i = (w_{i1}, ..., w_{iP})^\top$ individual vector of profile variables
c_i allocation variable

Likelihood:

$$L(\theta|Y, W) = \prod_{i=1}^{N} \sum_{g}^{\infty} P(c_i = g|\theta^c) \; f(W_i|c_i = g; \theta_g^W) \; \underbrace{f(Y_i|c_i = g; \theta_g^Y)}_{\text{Outcome}}$$

Sub-model for outcome: given cluster g,

$$Y_i \sim \mathcal{N}(\theta_g + \beta^\top X_i, \sigma_g^2)$$

Other types of outcomes:
Bernoulli, Poisson, Binomial, Categorical, Quantile, Survival

Estimated cluster-specific parameters

- MCMC Gibbs sampler: $\Theta = (\alpha, [\phi]_g, [\mu]_g, [V]_g, c, \beta)$

- Posterior similarity matrix S from pairwise co-clustering probability

- Selection of the representative clustering P^*

    Partitioning around medoids on dissimilarity matrix $1 - S$
    Average silhouette width

Estimated cluster-specific parameters

- MCMC Gibbs sampler: $\Theta = (\alpha, [\phi]_g, [\mu]_g, [V]_g, c, \beta)$

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$$[\phi]_g \sim f([\phi]_g \mid \alpha, [\mu]_g, [V]_g, c, \beta) \text{ etc...}$$

- Posterior similarity matrix S from pairwise co-clustering probability

- Selection of the representative clustering P^*

  Partitioning around medoids on dissimilarity matrix $1 - S$
  Average silhouette width

Estimation

Cluster-specific parameters as the average over the MCMC iterations:

$$\bar{\Theta}_g^{(k)} = \frac{1}{N_g} \sum_{i | c_i^* = g} \Theta_{c_i^{(k)}}$$

$\Theta_{c_i^{(k)}}$ parameter for the cluster subject i is allocated to, at iteration k

N_g the number of subjects in cluster g of P^*.

Estimation

Cluster-specific parameters as the average over the MCMC iterations:

$$\hat{\Theta}_g = \frac{1}{K} \sum_{k=1}^{K} \frac{1}{N_g} \sum_{i|c_i^*=g} \Theta_{c_i^{(k)}}$$

$\Theta_{c_i^{(k)}}$ parameter for the cluster subject i is allocated to, at iteration k
N_g the number of subjects in cluster g of P^*.

Estimation

Cluster-specific parameters as the average over the MCMC iterations:

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$\Theta_{c_i^{(k)}}$ parameter for the cluster subject i is allocated to, at iteration k

N_g the number of subjects in cluster g of P^*.

$\rightarrow$ Integration of the clustering uncertainty in the parameters estimation.

$\rightarrow$ Empirical credible intervals computed from MC sample of $\bar{\Theta}_g^{(k)}$

Convergence

Difficult to assess convergence based on parameters traces:

- Fixed effects converge quickly

- Cluster-specific parameters not traceable

- If stuck in local mode, α not good indicator (Hastie et al., 2014)

$\rightarrow$ Marginal partition posterior $p(C|Y, W)$

- identify runs that were significantly different from others, perhaps due to convergence issues

- which run explored the higher posterior probability regions

Application to ADNI data - (Rouanet et al. 2020)

Objective : Identify subgroups of the population associated with specific cognitive evolution patterns and brain imaging profiles.

- ○ North American Alzheimer's Disease Neuroimaging Initiative
- ○ Sample of 199 subjects, 55 years old and over, 8-year follow-up
- ○ Normalised Mini-Mental State Examination (Philipps et al., 2014)

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- ○ Profile variables:

    - → Standardised MRI brain volumes: whole brain, ventricles, hippocampus, entorhinal cortex, fusiform gyrus and middle temporal gyrus, standardised by the intracerebral volume

    - → Gender (1 for women, 0 for men) and Education (1 if greater than or equal to 16 years of education, 0 otherwise), APOE4 status (1 if 1 or 2 APOE4 alleles, 0 otherwise)

Model specification

Profile variables, given cluster g:

Gender, Sex, Education:
$W_i^{(1)} \sim Bernouilli(\phi_g)$ with $\phi_g \sim Dirichlet(a_j)$

Standardized MRI brain volumes:
$W_i^{(2)} \sim \mathcal{N}_P(\mu_g; V_g)$ with $\mu_g \sim \mathcal{N}_P(\mu_0; V_0)$, $V_g \sim InvWishart(R_0, K_0)$

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Longitudinal normalized MMSE, given cluster g:

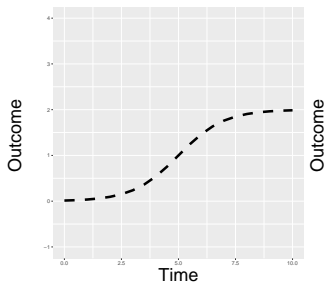$Y(t_i) = f_g(t_i) + \epsilon_g(t_i)$ with $\epsilon_g \sim \mathcal{N}(0, L_{1,g})$

$f_g(\cdot) \sim GP(\mathbf{0}, \mathcal{K}_g(\cdot, \cdot))$ with $\mathcal{K}_g(s, t) = L_{g,2} \exp\left(-\frac{(s-t)^2}{L_{g,3}}\right)$

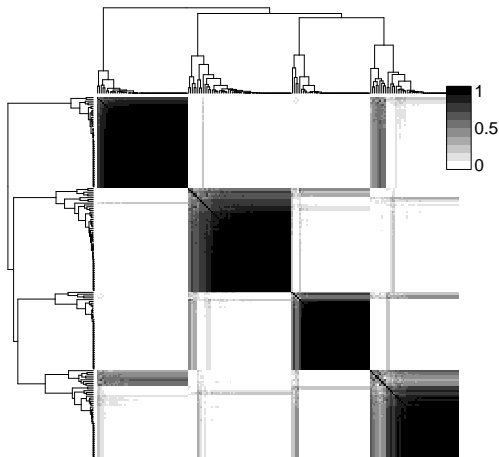$$\exp(L_{g,l}) \sim \mathcal{N}(0, \sigma_l^2)$$

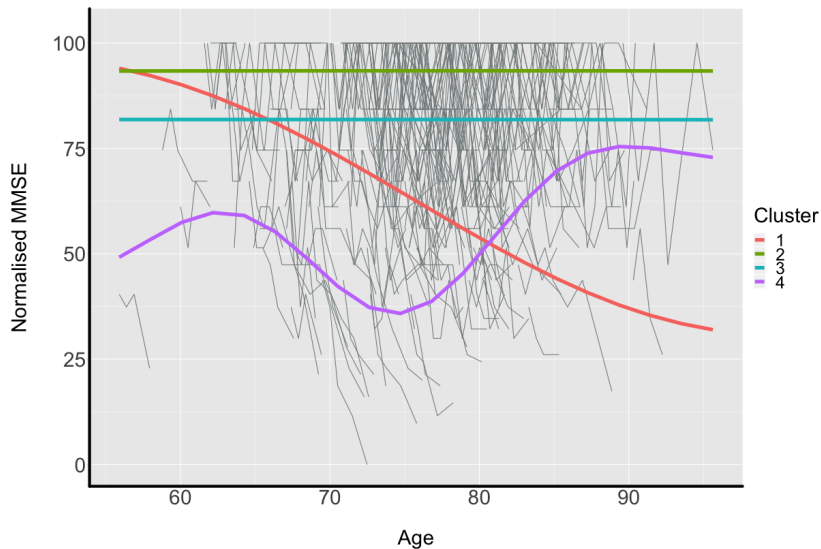# Gaussian Process prior

Given the cluster g :

$$Y_{ij} = f_g(t_{ij}) + \epsilon_{ijg} \text{ with } \epsilon_{ijg} \sim \mathcal{N}(0, L_{g,1})$$
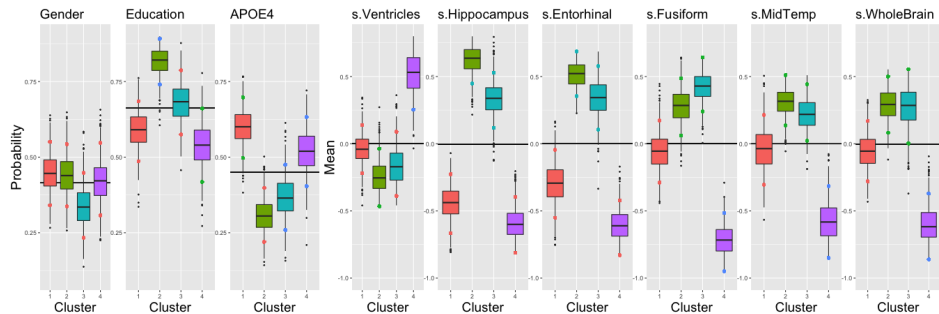$$f_g(\cdot) \sim GP(m_g(\cdot), \ \mathcal{K}_g(\cdot, \cdot))$$
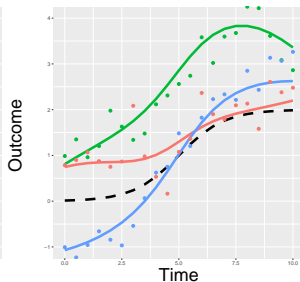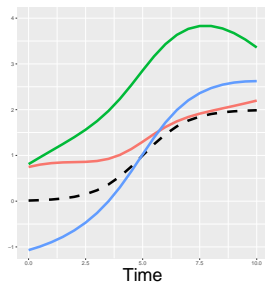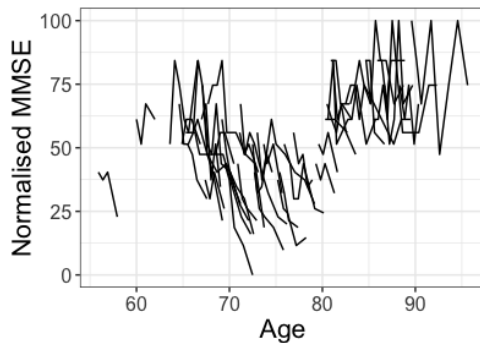
Posterior similarity matrix

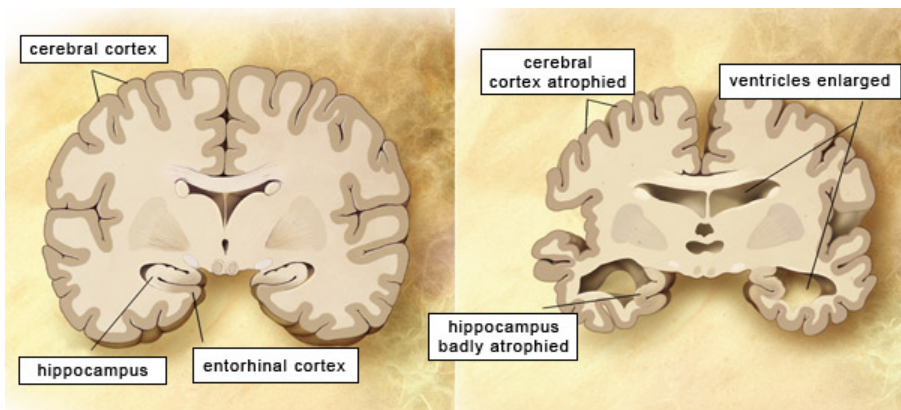# Cluster-specific cognitive patterns

Cluster profiles

Cognitive pattern in cluster 4

Discussion

Conclusion

Mixture model with unconstrained number of clusters

Outcome-guided clustering analysis

Integration of different types of profile variables

Extension of the ℝ package **PReMiuM**

Practical

Hands-on exercises on the PReMiuM package (profRegr function)

Data on cognitive decline from lcmm package

Details on DP parameters

References

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Rouanet A, et al. Bayesian profile regression with a longitudinal response.

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Bair, E. (2013). Semi-supervised clustering methods. Wiley Interdisciplinary Reviews: Computational Statistics, 5(5): 349–361.