Nonparametric bayesian modelling of individual co-exposures to various pesticides to determine cocktails

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Périclès project (ANR 2009-2011)

- For statisticians
  What are the cocktails of pesticides simultaneously present in the diet ?
  - Co-exposure assessment
  - Co-exposure clustering
- For toxicologists
  What are the possible combined effects of multiple residues of pesticides ?

Data

- **Contamination levels :** (DGCCRF, DGAL, SISE-EAUX)
  - $p = 1, \ldots, P = 79$ pesticides
  - $a = 1, \ldots, 121$ commodities
  - H : 0 if the value $< LOD$
- **Consumption :** the National French survey (INCA 2, 2006)
  - consumed quantities c_{ia} of $n = 3,337$ individuals
    $n = 1,439$ children (3-17 years) and $n = 1,898$ adults
  - 7 days detailed

Empirical exposure distribution x_{imp}

$$x_{imp} = \log_{10}\left(\sum_{a=1}^{A_p} c_{ia} \times q_{pam} / w_i\right)$$

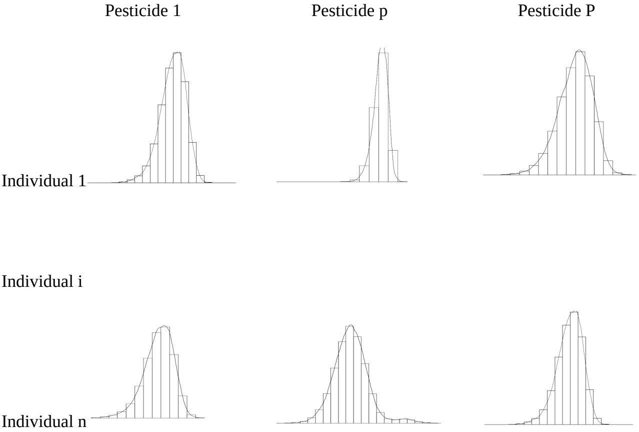
M=100 values computed by

- randomly sampling for each individual i and pesticide p
  - consumptions of food a observed on a day : c_{ia}
  - pesticide residue levels q_{pam} of the different commodities A_p
- dividing by the associated individual body weight w_i
- normalized the logarithm of exposures

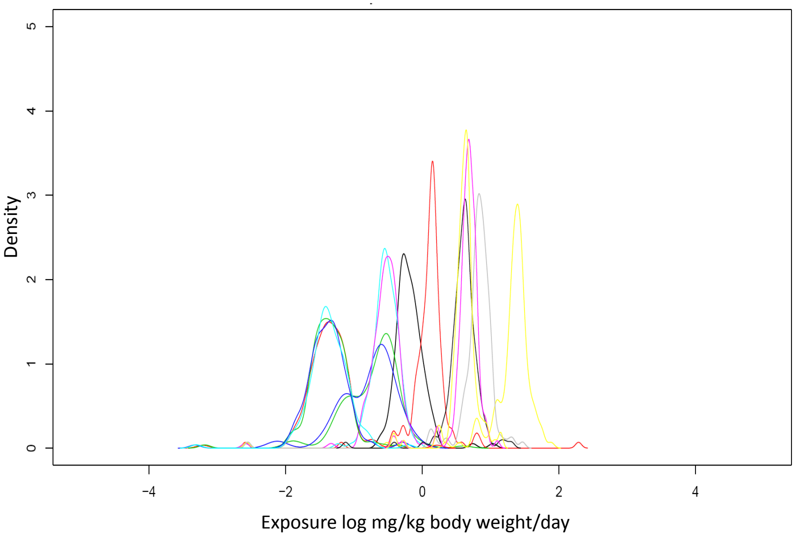
Exposure Structure

Co-exposures, $\{x_{imp}, i$:individuals ; m :residues levels ; p :pesticides$\}$

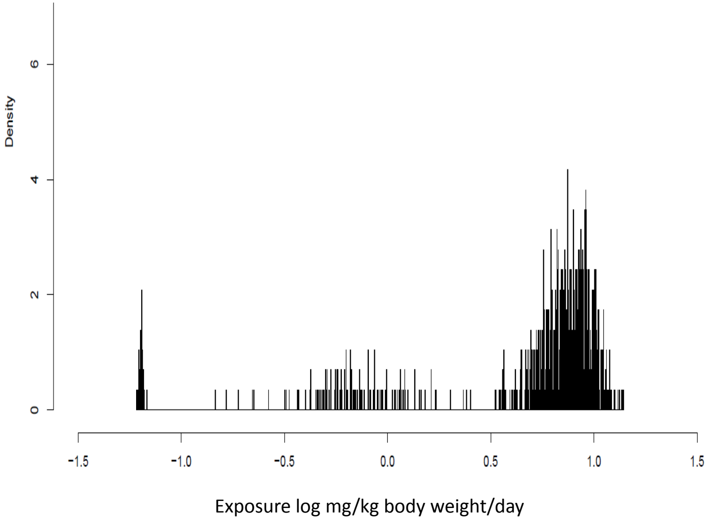
- $M = 1, 95^{th}$ percentile of exposure to each pesticide P
- $M = 100$, account for contamination variability



Co-exposures of 15 children to 79 pesticides



Children exposure to a single pesticide



Infinite Mixture Models
Non-parametric Bayesian Models

- A way of getting very flexible models
- No assumption on the number of mixture components
- No prior parametric assumption
- Infer an adequate model (size/complexity) without doing Bayesian model comparison (AIC, DIC...)
- Derived from finite parametric model with number of parameters going to infinity

Mixture Models

Let $x = (x_1, \ldots, x_n)$, with x_i a P dimensional vector $x_i = (x_{i1}, \ldots, x_{iP})$ distributed with a density of probability :

$$f(x) = \int_\Theta k(x|\theta)G(d\theta)$$

where

- $k(.|\theta)$ the known density of the mixture components,
- $\theta \in \Theta$ is a latent variable,
- G the unknown mixture distribution, infinite dim. parameter

How to place an appropriate prior on G ?

Dirichlet Process - DP

Define *a prior* on a unknown probability distribution

- $G|\gamma, H \sim \mathcal{D}(dG|\gamma, H)$ is a Dirichlet process with parameters
  - a real $\gamma > 0$
  - a probability measure H
- if and only if for any partition $B_1, \dots, B_K$ of Ω,

$$(G(B_1), \dots, G(B_K)) \sim \text{Dir}(\gamma H(B_1), \dots, \gamma H(B_K))$$

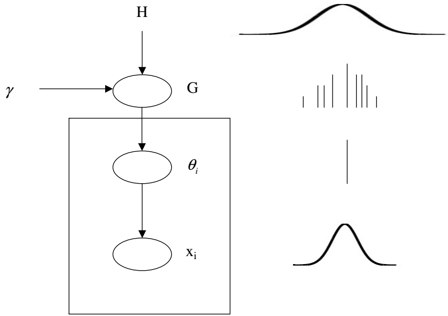
- $\mathbb{E}[G(B)] = H(B) \qquad \mathbb{V}[G(B)] = H(B)(1 - H(B))/(1 + \gamma)$

Dirichlet Process Mixture Models - DPM

$$G \sim DP(\gamma, H)$$

$$\theta_i | G \sim G$$

$$x_i | \theta_i \sim k(.|\theta_i)$$



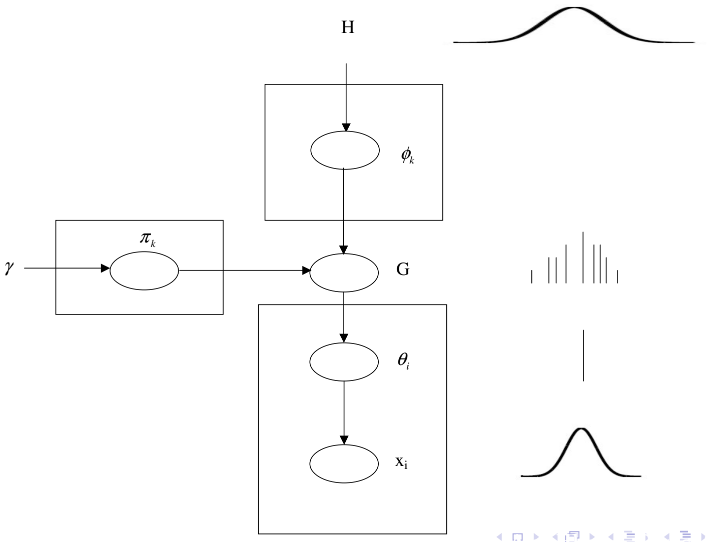
Stick-Breaking Representation - SB

Sample $G \sim DP(\gamma, H) \Leftrightarrow G = \sum_{k=1}^{\infty} \pi_k \delta_{\phi_k}$

- $\phi_k \sim H$
- Infinite mixing proportions, $\sum_{k=1}^{\infty} \pi_k = 1 : \pi_k = \beta_k \prod_{l=1}^{k-1} (1 - \beta_l)$
- Infinite sequence of Beta r.v. : $\beta_k \sim Beta(1, \gamma)$
- Good quality of approximation for reasonable $K < \infty$

  $G = \sum_{k=1}^{K} \pi_k \delta_{\phi_k}$ (Ishwaran and James 2001)

Stick-Breaking Representation - SB



Modeling co-exposure to pesticides $M = 1$

$x = (x_1, \ldots, x_n)$, with x_i a P dimensional vector $x_i = (x_{i1}, \ldots, x_{iP})$

$$
\begin{aligned}
x_i|\theta_i &\sim k(.|\theta_i) && (1)\\
\theta_i|G &\sim G && (2)\\
G &\sim DP(\gamma, H) && (3)
\end{aligned}
$$

- kernel k : a MultivariateNormal $\mathcal{N}(\mu, \tau)$, $\phi = (\mu, \tau)$
- base probability measure H : the conjugate Normal-Wishart

Model for cocktails of pesticides $M = 100$

One level of hierarchy

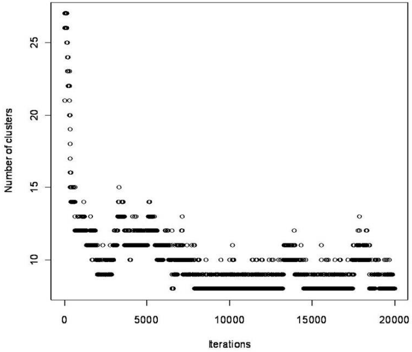
$x_{im} = (x_{pim}, p = 1, \ldots, P)$ with $i = 1, \ldots, n$ and $m = 1, \ldots, M$

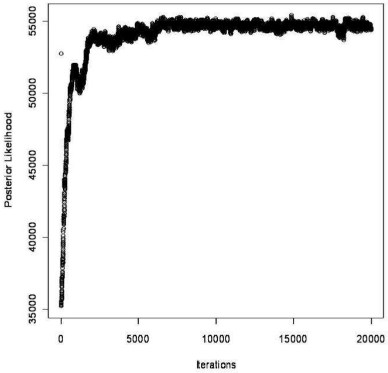
$$
\begin{aligned}
x_{im} | \theta_{im} &\sim k(.|\theta_{im}) && (4)\\
\theta_{im} | G_i &\sim G_i && (5)\\
G_i &\sim DP(\alpha_i, G_0) && (6)\\
G_0 &\sim DP(\gamma, H) && (7)
\end{aligned}
$$

Algorithm and Random Block

- Gibbs sampler based on the Stick-Breaking priors
- Random Block to reduce the heavy computational burden
  - at each Gibbs cycle select $d < P$ pesticides
  - a subset of random observations $x_i = (x_{il_1}, \ldots, x_{il_d})$ is used instead of $x_i = (x_{i1}, \ldots, x_{iP})$

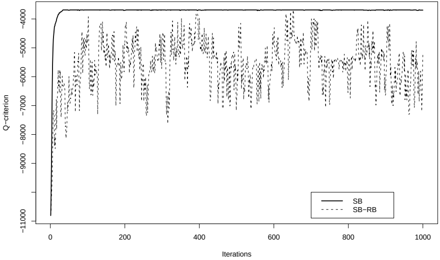
Example of convergence checking



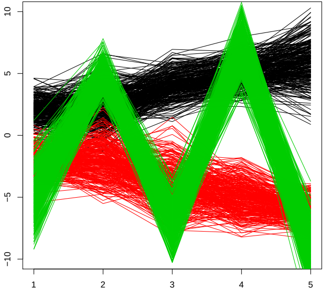


Validation data

Comparison between Stick-breaking (SB) and "Random-Block Stick-Breaking" (RB-SB) algorithms ($N = 30$ atomes, 30000 iterations)



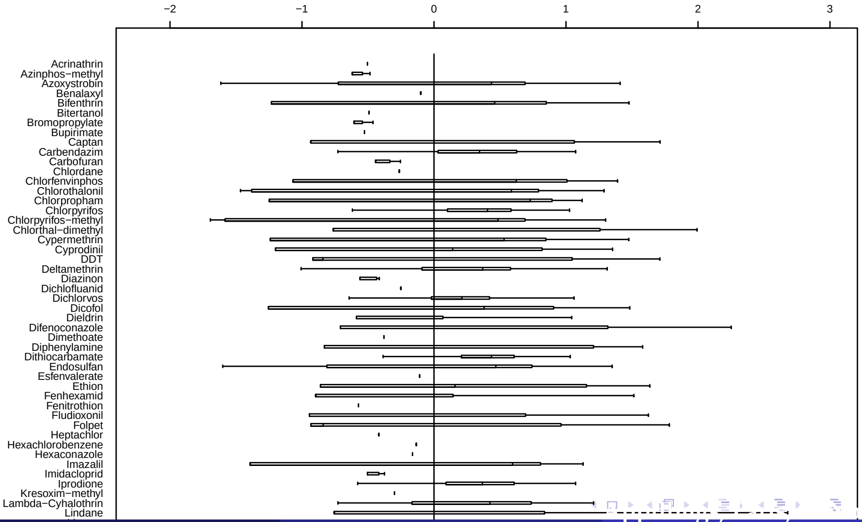
Q-criterion of the first $1,000$ iterations performed with the SB and the SB-RB algorithms



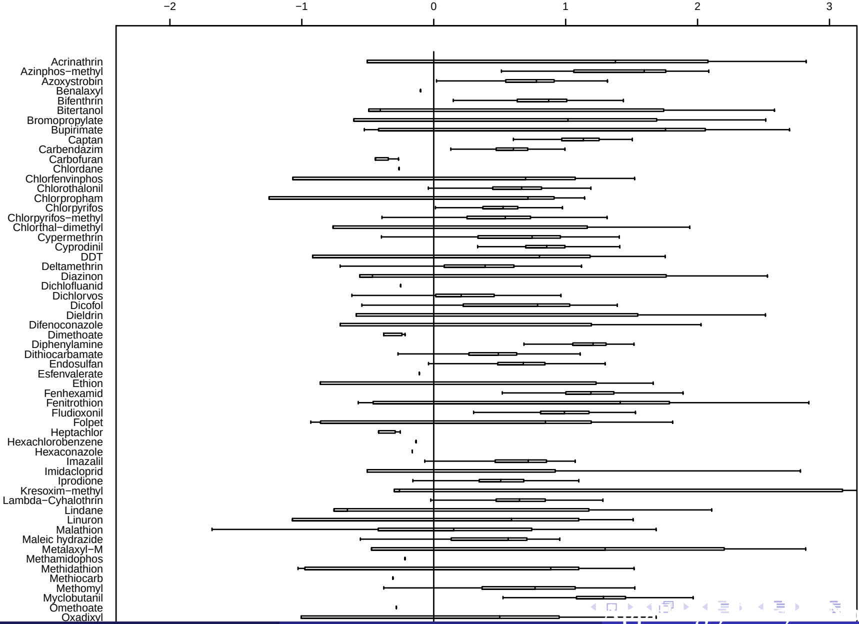
Optimal partion obtained with the SB algorithm : mixture of 3 gaussian distributions

Children co-exposure to pesticides

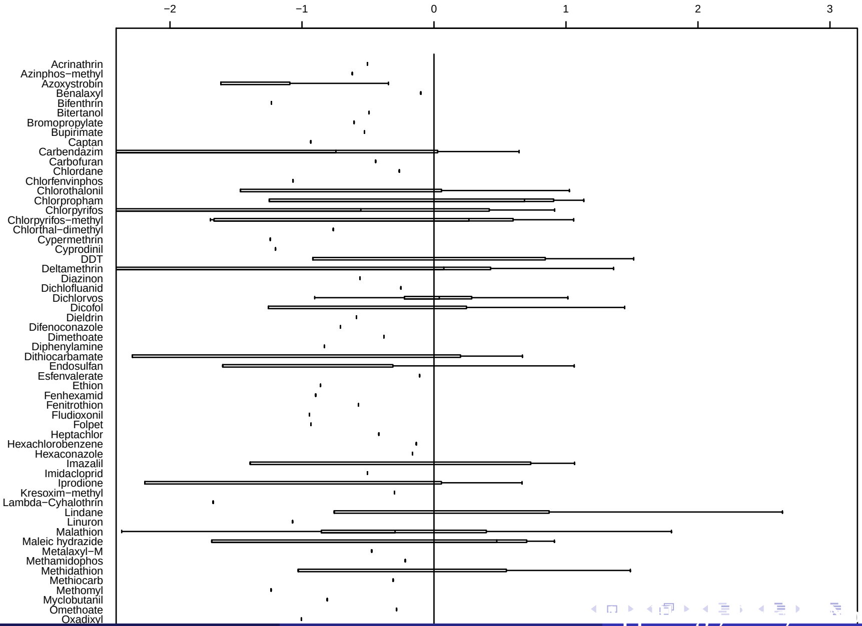
Three main clusters of children with similar co-exposures
Box-plot of the cluster 1 : 699 children



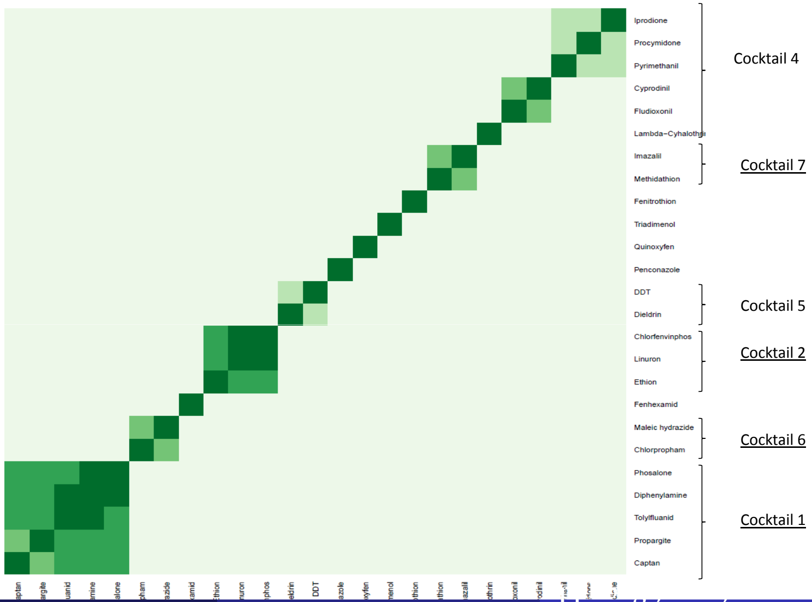
Box-plot of the cluster 2 : 238 children



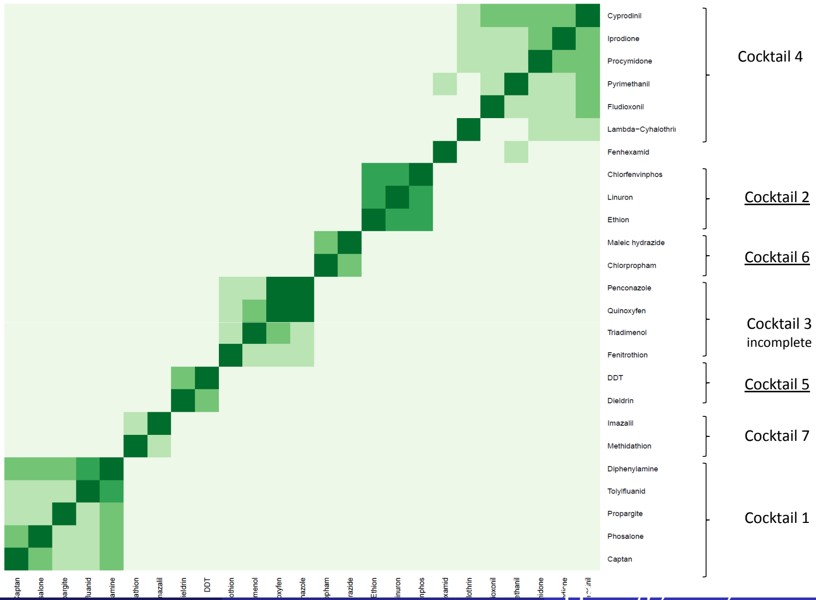
Box-plot of the cluster 3 : 239 children



Exposures correlations of cluster 1 : 699 children



Exposures correlations of cluster 2 : 238 children



Extensions

- Prior distribution on γ : $Gamma(a_\gamma, b_\gamma)$
- Use Poisson-Dirichlet process instead of DP : slow convergence
    - a_γ : $Uniform[0, 1]$
    - b_γ : $Gamma(0.01, 0.01)$

- Hierarchical model not really adapted

- Pareto kernel for k
- DP for censored data

- 3 of the 7 defined cocktails have toxicological effects

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