Bayesian measurement error models for air pollution and health studies

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Bayesian Biostatistics, 22nd June 2018

Environmental epidemiology

- Effect of environmental exposures on health conditions
- Used in the definition of health care policies and interventions
- Exposures: air and water pollutants, individual and ambient concentrations
- Risk assessment: health conditions and development of diseases
- High throughput molecular data: omics data (metabolome, genome, transcriptome,...)

Environmental epidemiology and the exposome

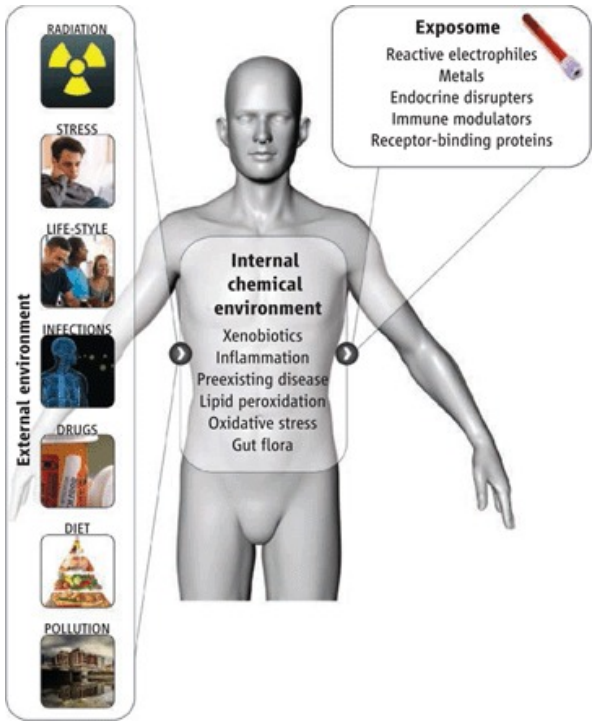


Figure: Overview of the exposome[1]

[1] **Rappaport and Smith, 2010.**

Measurement error in environmental exposures

- Particulary challenging on Traffic Related Air Pollution (TRAP)
- Different sources of ME:
  - Instrument imprecision
  - Difference between ambient concentration and individual exposure
  - Difference between average personal exposure (at home/work address,...) and actual individual exposure
- Mostly classical error

$$\mathbf{W} = \mathbf{X} + \mathbf{U}$$

$$\mathbf{U} \sim \mathrm{N}(0, \sigma^2_{em}\mathbf{I})$$

Bayesian measurement error models

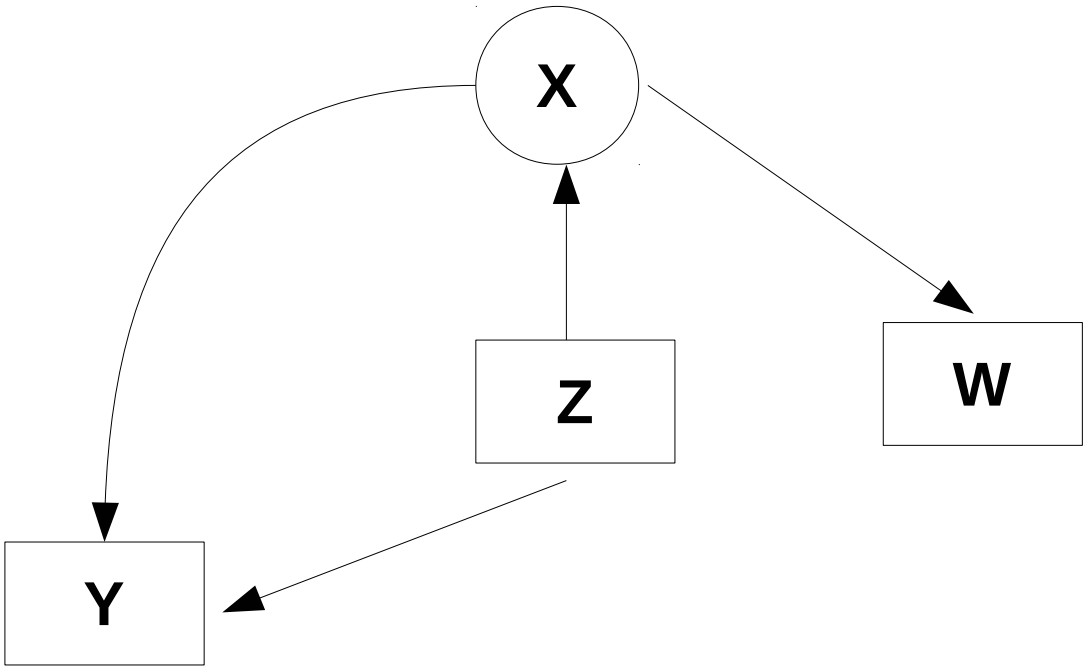


Figure: Graphical structure of the error models: $\boldsymbol{X}$ is the true covariate, $\boldsymbol{W}$ is the error-prone proxy, $\boldsymbol{Z}$ is an exact observable covariate and $\boldsymbol{Y}$ is the response[2].

[2] **Muff et al, 2015**.

Bayesian measurement error models

- Level 1: regression model $\boldsymbol{Y}|\boldsymbol{v}, \boldsymbol{\theta_1}$ of the response variable $\boldsymbol{Y}$ as if $\boldsymbol{X}$ were observed, depending on unknown parameters $\boldsymbol{v}$ and hyperparameters $\boldsymbol{\theta_1}$
- Level 2: latent error model $\boldsymbol{X}|\boldsymbol{W}, \boldsymbol{\theta_2}$ depending on hyperparameters $\boldsymbol{\theta_2}$
- Level 3: priors defined for the hyperparameters $(\boldsymbol{\theta_1}, \boldsymbol{\theta_2})$

Oxford Street II Study

- Randomized cross-over trial
- Part of Exposomics consortium
- 60 volunteers walking in Hyde Park (traffic free) and Oxford Street (highly polluted)
- 3 measurements per walking session: 6 measurements per individual
- Volunteers divided in three groups: healthy (20), COPD (20), IHD (20)
- Information on age, sex, BMI, caffeine intake, ...
- TRAP assessment: PM_{10}, $PM_{2.5}$, $CBLK$, UFP and NO_2
- Omics measurements: metabolomics, transcriptomics and adductomics

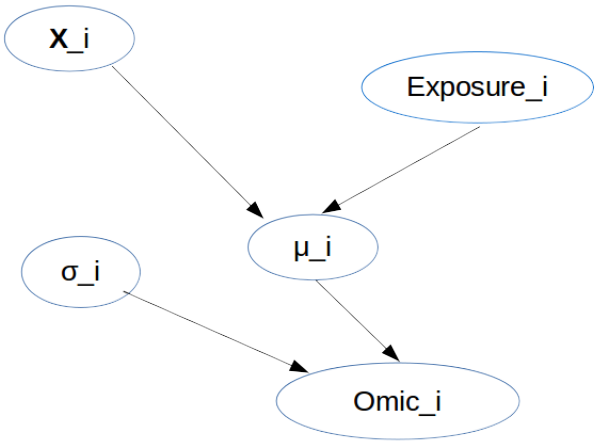
Model on TRAP and metabolomic signals

- On each pollutant
- 5749 metabolic features: selected features based on previous studies
- Fixed effects: sex, age, BMI, disease, caffeine intake

$$m_{ij} \sim \mathrm{N}(\mu_{ij}, \sigma_e^2)$$

$$\mu_{ij} = \alpha + \boldsymbol{\beta}^\top \boldsymbol{X}_{ij} + \beta_{expo} E_{ij} + ID_i + T * L_{ij}$$

- $\boldsymbol{E}$ = exposure to pollutant

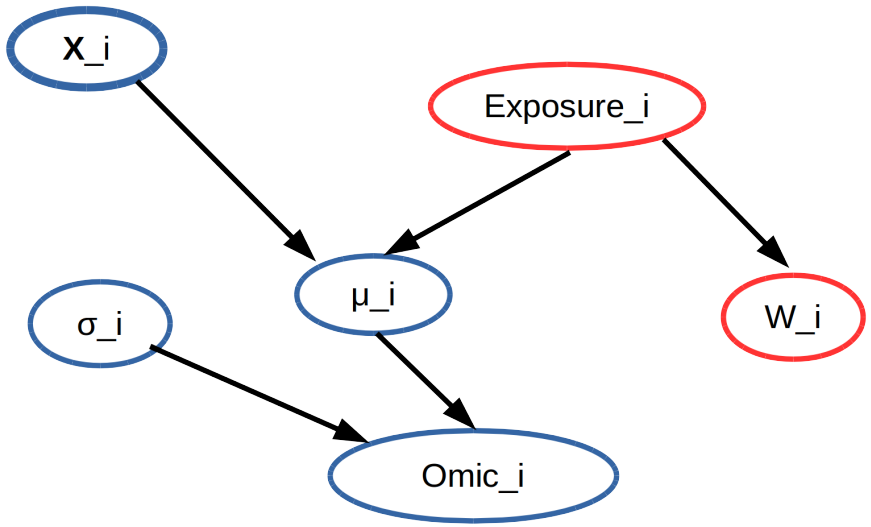


Measurement error on TRAP model

- ME on exposures

$$
\begin{aligned}
m_{ij} &\sim \mathrm{N}(\mu_{ij}, \sigma_e^2) \\
\mu_{ij} &= \alpha + \boldsymbol{\beta}^\top \boldsymbol{X}_{ij} + \beta_{expo} E_{ij} + ID_i + T * L_{ij} \\
W_{ij} &= E_{ij} + U_{ij} \\
U_{ij} &\sim \mathrm{N}(0, \sigma_U^2)
\end{aligned}
$$

- Normal priors to regression coefficients
- Inverse gamma priors to precisions of random effects



Dependency across omic signals

- Metabolic features are not independent in the same individual
- Multivariate response in the Bayesian model

$$\boldsymbol{m} \sim \boldsymbol{MVN}(\mathbf{0}, \Sigma)$$

$$\begin{bmatrix} \boldsymbol{m}(1) \\ \boldsymbol{m}(2) \\ \dots \\ \boldsymbol{m}(n) \end{bmatrix} = \boldsymbol{\mu} + \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\beta_{expo}}\boldsymbol{E} + \boldsymbol{Z}\boldsymbol{r}$$

$$\boldsymbol{W} = \boldsymbol{E} + \boldsymbol{U}$$

- Wishart prior for Σ

Dependency across different exposures

- TRAP exposures are not independent on the same individual and location
- Correlated exposures in the Bayesian model

$$\boldsymbol{m} \sim \boldsymbol{MVN}(\mathbf{0}, \Sigma)$$

$$\begin{bmatrix} \boldsymbol{m}(1) \\ \boldsymbol{m}(2) \\ \dots \\ \boldsymbol{m}(n) \end{bmatrix} = \mu + \boldsymbol{X}\beta + \beta_{\boldsymbol{expo_1}}\boldsymbol{E_1} + \beta_{\boldsymbol{expo_2}}\boldsymbol{E_2} + \dots + \beta_{\boldsymbol{expo_n}}\boldsymbol{E_n} + \boldsymbol{Z}\boldsymbol{r}$$

$$\boldsymbol{W} = \boldsymbol{E} + \boldsymbol{U}$$

Naive vs error-corrected BHM

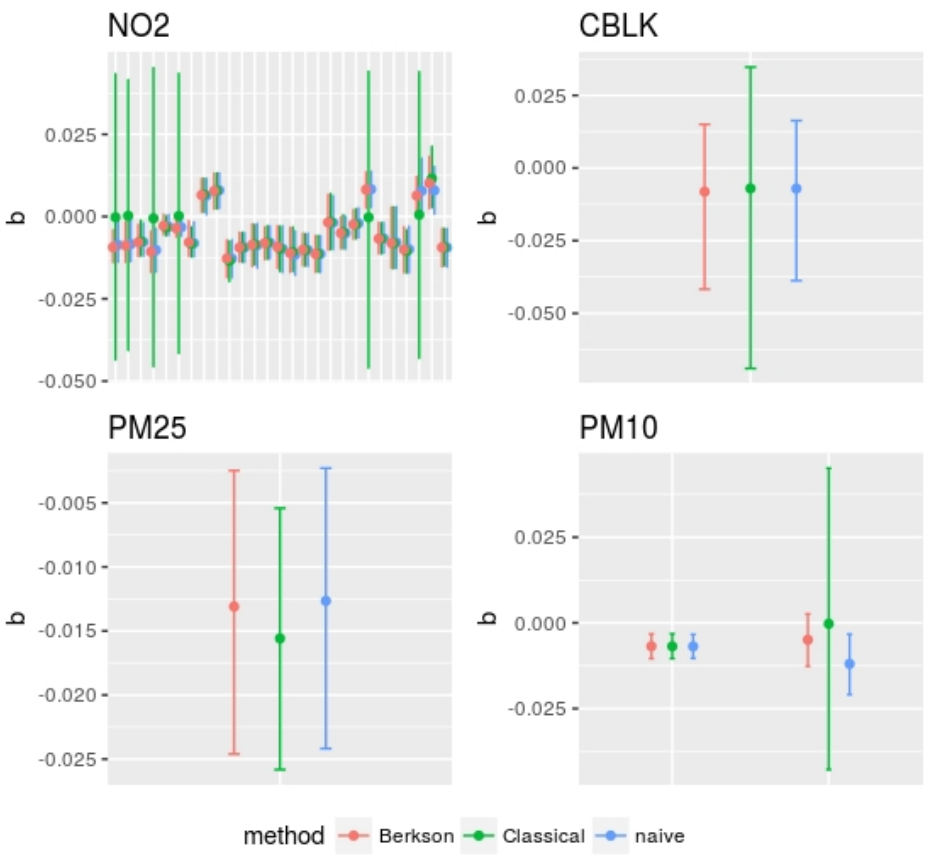


Figure: Regression coefficients with and without error modeling in JAGS. A classical and a Berkson error are assumed.

Multi-omics BHM

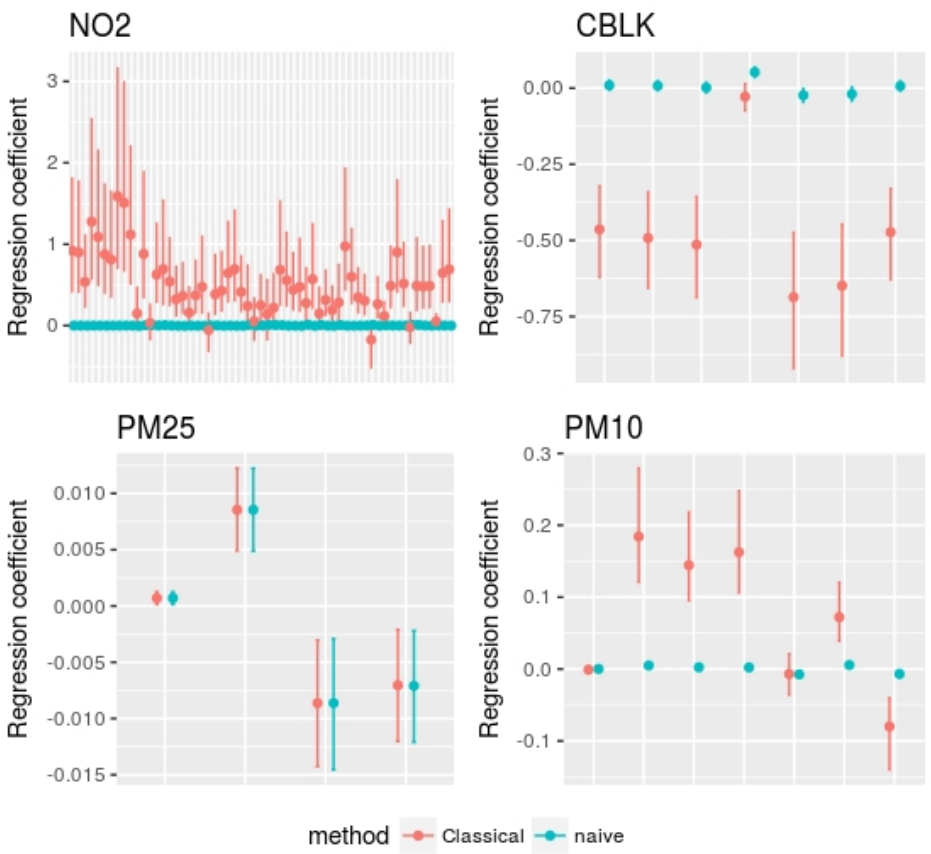


Figure: Regression coefficients with and without classical error modeling in `JAGS`. A correlated structure among omic signals is assumed.

Correlated exposure BHM

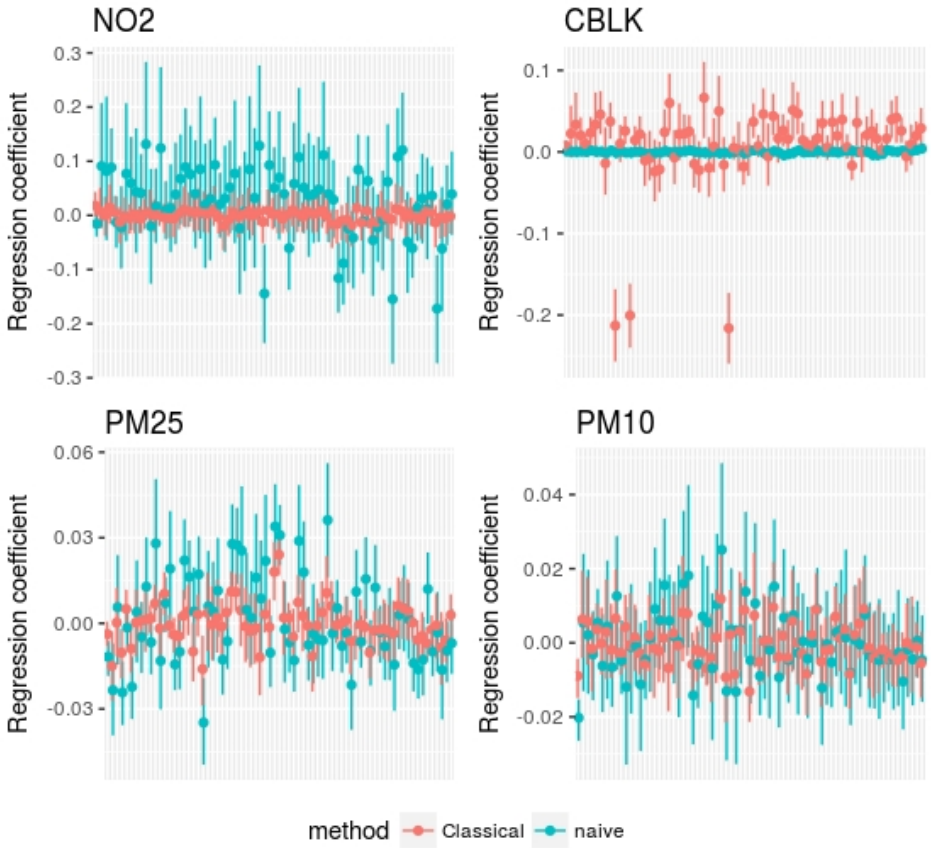


Figure: Regression coefficients with and without classical error modeling in `JAGS`. Dependencies among omic signals and among different TRAP exposures are assumed.

Conclusions and future work

- Effect of classical error
- No effect of Berkson error

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- No effect of Berkson error
- BHM flexibility: possible to account for dependencies
- Among omics: allows to identify more signals, no multiple testing problems
- Among pollutants
- Classical ME included in both models

Conclusions and future work

- Effect of classical error
- No effect of Berkson error
- BHM flexibility: possible to account for dependencies
- Among omics: allows to identify more signals, no multiple testing problems
- Among pollutants
- Classical ME included in both models
- Implemented in `JAGS`
- Working on `INLA` implementation: some difficulties with multiple omics, faster for single omic models

Thank you!