# Simple fitting of subject-specific curves for longitudinal data

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- Introduction
  - ⋆ The data
  - ⋆ P-splines
  - ⋆ Mixed model representation of P-splines

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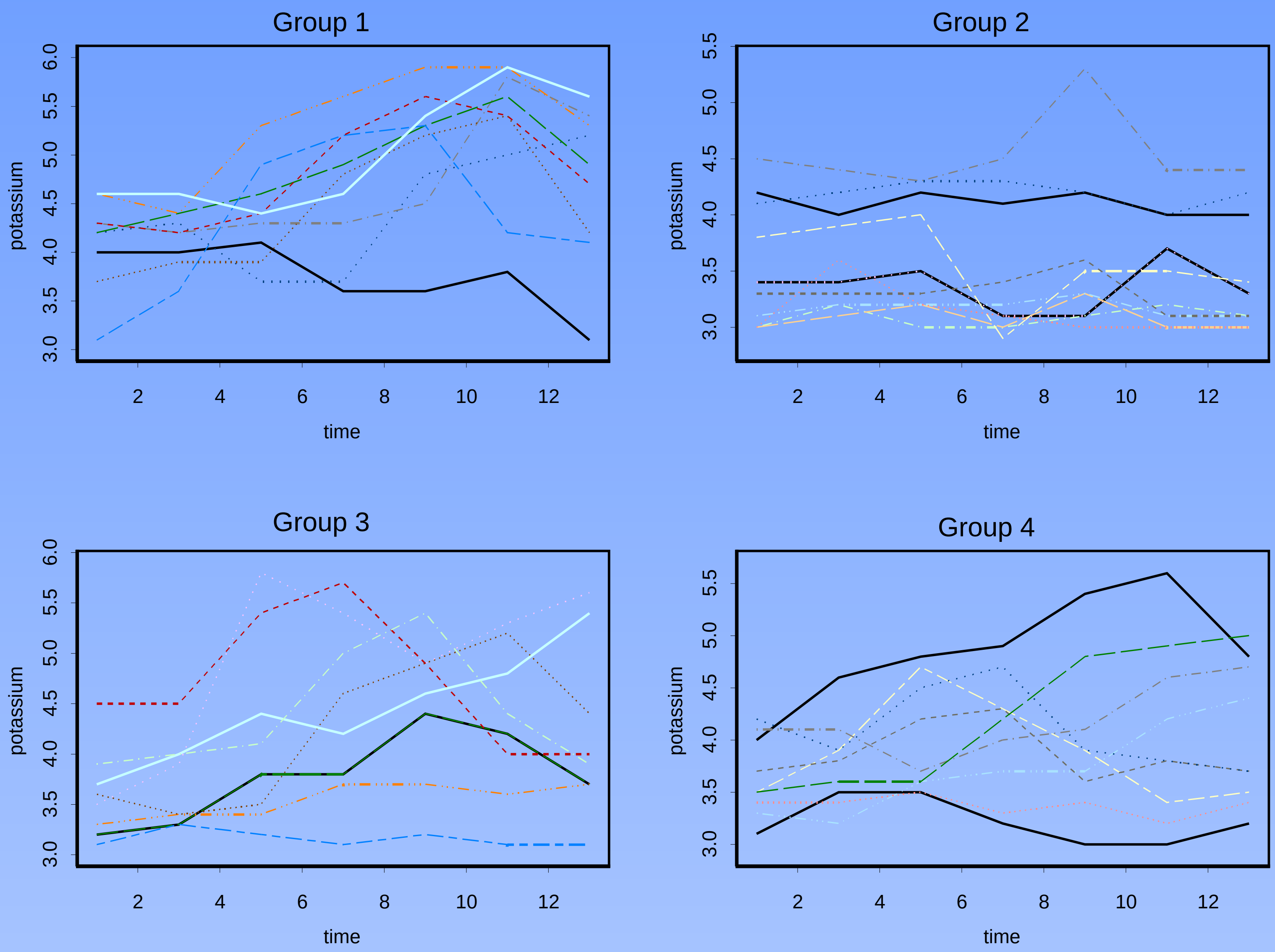
- P-spline models for longitudinal data.
  - ⋆ Subject-specific Curves
- Analysis of dogs data.

# The data

Objetive: Determine the effect of 4 surgical treatments on coronary sinus potasium in dogs

- 36 dogs
- 4 treatments
- 7 measurements per dog


Group 1
Group 2
Group 3
Group 4
potassium
time
2
4
6
8
10
12
3.0
3.5
4.0
4.5
5.0
5.5
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# Smoothing

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$$\boldsymbol{y} = f(\boldsymbol{t}) + \boldsymbol{\epsilon}$$

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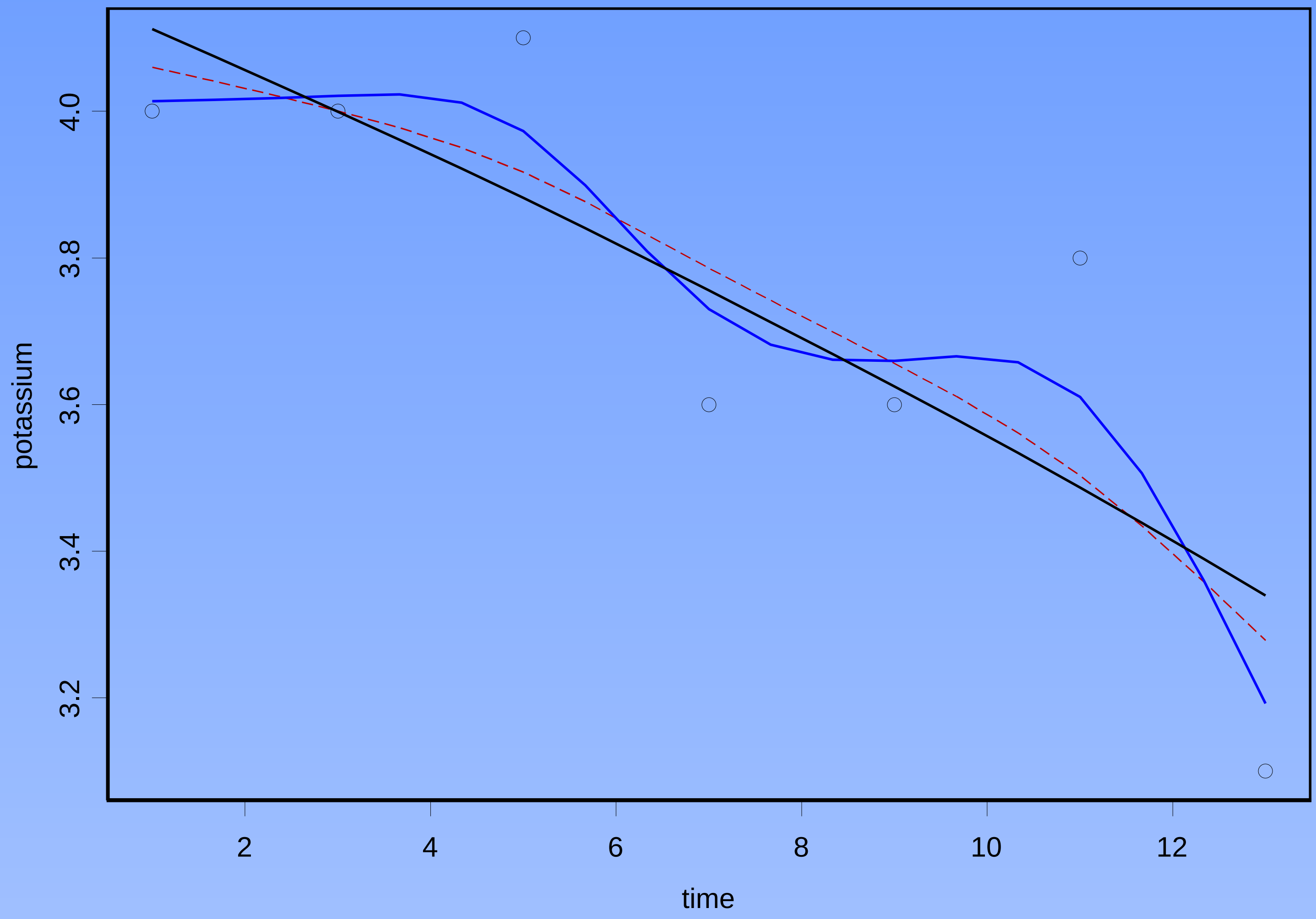
- Smoothing methods fall into two groups:

  ⋆ Specified by the fitting procedure: **Kernels**
  ⋆ Solution of a minimisation problem: **Splines**


potassium
4.0
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# B-splines

- We write $f = \boldsymbol{Ba}$, $\boldsymbol{B}$ is a B-spline basis and $\boldsymbol{a}$ are coefficients
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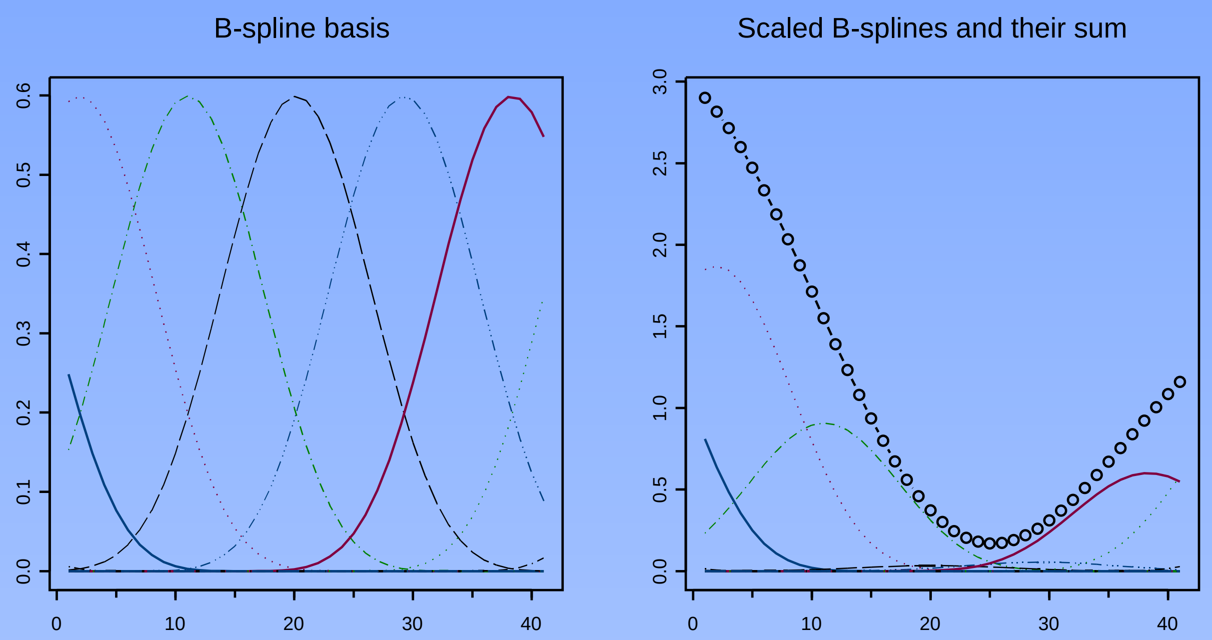

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$$\boldsymbol{y} = f(\boldsymbol{x}) + \boldsymbol{\epsilon} \quad f(\boldsymbol{x}) \approx \boldsymbol{B}\boldsymbol{a} \quad S = (\boldsymbol{y} - \boldsymbol{B}\boldsymbol{a})'(\boldsymbol{y} - \boldsymbol{B}\boldsymbol{a}) + \lambda \boldsymbol{a}'\boldsymbol{D}'\boldsymbol{D}\boldsymbol{a}$$

$$\hat{\boldsymbol{a}} = (\boldsymbol{B}'\boldsymbol{B} + \lambda \boldsymbol{D}'\boldsymbol{D})^{-1}\boldsymbol{B}'\boldsymbol{y}$$

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- Moderate dimension ($k$ between 10 and 40)
- Computationally faster than smoothing splines

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$\Downarrow$ $\boldsymbol{a}$ treated as mixed effects

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**Best Linear Unbiased Predictor = Penalized likelihood fit**

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- GAM $\Rightarrow$ GLMM

# P-splines with truncared lines basis

$$y_{ij} = f(t_{ij}) + \epsilon_{ij} \quad 1 \leq j \leq 7$$

$$f(t_{ij}) = \alpha_0 + \alpha_1 t_{ij} + \sum_{k=1}^{K} u_k (t_{ij} - \kappa_k)_+ \quad u_k \sim N(0, \sigma_u^2)$$

$$\Downarrow$$

$$\boldsymbol{y} = \boldsymbol{X\alpha} + \boldsymbol{Zu} + \boldsymbol{\epsilon} \quad Cov \begin{bmatrix} \boldsymbol{u} \\ \boldsymbol{\epsilon} \end{bmatrix} = \begin{bmatrix} \sigma_u^2 \boldsymbol{I} & 0 \\ 0 & \sigma^2 \boldsymbol{I} \end{bmatrix}$$

$$\boldsymbol{Z} = \begin{bmatrix} (t_{i1} - \kappa_1)_+ & \dots & (t_{i1} - \kappa_K)_+ \\ \vdots & \ddots & \vdots \\ (t_{i7} - \kappa_1)_+ & \dots & (t_{i7} - \kappa_K)_+ \end{bmatrix}$$

# P-spline models for longitudinal data

Basic Model $\quad y_{ij} = \alpha_0 + \alpha_1 t_{ij} + \beta_{i0} + \epsilon_{ij} \quad 1 \leq j \leq 7 \quad 1 \leq i \leq 36$

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Model B $y_{ij} = f_{gr(i)}(t_{ij}) + \beta_{i0} + \beta_{i1} t_{ij} + \epsilon_{ij}$

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$\Downarrow$ Subject specific curves

Model C $y_{ij} = f_{gr(j)}(t_{ij}) + g_i(t_{ij}) + \epsilon_{ij}$

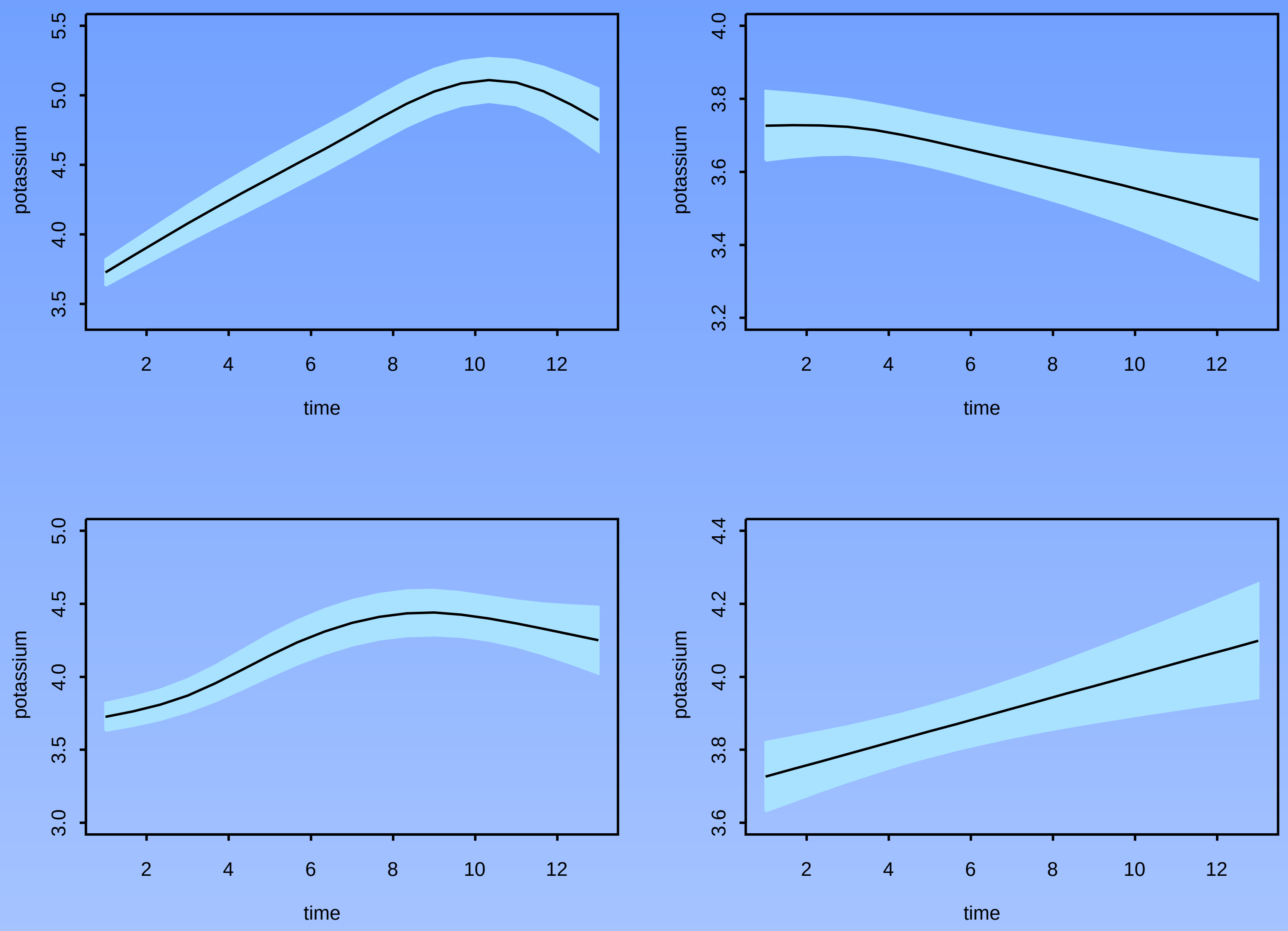
The mixed model associated to Model A is:



$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\alpha} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{\epsilon} \quad Cov \begin{bmatrix} \boldsymbol{u} \\ \boldsymbol{\epsilon} \end{bmatrix} = \begin{bmatrix} \sigma^2_{\beta_0}\boldsymbol{I} & 0 & 0 \\ 0 & \Sigma_{gr} & 0 \\ 0 & 0 & \sigma^2\boldsymbol{I} \end{bmatrix}$$

$$\boldsymbol{X} = \begin{bmatrix} \boldsymbol{X}_{\text{time}} \\ \vdots \\ \boldsymbol{X}_{\text{time}} \end{bmatrix} \quad \boldsymbol{X}_{\text{time}} = \begin{bmatrix} 1 & t_1 \\ \vdots & \vdots \\ 1 & t_7 \end{bmatrix} \quad \boldsymbol{Z} = \begin{bmatrix} \boldsymbol{Z}_1 & & & & 1 & 0 & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & & 1 & 0 & \cdots & 0 \\ & \boldsymbol{Z}_2 & & & 0 & 1 & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & & 0 & 1 & \cdots & 0 \\ & & \boldsymbol{Z}_3 & & \vdots & \vdots & \vdots & \vdots \\ & & & & 0 & 0 & \cdots & 1 \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & \boldsymbol{Z}_4 & 0 & 0 & \cdots & 1 \end{bmatrix}$$

$$\boldsymbol{Z}_{\text{gr(i)}} = \begin{bmatrix} \boldsymbol{Z}_{\text{time}} \\ \vdots \\ \boldsymbol{Z}_{\text{time}} \end{bmatrix} \quad \Sigma_{gr} = \begin{bmatrix} \sigma^2_1\boldsymbol{I} & & & \\ & \sigma^2_2\boldsymbol{I} & & \\ & & \sigma^2_3\boldsymbol{I} & \\ & & & \sigma^2_4\boldsymbol{I} \end{bmatrix}$$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The mixed model associated to Model B is:

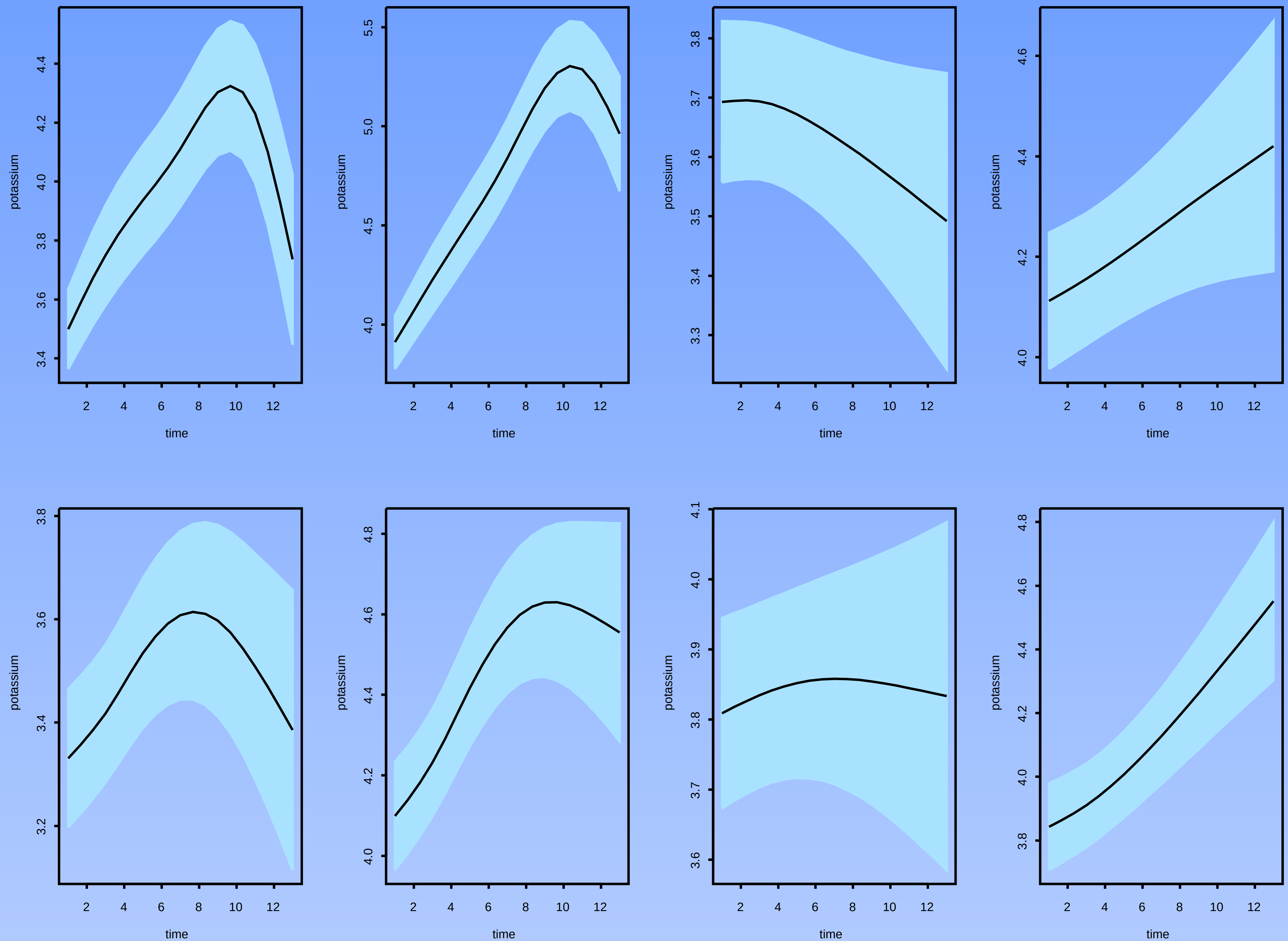
$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\alpha} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{\epsilon} \quad Cov\begin{bmatrix} \boldsymbol{u} \\ \boldsymbol{\epsilon} \end{bmatrix} = \begin{bmatrix} \Sigma_{gr} & 0 & 0 \\ 0 & blockdiag(\Sigma) & 0 \\ 0 & 0 & \sigma^2 \boldsymbol{I} \end{bmatrix}$$

$$\boldsymbol{Z} = \left[\begin{array}{cccccccc} \boldsymbol{Z}_1 & & & & \boldsymbol{X}_{\text{time}} & 0 & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & & \boldsymbol{X}_{\text{time}} & 0 & \cdots & 0 \\ & \boldsymbol{Z}_2 & & & 0 & \boldsymbol{X}_{\text{time}} & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & & 0 & \boldsymbol{X}_{\text{time}} & \cdots & 0 \\ & & \boldsymbol{Z}_3 & & \vdots & \vdots & \vdots & \vdots \\ & & & & 0 & 0 & \cdots & \boldsymbol{X}_{\text{time}} \\ & & & & \vdots & \vdots & \ddots & \vdots \\ & & & \boldsymbol{Z}_4 & 0 & 0 & \cdots & \boldsymbol{X}_{\text{time}} \end{array}\right]$$

The mixed model associated to Model C is:

$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\alpha} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{\epsilon} \quad Cov\begin{bmatrix} \boldsymbol{u} \\ \boldsymbol{\epsilon} \end{bmatrix} = \begin{bmatrix} \Sigma_{gr} & 0 & 0 & 0 \\ 0 & blockdiag(\Sigma) & 0 & 0 \\ 0 & 0 & \sigma_c^2\boldsymbol{I} & 0 \\ 0 & 0 & 0 & \sigma^2\boldsymbol{I} \end{bmatrix}$$

$$\boldsymbol{Z} = \begin{bmatrix} \boldsymbol{Z}_1 & & & & \boldsymbol{X}_{\mathsf{time}} & 0 & \cdots & 0 & \boldsymbol{Z}_{\mathsf{time}} & 0 & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ & & & & \boldsymbol{X}_{\mathsf{time}} & 0 & \cdots & 0 & \boldsymbol{Z}_{\mathsf{time}} & 0 & \cdots & 0 \\ & \boldsymbol{Z}_2 & & & 0 & \boldsymbol{X}_{\mathsf{time}} & \cdots & 0 & 0 & \boldsymbol{Z}_{\mathsf{time}} & \cdots & 0 \\ & & & & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ & & & & 0 & \boldsymbol{X}_{\mathsf{time}} & \cdots & 0 & 0 & \boldsymbol{Z}_{\mathsf{time}} & \cdots & 0 \\ & & \boldsymbol{Z}_3 & & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ & & & & 0 & 0 & \cdots & \boldsymbol{X}_{\mathsf{time}} & 0 & 0 & \cdots & \boldsymbol{Z}_{\mathsf{time}} \\ & & & & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ & & & \boldsymbol{Z}_4 & 0 & 0 & \cdots & \boldsymbol{X}_{\mathsf{time}} & 0 & 0 & \cdots & \boldsymbol{Z}_{\mathsf{time}} \end{bmatrix}$$


potassium
time

# Conclusions and work in progress

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- $P$-splines are useful tool to model longitudinal data
- P-splines as mixed models
- Easy to implement in standard sorfware
- Model selection

# References

# References


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