# Les 53èmes Journées de Statistique de la Société Française de Statistique

**Van Tuan NGUYEN**

vantuan.nguyen@califrais.fr

## Lights: a generalized joint model for high-dimensional multivariate longitudinal data and censored durations

S. Bussy [(1,2)], V.T. Nguyen[(1,2)], A. Barbieri [(3)], S. Zohar [(4)], A.S. Jannot [(4,5)]

[(1)]LOPF, Califrais' Machine Learning Lab, Paris, France
[(2)]LPSM, UMR 8001, CNRS, Sorbonne University, Paris, France
[(3)]INSERM, UMR 1219, Bordeaux Population Health Research Center, Univ. Bordeaux, France
[(4)]INSERM, UMRS 1138, Centre de Recherche des Cordeliers, Paris, France
[(5)]Biomedical Informatics and Public Health Department, EGPH, APHP, Paris, France

# I. Introduction

# Overview

- Deal with the problem of joint modeling of longitudinal data and censored durations

# Overview

- Deal with the problem of joint modeling of longitudinal data and censored durations
- Large number of both longitudinal and time-independent features are available

# Overview

- Deal with the problem of joint modeling of longitudinal data and censored durations
- Large number of both longitudinal and time-independent features are available
- Flexibility in modeling the dependency between the longitudinal features and the event time with appropriate penalties

# Overview





- Deal with the problem of joint modeling of longitudinal data and censored durations
- Large number of both longitudinal and time-independent features are available
- Flexibility in modeling the dependency between the longitudinal features and the event time with appropriate penalties
- Inference achieved using an efficient and novel Proximal Quasi-Newton Expectation Maximization algorithm

# Use cases

- Predict the risk for an event of interest to occur quickly, taking into account simultaneously a huge number of longitudinal signals in a high-dimensional context

# Use cases

- Predict the risk for an event of interest to occur quickly, taking into account simultaneously a huge number of longitudinal signals in a high-dimensional context
- Provides powerful interpretability by automatically pinpointing significant time-dependent and time-independent features

# Use cases

- Predict the risk for an event of interest to occur quickly, taking into account simultaneously a huge number of longitudinal signals in a high-dimensional context
- Provides powerful interpretability by automatically pinpointing significant time-dependent and time-independent features

## Real-time decision support

- Medical context $\rightarrow$ event of interest: survival time, re-hospitalization, relapse or disease progression ; longitudinal data: biomarkers or vital parameters measurements

# Use cases

- Predict the risk for an event of interest to occur quickly, taking into account simultaneously a huge number of longitudinal signals in a high-dimensional context
- Provides powerful interpretability by automatically pinpointing significant time-dependent and time-independent features

## Real-time decision support

- Medical context $\rightarrow$ event of interest: survival time, re-hospitalization, relapse or disease progression ; longitudinal data: biomarkers or vital parameters measurements
- Customer's satisfaction monitoring context $\rightarrow$ event of interest: time when a client churns ; longitudinal data: the client's activity recorded from account opening throughout the duration of the business relationship

# High-dimensional framework

- Survival analysis

$$T = T^\star \wedge C \quad \text{and} \quad \Delta = \mathbb{1}_{\{T^\star \leq C\}}$$

# High-dimensional framework

- Survival analysis

$$T = T^\star \wedge C \quad \text{and} \quad \Delta = \mathbb{1}_{\{T^\star \leq C\}}$$

- Time-independent features $X \in \mathbb{R}^p$ with $p \gg n$

# High-dimensional framework

- Survival analysis

$$T = T^\star \wedge C \quad \text{and} \quad \Delta = \mathbb{1}_{\{T^\star \leq C\}}$$

- Time-independent features $X \in \mathbb{R}^p$ with $p \gg n$
- $L$ longitudinal outcomes such that $L \gg n$ and

$$Y(t) = \big(Y^1(t), \dots, Y^L(t)\big)^\top \in \mathbb{R}^L$$

# High-dimensional framework

- Survival analysis

$$T = T^\star \wedge C \quad \text{and} \quad \Delta = \mathbb{1}_{\{T^\star \leq C\}}$$

- Time-independent features $X \in \mathbb{R}^p$ with $p \gg n$
- $L$ longitudinal outcomes such that $L \gg n$ and

$$Y(t) = \big(Y^1(t), \ldots, Y^L(t)\big)^\top \in \mathbb{R}^L$$

- Heterogeneity of the population: latent subclasses

$$G \in \{0, \ldots, K-1\}$$

# High-dimensional framework

- Survival analysis

$$T = T^\star \wedge C \quad \text{and} \quad \Delta = \mathbb{1}_{\{T^\star \leq C\}}$$

- Time-independent features $X \in \mathbb{R}^p$ with $p \gg n$
- $L$ longitudinal outcomes such that $L \gg n$ and

$$Y(t) = \big(Y^1(t), \ldots, Y^L(t)\big)^\top \in \mathbb{R}^L$$

- Heterogeneity of the population: latent subclasses

$$G \in \{0, \ldots, K-1\}$$

- Softmax link function for the latent class membership probability given time-independent features

$$\pi_{\xi_k}(x) = \mathbb{P}[G = k | X = x] = \frac{e^{x^\top \xi_k}}{\sum_{k=0}^{K-1} e^{x^\top \xi_k}}$$

# II. Model

# Submodels

## Class-specific marker trajectories

- $h_l\Big(\mathbb{E}[Y^l(t)|b^l, G=k]\Big) = m_k^l(t) = u^l(t)^\top \beta_k^l + v^l(t)^\top b^l$
  with fixed effect parameters $\beta_k^l \in \mathbb{R}^{q_l}$ and subject-and-longitudinal outcome specific random effects $b^l \in \mathbb{R}^{r_l} \sim \mathcal{N}(0, D_{ll})$

# Submodels

## Class-specific marker trajectories

- $h_l\Big(\mathbb{E}[Y^l(t)|b^l, G = k]\Big) = m_k^l(t) = u^l(t)^\top \beta_k^l + v^l(t)^\top b^l$
  with fixed effect parameters $\beta_k^l \in \mathbb{R}^{q_l}$ and subject-and-longitudinal outcome specific random effects $b^l \in \mathbb{R}^{r_l} \sim \mathcal{N}(0, D_{ll})$
- $\mathrm{Cov}[b^l, b^{l'}] = D_{ll'}$ and

$$D = \begin{bmatrix} D_{11} & \cdots & D_{1L} \\ \vdots & \ddots & \vdots \\ D_{1L}^\top & \cdots & D_{LL} \end{bmatrix}$$

  the global variance-covariance matrix

# Submodels





## Class-specific marker trajectories

- $h_l\big(\mathbb{E}[Y^l(t)|b^l, G = k]\big) = m_k^l(t) = u^l(t)^\top \beta_k^l + v^l(t)^\top b^l$
with fixed effect parameters $\beta_k^l \in \mathbb{R}^{q_l}$ and subject-and-longitudinal outcome specific random effects $b^l \in \mathbb{R}^{r_l} \sim \mathcal{N}(0, D_{ll})$
- $\text{Cov}[b^l, b^{l'}] = D_{ll'}$

## CLass-specific risk of event

- $$\lambda(t|\mathcal{Y}(t), G = k) = \lambda_0(t) \exp\Big\{ \underbrace{\sum_{l=1}^{L}\sum_{a=1}^{\mathcal{A}} \gamma_{k,a}^l \Psi_a^l(t)}_{\gamma_k^\top \Psi(t)} \Big\}$$
with $\mathcal{Y}(t) = \{Y(u), 0 \leq u < t\}$ and for each $l$-th longitudinal outcome, we consider $\mathcal{A} \in \mathbb{N}_+$ known functionals $\Psi_a^l$ extracted from $\mathcal{Y}^l(t)$ through a given representation mapping

# Submodels

## Class-specific marker trajectories

- $h_l\Big(\mathbb{E}[Y^l(t)|b^l, G=k]\Big) = m_k^l(t) = u^l(t)^\top \beta_k^l + v^l(t)^\top b^l$
  with fixed effect parameters $\beta_k^l \in \mathbb{R}^{q_l}$ and subject-and-longitudinal outcome specific random effects $b^l \in \mathbb{R}^{r_l} \sim \mathcal{N}(0, D_{ll})$
- $\mathrm{Cov}[b^l, b^{l'}] = D_{ll'}$

## CLass-specific risk of event

- $\lambda(t|\mathcal{Y}(t), G=k) = \lambda_0(t) \exp\Bigg\{ \underbrace{\sum_{l=1}^{L} \sum_{a=1}^{\mathcal{A}} \gamma_{k,a}^l \Psi_a^l(t)}_{\gamma_k^\top \Psi(t)} \Bigg\}$

  with $\mathcal{Y}(t) = \{Y(u), 0 \leq u < t\}$ and for each $l$-th longitudinal outcome, we consider $\mathcal{A} \in \mathbb{N}_+$ known functionals $\Psi_a^l$ extracted from $\mathcal{Y}^l(t)$ through a given representation mapping
- $\Psi(t) \in \mathbb{R}^{L\mathcal{A}}$ : high-dim representation features vector, highly flexible and independent of any modeling assumption !

# Notations

- $\mathcal{D}_n = \Big\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\Big\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$

# Notations

- $\mathcal{D}_n = \big\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\big\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$
- $y_i = ({y_i^1}^\top \cdots {y_i^L}^\top)^\top \in \mathbb{R}^{n_i}$ with $n_i = \sum_{l=1}^L n_i^l$

# Notations

- $\mathcal{D}_n = \Big\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\Big\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$
- $y_i = ({y_i^1}^\top \cdots {y_i^L}^\top)^\top \in \mathbb{R}^{n_i}$ with $n_i = \sum_{l=1}^L n_i^l$
- $b_i = ({b_i^1}^\top \cdots {b_i^L}^\top)^\top \in \mathbb{R}^{r}$ with $r = \sum_{l=1}^L r_l$

# Notations

- $\mathcal{D}_n = \left\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\right\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$
- $y_i = ({y_i^1}^\top \cdots {y_i^L}^\top)^\top \in \mathbb{R}^{n_i}$ with $n_i = \sum_{l=1}^L n_i^l$
- $b_i = ({b_i^1}^\top \cdots {b_i^L}^\top)^\top \in \mathbb{R}^{r}$ with $r = \sum_{l=1}^L r_l$
- Design matrices

$$U_i = \begin{bmatrix} U_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & U_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times q} \text{ and } V_i = \begin{bmatrix} V_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & V_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times r}$$

with $q = \sum_{l=1}^L q_l$ and where for all $l = 1, \ldots, L$, one writes

$$\begin{cases} U_{il} &= \left(u_i^l(t_{i1}^l)^\top \cdots u_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times q_l}, \\ V_{il} &= \left(v_i^l(t_{i1}^l)^\top \cdots v_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times r_l}. \end{cases}$$

# Notations



- $\mathcal{D}_n = \left\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\right\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$
- $y_i = ({y_i^1}^\top \cdots {y_i^L}^\top)^\top \in \mathbb{R}^{n_i}$ with $n_i = \sum_{l=1}^L n_i^l$
- $b_i = ({b_i^1}^\top \cdots {b_i^L}^\top)^\top \in \mathbb{R}^{r}$ with $r = \sum_{l=1}^L r_l$
- Design matrices

$$U_i = \begin{bmatrix} U_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & U_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times q} \text{ and } V_i = \begin{bmatrix} V_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & V_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times r}$$

with $q = \sum_{l=1}^L q_l$ and where for all $l = 1, \ldots, L$, one writes

$$\begin{cases} U_{il} &= \left(u_i^l(t_{i1}^l)^\top \cdots u_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times q_l}, \\ V_{il} &= \left(v_i^l(t_{i1}^l)^\top \cdots v_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times r_l}. \end{cases}$$

- $\beta_k = ({\beta_k^1}^\top \cdots {\beta_k^L}^\top)^\top \in \mathbb{R}^q$

# Notations

- $\mathcal{D}_n = \left\{(x_1, y_1^1, \ldots, y_1^L, t_1, \delta_1), \ldots, (x_n, y_n^1, \ldots, y_n^L, t_n, \delta_n)\right\}$ with $y_i^l = (y_{i1}^l, \ldots, y_{in_i^l}^l)^\top \in \mathbb{R}^{n_i^l}$ and $y_{ij}^l = Y_i^l(t_{ij}^l)$
- $y_i = ({y_i^1}^\top \cdots {y_i^L}^\top)^\top \in \mathbb{R}^{n_i}$ with $n_i = \sum_{l=1}^L n_i^l$
- $b_i = ({b_i^1}^\top \cdots {b_i^L}^\top)^\top \in \mathbb{R}^r$ with $r = \sum_{l=1}^L r_l$
- Design matrices

$$U_i = \begin{bmatrix} U_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & U_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times q} \text{ and } V_i = \begin{bmatrix} V_{i1} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & V_{iL} \end{bmatrix} \in \mathbb{R}^{n_i \times r}$$

with $q = \sum_{l=1}^L q_l$ and where for all $l = 1, \ldots, L$, one writes

$$\begin{cases} U_{il} &= \left(u_i^l(t_{i1}^l)^\top \cdots u_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times q_l}, \\ V_{il} &= \left(v_i^l(t_{i1}^l)^\top \cdots v_i^l(t_{in_i^l}^l)^\top\right)^\top \in \mathbb{R}^{n_i^l \times r_l}. \end{cases}$$

- $\beta_k = ({\beta_k^1}^\top \cdots {\beta_k^L}^\top)^\top \in \mathbb{R}^q$
- $M_{ik} = U_i \beta_k + V_i b_i \in \mathbb{R}^{n_i}$

# Likelihood

- $\theta = \left(\xi_0^\top \cdots \xi_{K-1}^\top, \beta_0^\top \cdots \beta_{K-1}^\top, \phi^\top, \text{vech}(D), \lambda_0^\top, \gamma_0^\top \cdots \gamma_{K-1}^\top\right) \in \mathbb{R}^\vartheta$

# Likelihood

- $\theta = \left(\xi_0^\top \cdots \xi_{K-1}^\top, \beta_0^\top \cdots \beta_{K-1}^\top, \phi^\top, \text{vech}(D), \lambda_0^\top, \gamma_0^\top \cdots \gamma_{K-1}^\top\right) \in \mathbb{R}^\vartheta$
- $f(y_i | b_i, G_i = k) = \exp\left\{(y_i \odot \Phi_i)^\top M_{ik} - c_\phi(M_{ik}) + d_\phi(y_i)\right\}$ with $\Phi_i = (\phi_1^{-1} \mathbf{1}_{n_i^1}{}^\top \cdots \phi_L^{-1} \mathbf{1}_{n_i^L}{}^\top)^\top \in \mathbb{R}^{n_i}$

# Likelihood



- $\theta = \left(\xi_0^\top \cdots \xi_{K-1}^\top, \beta_0^\top \cdots \beta_{K-1}^\top, \phi^\top, \text{vech}(D), \lambda_0^\top, \gamma_0^\top \cdots \gamma_{K-1}^\top\right) \in \mathbb{R}^\vartheta$
- $f(y_i|b_i, G_i = k) = \exp\left\{(y_i \odot \Phi_i)^\top M_{ik} - c_\phi(M_{ik}) + d_\phi(y_i)\right\}$ with $\Phi_i = (\phi_1^{-1}\mathbf{1}_{n_i^1}{}^\top \cdots \phi_L^{-1}\mathbf{1}_{n_i^L}{}^\top)^\top \in \mathbb{R}^{n_i}$
- Survival part:

$$\begin{aligned} f(t_i, \delta_i | G_i = k; \theta) = &\left[\lambda(t_i|\mathcal{Y}(t_i), G_i = k)\right]^{\delta_i} \\ &\times \exp\left\{ - \int_0^{t_i} \lambda(s|\mathcal{Y}(s), G_i = k)\mathrm{d}s \right\} \end{aligned}$$

# Likelihood





- $\theta = \left(\xi_0^\top \cdots \xi_{K-1}^\top, \beta_0^\top \cdots \beta_{K-1}^\top, \phi^\top, \text{vech}(D), \lambda_0^\top, \gamma_0^\top \cdots \gamma_{K-1}^\top\right) \in \mathbb{R}^\vartheta$
- $f(y_i|b_i, G_i = k) = \exp\left\{(y_i \odot \Phi_i)^\top M_{ik} - c_\phi(M_{ik}) + d_\phi(y_i)\right\}$ with $\Phi_i = (\phi_1^{-1}\mathbf{1}_{n_i^1}{}^\top \cdots \phi_L^{-1}\mathbf{1}_{n_i^L}{}^\top)^\top \in \mathbb{R}^{n_i}$
- Survival part:

$$f(t_i, \delta_i | G_i = k; \theta) = \Big[\lambda(t_i | \mathcal{Y}(t_i), G_i = k)\Big]^{\delta_i} \times \exp\left\{ - \int_0^{t_i} \lambda(s | \mathcal{Y}(s), G_i = k) \mathrm{d}s \right\}$$

- Then, the log-likelihood (JLCMs type) writes

$$\ell_n(\theta) = n^{-1} \sum_{i=1}^{n} \log \sum_{k=0}^{K-1} \pi_{\xi_k}(x_i) f_\theta(t_i, \delta_i | G_i = k) f_\theta(y_i | G_i = k) \mathrm{d}b_i$$

# III. Inference

# Penalization

- Penalized objective

$$\ell_n^{\text{pen}}(\theta) = -\ell_n(\theta) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$$

with the elasticnet penalty

$$\|z\|_{\text{en},\eta} = (1-\eta)\|z\|_1 + \frac{\eta}{2}\|z\|_2^2$$

and the sparse group lasso penalty

$$\|z\|_{\text{sg}l_1,\tilde{\eta}} = (1-\tilde{\eta})\|z\|_1 + \tilde{\eta}\sum_{l=1}^{L}\|z^l\|_2$$

# Penalization





- Penalized objective

$$\ell_n^{\text{pen}}(\theta) = -\ell_n(\theta) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$$

with the elasticnet penalty

$$\|z\|_{\text{en},\eta} = (1-\eta)\|z\|_1 + \frac{\eta}{2}\|z\|_2^2$$

and the sparse group lasso penalty

$$\|z\|_{\text{sg}l_1,\tilde{\eta}} = (1-\tilde{\eta})\|z\|_1 + \tilde{\eta} \sum_{l=1}^{L} \|z^l\|_2$$

- Resulting optimization problem

$$\hat{\theta} \in \text{argmin}_{\theta \in \mathbb{R}^{\vartheta}} \ \ell_n^{\text{pen}}(\theta)$$

# prox-QNEM algorithm (1/2)

- $\ell_n^{\text{comp}}(\theta) = \ell_n^{\text{comp}}(\theta; \mathcal{D}_n, \boldsymbol{b}, \boldsymbol{G})$

# prox-QNEM algorithm (1/2)

- $\ell_n^{\text{comp}}(\theta) = \ell_n^{\text{comp}}(\theta; \mathcal{D}_n, \boldsymbol{b}, \boldsymbol{G})$

## E-step

- $\mathcal{Q}_n(\theta, \theta^{(w)}) = \mathbb{E}_{\theta^{(w)}}[\ell_n^{\text{comp}}(\theta) | \mathcal{D}_n]$

# prox-QNEM algorithm (1/2)



- $\ell_n^{\text{comp}}(\theta) = \ell_n^{\text{comp}}(\theta; \mathcal{D}_n, \boldsymbol{b}, \boldsymbol{G})$

## E-step

- $\mathcal{Q}_n(\theta, \theta^{(w)}) = \mathbb{E}_{\theta^{(w)}}[\ell_n^{\text{comp}}(\theta) | \mathcal{D}_n]$
- Requires to compute expectations of the form

$$\mathbb{E}_{\theta^{(w)}}[g(b_i, G_i) | t_i, \delta_i, y_i] = \sum_{k=0}^{K-1} \pi_{ik}^{\theta^{(w)}} \int_{\mathbb{R}^r} g(b_i, G_i) f_{\theta^{(w)}}(b_i | t_i, \delta_i, y_i) \mathrm{d} b_i$$

for different functions $g$, where we denote

$$\pi_{ik}^{\theta^{(w)}} = \mathbb{P}_{\theta^{(w)}}[G_i = k | t_i, \delta_i, y_i]$$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \; \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \; \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^{n} \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \ \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^n \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^n \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^{\vartheta}} \; \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^{n} \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^{n} \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$
- $\xi_k^{(w+1)} \in \text{argmin}_{\xi_k \in \mathbb{R}^p} \, P_{n,k}^{(w)}(\xi_k) + \zeta_{1,k} \|\xi_k\|_{\text{en},\eta}$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \; \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^n \hat{\mathbb{E}}_{\theta^{(w)}} [b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^n \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$
- $\xi_k^{(w+1)} \in \text{argmin}_{\xi_k \in \mathbb{R}^p} P_{n,k}^{(w)}(\xi_k) + \zeta_{1,k} \|\xi_k\|_{\text{en},\eta}$
- L-BFGS-B to solve the problem

$$\begin{aligned}
\text{minimize} \quad & P_{n,k}^{(w)}(\xi_k^+ - \xi_k^-) + \zeta_{1,k} \Big( (1-\eta) \sum_{j=1}^p (\xi_{k,j}^+ + \xi_{k,j}^-) + \frac{\eta}{2} \|\xi_k{}^+ - \xi_k{}^-\|_2^2 \Big) \\
\text{subject to} \quad & \xi_{k,j}^+ \geq 0 \text{ and } \xi_{k,j}^- \geq 0 \text{ for } j = 1, \dots, p
\end{aligned}$$

# prox-QNEM algorithm (2/2)



## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^{\vartheta}} \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^{n} \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^{n} \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$
- $\xi_k^{(w+1)} \in \text{argmin}_{\xi_k \in \mathbb{R}^p} P_{n,k}^{(w)}(\xi_k) + \zeta_{1,k} \|\xi_k\|_{\text{en},\eta}$
- L-BFGS-B to solve the problem

$$
\begin{aligned}
\text{minimize} \quad & P_{n,k}^{(w)}(\xi_k^+ - \xi_k^-) + \zeta_{1,k}\Big((1-\eta)\sum_{j=1}^{p}(\xi_{k,j}^+ + \xi_{k,j}^-) + \frac{\eta}{2}\|\xi_k{}^+ - \xi_k{}^-\|_2^2\Big) \\
\text{subject to} \quad & \xi_{k,j}^+ \geq 0 \text{ and } \xi_{k,j}^- \geq 0 \text{ for } j = 1, \ldots, p
\end{aligned}
$$

- Closed-form update for $\beta_k^{(w+1)}$

# prox-QNEM algorithm (2/2)



## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \ \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^{n} \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^{n} \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$
- $\xi_k^{(w+1)} \in \text{argmin}_{\xi_k \in \mathbb{R}^p} P_{n,k}^{(w)}(\xi_k) + \zeta_{1,k} \|\xi_k\|_{\text{en},\eta}$
- L-BFGS-B to solve the problem

$$
\begin{aligned}
\text{minimize} \quad & P_{n,k}^{(w)}(\xi_k^+ - \xi_k^-) + \zeta_{1,k}\Big((1-\eta)\sum_{j=1}^{p}(\xi_{k,j}^+ + \xi_{k,j}^-) + \frac{\eta}{2}\|\xi_k{}^+ - \xi_k{}^-\|_2^2\Big) \\
\text{subject to} \quad & \xi_{k,j}^+ \geq 0 \text{ and } \xi_{k,j}^- \geq 0 \text{ for } j = 1, \ldots, p
\end{aligned}
$$

- Closed-form update for $\beta_k^{(w+1)}$
- Proximal gradient (ISTA) for the $\gamma_k^{(w+1)}$ update, based on Lemma 1 that states $\text{prox}_{\text{sg}l_1,\tilde{\eta},\zeta} = \text{prox}_{\zeta\tilde{\eta}\sum_{l=1}^{L}\|\cdot\|_{2,l}} \circ \text{prox}_{\zeta(1-\tilde{\eta})\|\cdot\|_1}$

# prox-QNEM algorithm (2/2)

## Proximal Quasi-Newton M-step

- $\theta^{(w+1)} \in \text{argmin}_{\theta \in \mathbb{R}^\vartheta} \ \mathcal{Q}_n(\theta, \theta^{(w)}) + \sum_{k=0}^{K-1} \zeta_{1,k} \|\xi_k\|_{\text{en},\eta} + \zeta_{2,k} \|\gamma_k\|_{\text{sg}l_1,\tilde{\eta}}$
- $D^{(w+1)} = n^{-1} \sum_{i=1}^n \hat{\mathbb{E}}_{\theta^{(w)}}[b_i b_i^\top | t_i, \delta_i, y_i]$
- $P_{n,k}^{(w)}(\xi_k) = -n^{-1} \sum_{i=1}^n \hat{\pi}_{ik}^{\theta^{(w)}} \log \pi_{\xi_k}(x_i)$
- $\xi_k^{(w+1)} \in \text{argmin}_{\xi_k \in \mathbb{R}^p} P_{n,k}^{(w)}(\xi_k) + \zeta_{1,k} \|\xi_k\|_{\text{en},\eta}$
- L-BFGS-B to solve the problem

$$\begin{aligned} &\text{minimize} && P_{n,k}^{(w)}(\xi_k^+ - \xi_k^-) + \zeta_{1,k}\Big((1-\eta)\sum_{j=1}^p (\xi_{k,j}^+ + \xi_{k,j}^-) + \frac{\eta}{2}\|\xi_k{}^+ - \xi_k{}^-\|_2^2\Big) \\ &\text{subject to} && \xi_{k,j}^+ \geq 0 \text{ and } \xi_{k,j}^- \geq 0 \text{ for } j = 1, \ldots, p \end{aligned}$$

- Closed-form update for $\beta_k^{(w+1)}$
- Proximal gradient (ISTA) for the $\gamma_k^{(w+1)}$ update, based on Lemma 1 that states $\text{prox}_{\text{sg}l_1,\tilde{\eta},\zeta} = \text{prox}_{\zeta\tilde{\eta}\sum_{l=1}^L \|\cdot\|_{2,l}} \circ \text{prox}_{\zeta(1-\tilde{\eta})\|\cdot\|_1}$
- $\lambda_0^{(w+1)}(t) = \dfrac{\sum_{i=1}^n \delta_i \mathbb{1}_{\{t=t_i\}}}{\sum_{i=1}^n \sum_{k=0}^{K-1} \hat{\pi}_{ik}^{\theta^{(w)}} \exp\Big\{\gamma_k^{(w+1)\top} \Psi_i(t_i)\Big\} \mathbb{1}_{\{t_i \geq t\}}}$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor \text{ random samples without replacement} \big\}$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor \text{ random samples without replacement} \big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0,1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \big\lfloor \frac{L r_s}{K} \big\rfloor + 1, \ldots, (k+1) \big\lfloor \frac{L r_s}{K} \big\rfloor \Big\}$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0,1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \big\lfloor \dfrac{L r_s}{K} \big\rfloor + 1, \ldots, (k+1) \big\lfloor \dfrac{L r_s}{K} \big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left( \mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix} \right)$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \Big\lfloor \dfrac{Lr_s}{K} \Big\rfloor + 1, \ldots, (k+1) \Big\lfloor \dfrac{Lr_s}{K} \Big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left( \mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix} \right)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big( (1, t)^\top \beta_k^l + (1, t)^\top b_i^l \big)$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0,1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor \text{ random samples without replacement} \big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \big\lfloor \dfrac{Lr_s}{K} \big\rfloor + 1, \ldots, (k+1) \big\lfloor \dfrac{Lr_s}{K} \big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left( \mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix} \right)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big( (1, t)^\top \beta_k^l + (1, t)^\top b_i^l \big)$
- $\big( \tilde{\Psi}_{k,a}(t, \beta_k, b_i^l) \big)_{a \in \{1,2\}} = \big( \beta_{k,1}^l + \beta_{k,2}^l t + b_{i,1}^l + b_{i,2}^l t \ , {b_i^l}^\top \big)$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0,1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n\times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \dots, s$
- $\xi = (\underbrace{\varsigma_1, \dots, \varsigma_1}_{s}, 0, \dots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \big\lfloor \dfrac{Lr_s}{K} \big\rfloor + 1, \dots, (k+1) \big\lfloor \dfrac{Lr_s}{K} \big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left(\mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix}\right)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big((1,t)^\top \beta_k^l + (1,t)^\top b_i^l\big)$
- $\big(\tilde{\Psi}_{k,a}(t, \beta_k, b_i^l)\big)_{a \in \{1,2\}} = \big(\beta_{k,1}^l + \beta_{k,2}^l t + b_{i,1}^l + b_{i,2}^l t \ , {b_i^l}^\top\big)$
- $\tilde{\gamma}_{k,a}^l = \varsigma_2 \mathbb{1}_{\{l \in \mathcal{S}_k,\ a \in \{1,2\}\}}$

# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \big\lfloor \dfrac{Lr_s}{K} \big\rfloor + 1, \ldots, (k+1) \big\lfloor \dfrac{Lr_s}{K} \big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left( \mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix} \right)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big( (1, t)^\top \beta_k^l + (1, t)^\top b_i^l \big)$
- $\big( \tilde{\Psi}_{k,a}(t, \beta_k, b_i^l) \big)_{a \in \{1,2\}} = \big( \beta_{k,1}^l + \beta_{k,2}^l t + b_{i,1}^l + b_{i,2}^l t \ , {b_i^l}^\top \big)$
- $\tilde{\gamma}_{k,a}^l = \varsigma_2 \mathbb{1}_{\{l \in \mathcal{S}_k, \ a \in \{1,2\}\}}$
- $\lambda_i(t | G_i = k) = \lambda_0(t) \exp \big\{ \iota_{i,k,1} + \iota_{i,k,2} t \big\}$

# High-dimensional simulation study

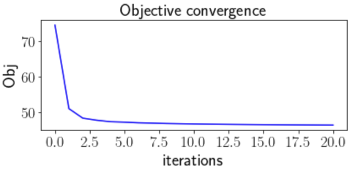
- High-risk subjects proportion $\pi_1 \in [0,1]$
- $\mathcal{H} = \big\{\lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n\times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k\big\lfloor \frac{Lr_s}{K} \big\rfloor + 1, \ldots, (k+1)\big\lfloor \frac{Lr_s}{K} \big\rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\Big(\mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix}\Big)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big((1,t)^\top \beta_k^l + (1,t)^\top b_i^l\big)$
- $\big(\tilde{\Psi}_{k,a}(t, \beta_k, b_i^l)\big)_{a \in \{1,2\}} = \big(\beta_{k,1}^l + \beta_{k,2}^l t + b_{i,1}^l + b_{i,2}^l t \ , b_i^{l}{}^\top\big)$
- $\tilde{\gamma}_{k,a}^l = \varsigma_2 \mathbb{1}_{\{l \in \mathcal{S}_k,\ a \in \{1,2\}\}}$
- $\lambda_i(t|G_i = k) = \lambda_0(t) \exp\big\{\iota_{i,k,1} + \iota_{i,k,2} t\big\}$
- Gompertz baseline $\lambda_0(t) = \kappa_1 \kappa_2 \exp(\kappa_2 t)$

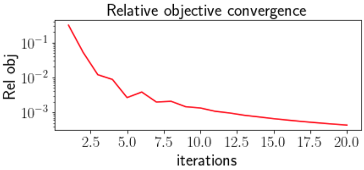
# High-dimensional simulation study

- High-risk subjects proportion $\pi_1 \in [0, 1]$
- $\mathcal{H} = \big\{ \lfloor \pi_1 n \rfloor$ random samples without replacement$\big\}$
- $[x_{ij}] \in \mathbb{R}^{n \times p} \sim \mathcal{N}\big(0, \Sigma_1(\rho_1)\big)$
- $x_{ij} \leftarrow x_{ij} + (-1)^{\mathbb{1}_{\{i \notin \mathcal{H}\}}} gap$ for $j = 1, \ldots, s$
- $\xi = (\underbrace{\varsigma_1, \ldots, \varsigma_1}_{s}, 0, \ldots, 0) \in \mathbb{R}^p$
- $G_i \sim \mathcal{B}\big(\pi_\xi(x_i)\big)$
- $\mathcal{S}_k = \Big\{ k \lfloor \dfrac{Lr_s}{K} \rfloor + 1, \ldots, (k+1) \lfloor \dfrac{Lr_s}{K} \rfloor \Big\}$
- $\beta_k^l \sim \mathbb{1}_{\{l \in \mathcal{S}_k\}} \mathcal{N}\left( \mu_k, \begin{bmatrix} \rho_3 & 0 \\ 0 & \rho_3 \end{bmatrix} \right)$
- $Y_i^l(t) = \epsilon_i^l(t) + \mathbb{1}_{\{l \in \mathcal{S}_k\}} \sum_{k=0}^{K-1} \mathbb{1}_{\{G_i = k\}} \big( (1, t)^\top \beta_k^l + (1, t)^\top b_i^l \big)$
- $\big(\tilde{\Psi}_{k,a}(t, \beta_k, b_i^l)\big)_{a \in \{1,2\}} = \big( \beta_{k,1}^l + \beta_{k,2}^l t + b_{i,1}^l + b_{i,2}^l t \ , b_i^l{}^\top \big)$
- $\tilde{\gamma}_{k,a}^l = \varsigma_2 \mathbb{1}_{\{l \in \mathcal{S}_k, \ a \in \{1,2\}\}}$
- $\lambda_i(t | G_i = k) = \lambda_0(t) \exp\big\{ \iota_{i,k,1} + \iota_{i,k,2} t \big\}$
- Gompertz baseline $\lambda_0(t) = \kappa_1 \kappa_2 \exp(\kappa_2 t)$
- $T_i^\star | G_i = k \sim \dfrac{1}{\iota_{i,k,2} + \kappa_2} \log \left( 1 - \dfrac{(\iota_{i,k,2} + \kappa_2) \log U_i}{\kappa_1 \kappa_2 \exp \iota_{i,k,1}} \right)$

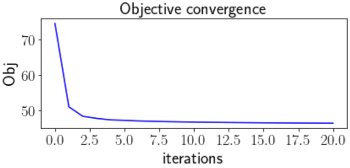
# First results (1/2)

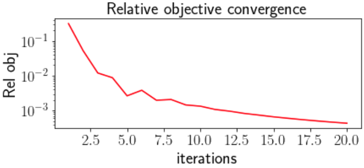


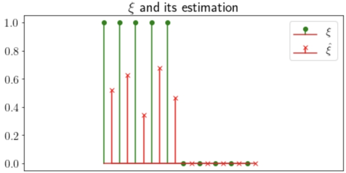


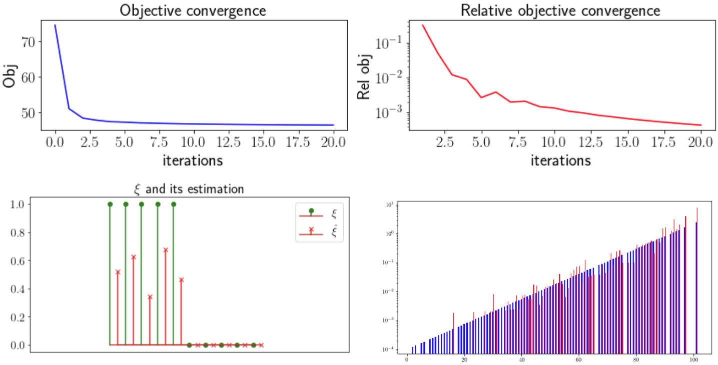
# First results (1/2)



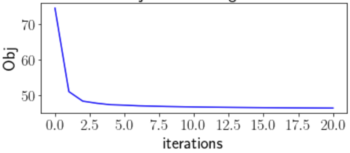



# First results (1/2)

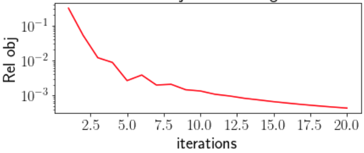


# First results (1/2)

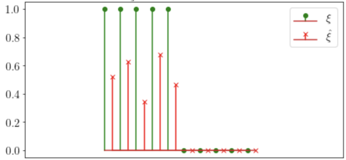
Objective convergence

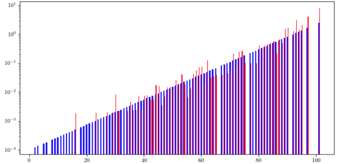



Relative objective convergence

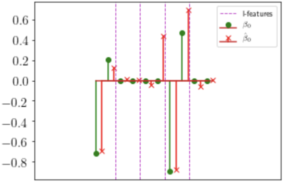



$\xi$ and its estimation

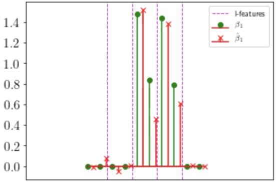


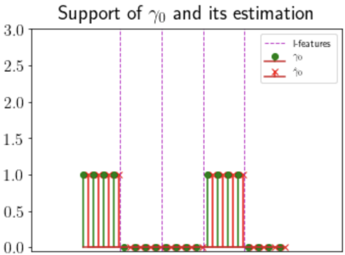

$\beta_0$ and its estimation

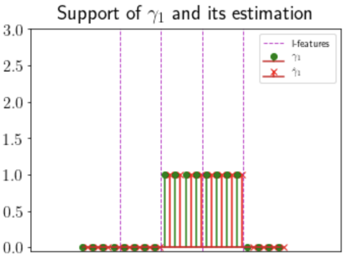



$\beta_1$ and its estimation

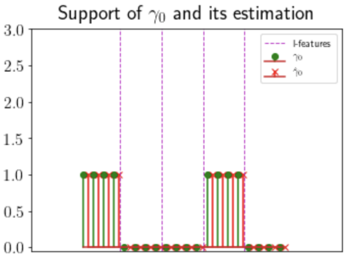


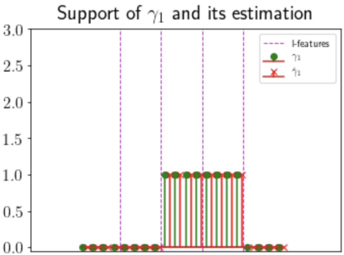
# First results (2/2)

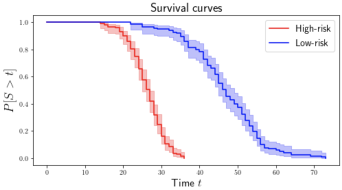


# First results (2/2)

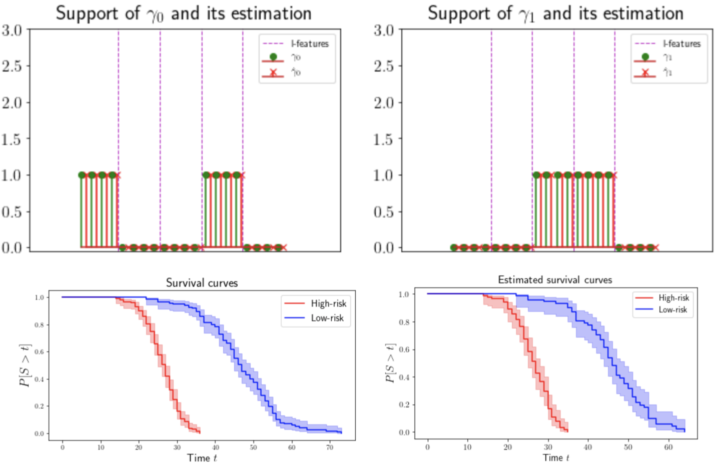


# First results (2/2)





# V. Conclusion

# Conclusion

- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available

# Conclusion

- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available
- Penalization of the likelihood in order to perform feature selection and to prevent overfitting

# Conclusion

- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available
- Penalization of the likelihood in order to perform feature selection and to prevent overfitting
- New efficient estimation algorithm (prox-QNEM) has been derived

# Conclusion

- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available
- Penalization of the likelihood in order to perform feature selection and to prevent overfitting
- New efficient estimation algorithm (prox-QNEM) has been derived
- Automatically determines significant prognostic longitudinal features

# Conclusion

- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available
- Penalization of the likelihood in order to perform feature selection and to prevent overfitting
- New efficient estimation algorithm (prox-QNEM) has been derived
- Automatically determines significant prognostic longitudinal features

## Python 3 package

- Available at https://github.com/Califrais/lights

# Conclusion



- Prognostic method called lights introduced to deal with the problem of joint modeling of longitudinal data and censored durations, where a large number of longitudinal features are available
- Penalization of the likelihood in order to perform feature selection and to prevent overfitting
- New efficient estimation algorithm (prox-QNEM) has been derived
- Automatically determines significant prognostic longitudinal features

## Python 3 package

- Available at `https://github.com/Califrais/lights`
- Applications of the model available soon

# Thank you!

# References