Dynamic Prediction of Generalized Functional Data

Ying Jin, Andrew Leroux

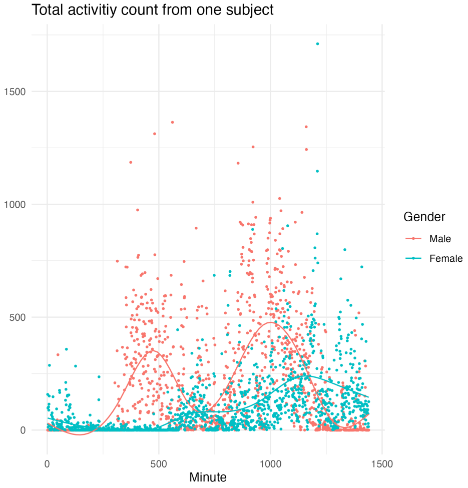
December 8th, 2023

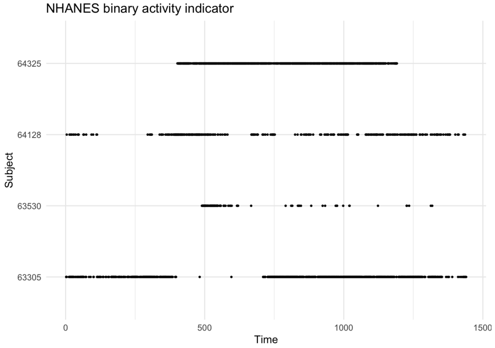
Introduction

Functional data

- Functional data
  - Unit of observations is a function for each subject
  - Arising from a smooth underlying function: $E(Y(t)) = \mu(t)$
  - Observed as repeated measures densely collected across the study domain
- Generalized functional data
  - Functional data with discrete value (e.g., binary outcome)
  - Following exponential family distribution characterized by a continuous latent function: $g(E(Y(t))) = \eta(t)$

Examples


Total activitiy count from one subject
1500
1000
500
0
0
500
1000
1500
Minute
Gender
Male
Female


NHANES binary activity indicator
64325
64128
63530
63305
Subject
0
500
1000
1500
Time

Dynamic prediction

- Dynamic prediction

  When there are repeated measures
  - To predict future outcomes based on historical data from the same subject
  - Prediction updates as extra measures are collected For example, to predicted activities in the afternoon \ given activities in the morning
- Challenges of generalized functional data
  - Density NHANES minute-by-minute activity indicator, 1440 measure per subject
  - Complexity
  - Estimation of out-of-sample random effect
- Goal: to develop a fast, scalable method for dynamic prediction of generalized functional outcomes

Method

Assumptions

For each subject i in the population

- A generalized outcome $Y_i(t)$ is generated along a variable t (for example, time), where $t \in (0, T]$
- The outcome, at any specific t, follows an exponential family distribution characterized by a (latent) continuous function $\eta_i(t)$
- The latent function $\eta_i(t)$ consists of a functional fixed effect (population-level) and a random effect (subject-level)

$$g[E(Y_i(t))] = \eta_i(t) = \beta_0(t) + b_i(t)$$

Functional extension of the mixed model framework

Observed data

- In practice we would observe the discrete realization of $\{Y_i(t), t\}$ along a dense grid
- Domain of t: $(0, T]$
- Measurement index $j = 1...J$

At each j, we have the value of t, and the value of outcome Y

- Value of t at jth observation: t_j
- Value of outcome at jth observation: $Y_i(t_j)$

Generalized Functional Principal Component Analysis (GFPCA)

In FPCA, the expectation of functional outcome is decomposed. In GFPCA, the transformation of mean is decomposed.

- Functional PCA of non-Gaussian functional data

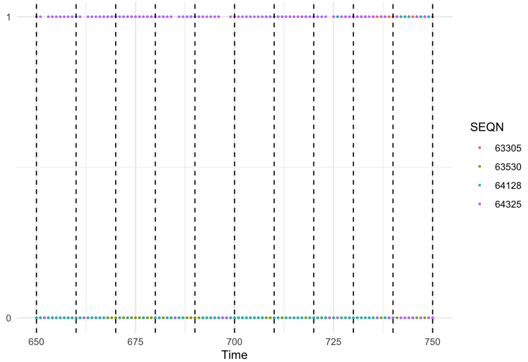
$$g(E(Y_i(t))) = f_0(t) + \sum_{k=1}^{K} \xi_{ik}\phi_k(t)$$

  - f_0 is the population mean function
  - ϕ_k are orthogonal principal component functions (PC)
  - ξ_{ik} are mutually independent scores/loadings. $\xi_{ik} \sim N(0, \lambda_k)$
- Existing methods tend to be slow in implementation
- Fast implementation of FPCA exists for Gaussian outcomes (e.g., FACE)

Fast implementation of GFPCA (fGFPCA)

Example: a 100-min section taken from one day

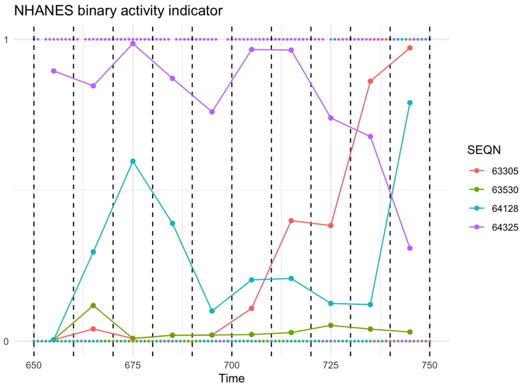
NHANES binary activity indicator



Bin the observed outcomes in to small, non-overlapping, equal length bins.

- Bin index: $s \in \{1, 2, ...S\}$
- Midpoint index of the sth bin: m_s
- Value of t at bin midpoints: t_{m_s}
- If bins have equal length w, then the sth bin is $(t_{m_s} - \frac{w}{2}, t_{m_s} + \frac{w}{2}]$

Fast implementation of GFPCA (fGFPCA)

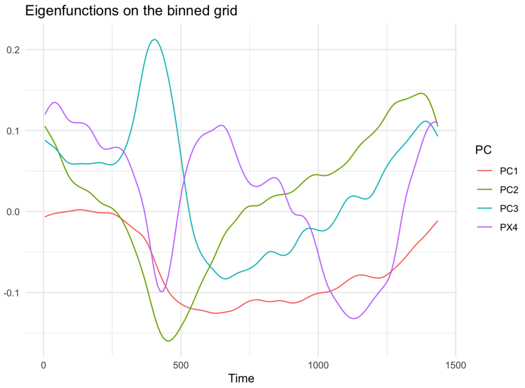


Fit a local, intercept-only generalized linear mixed model at every bin:

$$g[E(Y_i(t_j))] = \eta_i(t_{m_s}) = \beta_0(t_{m_s}) + b_i(t_{m_s})$$
$$t_j \in (t_{m_s} - \frac{w}{2}, t_{m_s} + \frac{w}{2}]$$

Estimate subject-level latent function tracks on the binned grid $\hat{\eta}_i(t_{m_s})$

Fast implementation of GFPCA (fGFPCA)



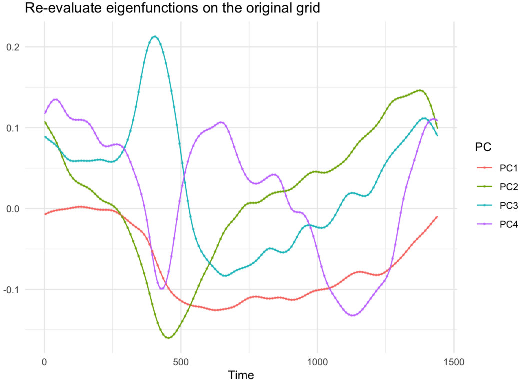
Fit FPCA on the estimated latent functions:

$$\hat{\eta}_i(t_{m_s}) = f_0(t_{m_s}) + \sum_{k=1}^{K} \xi_{ik}\phi_k(t_{m_s}) + \epsilon_i(t_{m_s})$$

to obtain a set of estimates:

- Basis functions $\hat{\mathbf{\Phi}} = \{\hat{\phi}_1(t_{m_s}), ..., \hat{\phi}_K(t_{m_s}))\}$
- Variance of scores $\hat{\lambda}_1 ... \hat{\lambda}_K$

Fast implementation of GFPCA (fGFPCA)



Special case of splines interpolation

- $\hat{\phi}_K(t_{m_s})$ are estiamted on the binned grid
  - Use spline basis the to re-evaluated on the original grid t_j
- $\hat{\phi}_K(t_{m_s})$ and $\hat{\lambda}_k$ are biased by a multiplicative factor
  - Use a GLMM model to de-biased
- This step also re-estimates the population mean function $\hat{f}_0$

Out-of-sample dynamic prediction

- Assume we have a new observations u who is partiall observed with J_u measures ($J_u < J$)
- Prediction of unobserved track: $\hat{\eta_u}(t_j) = \hat{f}_0(t_j) + \sum_{k=1}^{K} \hat{\xi}_{uk}\hat{\phi}_k(t_j), J_u < j \leq J$
- Since the outcome follows an exponential family distribution $p(Y_i(t)|\eta_i(t)) = h(Y_i(t))exp\{\eta_i(t)T[Y_i(t)] - A(\eta_i(t))\}$, the Log-likelihood of this new subject:

$$l_u(\boldsymbol{\xi}_u) = \sum_{j<J_u} log(h(Y_u(t_j))) + \eta_u(t_j)T(Y_u(t_j)) - log(A[\eta_u(t_j)])$$
$$\boldsymbol{\xi}_u = [\xi_{u1}, ..., \xi_{uK}]$$

- Use Bayes method to maximum the likelihood:
  - Prior distribution: $\xi_{uk} \sim N(0, \hat{\lambda}_k)$
  - Posterior distribution: the likelihood of $P(Y_u(t_j)|\xi_u) = l_u(\boldsymbol{\xi}_u)$

Simulation

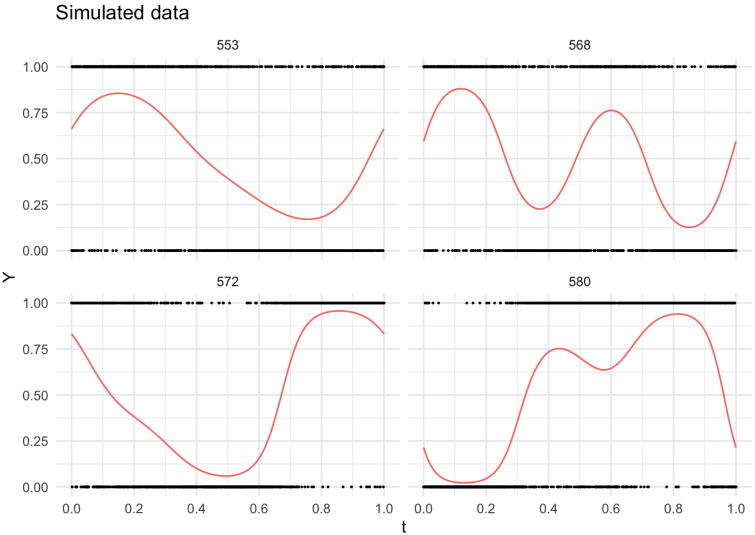
Simulation 1

- Training sample size N=500
- Each subject has 1000 observations along $t \in (0, 1]$ (J = 1000)
- Binary functional outcomes:

$$Y_i(t) \sim Bernoulli(\frac{exp(\eta_i(t))}{1 + exp(\eta_i(t))})$$
$$\eta_i(t) = f_0(t) + \xi_{i1}\sqrt{2}sin(2\pi t) + \xi_{i2}\sqrt{2}cos(2\pi t) +$$
$$\xi_{i3}\sqrt{2}sin(4\pi t) + \xi_{i4}\sqrt{2}cos(4\pi t)$$ cyclice pattern

  - $f_0(t) = 0$
  - $\xi_{ik} \sim N(0, 0.5^{k-1}),\ k \in \{1, 2, 3, 4\}$
- Additional 100 subjects for testing
- Repeat 500 times

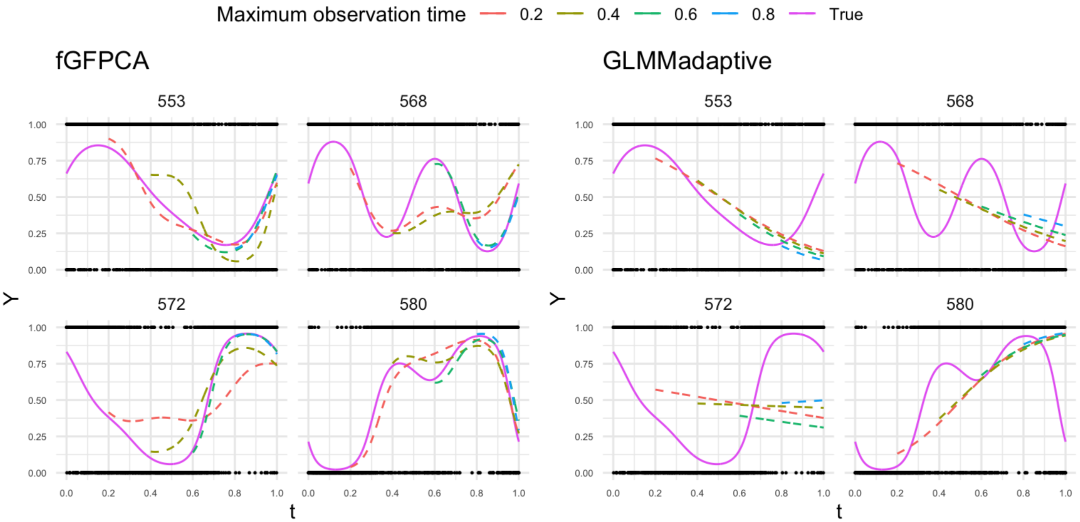
Example


Simulated data
553
568
572
580
1.00
0.75
0.50
0.25
0.00
0.0
0.2
0.4
0.6
0.8
1.0
Y
t

Evaluation

- Compare predictive performance of two methods
  - fGFPCA
  - GLMM using Adaptive Gaussian Quadrature (GLMMadaptive)
    - Limited in terms of model flexibility: $g(E(Y_i)) = \beta_0 + \beta_1 t + b_{i0} + b_{i1} t$
    - Incorporate spline basis: computationally unfeasible
- Evaluation metrics
  - Integrated Squared Error (ISE) for latent function
  - Area-Under-the-Receiver-Operator-Curve (AUC) for the observed binary outcome

Indivivdual predicted tracks



Intergrated squared error

	Maximum observation time							
	fGFPCA				GLMMadaptive			
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8
(0.2, 0.4]	146.407				387.708			
(0.4, 0.6]	183.967	74.977			291.579	269.799		
(0.6, 0.8]	218.265	49.275	15.776		315.778	282.736	278.242	
(0.8, 1.0]	108.918	77.981	17.747	12.005	563.011	477.485	597.746	600.34

for example: subject 580 red line

Because of the cyclic pattern, start and end of one cycle are close to each other

Area under the ROC curve

	Maximum observation time							
	fGFPCA				GLMMadaptive			
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8
(0.2, 0.4]	0.748				0.591			
(0.4, 0.6]	0.664	0.734			0.524	0.596		
(0.6, 0.8]	0.715	0.790	0.803		0.669	0.694	0.687	
(0.8, 1.0]	0.740	0.755	0.781	0.784	0.514	0.556	0.526	0.564

Computation time (minutes)

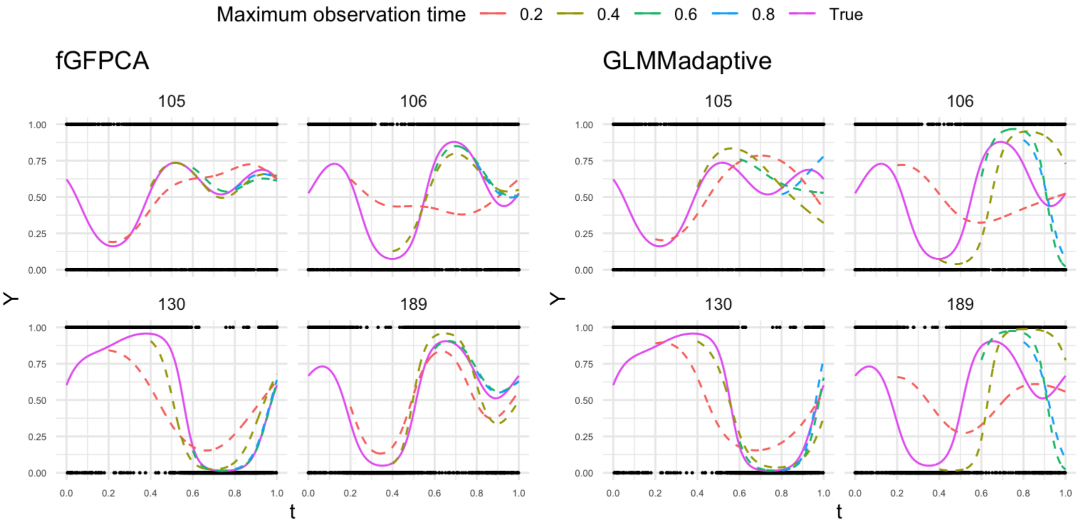
Method	Fit	Prediction
fGFPCA	0.725	1.592
GLMMadaptive	2.287	0.017

Simulation 2

- Use smaller datasets so that GLMMadaptive achieves higher flexibility
  - Training sample size N $=$ 100
  - Fit GLMMadaptive on 10% of the measurements
  - Repeat 100 times
- Reference model:

$$g(E(Y_i(t))) = \sum_{k=1}^{4} \zeta_k B_k(t) + \sum_{l=1}^{4} \xi_{il} \phi_l(t)$$

Individual predicted tracks



Integrated squared error

	Observation track							
	fGFPCA				GLMMadaptive			
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8
(0.2,0.4]	151.709				374.368			
(0.4,0.6]	189.147	77.904			268.805	464.796		
(0.6,0.8]	226.314	51.773	17.050		321.530	286.806	230.564	
(0.8, 1.0]	113.007	81.718	19.576	13.244	227.965	472.162	341.146	136.831

Area under the ROC curve

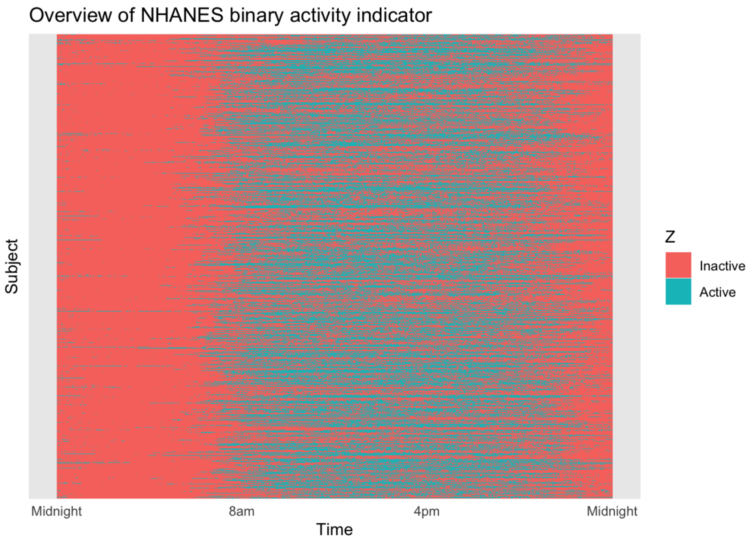
	Observation track							
	fGFPCA				GLMMadaptive			
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8
(0.2,0.4]	0.745				0.674			
(0.4,0.6]	0.663	0.733			0.623	0.671		
(0.6,0.8]	0.712	0.789	0.802		0.691	0.700	0.732	
(0.8, 1.0]	0.741	0.755	0.782	0.785	0.680	0.627	0.679	0.743

Computation time (minutes)

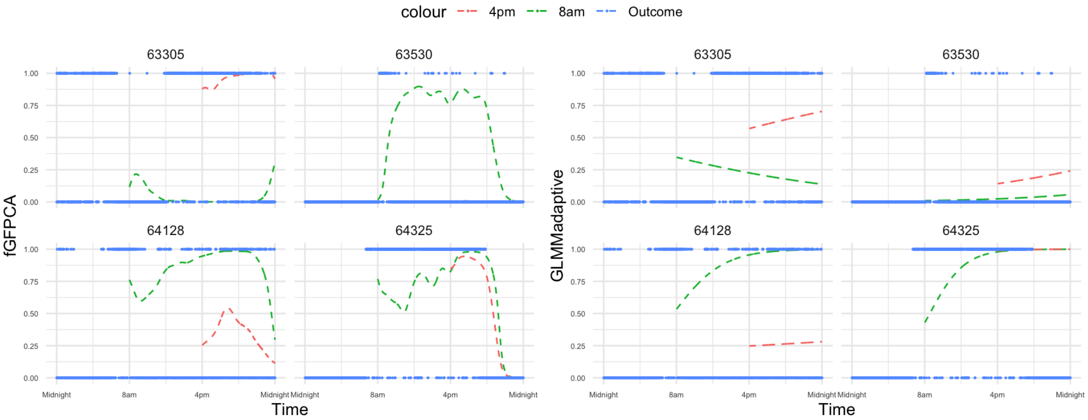
Method	Fit	Prediction
fGFPCA	0.043	1.405
GLMMadaptive	5.842	0.023

Data application

NHANES binary activity indicator



Individual predicted tracks



Area under the ROC curve

	Maximum observation time			
	fGFPCA		GLMMadaptive	
Window	8am	4pm	8am	4pm
8am-4pm	0.587		0.628	
4am-midnight	0.680	0.766	0.448	0.613

Discussion

Discussion

- fGFPCA can accommodate more flexible correlation structure between repeated measure
- fGFPCA reduced time spent on model fitting
- However, when ever larger dataset, fGFPCA is still not efficient enough
    - The GLMM model for re-evaluation of estimates in step 4
    - Laplace Approximation for out-of-sample prediction

Thank you!

References

Douglas Bates, Martin Mächler, Ben Bolker, and Steve Walker.
Fitting linear mixed-effects models using lme4.
Journal of Statistical Software, 67(1):1–48, 2015.

Jeff Goldsmith, Fabian Scheipl, Lei Huang, Julia Wrobel, Chongzhi Di, Jonathan Gellar, Jaroslaw Harezlak, Mathew W. McLean, Bruce Swihart, Luo Xiao, Ciprian Crainiceanu, and Philip T. Reiss.
refund: Regression with Functional Data, 2022.
R package version 0.1-28.

Mithat Gonen and Glenn Heller.
Concordance probability and discriminatory power in proportional hazards regression.
Biometrika, 92(4):965–970, 2005.

Patrick J. Heagerty and Yingye Zheng.
Survival model predictive accuracy and roc curves.
Biometrics, 61(1):92–105, 2005.

Appendix

Example: binary data

- Maximize the posterior log-likelihood:

$$l(\boldsymbol{\xi}_u|\boldsymbol{Y}_u, \hat{\boldsymbol{\Theta}}) \propto l(\boldsymbol{Y}_u|\boldsymbol{\xi}_u, \hat{\boldsymbol{\Theta}}) + l(\boldsymbol{\xi}_u|\hat{\boldsymbol{\Theta}})$$

- Log-likelihood of $\boldsymbol{Y}_u$:

$$l(\boldsymbol{Y}_u|\boldsymbol{\xi}_u, \hat{\boldsymbol{\Theta}}) = \sum_{s=1}^{s_{max}} h_s \eta(s) - \sum_{s=1}^{s_{max}} n_s log(1 + exp(\eta(s))), \quad \eta(s) = \hat{f}_0(s) + \sum_{k=1}^{K} \xi_{uk} \hat{\phi}_k(s)$$

  - n_s indicates the number of observation in the sth bin
  - h_s indicates the number of events/sucesses in the sth bin
  - t_m is in bin s_{max}
- Log-likelihood of $\boldsymbol{\xi}_u$:

$$l(\boldsymbol{\xi}_u|\hat{\boldsymbol{\Theta}}) \propto -\boldsymbol{\xi}_u^T \boldsymbol{\Gamma}^{-1} \boldsymbol{\xi}_u / 2, \quad \boldsymbol{\Gamma} = \begin{bmatrix} \hat{\lambda}_1 & \dots \\ \dots & \dots \\ \dots & \hat{\lambda}_K \end{bmatrix}$$

Example: binary data

$$l(\xi_u|\boldsymbol{Y}_u, \hat{\boldsymbol{\Theta}}) \propto \sum_{s=1}^{s_{max}} h_s \eta(s) - \sum_{s=1}^{s_{max}} n_s log(1 + exp(\eta(s)) - \xi_u^T \boldsymbol{\Gamma}^{-1} \xi_u / 2$$

$$\frac{dl(\xi_u|\boldsymbol{Y}_u, \hat{\boldsymbol{\Theta}})}{d\xi_u} = \sum_{s=1}^{s_{max}} h_s \phi(s) - \sum_{s=1}^{s_{max}} n_s \frac{exp(\eta(s))}{1 + exp(\eta(s))} \phi(s) - \xi_u^T \boldsymbol{\Gamma}^{-1} = 0$$

- The numeric solution of the score equation can be found efficiently