Manuscript progress report

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Contents

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 $\eta_i(t)$:

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

$$p(Y_i(t)) = h(Y_i(t))exp\{\eta_i(t)T[Y_i(t)] - A(\eta_i(t))\}$$

- The continuous latent function consists of a population-level fixed process and an individual-level random process

$$\eta_i(t) = \beta_0(t) + b_i(t)$$

Observed data

In practice we would observe the discrete realization of $\{Y_i(t), t\}$ along a dense grid. For simplicity, we assume the observation grid is regular (same across sample). When we have J observations points in $(0, T]$, then for the jth observation point, we denote the corresponding value of t as t_j, and the corresponding outcome at this point $Y_i(t_j)$.

fGFPCA Algorithm

Bin data:

Choose a proper bin width w considering model complexity and identifiability. For now let's say the bins are equal-length and non-overlapping.

- Bin index $s = 1...S$
- Index of bin midpoints m_s
- Value of t corresponding to bin midpoints t_{m_s}
- Bin endpoints: $(t_{m_s} - \frac{w}{2}, t_{m_s} + \frac{w}{2}]$

Local GLMMs

At the every bin, we fit a local intercept-only model:

$$g[E(Y_i(t_j))] = \eta_i(t_{m_s}) = \beta_0(t_{m_s}) + b_i(t_{m_s})$$

where $t_j \in (t_{m_s} - \frac{w}{2}, t_{m_s} + \frac{w}{2}]$.

Here we are basically saying that the value of latent function is constant within the same bin, which clearly is a misspecification of the true latent process.

From the model above. we will be able to estimate a $\hat{\eta}_i(t_{m_s})$ on the binned grid for every individual in the training sample.

FPCA

Here, we fit a FPCA model on the $\hat{\eta}_i(t_{m_s})$ obtained from step 2:

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

where ξ_{ik} independently follows normal distribution $N(0, \lambda_k)$, and $\epsilon_i(t_{m_s})$ at each point follows $N(0, \sigma_2)$.

From this model, we will be able to obtain the following estimates which are shared across population:

- Population mean $\hat{f}_0(t_{m_s})$
- Basis functions $\hat{\boldsymbol{\Phi}} = \{\hat{\phi}_1(t_{m_s}), ..., \hat{\phi}_K(t_{m_s}))\}$
- Estimates of variance of scores $\hat{\lambda}_1 ... \hat{\lambda}_K$

Projection and Debias

The mean and basis functions are evaluated on the binned grid. To extend it to the original measurement grid data was collected on, we project the estimated eigenfunctions $\hat{\boldsymbol{\Phi}}$ back use spline basis. Now we have extend the $\hat{\phi}_k(t_{m_s})$ to the original grid $\hat{\phi}_k(t_j)$

Because of the misspecification of local GLMMs, the estimated eigenfunctions and eigenvalues are also biased by a constant multiplicative effect. Therefore, we use a GLMM to re-evaluate the mean function, eigenfunctions and eigenvalues.

Out-of-sample prediction

Now, let's assume we have a new subject u with J_u observations ($J_u < J$). Then the log-likelihood of this new subject would be:

$$l_u = \sum_{t_j < t_{J_u}} log(h(Y_u(t_j))) + \hat{\eta}_u(t_j)T(Y_u(t_j)) - log(A[\hat{\eta}_u(t_j)])$$

where $\hat{\eta}_u(t_j) = \hat{f}_0(t_j) + \sum_{k=1}^{K} \xi_{uk}\hat{\phi}(t_j)$.

With estimates for the population-level parameters from fGFPCA algorithms above, we can estimate ξ_{uk} by maximization of l_u. Direct maximization some times does not have closed form solution. Numeric maximization methods seem not very stable as well. So I have decided to used a Bayes approach (Laplace Approximation):

- Prior distribution: $\xi_{uk} \sim N(0, \hat{\lambda}_k)$
- Posterior distribution: the likelihood of $l_u = l(Y_u(t_j)|\xi_u)$

Laplace Approximation would get the posterior mode of ξ_{uk} through quadratic approximation.

Reference method

GLMMadaptive

- For large datasets, we can fit a model with random intercept and slope for time. It is doable on 500 datasets, but obviously too simple for the data generation scheme. We would expect it to perform terribly.

$$g(E(Y_i(t))) = \beta_0 + \beta_1 t + b_{i0} + b_{i1} t$$

- For small datasets, we would like to fit fGFPCA and GLMMadaptive on a dataset with smaller sample size and/or smaller measurement density. For the GLMMadaptive model, we would set it up with spline basis functions so that its flexibility is comparable with fGFPCA model, such as:

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

Generalized functional-on-scalar regression

We would like to use a second reference method for predictive performance comparision. In this model, predictions on a specific interval are all made using the last few observations in the observed window. For example, if we are given observations on [0, 0.2] (j = $1 \dots 200$), we may use L observations taken right before t=0.2 ($t_j : j = 200, ...200 - (L-1)$) as time-fixed covariate to predict any future time.

Let's write out the model expression (with questionable notation). If the observations if up to t_m, then:

$$\begin{aligned} g(E[Y_i(t)]) &= \beta_0(t) + \sum_{l=1}^{L} \beta_l(t) Y_i(t_l) \\ l &= m, ...m - (j-1) \\ t &> t_m \end{aligned}$$

This is a simple function-on-scalar model with no random effect, meaning all subject with the same last observed outcome would have the same estimated/predicted latent track. This is clearly anti-intuitive. But adding random effects would make out-of-sample prediction impossible.

Under both frameworks, for each dataset we need to fit four models (similar to the GLMMadaptive method):

- Given 0-0.2, predict 0.2-1
- Given 0-0.4, predict 0.4-1
- Given 0-0.6, predict 0.6-1
- Given 0-0.8, predict 0.8-1

But prediction performance will be reported by equal-length time window.

Larger-scale simulation

Simulation set up

Here we simulate binary data from cyclic latent process:

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

where:

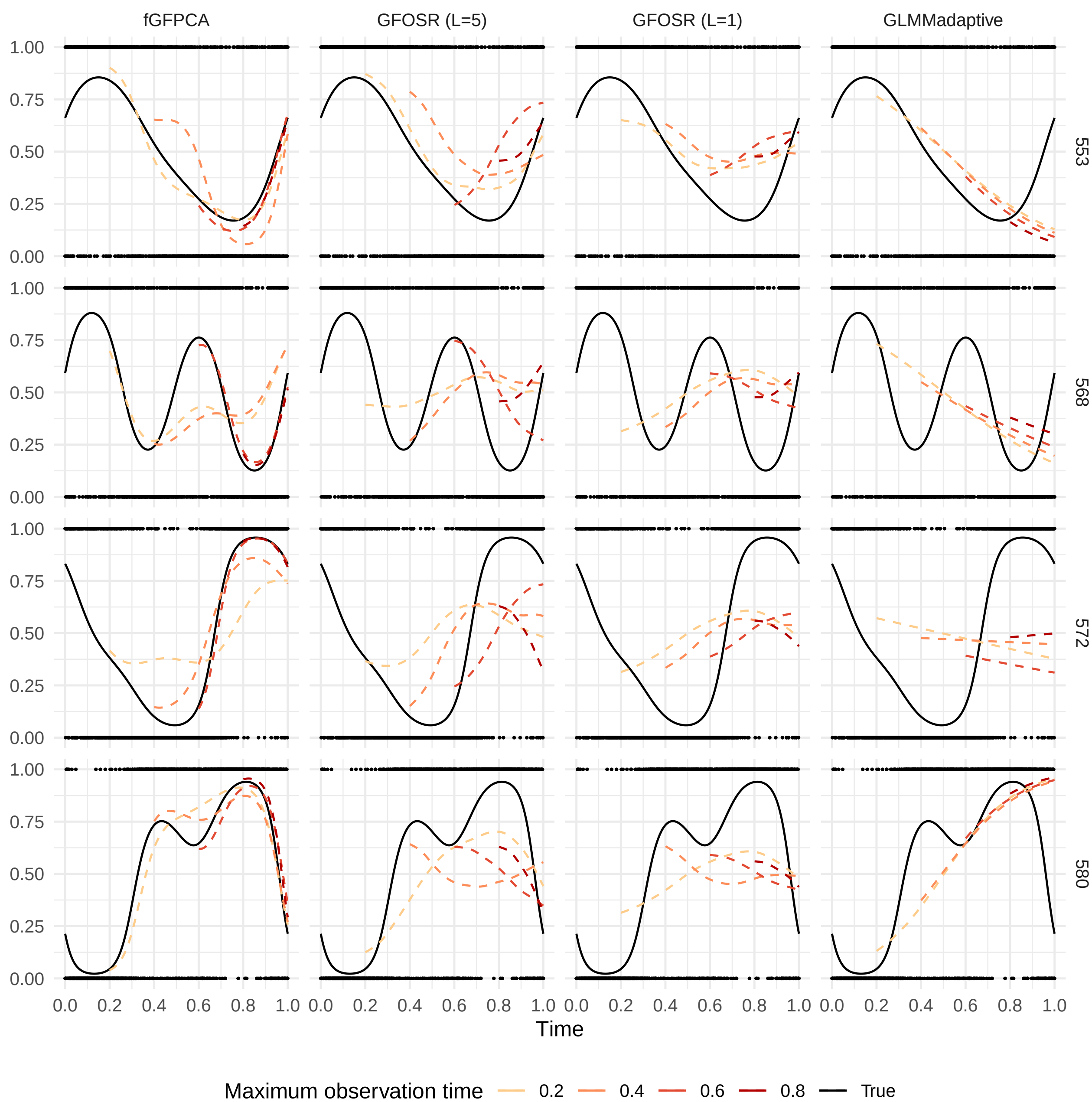
- t is 1000 equal-spaced observations points on $[0, 1]$ (J = 1000).
- $f_0(t) = 0$
- $\xi_k \sim N(0, \lambda_k)$, and $\lambda_k = 1, 0.5, 0.25, 0.125$ for k = 1, 2, 3, 4 respectively.
- Sample size $N = 500$
- In the binning step, we bin every 10 observations
- 500 simulations were implemented

Figures

```
load(here("Data/SimOutput_fGFPCA.RData"))
load(here("Data/SimOutput_GLMMadaptive.RData"))
load(here("Data/SimOutput_GFOSR_L1.RData"))
pred_list_gfosr_l1 <- pred_list_gfofr
t_vec_gfosr_l1 <- t_vec_gfofr
rm(pred_list_gfofr, t_vec_gfofr)
load(here("Data/SimOutput_GFOSR_L5.RData"))
pred_list_gfosr_l5 <- pred_list_gfofr
t_vec_gfosr_l5 <- t_vec_gfofr
rm(pred_list_gfofr, t_vec_gfofr)

rand_id <- sample(501:600, size = 4)
```

```
bind_rows(
  pred_list_all[[1]] %>% filter(id %in% rand_id) %>%
    mutate(method="fGFPCA"),
  pred_list_ref[[1]] %>% filter(id %in% rand_id) %>%
    mutate(method = "GLMMadaptive"),
  pred_list_gfosr_l1[[1]] %>% filter(id %in% rand_id) %>%
    mutate(method = "GFOSR (L=1)") %>%
    rename(pred0.2=pred_w1, pred0.4=pred_w2, pred0.6=pred_w3, pred0.8=pred_w4),
  pred_list_gfosr_l5[[1]] %>% filter(id %in% rand_id) %>%
    mutate(method = "GFOSR (L=5)") %>%
    rename(pred0.2=pred_w1, pred0.4=pred_w2, pred0.6=pred_w3, pred0.8=pred_w4)
) %>% mutate_at(vars(eta_i, pred0.2, pred0.4, pred0.6, pred0.8),
                .funs = function(x){exp(x)/(1+exp(x))}) %>%
  mutate(method=factor(method,
         levels = c("fGFPCA", "GFOSR (L=5)", "GFOSR (L=1)","GLMMadaptive"))) %>%
  ggplot()+
```

```r
  geom_point(aes(x=t, y=Y), size = 0.2)+
  geom_line(aes(x=t, y=eta_i, col = "True"))+
  geom_line(aes(x=t, y=pred0.2, col = "0.2"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.4, col = "0.4"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.6, col = "0.6"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.8, col = "0.8"), linetype="dashed", na.rm=T)+
  facet_grid(rows = vars(id), cols = vars(method))+
  labs(col = "Maximum observation time", x = "Time", y="")+
  scale_x_continuous(breaks = seq(0, 1, by = 0.2))+
  theme(legend.position = "bottom")+
  scale_color_manual(values = cols)
```



ISE and AUC

```r
## ISE container
ise_fgfpca <- ise_adglmm <- ise_gfosr_l1 <- ise_gfosr_l5 <-
  array(NA, dim = c(length(window)-2, length(window)-2, M))
# dims: prediction window, max obs time, simulation iter
```

```r
## calculation
for(m in 1:M){
  # this_df <- pred_list_all[[m]]
  ise_tb <- pred_list_all[[m]] %>%
    mutate(err1 = (pred0.2-eta_i)^2,
           err2 = (pred0.4-eta_i)^2,
           err3 = (pred0.6-eta_i)^2,
           err4 = (pred0.8-eta_i)^2) %>%
    select(id, t, starts_with("err")) %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("err"))
  ise_fgfpca[, ,m] <- as.matrix(ise_tb)


}

mean_ise_fgfpca <- apply(ise_fgfpca, c(1, 2), mean)

# mean_ise <- data.frame(mean_ise) %>%
#   mutate(Window = c("(0.2, 0.4]", "(0.4, 0.6]", "(0.6, 0.8]", "(0.8, 1.0]"),
#          .before = 1)
colnames(mean_ise_fgfpca) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
## calculation
for(m in 1:M){
  # this_df <- pred_list_gfosr_l1[[m]]
  ise_tb <- pred_list_ref[[m]] %>%
    mutate(err1 = (pred0.2-eta_i)^2,
           err2 = (pred0.4-eta_i)^2,
           err3 = (pred0.6-eta_i)^2,
           err4 = (pred0.8-eta_i)^2) %>%
    select(id, t, starts_with("err")) %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("err"))
  ise_adglmm[, ,m] <- as.matrix(ise_tb)
}
```

```r
mean_ise_adglmm <- apply(ise_adglmm, c(1, 2), mean)
colnames(mean_ise_adglmm) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
## calculation
for(m in 1:M){
  # this_df <- pred_list_ref[[m]]
  ise_tb <- pred_list_gfosr_l1[[m]] %>%
    mutate(err1 = (pred_w1-eta_i)^2,
           err2 = (pred_w2-eta_i)^2,
           err3 = (pred_w3-eta_i)^2,
           err4 = (pred_w4-eta_i)^2) %>%
    select(id, t, starts_with("err"), window) %>%
    # mutate(window = factor(window, levels = 1:5,
    #                        labels = c("[0,0.2]", "(0.2,0.4]", "(0.4,0.6]",))) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != 1) %>%
    select(starts_with("err"))
  ise_gfosr_l1[, ,m] <- as.matrix(ise_tb)
}

mean_ise_gfosr_l1 <- apply(ise_gfosr_l1, c(1, 2), mean)
colnames(mean_ise_gfosr_l1) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
## calculation
for(m in 1:M){
  # this_df <- pred_list_ref[[m]]
  ise_tb <- pred_list_gfosr_l5[[m]] %>%
    mutate(err1 = (pred_w1-eta_i)^2,
           err2 = (pred_w2-eta_i)^2,
           err3 = (pred_w3-eta_i)^2,
           err4 = (pred_w4-eta_i)^2) %>%
    select(id, t, starts_with("err"), window) %>%
    # mutate(window = factor(window, levels = 1:5,
    #                        labels = c("[0,0.2]", "(0.2,0.4]", "(0.4,0.6]",))) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != 1) %>%
    select(starts_with("err"))
  ise_gfosr_l5[, ,m] <- as.matrix(ise_tb)
}

mean_ise_gfosr_l5 <- apply(ise_gfosr_l5, c(1, 2), mean)
colnames(mean_ise_gfosr_l5) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
## a function to calculate AUC
get_auc <- function(y, pred){
  if(sum(is.na(y))>0 | sum(is.na(pred))>0){
```

```r
    auc <- NA
  }
  else{
    this_perf <- performance(prediction(pred, y), measure = "auc")
    auc <- this_perf@y.values[[1]]
  }
  return(auc)
}
```

```r
## auc container
auc_fgfpca <- auc_adglmm <- auc_gfosr_l1 <- auc_gfosr_l5 <-
  array(NA, dim = c(length(window)-2, length(window)-2, M))
```

```r
for(m in 1:M){
  this_df <- pred_list_all[[m]]
  auc_tb <- this_df %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred0.2),
              auc2 = get_auc(Y, pred0.4),
              auc3 = get_auc(Y, pred0.6),
              auc4 = get_auc(Y, pred0.8)) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("auc"))
  auc_fgfpca[, ,m] <- as.matrix(auc_tb)
}


mean_auc_fgfpca <- apply(auc_fgfpca, c(1, 2), mean)
# mean_auc <- data.frame(mean_auc) %>%
#   mutate(Window = c("(0.2, 0.4]", "(0.4, 0.6]", "(0.6, 0.8]", "(0.8, 1.0]"),
#          .before = 1)
colnames(mean_auc_fgfpca) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
for(m in 1:M){
  this_df <- pred_list_ref[[m]]
  auc_tb <- this_df %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred0.2),
              auc2 = get_auc(Y, pred0.4),
              auc3 = get_auc(Y, pred0.6),
              auc4 = get_auc(Y, pred0.8)) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("auc"))
  auc_adglmm[, ,m] <- as.matrix(auc_tb)

}


mean_auc_adglmm <- apply(auc_adglmm, c(1, 2), mean)
```

```r
colnames(mean_auc_adglmm) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
for(m in 1:M){
  this_df <- pred_list_gfosr_l1[[m]]
  auc_tb <- this_df %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred_w1),
              auc2 = get_auc(Y, pred_w2),
              auc3 = get_auc(Y, pred_w3),
              auc4 = get_auc(Y, pred_w4)) %>%
    filter(window != 1) %>%
    select(starts_with("auc"))
  auc_gfosr_l1[, ,m] <- as.matrix(auc_tb)

}


mean_auc_gfosr_l1 <- apply(auc_gfosr_l1, c(1, 2), mean)
colnames(mean_auc_gfosr_l1) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
for(m in 1:M){
  this_df <- pred_list_gfosr_l5[[m]]
  auc_tb <- this_df %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred_w1),
              auc2 = get_auc(Y, pred_w2),
              auc3 = get_auc(Y, pred_w3),
              auc4 = get_auc(Y, pred_w4)) %>%
    filter(window != 1) %>%
    select(starts_with("auc"))
  auc_gfosr_l5[, ,m] <- as.matrix(auc_tb)

}


mean_auc_gfosr_l5 <- apply(auc_gfosr_l5, c(1, 2), mean)
colnames(mean_auc_gfosr_l5) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
fgfpca1 <- rbind(mean_ise_fgfpca ,mean_auc_fgfpca) %>% as_tibble() %>%
  mutate(Window = rep(c("(0.2, 0.4]", "(0.4, 0.6]", "(0.6, 0.8]", "(0.8, 1.0]"), 2), .before=1)
gfosr_l5_1 <- rbind(mean_ise_gfosr_l5 ,mean_auc_gfosr_l5) %>% as_tibble()
gfosr_l1_1 <- rbind(mean_ise_gfosr_l1 ,mean_auc_gfosr_l1) %>% as_tibble()
adglmm1 <- rbind(mean_ise_adglmm ,mean_auc_adglmm) %>% as_tibble()

bind_cols(fgfpca1, gfosr_l5_1, gfosr_l1_1, adglmm1, .name_repair = "minimal") %>%
  kable(digits = 3, booktabs=T,
        table.attr="style=\"color:black;\"") %>%
  kable_styling(full_width = F) %>%
  add_header_above(c(" " = 1, "fGFPCA" = 4, "GFOSR (L=5)" = 4,
                     "GFOSR (L=1)" = 4, "GLMMadaptive" = 4)) %>%
  add_header_above(c(" " = 1, "Maximum observation time" = 16)) %>%
```

```
group_rows(index = c("ISE"= 4, "AUC" = 4)) %>%
landscape()
```

	Maximum observation time														
	fGFPCA				GFOSR (L=5)				GFOSR (L=1)				GLMMadaptive		
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8	0.2	0.4	0.6
ISE															
(0.2, 0.4]	146.407				274.947				362.476				387.708		
(0.4, 0.6]	183.967	74.977			277.438	220.209			286.614	262.552			291.579	269.799	
(0.6, 0.8]	218.265	49.275	15.776		322.338	373.108	325.017		385.701	410.508	389.305		315.778	282.736	278.242
(0.8, 1.0]	108.918	77.981	17.747	12.005	290.982	318.079	350.850	333.580	328.482	341.274	354.211	347.067	563.011	477.485	597.746
AUC															
(0.2, 0.4]	0.748				0.686				0.624				0.591		
(0.4, 0.6]	0.664	0.734			0.563	0.630			0.543	0.590			0.524	0.596	
(0.6, 0.8]	0.715	0.790	0.803		0.669	0.628	0.676		0.604	0.577	0.615		0.669	0.694	0.687
(0.8, 1.0]	0.740	0.755	0.781	0.784	0.626	0.606	0.552	0.584	0.588	0.564	0.537	0.551	0.514	0.556	0.526

Method	Time
fGFPCA	2.317
GLMMadaptive	2.304
GFOSR (L=1)	0.025
GFOSR (L=5)	0.144

Time (minutes)

I chose not to report fitting and prediction time separately because it is too difficult to tell them apart for the GFOSR models.

```
data.frame(
  "Method" = c("fGFPCA", "GLMMadaptive", "GFOSR (L=1)", "GFOSR (L=5)"),
  "Time" = c(mean(fit_time/60+pred_time),
             mean(fit_time_ref+pred_time_ref/60),
             mean(t_vec_gfosr_l1/60),
             mean(t_vec_gfosr_l5/60))) %>%
  kable(digits = 3, booktabs = T, table.attr = "style = \"color:black;\"") %>%
  kable_styling(full_width = F)
```

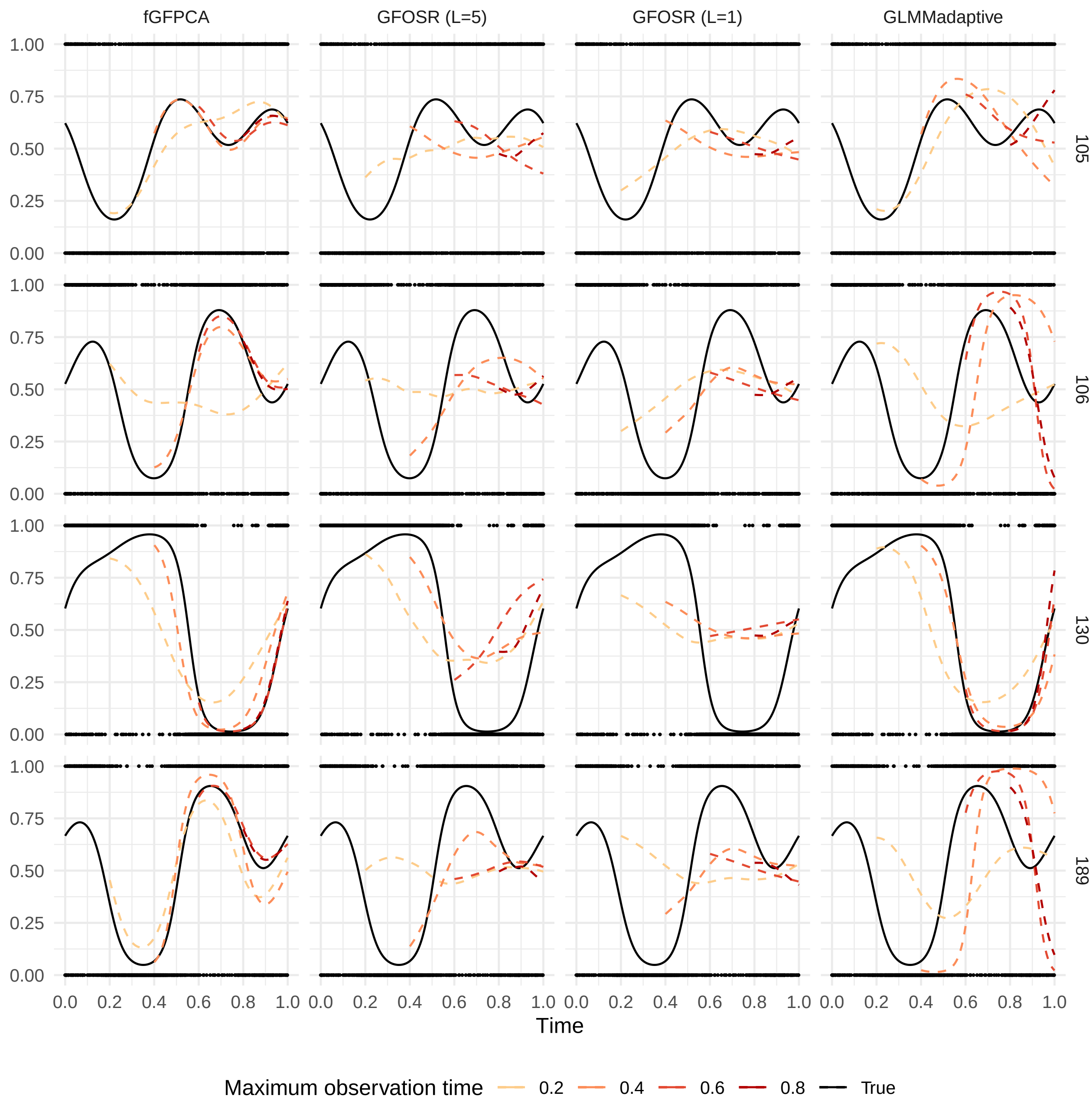
Small-scale simulation

I have used 100 subjects for training and testing, and repeated 500 times. When fitting GLMMadpative, I reduce the number of measurements in the training dataset to 1/10 by taking one every 10 observations. The prediction is on the original grid.

```
load(here("Data/SubSimOutput_GLMMadaptive.RData"))

load(here("Data/SubSimOutput_fGFPCA.RData"))
pred_subset_adglmm <- pred_subset_adglmm[!num_probs]
fit_time_subset_adglmm <- fit_time_subset_adglmm[!num_probs]
pred_time_subset_adglmm <- pred_time_subset_adglmm[!num_probs]

load(here("Data/SubSimOutput_GFOSR_L1.RData"))
pred_subset_gfosr_l1 <- pred_list_gfofr_subset
t_subset_gfosr_l1 <- t_vec_gfofr_subset
rm(pred_list_gfofr_subset, t_vec_gfofr_subset)

load(here("Data/SubSimOutput_GFOSR_L5.RData"))
pred_subset_gfosr_l5 <- pred_list_gfofr_subset
t_subset_gfosr_l5 <- t_vec_gfofr_subset
rm(pred_list_gfofr_subset, t_vec_gfofr_subset)

rand_id <- sample(101:200, size = 4)
```

Figure

```r
bind_rows(
  pred_subset_fGFPCA[[1]] %>% filter(id %in% rand_id) %>% mutate(method="fGFPCA"),
  pred_subset_gfosr_l5[[1]] %>% filter(id %in% rand_id) %>% mutate(method = "GFOSR (L=5)") %>%
    rename(pred0.2=pred_w1, pred0.4=pred_w2, pred0.6=pred_w3, pred0.8=pred_w4),
  pred_subset_gfosr_l1[[1]] %>% filter(id %in% rand_id) %>% mutate(method = "GFOSR (L=1)") %>%
    rename(pred0.2=pred_w1, pred0.4=pred_w2, pred0.6=pred_w3, pred0.8=pred_w4),
  pred_subset_adglmm[[1]] %>% filter(id %in% rand_id) %>% mutate(method = "GLMMadaptive")) %>%
  mutate_at(vars(eta_i, pred0.2, pred0.4, pred0.6, pred0.8),
              .funs = function(x){exp(x)/(1+exp(x))}) %>%
  mutate(method=factor(method,
         levels = c("fGFPCA", "GFOSR (L=5)", "GFOSR (L=1)","GLMMadaptive"))) %>%
  ggplot()+
  geom_point(aes(x=t, y=Y), size = 0.2)+
  geom_line(aes(x=t, y=eta_i, col = "True"))+
  geom_line(aes(x=t, y=pred0.2, col = "0.2"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.4, col = "0.4"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.6, col = "0.6"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=t, y=pred0.8, col = "0.8"), linetype="dashed", na.rm=T)+
  facet_grid(rows = vars(id), cols = vars(method))+
  labs(col = "Maximum observation time", x = "Time", y="")+
  scale_x_continuous(breaks = seq(0, 1, by = 0.2))+
  theme(legend.position = "bottom")+
  scale_color_manual(values = cols)
```



ISE and AUC

```
## ISE container
ise_fgfpca2 <- ise_adglmm2 <- ise_gfosr_l1_2 <- ise_gfosr_l5_2 <-
  array(NA, dim = c(length(window)-2, length(window)-2, M))
# dims: prediction window, max obs time, simulation iter
```

```
for(m in 1:length(pred_subset_fGFPCA)){
  this_df <- pred_subset_fGFPCA[[m]]
  ise_tb_m <- this_df %>%
    mutate(err1 = (pred0.2-eta_i)^2,
```

```
          err2 = (pred0.4-eta_i)^2,
          err3 = (pred0.6-eta_i)^2,
          err4 = (pred0.8-eta_i)^2) %>%
    select(id, t, starts_with("err")) %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("err")) %>% as.matrix()
  ise_fgfpca2[,,m] <- ise_tb_m
}

mean_ise_fgfpca2 <- apply(ise_fgfpca2, c(1, 2), mean)

colnames(mean_ise_fgfpca2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
for(m in 1:length(pred_subset_adglmm)){
  this_df <- pred_subset_adglmm[[m]]
  ise_tb_m <- this_df %>%
    mutate(err1 = (pred0.2-eta_i)^2,
          err2 = (pred0.4-eta_i)^2,
          err3 = (pred0.6-eta_i)^2,
          err4 = (pred0.8-eta_i)^2) %>%
    select(id, t, starts_with("err")) %>%
    mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != "[0,0.2]") %>%
    select(starts_with("err")) %>% as.matrix()
  ise_adglmm2[,,m] <- ise_tb_m
}

mean_ise_adglmm2<- apply(ise_adglmm2, c(1, 2), mean, na.rm = T)

colnames(mean_ise_adglmm2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
for(m in 1:length(pred_subset_gfosr_l1)){
  this_df <- pred_subset_gfosr_l1[[m]]
  ise_tb_m <- this_df %>%
    mutate(err1 = (pred_w1-eta_i)^2,
          err2 = (pred_w2-eta_i)^2,
          err3 = (pred_w3-eta_i)^2,
          err4 = (pred_w4-eta_i)^2) %>%
    select(id, t, starts_with("err"), window) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != 1) %>%
```

```r
    select(starts_with("err")) %>% as.matrix()
  ise_gfosr_l1_2[,,m] <- ise_tb_m
}

mean_ise_gfosr_l1_2<- apply(ise_gfosr_l1_2, c(1, 2), mean, na.rm = T)

colnames(mean_ise_gfosr_l1_2) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
for(m in 1:length(pred_subset_gfosr_l5)){
  this_df <- pred_subset_gfosr_l5[[m]]
  ise_tb_m <- this_df %>%
    mutate(err1 = (pred_w1-eta_i)^2,
           err2 = (pred_w2-eta_i)^2,
           err3 = (pred_w3-eta_i)^2,
           err4 = (pred_w4-eta_i)^2) %>%
    select(id, t, starts_with("err"), window) %>%
    group_by(window, id) %>%
    summarise_at(vars(err1, err2, err3, err4), sum) %>%
    group_by(window) %>%
    summarize_at(vars(err1, err2, err3, err4), mean) %>%
    filter(window != 1) %>%
    select(starts_with("err")) %>% as.matrix()
  ise_gfosr_l5_2[,,m] <- ise_tb_m
}

mean_ise_gfosr_l5_2 <- apply(ise_gfosr_l5_2, c(1, 2), mean, na.rm = T)

colnames(mean_ise_gfosr_l5_2) <- c("0.2", "0.4", "0.6", "0.8")
```

```r
## auc container
auc_fgfpca2 <- auc_adglmm2 <- auc_gfosr_l1_2 <- auc_gfosr_l5_2 <-
  array(NA, dim = c(length(window)-2, length(window)-2, M))
```

```r
for(m in 1:length(pred_subset_fGFPCA)){
  this_df <- pred_subset_fGFPCA[[m]]
  auc_tb_m <- this_df %>%
  mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
  select(Y, starts_with("pred"), window) %>%
  group_by(window) %>%
  summarise(auc1 = get_auc(Y, pred0.2),
            auc2 = get_auc(Y, pred0.4),
            auc3 = get_auc(Y, pred0.6),
            auc4 = get_auc(Y, pred0.8)) %>%
  filter(window != "[0,0.2]") %>%
  select(starts_with("auc")) %>% as.matrix()

  auc_fgfpca2[, , m] <- auc_tb_m

}

mean_auc_fgfpca2 <- apply(auc_fgfpca2, c(1,2), mean)
colnames(mean_auc_fgfpca2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
for(m in 1:length(pred_subset_adglmm)){
  this_df <- pred_subset_adglmm[[m]]
  auc_tb_m <- this_df %>%
  mutate(window = cut(t, breaks = window, include.lowest = T)) %>%
  select(Y, starts_with("pred"), window) %>%
  group_by(window) %>%
  summarise(auc1 = get_auc(Y, pred0.2),
            auc2 = get_auc(Y, pred0.4),
            auc3 = get_auc(Y, pred0.6),
            auc4 = get_auc(Y, pred0.8)) %>%
  filter(window != "[0,0.2]") %>%
  select(starts_with("auc")) %>% as.matrix()

  auc_adglmm2[, , m] <- auc_tb_m

}

mean_auc_adglmm2 <- apply(auc_adglmm2, c(1,2), mean, na.rm = T)
colnames(mean_auc_adglmm2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
for(m in 1:length(pred_subset_gfosr_l1)){
  this_df <- pred_subset_gfosr_l1[[m]]
  auc_tb_m <- this_df %>%
  select(Y, starts_with("pred"), window) %>%
  group_by(window) %>%
  summarise(auc1 = get_auc(Y, pred_w1),
            auc2 = get_auc(Y, pred_w2),
            auc3 = get_auc(Y, pred_w3),
            auc4 = get_auc(Y, pred_w4)) %>%
  filter(window != 1) %>%
  select(starts_with("auc")) %>% as.matrix()

  auc_gfosr_l1_2[, , m] <- auc_tb_m

}

mean_auc_gfosr_l1_2 <- apply(auc_gfosr_l1_2, c(1,2), mean)
colnames(mean_auc_gfosr_l1_2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
for(m in 1:length(pred_subset_gfosr_l5)){
  this_df <- pred_subset_gfosr_l5[[m]]
  auc_tb_m <- this_df %>%
  select(Y, starts_with("pred"), window) %>%
  group_by(window) %>%
  summarise(auc1 = get_auc(Y, pred_w1),
            auc2 = get_auc(Y, pred_w2),
            auc3 = get_auc(Y, pred_w3),
            auc4 = get_auc(Y, pred_w4)) %>%
  filter(window != 1) %>%
  select(starts_with("auc")) %>% as.matrix()

  auc_gfosr_l5_2[, , m] <- auc_tb_m
```

```
}

mean_auc_gfosr_l5_2 <- apply(auc_gfosr_l5_2, c(1,2), mean)
colnames(mean_auc_gfosr_l5_2) <- c("0.2", "0.4", "0.6", "0.8")
```

```
fgfpca2 <- rbind(mean_ise_fgfpca2 ,mean_auc_fgfpca2) %>% as_tibble() %>%
  mutate(Window = rep(c("(0.2, 0.4]", "(0.4, 0.6]", "(0.6, 0.8]", "(0.8, 1.0]"), 2), .before=1)
gfosr_l5_2 <- rbind(mean_ise_gfosr_l5_2 ,mean_auc_gfosr_l5_2) %>% as_tibble()
gfosr_l1_2 <- rbind(mean_ise_gfosr_l1_2 ,mean_auc_gfosr_l1_2) %>% as_tibble()
adglmm2 <- rbind(mean_ise_adglmm2 ,mean_auc_adglmm2) %>% as_tibble()

bind_cols(fgfpca2, gfosr_l5_2, gfosr_l1_2, adglmm2, .name_repair = "minimal") %>%
  kable(digits = 3, booktabs=T,
        table.attr="style=\"color:black;\"") %>%
  kable_styling(full_width = F) %>%
  add_header_above(c(" " = 1, "fGFPCA" = 4, "GFOSR (L=5)" = 4,
                     "GFOSR (L=1)" = 4, "GLMMadaptive" = 4)) %>%
  add_header_above(c(" " = 1, "Maximum observation time" = 16)) %>%
  group_rows(index = c("ISE"= 4, "AUC" = 4)) %>%
  landscape()
```

	Maximum observation time														
	fGFPCA				GFOSR (L=5)				GFOSR (L=1)				GLMMadaptive		
Window	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8	0.2	0.4	0.6
ISE															
(0.2, 0.4]	150.641				286.853				367.282				374.836		
(0.4, 0.6]	188.065	77.380			286.628	227.225			290.781	265.809			268.390	463.337	
(0.6, 0.8]	224.001	51.533	16.879		328.612	374.572	326.522		386.705	408.427	388.427		319.731	287.001	233.510
(0.8, 1.0]	112.163	81.368	19.592	13.399	301.165	324.817	353.888	335.139	331.488	342.935	354.800	347.627	228.335	469.769	331.509
AUC															
(0.2, 0.4]	0.746				0.679				0.620				0.672		
(0.4, 0.6]	0.662	0.734			0.549	0.627			0.536	0.590			0.622	0.671	
(0.6, 0.8]	0.710	0.787	0.801		0.656	0.617	0.668		0.598	0.574	0.613		0.689	0.698	0.731
(0.8, 1.0]	0.740	0.754	0.781	0.784	0.611	0.588	0.551	0.578	0.580	0.556	0.536	0.551	0.681	0.629	0.679

Method	Time
fGFPCA	1.629
GLMMadaptive	5.479
GFOSR (L=1)	0.010
GFOSR (L=5)	0.054

Among 500 hundred iterations, 6 did not converge for the GLMMadaptive model. No numeric issue for fGFPCA.

Time

```
data.frame(
  "Method" = c("fGFPCA", "GLMMadaptive", "GFOSR (L=1)", "GFOSR (L=5)"),
  "Time" = c(mean(fit_time_subset_fGFPCA/60+pred_time_subset_fGFPCA),
             mean(fit_time_subset_adglmm+pred_time_subset_adglmm/60),
             mean(t_subset_gfosr_l1/60),
             mean(t_subset_gfosr_l5/60))) %>%
  kable(digits = 3, booktabs = T, table.attr = "style = \"color:black;\"") %>%
  kable_styling(full_width = F)
```

NHANES data application

We take 60% subjects (N = 5257) for training, 40% (n = 3506) for out-of-sample prediction. When using the full sample The debiase step (mgcv::bam) in fGFPCA took a really a long time, and GLMM adaptive only works for intercept-only model. In the debias step, re-evaluated eigenvalues also lost their decreasing nature.

```
# df_nhanes <- read_rds(here("Data/nhanes_bi.rds"))
load(here("Data/ApplOutput_fGFPCA.RData"))
load(here("Data/ApplOutput_GLMMadaptive.RData"))

load(here("Data/Appl_GFOSR_L5.RData"))
load(here("Data/Appl_GFOSR_L1.RData"))

pred_appl_gfosr_l1 <- pred_appl_gfosr_l1 %>%
  rename(pred360=pred_w1, pred720=pred_w2, pred1080=pred_w3)
pred_appl_gfosr_l5 <- pred_appl_gfosr_l5 %>%
  rename(pred360=pred_w1, pred720=pred_w2, pred1080=pred_w3)
```

```
df_nhanes %>% select(SEQN, Z, sind) %>%
  filter(SEQN %in% unique(nhanes_pred_adglmm$id) | SEQN %in% unique(nhanes_pred_fgfpca$id)) %>%
  mutate(Z = factor(Z, levels = 0:1, labels = c("Inactive", "Active"))) %>%
  mutate(SEQN = factor(SEQN)) %>%
  ggplot()+
  geom_tile(aes(x=sind, y = SEQN, fill = Z))+
  labs(x="Time", y="Subject", title = "Overview of NHANES binary activity indicator")+
  theme(axis.text.y = element_blank())+
```

```
  scale_x_continuous(breaks = seq(0, 1440, by = 480),
                     labels = c("Midnight", "8am", "4pm", "Midnight"))
```

AUC

```
# window
window <- seq(0, 1440, by = 360)
```

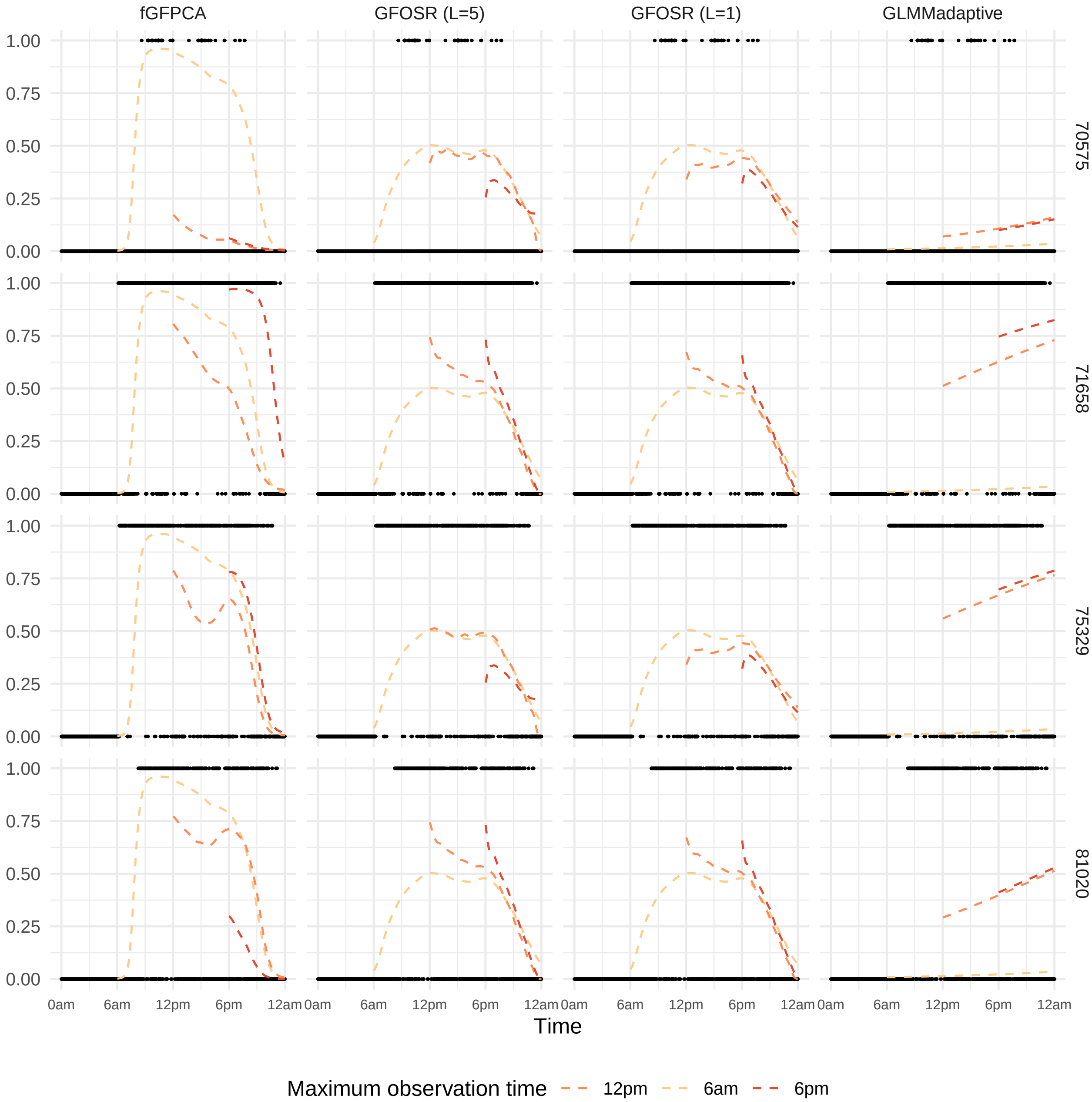
```
auc_appl_fgfpca <- pred_nhanes_fgfpca %>%
    mutate(window = cut(sind, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred360),
              auc2 = get_auc(Y, pred720),
              auc3 = get_auc(Y, pred1080)) %>%
    filter(window != "[0,360]") %>%
    select(starts_with("auc"))

auc_appl_gfosr_l5 <- pred_appl_gfosr_l5 %>%
  select(-window) %>%
    mutate(window = cut(sind, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred360),
              auc2 = get_auc(Y, pred720),
              auc3 = get_auc(Y, pred1080)) %>%
    filter(window != "[0,360]") %>%
    select(starts_with("auc"))

auc_appl_gfosr_l1 <- pred_appl_gfosr_l1 %>%
  select(-window) %>%
    mutate(window = cut(sind, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred360),
              auc2 = get_auc(Y, pred720),
              auc3 = get_auc(Y, pred1080)) %>%
    filter(window != "[0,360]") %>%
    select(starts_with("auc"))

auc_appl_adglmm <- pred_nhanes_adglmm %>%
    mutate(window = cut(sind, breaks = window, include.lowest = T)) %>%
    select(Y, starts_with("pred"), window) %>%
    group_by(window) %>%
    summarise(auc1 = get_auc(Y, pred360),
              auc2 = get_auc(Y, pred720),
              auc3 = get_auc(Y, pred1080)) %>%
    filter(window != "[0,360]") %>%
    select(starts_with("auc"))

colnames(auc_appl_fgfpca) <- colnames(auc_appl_gfosr_l5) <- colnames(auc_appl_gfosr_l1) <- colnames(auc_
```

```r
bind_cols(Window = c("6am-12pm", "12pm-6pm", "6pm-12am"),
          auc_appl_fgfpca, auc_appl_gfosr_l5, auc_appl_gfosr_l1, auc_appl_adglmm,
          .name_repair = "minimal") %>%
  kable(digits = 3, booktabs=T,
        table.attr="style=\"color:black;\"") %>%
  kable_styling(full_width = F) %>%
  add_header_above(c(" " = 1, "fGFPCA" = 3, "GFOSR (L=5)" = 3,
                     "GFOSR (L=1)" = 3, "GLMMadaptive" = 3)) %>%
  add_header_above(c(" " = 1, "Maximum observation time" = 12)) %>%
  landscape()
```

	Maximum observation time											
	fGFPCA			GFOSR (L=5)			GFOSR (L=1)			GLMMadaptive		
Window	6am	12pm	6pm	6am	12pm	6pm	6am	12pm	6pm	6am	12pm	6pm
6am-12pm	0.703			0.689			0.684			0.581		
12pm-6pm	0.536	0.709		0.519	0.699		0.520	0.654		0.532	0.701	
6pm-12am	0.716	0.679	0.773	0.677	0.678	0.723	0.677	0.676	0.708	0.514	0.565	0.626

Figure

```
rand_id <- sample(unique(pred_nhanes_adglmm$id), 4)
cols <- cols[1:3]
names(cols) <- c("6am", "12pm", "6pm")
bind_rows(
  pred_nhanes_fgfpca %>% filter(id %in% rand_id) %>% mutate(method="fGFPCA"),
  pred_appl_gfosr_l5 %>% filter(id %in% rand_id) %>% mutate(method = "GFOSR (L=5)"),
  pred_appl_gfosr_l1 %>% filter(id %in% rand_id) %>% mutate(method = "GFOSR (L=1)"),
  pred_nhanes_adglmm %>% filter(id %in% rand_id) %>% mutate(method = "GLMMadaptive")) %>%
  mutate_at(vars(pred360, pred720, pred1080),
               .funs = function(x){exp(x)/(1+exp(x))}) %>%
  mutate(method=factor(method,
         levels = c("fGFPCA", "GFOSR (L=5)", "GFOSR (L=1)","GLMMadaptive"))) %>%
  ggplot()+
  geom_point(aes(x=sind, y=Y), size = 0.2)+
  geom_line(aes(x=sind, y=pred360, col = "6am"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=sind, y=pred720, col = "12pm"), linetype="dashed", na.rm=T)+
  geom_line(aes(x=sind, y=pred1080, col = "6pm"), linetype="dashed", na.rm=T)+
  facet_grid(rows = vars(id), cols = vars(method))+
  labs(col = "Maximum observation time", x = "Time", y="")+
  scale_x_continuous(breaks = seq(0, 1440, by = 360),
                     labels = c("0am", "6am", "12pm", "6pm", "12am"))+
  theme(legend.position = "bottom", axis.text.x = element_text(size = 7))+
  scale_color_manual(values = cols)
```



Additional figures