Functional Mixed Effects Spectral Analysis

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Outline

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Functional data analysis uses a curve as the basic unit, such as functional linear model, fPCA, curve registration etc (Ramsay and Silverman, 2005).

When the curves can be potentially correlated: functional mixed effects models (e.g. Guo, 2002, Morris and Carroll, 2006).

When multiple time series are collected from same subjects: the focus is in the second moments.

Functional mixed effects spectral model.
A motivating example

- A study on insomnia using heart rate variability.
- 125 men and women ages 60-89
- 76 insomnia, 49 stressed caregivers
- Three short segments of heart rate variability (T=500, heart beats) from the first 3 NREM sleep cycles from each subject
- HRV spectra in different sleep stages provides indirect measures of subconscious nervous system. And are related to stress and insomnia (Malik et al, 1996, Hall et al, 2004)
- Questions: how does the HRV spectra progress through the night and what are the differences between two groups?
Figure: Heart rate variability, log-periodogram, and estimated best linear unbiased log-spectral predictor from the first three periods of NREM of a caregiver subject.
Challenges

- The basic unit of the functional data analysis is a time series with mean zero.
- The interest is the covariate effects on the second moment, implying regularity conditions on higher moments.
- The time series within each subject are correlated (LDA in time series data)
- Solution: use the log-spectrum as the basic unit and use functional mixed effects model to account for correlations.
Functional mixed effects model

e.g. Guo, 2002, Morris and Carroll, 2006

\[ y_{ij} = U_{ij}\beta(t_{ij}) + V_{ij}\alpha_i(t_{ij}) + e_{ij}, \quad e_{ij} \sim N(0, \sigma_e^2), \]

where

► \( \beta(t) = \{\beta_1(t), \ldots, \beta_p(t)\}^T \) is a \( p \times 1 \) vector of fixed functions;

► \( \alpha_i(t) = \{\alpha_{1i}(t), \ldots, \alpha_{qi}(t)\}^T \) is a \( q \times 1 \) vector of random functions, that are modeled as realizations of some stochastic processes with zero means;

► \( U_{ij} \ (1 \times p) \) and \( V_{ij} \ (1 \times q) \) are design matrices

► Fixed and random functional effects can be modeled through B-spline, Smoothing splines, Wavelets, P-splines or other basis (Many recent work)
Related works in replicated time series

- Diggle and Al Wasel (1997) Use log-linear parametric mixed effects model to model the a group of log-periodograms with a nested structure.
- Iannaccone and Coles (2001) generalize this with a spline estimate for the population average curve.
- Freyermuth et al (2010) use a global tree structure for the same frame work so that the population-average can be calculated within each segment.

Limitations:
- They require the time series to be mutually independent.
- The ”random log-periodograms” have not been formally defined.
Spectral analysis for stationary time series

Let \( \{X_t, t = 1, \cdots, T\} \) be a zero-mean real stationary time series.

- The Cramér representation:
  \[
  X_t = \int A(\omega) e^{i2\pi \omega t} dZ(\omega),
  \]

- The spectrum \( f(\omega) = A(\omega)A(\omega)' \).

- DFT: \( d(\omega_k) = \sum_{t=1}^T X_t e^{i2\pi \omega_k t} \).

- Periodogram: \( I(\omega_k) = (1/T) d(\omega_k) d(\omega_k)' \)

- Smooth \( I(\omega_k) \): \( \hat{I}(\omega_k) \sim f(\omega_k) \chi^2_2/2 \) for \( k \neq 1, T/2, T \);
  \( \sim f(\omega_k) \chi^2_1 \) otherwise.

- \( \log\{I(\omega_k)\} \approx \log f(\omega_k) + \gamma_k + e_k \).

- Wahba (1980, JASA) model \( \log f(\omega_k) \) by a periodic cubic spline.
We define the $k$th replicate time series of the $j$th independent unit (subject) $\{X_{jkt}\}$ for $k = 1, \ldots, n_j$ and $j = 1, \ldots, N$ as:

$$
X_{jkt} = \int_{-1/2}^{1/2} A_0(\omega; U_{jk}) A_j(\omega; V_{jk}) e^{2\pi i \omega t} dZ_{jk}(\omega) \quad (1)
$$

$A_0(\omega; U_{jk})$ is fixed part of the transfer function

$A_j(\omega; V_{jk})$ is unit-specific random deviation from the fixed transfer function.

The resultant unit-specific random spectrum takes the following form

$$
f_{jk}(\omega; U_{jk}, V_{jk}) = |A_0(\omega; U_{jk})|^2 |A_j(\omega; V_{jk})|^2, \quad (2)
$$

where $E \{ \log |A_j(\omega; V_{jk})|^2 \} = 0$
Assume that the effects of the design matrices are multiplicative on spectrum,

\[
\log |A_0(\omega; U_{jk})|^2 = U_{jk}^T \beta(\omega),
\]

\[
\log |A_j(\omega; V_{jk})|^2 = V_{jk}^T \alpha_j(\omega),
\]

we have functional mixed effects spectral model in the log-spectrum

\[
\log f_{jk}(\omega; U_{jk}, V_{jk}) = U_{jk}^T \beta(\omega) + V_{jk}^T \alpha_j(\omega),
\]

(3)

- \(\beta(\omega)\) are the functional mixed effects modeled as periodic smoothing spline.
- \(\alpha_j(\omega)\) are the functional random effects, with \(\Gamma(\omega, \nu) = E \{ \alpha_j(\omega) \alpha_j(\nu) \}\) to be estimated in a Sobolev space.
With some regularity conditions, we can show \( \{ l_{jk}(\omega_l) | \alpha_j(\omega_k) \} \) are asymptotically \( f_{jk}(\omega_l) \chi_2^2 / 2 \) for \( l \neq 0, \frac{T}{2}, T \) and \( f_{jk}(\omega_l) \chi_1^2 \) otherwise.

Letting \( y_{jkl} = \log l_{jkl} + \gamma_l \), the log-periodograms approximately follow the functional mixed effects model

\[
y_{jkl} \approx U_{jk}^T \beta(\omega_l) + V_{jk}^T \alpha_j(\omega_l) + \epsilon_{jkl}
\]  \hspace{1cm} (4)

where \( \epsilon_{jkl} \) are mean-zero independent random variables for \( l = 0, \ldots, L \) with \( \text{var} (\epsilon_{jkl}) = \sigma_l^2 \).
We adopt a similar iterative approach of Yao and Lee (2006),

- We estimate the fixed effects by a periodic smoothing spline.
- Remove the fixed effects and use a Kullback-Leibler criterion-based algorithm to estimate the functional covariance (Krafft et al, 2008)
- Estimate the BLUPS of the random effects.
- Update the estimate of the fixed effects using the estimated functional covariance.
Minimizing the penalized sums-of-squares in a periodic RKHS

\[
\frac{1}{nT} \sum_{j=1}^{N} \sum_{k=1}^{n_j} \sum_{\ell=1-L}^{L} \left\{ y_{jk\ell} - U^T_{jk} \beta(\omega_\ell) \right\}^2 + \sum_{p=1}^{p} \lambda_p \int_{-1/2}^{1/2} \beta''_p(\omega)^2 \, d\omega
\]

(5)

Conditional of the GCV estimate of the smoothing parameters, we have

\[
\hat{\beta}(\omega) = \frac{1}{T} \sum_{\ell=1-L}^{L} \sum_{m=1-L}^{L} \left\{ U^T U + n(2\pi m)^4 \Lambda \right\}^{-1} U^T Y_\ell e^{2\pi im(\omega-\omega_\ell)}.
\]

(6)
Define the residuals $y_{jk}^* = y_{jk} - U_{jk}^T \hat{\beta}(\omega_\ell)$ and $Y_{j\ell}^* = (y_{j1\ell}^*, \ldots, y_{jn_j\ell}^*)^T$.

\[
\hat{\Gamma}_q(\omega, \nu) = N^{-1} \sum_{j=1}^{N} \tilde{\alpha}_{jq}(\omega)\tilde{\alpha}_{jq}(\nu)
\] (7)

where $\tilde{\alpha}_j = (\tilde{\alpha}_{j1}, \ldots, \tilde{\alpha}_{jQ})^T$ is based on minimizing

\[
\frac{1}{n_j T} \sum_{k=1}^{n_j} \sum_{\ell=1-L}^{L} \left\{ y_{jk\ell}^* - V_{jk}^T \alpha_j(\omega_\ell) \right\}^2 + \sum_{q=1}^{Q} \theta_q \int_{-1/2}^{1/2} \alpha_{jq}''(\omega)^2 \, d\omega
\]
The goal is to optimally estimate the covariance function, not to optimally smooth each functional random effect $\alpha_{jq}(\omega)$.

The smoothing parameters are estimated by a KL-criterion based cross validation.

$$K(\Theta) = \sum_{j=1}^{N} \log \left| \hat{\Sigma}_{-j}(\Theta) \right|_+ + Y_j^T \hat{\Sigma}_{-j}(\Theta)^{-1} Y_j^*.$$ 

where $\hat{\Sigma}_{-j}(\Theta)$ is the estimated covariance without the $j$th time series.

With the estimated functional covariance, the fixed effects can be updated using penalized weighted least squares estimates (e.g. Lin et al, 2004, Krafty et al, 2008).
The BLUPS of $\alpha_j(\omega)$ are just the posterior means based on $Y_j^*$

$$\hat{\alpha}_j(\omega) = \left\{ \hat{\Gamma}(\omega, \omega_{1-L}), \ldots, \hat{\Gamma}(\omega, \omega_L) \right\} \left( I_L \otimes V_j^T \right)$$

$$\left\{ (I_T \otimes V_j) \hat{W} \left( I_T \otimes V_j^T \right) + (\Sigma_\epsilon \otimes I_{n_j}) \right\}^{-1} Y_j^*$$
Following the result of Dai and Guo (2004), we can generate a time series from the estimated transfer function:

\[
\log \hat{f}_{jk}(\omega) = U_{jk}^{T} \hat{\beta}(\omega) + V_{jk}^{T} \hat{\alpha}_{j}(\omega),
\]

\[
\hat{A}_{jk}(\omega) = \sqrt{\hat{f}_{jk}(\omega)},
\]

\[
X_{jkt} = \sum_{l=1}^{T} \hat{A}_{jk}(\omega_l) \exp(2\pi i \omega_l t) dZ_l,
\]

where \(\omega_l = l/T\) and \(dZ_l\) are residuals. The resultant spectrum \(f_{jk}^{T}(\omega)\) of the generated time series \(X_{jkt}(t = 1, \cdots, T)\) has the following properties:

\[
f_{jk}^{T}(\omega_l) = f_{ik}(\omega_l)
\]

\[
f_{jk}(\omega) = f_{ik}(\omega) + O(T^{-1})
\]
Consistency

\[ \sup_{p=1,\ldots,P; \omega \in \mathbb{R}} E \left\{ \left| \hat{\beta}_p(\omega) - \beta_p(\omega) \right|^2 \right\} = O \left( N^{-4/5} T^{-4/5} \right) + O \left( T^{-1} \right) + O \left( N^{-1} \right). \]

\[ \sup_{q=1,\ldots,Q; \omega,\nu \in \mathbb{R}} E \left\{ \left| \hat{\Gamma}_q(\omega,\nu) - \Gamma_q(\omega,\nu) \right|^2 \right\} = O \left( N^{-2/3} + T^{-1} \right). \]

- The fixed effects estimates have the same rate as in independent case.
- The optimal rate in the functional covariance is slower, suggesting under-smoothing is needed.
Model:

\[ \log f_{jk}(\omega; U_{jk}, V_{jk}) = U_{jk}^T \beta(\omega) + V_{jk}^T \alpha_j(\omega) \]

where

\[
\begin{bmatrix}
U_{j1}^T \\
U_{j2}^T \\
U_{j3}^T
\end{bmatrix} = \begin{bmatrix}
1 & 0 & 0 & \tau_j & 0 & 0 \\
0 & 1 & 0 & 0 & \tau_j & 0 \\
0 & 0 & 1 & 0 & 0 & \tau_j
\end{bmatrix},
\begin{bmatrix}
V_{j1}^T \\
V_{j2}^T \\
V_{j3}^T
\end{bmatrix} = \begin{bmatrix}
1 \\
1 \\
1
\end{bmatrix}
\]

\( \tau_j \) is the indicator variable for the \( j \)th subject being an insomniac.

- The fixed effects \( \beta_1, \beta_2, \beta_3 \) are the mean log-spectrum at NREM periods 1, 2 and 3 for caregivers.
- \( \beta_4, \beta_5, \beta_6 \) are the differences in the mean log-spectra between insomnia and caregivers.
- Random intercept to account for correlation between the cycles.
Figure: Estimated log-spectral fixed effects and point-wise 95% confidence intervals for the analysis of heart rate variability.
Results

- In both groups, there is a shift of power towards higher frequency as the night progresses, indicating the subjects are more relaxed.

- The monotonic decreasing pattern in $\beta_4, \beta_5, \beta_6$, which are the differences between insomnia from the caregivers, indicating the caregivers in general more relaxed than the insomnia subjects.
A new type of functional data analysis where the basic unit is a time series segment and multiple segments can be collected from a subject.

The interest is how the covariates impact the second moment.

We propose a mixed effects Cramér spectral representation.

Generalize the definition of ”population-average” and subject-specific”.

The resultant log-spectrum has a functional mixed effects representation in the frequency domain.

Assuming that the functional effects are smooth, we proposed an iterative procedure for estimation.