Functional data analysis in longitudinal settings using smoothing splines

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• Connection between smoothing splines and linear mixed–effects model: Penalized least square

• Equivalence to LME but the interpretation is not the same

• Connection to Bayesian Hierarchical Models (Prior on the underlying function)

\[ f(t) = B_1 + B_2 t + w(t) \]
Current - Multiple curves (Longitudinal setting)
(Perform: Longitudinal Data Analysis)

\[ \begin{align*}
\beta_k(t) &= B_{1k} + B_{2k}t + w_{bk}(t), & k &= 1, \ldots, p \\
\alpha_l(t) &= A_{1l} + A_{2l}t + w_{al}(t), & l &= 1, \ldots, q
\end{align*} \]

Fixed effects and Random effects

a. Gaussian Process (Equivalent to the prior on the underlying function)

b. Fixed-effects – Diffuse priors on the null space

c. Random-effect: Well defined prior on the linear component

Note: Presentation of the entire framework is in terms of cubic smoothing spline
• Functional ANOVA and Regression

• Non parametric longitudinal models

• Mixed-effects smoothing spline ANOVA
Limitation of Assuming Parametric form?

Random effects curves necessarily need to share same degree smoothness?

Random and fixed-effects need to have similar form?

What about missing data?

Thoughts on why Generalized Additive Model and Generalized Additive Mixed Models
Estimating smoothing parameter

Generalized Maximum Likelihood equivalent to Restricted Maximum Likelihood

Other: Generalized Cross Validation, Unbiased Risk Minimization

• Hence SAS Proc Mixed (Limitations??)
Inference

• Test inverse of smoothing parameter $\Leftrightarrow$ test the variance component $= 0$

• Asymptotic distribution of LRT $\rightarrow$ 50:50 mixture of chi-square (1) and 0

• Test fixed effects $= 0$

• Asymptotic distribution of LRT $\rightarrow$ 50:50 mixture of chi-squares (dfs 2 and 3)
95% Component-Wise Confidence Intervals

CIs can be constructed using the Bayesian connection:

Posterior distribution of fixed and random effects

Across the function coverage properties