A Proposed Methodology for Performing Follow-up Tests to Compare Pairs of Treatment Levels in Functional Linear Models

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Introduction

- Functional data analysis (FDA) concerns situations in which collected data are curves.
- Functional ANOVA tests for a difference in a mean curve from k populations.
- The general mean function is defined as an intersection of the individual hypotheses.
- The mapping of the partial test statistics to a global one is done via a combining function.

The Closure Principle and Combining Functions

- Marcus et al. (1976) defined a closure principle for multiple adjustments for subregions of hypotheses as well as individual adjustments.
- The global test statistic should be based on a combination of the partial test statistics.

Proposed Methodology

- We propose performing a follow-up test based on subregions of the functional response domain and use the closure principle to adjust for multiplicity.
- The elementary null hypothesis $H_0$ corresponds to the subinterval $[a_i, b_i]$.
- For each subinterval, find the elementary test statistic $F_i$.

\[ F = \frac{\sum_{j=1}^{n} \left( y_j(t) - \hat{\mu}_j(t) \right)^2 dt}{\sum_{j=1}^{n} \left( \frac{\sum_{i=1}^{k} \left( y_{ij}(t) - \hat{\mu}_i(t) \right)^2 dt}{(k-1)} \right)} \]

- To test a subset of hypotheses, $H_{ij}$, construct the intersection test statistic $F_{ij}$ over $[a_i, b_i] \cup [a_j, b_j]$.

- Construction of the test statistic is equivalent to the unweighted sum combining function.
- The unadjusted p-values are found via permutations and than adjusted according to the closure principle.

Application

- The study investigated an influence of procaine on the hemolysis of erythrocytes.
- Measurements were taken every 15 seconds for 12 minutes.
- The experiment was repeated 5 times for each dosage/incubation combination.

Summary of the Findings

- No significant overall difference with 0 min incubation time ($p_{value/Bonf} = 1.000$).
- Procaine did not have enough time to react with erythrocyte suspension.
- Overall significance after 15 min incubation ($p_{value/Bonf} = 0.006$).
- Hemolysis of the least stable red blood cells (61-165 sec): $p_{value} = 0.022$.
- Hemolysis of the general red blood cells population (166-240 sec): $p_{value} = 0.060$.
- Plateau: $p_{value} = 0.006$.
- Overall significance after 30 min incubation ($p_{value/Bonf} = 0.018$).
- Hemolysis of the least stable red blood cells (61-165 sec): $p_{value} = 0.018$.
- Hemolysis of the general red blood cells population (166-240 sec): $p_{value} = 0.029$.
- Plateau: $p_{value} = 0.018$.
- No significant difference was found for the rest of the incubation times.

Statistical Methods

- We performed six separate analysis for the 6 different incubation times.
- Once the incubation times with the overall significance were identified, we used the proposed methodology to investigate periods of times with significant differences as well as pair-wise comparison of dosage levels within those periods.

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