Analysis of Variance for functional data using the R package ERP

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Keywords : Functional Analysis of Variance, Event-Related Potentials data.

Functional data are noisy and discrete observations generated from underlying continuous functions. Progress in instrumentations and techniques for measurements has produced massive data that are functional in nature, such as measurements over fine time or space grids, and images with many pixels per frame over time. Examples are recordings of electrical activity along locations on the scalp (electroencephalography or EEG) and changes of brain function associated with oxygen supply in blood flow in functional magnetic resonance imaging (fMRI).

Event-related potentials (ERP) are electroencephalograms time-locked to an event. Cognitive scientists use them to chart the time course of mental processes, yielding information not available from behavioral studies alone. In clinical research, ERPs are one of several noninvasive biomarkers that have been proposed for evaluating neurological and psychiatric disorders such as Alzheimer's disease, amnestic mild cognitive impairment, impulsive control disorder, among others.

As in traditional univariate or multivariate statistical analysis, functional data are similarly analyzed for covariate effects, both in experiment designs and in measuring effect sizes by p-values. The purpose of the R package ERP is to implement functional Analysis of Variance procedures in situations where the response is a curve (see Zhang (2013) for a review). For significance testing of the mean difference of groups of curves, the one-way design is the most common (see Cuevas *et al.*, 2004). To cover a broad spectrum of experimental designs in ERP studies, the general framework of the package ERP is a time-varying coefficient multivariate regression model with fixed-time covariates.

We first propose to review a broad spectrum of R packages designed to test for experimental effects on curves. Assuming that curves are observations of continuous-time Gaussian stochastic processes at discrete time points, the most famous method is due to Ramsay & Silverman (2005), who addressed the significance testing of an effect curve by deriving pointwise test statistics for the null hypotheses that no association exist between the response at time t and the covariates. Zhang (2013) reviewed the main strategies for testing the global null hypothesis by aggregating the pointwise tests statistics. One approach consists in deriving a simultaneous confidence interval for the effect curve, which amounts to controlling the Family-Wise Error-Rate (FWER) of a multiple testing procedure. However, in high-dimensional context, the FWER-controlling methods are known to be very conservative. Moreover, under strong dependence, it is not clear these methods actually control the FWER at the desired level.

Lastly, Donoho & Jin (2004) proposed the Higher Criticism Thresholding method to aggregate pointwise test statistics for signal detection when the signal, namely the curve of true effect parameters, is both rare and weak. Higher Criticism Thresholding is based on a Kolmogorov-Smirnov type statistic measuring the distance between the empirical distribution of the pointwise p-values and the theoretical uniform null distribution. If the pointwise test statistics are independent and if the Rare-and-Weak paradigm holds, Donoho & Jin (2004) showed that the Higher Criticism Thresholding method reaches optimal detection bounds. Indeed, ERP waveforms appear to contain only barely detectable peaks and troughs for brief time intervals in many studies. Moreover, the huge within-subject variability of ERP curves combined with small absolute values of the differential brain activity leads to a weak signal.

For testing differential ERP waveforms between treatments, Bugli & Lambert(2006) also derived Analysis of Variance F-test statistics in a time-varying coefficient regression model with random effects. The introduction of a within-curve random effect amounts to considering the amplitudes of an ERP curve as repeated measurements over time with a lag-1 auto-regressive structure. In aggregating pointwise test statistics by the integral of their squared value over time, the L_2–norm F-statistic is not designed to be optimal for functional data like ERP curves with complex temporal dependence. To improve on the detection of ERP signals under standard experimental designs, the package ERP implements optimal likelihood-ratio tests under an arbitrary time dependence pattern, based on a rank-reduced model for the correlation function in time (see Sheu *et al.*, 2016 and Causeur *et al.*, 2018).

The presentation will introduce an ERP study to illustrate the comparison between the testing methods implemented in the package ERP and many alternative methods introduced above. It will also highlight the functionalities of the package to identify significant intervals and produce plots displaying the effect curves, with options for confidence intervals and smoothing.

Références

[1] Bugli, C. & Lambert, P. (2006). Functional ANOVA with random functional effects: an application to event-related potentials modelling for electroencephalograms analysis. *Statistics in Medicine* **25**, 21, 3718–3739.

[2] Causeur, D., Sheu, C. F., Perthame, E. & Rufini, F. (2018). A Generalized Functional Likelihood-Ratio Test for Event-Related Potentials Signal Detection. *Submitted paper.*

[3] Cuevas, A. and Febrero, M. & Fraiman, R. (2004). An ANOVA test for functional data. *Computational Statistics & Data Analysis* **47**, 1, 111–122.

[4] Donoho, D. & Jin, J. (2004). Higher criticism for detecting sparse heterogeneous mixtures. *The Annals of Statistics* **32**, 3, 962–994.

[5] Ramsay, J. O. & Silverman, B. W. (2005). *Functional Data Analysis, 2nd edition.* Springer Series in Statistics. New-York.

[6] Sheu, C. F., Perthame, E., Lee, Y. S. & Causeur, D. (2016). Accounting for time dependence in large-scale multiple testing of event-related potential data. *Annals of Applied Statistics* **10**, 1, 219–245.

[7] Zhang, J. T. (2013). *Analysis of Variance for Functional Data.* Chapman & Hall. London.