Robust Mixed-Effects Model for Clustered Failure Time Data: Application to Huntington’s Disease Event Measures

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Thursday, February 23, 2017
4:15 p.m.
Marrs McLean Science Building 301

Abstract: An important goal in clinical and statistical research is properly modeling the distribution for clustered failure times which have a natural intra-class dependency and are subject to censoring. We handle these challenges with a novel approach that does not impose restrictive modeling or distributional assumptions. Using a logit transformation, we relate the distribution for clustered failure times to covariates and a random, subject-specific effect. The covariates are modeled with unknown functional forms, and the random effect may depend on the covariates and have an unknown and unspecified distribution. We introduce pseudo-values to handle censoring and splines for functional covariate effects and frame the problem into fitting an additive logistic mixed effects model. Unlike existing approaches for fitting such models, we develop semiparametric techniques that estimate the functional model parameters without requiring specifying or estimating the random effect distribution. We show both theoretically and empirically that the resulting estimators are consistent for any choice of random effect distribution and any dependency structure between the random effect and covariates. Lastly, we illustrate the method’s utility in an application to a Huntington’s disease study where our method provides new insights into differences between motor and cognitive impairment event times in at-risk subjects.

Tanya Garcia is an Assistant Professor in the Department of Epidemiology and Biostatistics at Texas A&M University. She is the recent recipient of a Faculty Development Award (K01) from NIH National Institute of Neurological Disorders and Stroke (NINDS). Her research interests are in developing innovative statistical methods that solve important neuroscience and biomedical problems, with particular emphasis in semiparametric theory, high-dimensional inference and survival analysis.

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